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Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States: A systematic review

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Complete List of Authors:	Celaya, Martín; Arizona Department of Health Services, Bureau of Assessment and Evaluation; The University of Arizona Mel and Enid Zuckerman College of Public Health, Health Promotion Sciences Zahlan, Alaa I; The University of Arizona Mel and Enid Zuckerman College of Public Health Rock, Chelsea; Arizona State University Nathan, Akshay ; Boston University Acharya, Aishwarya; The University of Arizona Mel and Enid Zuckerman College of Public Health Madhivanan, Purnima ; The University of Arizona Mel and Enid Zuckerman College of Public Health Ehiri, John; The University of Arizona Mel and Enid Zuckerman College of Public Health Hu, Chengcheng; The University of Arizona Mel and Enid Zuckerman College of Public Health Hu, Chengcheng; The University of Arizona Mel and Enid Zuckerman College of Public Health Pettygrove, Sydney ; The University of Arizona Mel and Enid Zuckerman College of Public Health McClelland, D. Jean ; The University of Arizona Mel and Enid Zuckerman College of Public Health McClelland, D. Jean ; The University of Arizona Mel and Enid Zuckerman College of Public Health McClelland, D. Jean ; The University of Arizona Mel and Enid Zuckerman College of Public Health Bellucci, Laura; Arizona Department of Health Services, Bureau of Women's and Children's Health
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TITLE

Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States: A systematic review

AUTHORS AND AFFILIATION

Martín F. Celaya^{1,2}, Alaa I. Zahlan², Chelsea Rock³, Akshay Nathan⁴, Aishwarya Acharya²,

Purnima Madhivanan², John Ehiri², Chengcheng Hu², Sydney Pettygrove², Jean McClelland⁵,

Velia Leybas Nuño², Laura Luna Bellucci¹

1. Arizona Department of Health Services, Phoenix, Arizona, United States

2. Mel & Enid Zuckerman College of Public Health, University of Arizona, Tucson, Arizona,

United States

3. College of Health Solutions, Arizona State University, Phoenix, Arizona, United States

4. Boston University, Boston, Massachusetts, United States

5. Health Sciences Library, The University of Arizona, Tucson, Arizona, United States

AUTHORS' E-MAIL ADDRESSES

Martín F. Celaya, <u>martin.celaya@azdhs.gov</u>; Alaa I Zahlan, <u>azahlan@arizona.edu</u>; Chelsea Rock, <u>chelsea.rock@azdhs.gov</u>; Akshay Nathan, <u>shayaknathan@gmail.com</u>; Aishwarya Acharya, <u>aishwaryaacharya@arizona.edu</u>; Purnima Madhivanan, <u>pmadhivanan@arizona.edu</u>; John Ehiri, jehiri@arizona.edu; Chengcheng Hu, <u>hucc@arizona.edu</u>; Sydney Pettygrove, <u>sydneyp@arizona.edu</u>; Jean McClelland, jmcc@arizona.edu, Velia Leybas Nuño, <u>vleybas@arizona.edu</u>

SUBMITTING AND CORRESPONDING AUTHOR

Martín F. Celaya, martin.celaya@azdhs.gov

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- Table 1. Outcomes of interest
- Table 2. Risk factors and outcomes by volume of studies
- Table 3. Summary of risk factors and outcomes by risk/association category

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Figure 1. PRISMA flow diagram

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- Appendix 1. Search strategy by database
- Appendix 2. Table of included studies
- Appendix 3. Results of NIH Quality Assessments for included studies

KEYWORDS: American Indian or Alaska Native, Mothers, Morbidity

ABSTRACT

Introduction and objective

Maternal morbidity and mortality (MMM) is a public health concern in the US, with Native American (NA) women experiencing higher rates than non-Hispanic White women. However, research examining specific risk factors (RF) for MMM outcomes experienced by NA women is limited. This systematic review comprehensively synthesizes and critically appraises the literature on individual and community risk factors for MMM.

Methods and analysis

A systematic search was performed in PubMed, Embase, CINAHL, and Scopus for articles published since 2012 using database-specific controlled vocabulary for MMM and NA. Selection criteria included studies with an observational study design, set in the US, including NA women in the perinatal period, and examining the relationship between an RF and an MMM outcome. Three reviewers screened and extracted data from the included studies. Risk of bias was assessed using the NIH's quality assessment tools for cohort, cross-sectional, and case-control studies. The data were analyzed using a descriptive approach.

Results

Fifteen studies were analyzed. NA women were the primary study population in 7 studies. All studies used administrative databases. The study settings were nationwide (7 studies), statewide (4 studies), and on Indian reservations (4 studies). Nine MMM outcomes were identified (e.g., postpartum hemorrhage and disseminated intravascular coagulation). Most studies examined hypertensive disorders of pregnancy (8 studies) and composite MMM (4 studies) as outcomes. Twenty-six RFs were identified. Twenty-four were individual-level RFs, and two were

community-level. Being of NA race (6 studies), rural maternal residency (4 studies), overweight/obese BMI (2 studies), maternal age (2 studies), nulliparity (2 studies), and

preexisting medical conditions (1 study) demonstrated increased risk with an MMM outcome.

Conclusion

These findings underscore the scarcity of research on the role of RFs and MMM outcomes for NA women. This scarcity confines the ability of healthcare and public health organizations to design and implement tailored approaches to reduce disparities.

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PROSPERO registration number CRD42022363405.

ARTICLE SUMMARY

Strenghts and limitations of this study

- The review searched a variety of databses to identify a wide range of studies on maternal morbidity and mortality in Native American women in the United States.
- The review incorporated studies conducted on Indian reservations and within specific tribal health systems, providing insights tailored to the unique contexts and experiences of Native American women.
- The review synthesizes and critically appraises the limited existing literature on risk factors for maternal morbidity and mortality specifically among Native American women in the United States.
- Many included studies had small sample sizes or low percentages of Native American women, limiting the generalizability of the findings to this specific population.
- Included studies relied on administrative databases, which introduce potential reporting biases and misclassification issues, especially concerning the racial categorization of Native American participants.

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INTRODUCTION

Maternal morbidity and mortality (MMM) are alarming public health problems in the United States. The Centers for Disease Control and Prevention (CDC) defines maternal mortality as the death of a woman during pregnancy, at delivery, or soon after delivery. [1] Severe maternal morbidity (SMM) refers to complications during labor and delivery with short- and long-term health consequences (e.g., sepsis, blood transfusion, preeclampsia, or hysterectomy). [2,3] The US has one of the highest maternal mortality ratios of any high-income country, reporting 26.4 maternal deaths per 100,000 live births. In contrast, Finland has the lowest maternal mortality ratio of 3.8 maternal deaths per 100,000 live births, a value nearly seven times lower than the US. [4] The causes behind the rising MMM rates are not fully understood but involve complex interactions of factors at patients and families, providers or facilities, overall systems, and within the community at various points in the reproductive life cylce. [5]

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Significant racial and ethnic health inequities persist in maternal health. [6–9] Native American women are three to four times more likely to die than non-Hispanic White women from pregnancy-related complications in the US and are three to five times more likely to experience SMM than non-Hispanic White women. [6,10,11] Historical trauma, racism, colonization, genocide, forced migration, reproductive coercion, and cultural erasure contribute to these adverse outcomes. [12–14] Native American women experience unique prolonged systemic barriers that create inequitable social conditions compared to other groups. [14–16] Some systemic barriers affecting include limited access to providers and birthing facilities. [14,17,18] In addition, a history of forced sterilization and forced infant and child separations has led to a strong distrust of the healthcare systems and providers, including the Indian Health Service. [19–

21]

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Rationale

Despite these concerns, only a sparse amount of research supports the presence MMM risk factors specific to Native American women. A recent scoping review on Native American women and the leading causes of maternal mortality in the US identified risk factors like historical trauma, inequities in healthcare availability, access and utilization, preexisting health conditions, and rurality. [22] A separate review of social determinants of pregnancy-related mortality and morbidity identified that race was a significant factor for MMM. [3] However, the review did not provide a list of risk factors specific to Native American women. [3] There is a need to explore further and assess the quality of research specific to MMM risk factors experienced by Native American women. Identifying this information can help identify areas for prevention focused on Native American communities. Therefore, this systematic review aims to comprehensively synthesize and critically appraise the literature on MMM risk factors experienced by Native American women.

Objective

To assess and critically appraise individual and community-level risk factors for pregnancyrelated morbidity and mortality experienced by Native American women in the US.

METHODS

Eligibility criteria

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Mata-Analyses (PRISMA) guidelines. [23] Inclusion criteria for studies were: 1) observational study design; 2) study set in the United States; 3) population was Native American women in the

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perinatal or puerperium period; 4) outcomes focused on measures of pregnancy-related mortality and morbidity; 5) examined the relationship between a risk factor/exposure and stated outcomes. Studies focusing on a different population were included if they offered a stratified analysis by race and contained a racial category for Native Americans. Studies were excluded if: 1) studies focused only on birth, neonatal, or infant outcomes; 2) studies that did not examine the relationship between a risk factor/exposure and stated outcomes; 3) studies with settings outside of the United States; 4) studies that did not include findings for Native American women; and 5) studies that focus on the preconception or postpartum phases.

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Information sources and search strategy

The review searched databases (PubMed, Embase, CINAHL, and Scopus) from 1 January 2012 to 10 October 2022. This timeframe was chosen because the CDC released a new standard for monitoring severe maternal morbidity on 12 November 2012. [2] With technical assistance from a specialized health sciences librarian, the team used search tools and strategies, including shortening keywords where appropriate, using thesaurus terms, and using database-specific controlled vocabulary (e.g., Medical Subject Headings, MeSH). The search strategy combined terms and search strings with the appropriate Boolean operators.

Selection process

Two independent reviewers screened the titles and abstracts based on the eligibility criteria to. If any disagreement occurred, a third reviewer helped arbitrate. After the title and abstract were screened, two independent reviewers screened full-text article. Each excluded article's reason for exclusion was noted at each stage.

Data collection process

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Two independent reviewers extracted data using Covidence. [24] The data collected included study details such as location, study design, and eligibility criteria, methods, year of the article, year(s) of study, data source, objectives, sample size and population, independent (risk factors) and dependent (outcomes) variables, key findings, measures of effect/association with p-values and confidence intervals, and limitations. If there were disagreements between the reviewers, a third reviewer arbitrated. For any missing information, the lead author contacted corresponding authors to request for information. Authors were contacted three times via email or phone. Any discrepancies within data extraction were reviewed and discussed in a team setting.

Data items

Primary outcomes of interest were maternal morbidity and mortality, including severe maternal morbidity (SMM) based on the CDC's list of 21 diagnoses and procedures (Table 1). [25]

Table 1Outcomes of interest	
Mortality and near-misses	
Severe maternal morbidity diagnostic or procedural outcomes	Acute myocardial infarctionAcute renal failureAdult respiratory Distress SyndromeAmniotic fluid embolismAneurysmCardiac arrestDisseminated intravascular coagulationEclampsiaHeart failurePuerperal cerebrovascular disordersPulmonary edemaSepsisSevere anesthesia complicationsShockSickle cell anemia with crisisThrombotic embolismBlood transfusionConversion of cardiac rhythmHysterectomy

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	Temporary tracheostomy
	Ventilation
Additional morbidity outcomes	Postpartum hemorrhage
	Ectopic pregnancy
	Placental abruption
	Uterine atony

This list was used to identify additional articles that did not utilize a composite outcome of severe maternal morbidity or mortality and instead had a more focused outcome in their investigation. Given the scope of this review, the terms "pregnancy complications," "obstetric complications," "labor complications," and "near-miss" were added to the list of outcomes to increase the sensitivity of the review. Pregnancy, labor, and obstetric complications all refer to conditions or pathological processes associated with pregnancy. [26] They can occur during or after pregnancy, ranging from minor discomforts to severe diseases requiring medical interventions. These include diseases in pregnant women, and pregnancies in women with diseases. Near-miss refers to an event that presented a risk but did not result in death. Maternal mortality refers to the death of a woman while pregnant or within one year of the end of a pregnancy, regardless of the outcome, duration or site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes.[27]

The search strategy was pilot tested in PubMed, finalized, and adapted to other databases. The complete search strategy is available in Appendix 1. The results from each database-specific search strategy were downloaded from the respective databases and uploaded to the EndNote version 20 reference manager software. [28] After removing the duplicates, the citations were imported into Covidence.

Study risk of bias assessment and certainty assessment

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Risk of bias was assessed using the NIH's Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, and Case-Control Studies to examine critical concepts for each study's validity. [29] Two independent reviewers used the tool criteria and rated articles as "good," "fair," or "poor" quality. A rating of "good" meant that there was the least risk of bias, and the results were considered valid. [29] A "fair" rating indicated susceptibility to some bias but was still insufficient to invalidate its results and would vary in their strengths and weaknesses. [29] A "poor" rating indicated a significant risk of bias and invalidated its results. [29] When the ratings differed, a third reviewer arbitrated the article's rating to reach a consensus.

Effect measures

Measures of effect such as risk and odds ratios with 95% confidence intervals were extracted. Descriptive statistics like prevalence and incidence were also included.

Synthesis methods

A description of the findings for each study included in the review is provided in Appendix 2. This table includes the risk factors and outcomes of interest and study characteristics. A descriptive synthesis of the results was the most appropriate for this review since there was a large diversity of study designs, risk factors, and outcomes. The variety of the studies included in this review hindered any quantitative synthesis of the identified risk factors' effect sizes. The identified risk factors are also organized into socioecological levels (i.e., individual, family, community, society, or systems). Risk factors were grouped by outcome examined. The information that was reported for each risk factor included 1) the number of studies that analyzed the risk factor, 2) the number of studies that had a measure of effect for a risk factor and was

reported to be statistically significant, and 3) the number of studies that had a measure of effect for a risk factor, and was not statistically significant. Ratings and descriptive information for each article are provided in a tabular format.

[INSERT FIGURE 1]

RESULTS

Study Selection and study characteristics

A total of 8,220 articles were identified, of which 357 duplicates were removed, resulting in 7,863 articles for screening (Figure 1). During the screening process, there were 6,967 agreements for inclusion and 896 conflicts resolved by an arbitrator, for an overall percent agreement of 88.6%. The selection process yielded a total of 145 articles, of which 15 were included in the review. [10,11,30–39] The most common reasons for study exclusion were: wrong patient population (41 studies), wrong setting (22 studies), and wrong type of publication (21 studies). Most (80.0%) studies used secondary data to examine associations between risk factors and outcomes. There was an equal number of studies across three study designs (5 studies each). The sample size across all studies ranged from 196 to 51,685,525 with a mean sample size of 4,479,962, a median of 72,697, a standard deviation of 12,732,821.6, and an interguartile range of 2,123,375.0. Seven studies focused primarily on Native American women (i.e., the study sample made up mainly of Native American women).[32–34,36–38,40] The remaining eight studies included Native American women as a subgroup in their sample.[10,11,30,31,35,39,41,42] Of these eight studies, the percentage of Native American women that were part of the overall sample ranged from 0.41% to 10.1%, and six of these studies BMJ Open: first published as 10.1136/bmjopen-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de Enseignement Superieur (ABES)

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had a proportion of Native American women in their sample that was $\leq 1.35\%$. The total number

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of Native American participants across all studies ranged from 196 to 492,771 with a mean of 57,266.5, a median of 7,107, a standard deviation of 129,234.2, and an interquartile range of 26,817.0. Study settings included nationwide (7/15 studies) [10,11,35,36,39,41,42], statewide (4/15 studies) [30,31,37,38], and on Indian reservations (4/15 studies) [32–34,40]. All studies used administrative databases such as birth vital records or hospital medical/discharge records.

Risk of bias in studies

Thirteen studies were rated as "good" and two were rated as "fair" according to the NIH's Study Quality Assessment Tools. See Appendix 3 for individual assessments of quality. Amongst the cohort and cross-sectional studies, fourteen were rated "good," [11,30,31,35,39–43] while one was rated "fair." [36] Most studies did not assess the exposure more than once over time (7/10 studies). [30,31,35,39–41,43] A smaller proportion were unable to demonstrate that the exposure of interest was measured before the outcome being measured (5/10 studies) [11,36,39,42,43] or did not adjust models to include potential confounders to assess their impact on the relationship between exposure(s) and outcome(s) (3/10 studies).[36,40,42] The reviewers were unable to find evidence in some studies if the outcome assessors were blinded to the exposure status of participants (3/10 studies) [11,36,42] or whether there was a loss to follow-up amongst the cohort studies (3/5 studies). [30,35,40] Amongst the case-control studies, four were rated as "good" [32–34,37] while one was rated as "fair." [38] The reviewers ascertained that some studies failed to provide a sample size justification (3/5 studies) [32–34] or did not randomly select cases and/or controls from the eligible study population (2/5 studies). [33,38]

Results of individual studies and syntheses

Nine outcomes were identified in the studies: hypertensive disorders of pregnancy (preeclampsia, severe preeclampsia, gestational hypertension, and hypertensive disorders of pregnancy), blood transfusions, postpartum hemorrhage, disseminated intravascular coagulation (DIC), hysterectomy, ectopic pregnancy, uterine atony, placental abruption, and SMM and/or mortality as a composite outcome. Twenty-six risk factors were identified, 24 of these were individual risk factors while two were community risk factors. No studies examined interpersonal/relationship (e.g. marital status or social support) or societal levels (e.g. historical trauma, structural racism, or discrimination) risk factors.

Table 2 lists the frequency by which each risk factor and outcome was studied in the literature. A majority of studies examined "hypertensive disorders of pregnancy" (8/15 studies) [30–35,37,42] and "severe maternal morbidity and/or mortality" (4/15 studies) [10,11,39,41] as outcomes. Fewer studies examined the remaining outcomes. A majority of studies examined body mass index (BMI) (6/15 studies) [30–34,38], maternal age (6/15 studies) [32–36,40], maternal race (5/15 studies) [10,31,39–41], and parity (5/15 studies) [32–34,38,40] as risk factors for various outcomes. Table 3 is a summary table that reports the number of studies grouped by outcome, the risk factors examined for associations, and the direction of those associations. Appendix 2 summarizes additional details on study design, sample size, and data sources; exposures and outcome variables; covariates; key findings including the measures of effect and study quality ratings.

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Risk Factor	

Outcome*

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	SMM M	HD P†	ВТ	РРН	DIC	Hyst	EP	UA	РА	No. of Studies Examinin Each Ris Factor
Body mass index	0	5	0	1	0	0	1	1	0	7
Age	0	4	0	1	0	0	1	1	0	6
Maternal race	3	1	2	1	1	1	0	1	0	5
Parity Maternal	0	3	0	1	0	0	0	1	0	5
residence	2	1	2	0	1	1	0	0	0	3
Gene expressions	0	3	0	0	0	0	0	0	0	3
Tobacco use	0	2	0	0	0	0	0	0	1	2
Birth primary payer type	1	0	1	0	0	0	0	0	0	1
Mag Sulfate Use	0	0	0	2	0	0	0	1	0	2
Inpatient induction	0	0	0	2	0	0	0	1	0	2
Augmentatio n	0	0	0	1	0	0	0	1	0	1
Birthweight	0	0	0	1	0	0	0	1	0	1
Physical health/ chronic health status	1	0	0	0	0	0	0	0	0	1
Gestational diabetes	0	1	0	0	0	0	0	0	0	1
Behavioral health status	1	0	0	0	0	0	0	0	0	1
Indian Health Service region	0	0	0	0	0	0	1	0	0	1
Gravidity	0	0	0	0	1	0	0	1	0	1
Routine aspirin use	0	0	0	1	0	0	0	0	0	1
Prior uterine incision or VBAC	0	0	0	1	0	0	0	0	0	1
Macrosomia	0	0	0	1	0	0	0	0	0	1
Antepartum Bleeding	0	0	0	1	0	0	0	0	0	1
Previous PPH	0	0	0	1	0	0	0	0	0	1

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Length of labor	0	0	0	1	0	0	0	0	0	1
Oxytocin use	0	0	0	1	0	0	0	0	0	1
Chorioamnio nitis	0	0	0	1	0	0	0	1	0	1
Retained placenta	0	0	0	1	0	0	0	1	0	1
No. of Studies Examining Each Outcome	4	8	2	2	2	1	1	1	1	15

*Acronyms: severe maternal morbidity and mortality (SMM), hypertensive disorders of pregnancy (HDP), blood transfusion (BT), postpartum hemorrhage (PPH), disseminated intravascular coagulation (DIC), hysterectomy (Hyst), ectopic pregnancy (EP), uterine atony (UA), and placental abruption (PA)

⁺ The HDP category includes pre-eclampsia, severe pre-eclampsia, gestational hypertension, and hypertensive disorders of pregnancy.

Outcome	↑Increased risk or positive association	—No association	↓Decreased risk or negative association
Hypertensive disorders o (8 studies)	f pregnancy		
Pregnancy induced hypertension	Rural maternal residency ¹¹⁷⁸ Maternal age 35 years or older and smoked during pregnancy ¹³⁷¹	Continuous smokeless tobacco use ²²³⁰ Continuous cigarette smoking ²²³⁰	Maternal age<35 years and smoked during pregnancy ¹³⁷¹
Pre-eclampsia	Native American maternal race ⁸¹⁴¹ <i>Overweight/obese</i> <i>BMI</i> ^{7372, 835, 836, 837 <i>Age at delivery</i>^{835, 836 <i>Nulliparity</i>^{835, 836, 837 Gestational diabetes⁸³⁷ Genetic factors CRP_A, rs3093077, (T allele additive)⁸³⁶ MBL2, rs1800451, (T allele dominant) ⁸³⁶ IL1A, rs3273550, (T allele dominant) ⁸³⁶ CTLA4, rs21775, (A allele dominant) ⁸³⁶ CRP, rs3093068, (G allele additive)⁸³⁷ CRP, rs876538, (C allele additive)⁸³⁷ CRP, rs876538, (C allele recessive)⁸³⁷}}}	Continuous smokeless tobacco use ²²³⁰ Continuous cigarette smoking ²²³⁰ Age at delivery ⁸³⁷ BMI ⁸¹⁴¹	Genetic factors CRP_B, rs1205, (A allele dom) ⁸³⁶ CRP_C, rs1130864, (T allele dom) ⁸³⁶ CRP, rs876538, (C allele dominant) ⁸³⁷

Table 3. Summary of risk factors and outcomes by risk/association category*

eclampsia	Obese BMI 836,837 Age at delivery 836 Gestational diabetes 837 Genetic factorsMBL2, rs1800451, (T allele dominant) 836 IL1A, rs3273550, (T allele dominant) 836 CTLA4, rs21775, (A allele dominant) 836 CRP, rs3093068, (G allele additive) 837 CRP, rs3093068, (G allele dominant) 837 CRP, rs876538, (C allele additive) 837 CRP, rs876538, (C allele additive) 837		CRP_A, rs3093077, (T allele additive) <i>CRP_B, rs120</i> . (<i>A allele dom</i>) ⁶ CRP_C, rs1130864, (T allele dom) ⁸³⁶ CRP, rs876538 allele dominan
Severe Maternal Morbidit (4 studies) Severe maternal morbidity (SMM) with transfusions	ty and/or Mortality Native American maternal race ¹¹⁹ Any physical health condition ¹¹⁹ Any behavioral health condition ¹¹⁹ Multiple chronic	Native American maternal race ⁹⁵²	
Severe maternal morbidity without transfusions	conditions	Rural maternal residency ⁴⁰¹⁰	
Severe maternal	Rural maternal	Urban maternal residency ³⁴²¹	
mortality (SMMM)	Native American race ⁴⁰¹⁰ Medicaid funded births ³⁴²¹		
Blood Transfusions (2 studies)	Native American race ⁴⁰¹⁰ Medicaid funded births ³⁴²¹		
Blood Transfusions (2 studies)	Native American race ⁴⁰¹⁰ Medicaid funded births ³⁴²¹ Rural maternal residency ^{3421, 4010} Medicaid-funded births ³⁴²¹		

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	Native AmericanMaternal race 1331 Gravidity<51131	Prior uterine incision ²⁹⁴⁴	
Uterine Atony			
(1 study)			
	Native American maternal race ¹³³¹ Birthweight>4500g ¹³³¹	Gravidity<5 ¹³³¹ Induction augmentation ¹³³¹ Chorioamnionitis ¹³³¹	
Ectopic Pregnancy (1 study)			
	Maternal age>19 years ¹⁸⁶¹ IHS region ¹⁸⁶¹		
Placental Abruption (1 study)			
	Continuous use of smokeless tobacco ²²³⁰ Continuous cigarette smoking ²²³⁰		
Disseminated Intravascul (1 study)	ar Coagulation		
	Native American race ⁴⁰¹⁰	Rural maternal residency ⁴⁰¹⁰	
Hysterectomy (1 study)			

Native American race ⁴⁰¹⁰
Rural maternal
residency ⁴⁰¹⁰

*BMI, body mass index; h, hours; m, minutes; significant associations are italicized and bolded, significant association in the same direction as categorized

Specific to hypertensive disorders of pregnancy as an outcome having a rural residency (1/1 studies), an overweight or obese BMI (4/5 studies), age above 35 years also referred to as "advanced maternal age" (1/4 studies), and nulliparity (3/3 studies) were significantly associated with increased risk. [30,32–34,42] Genetic predispositions to hypertensive disorders of pregnancy were not significantly associated with increased risk (3/3 studies). [32–34] Studies that focused on severe maternal morbidity and/or mortality as a distinct composite outcome identified being a Native American race (2/3 studies), having a physical health condition (1/1)study), a rural residency (1/2 studies), and Medicaid funded births (1/1 study) as significantly associated with increased risk. The risk of blood transfusions was significantly associated with Native American race (1/1 study), rural residency (2/2 studies), and Medicaid-funded births (1/1 study)study). [10,11,39] Postpartum hemorrhage risk was significantly associated with being of Native American race when compared to other racial/ethnic groups, a gravidity <5, a birthweight of 4500g, having a retained placenta, magnesium sulfate use (2/2 studies), antepartum bleeding, previous postpartum hemorrhage, being in third stage labor greater than 20 minutes, maternal rural residency, fetal macrosomia, and oxytocin use for longer than 12 hours. [38,40] Other outcomes, such as uterine atony, ectopic pregnancy, hysterectomy, and positively associated risk factors, are further described in Appendix 2. This systematic review did not identify risk factors significantly associated with placental abruptions.

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This systematic review also identified factors that demonstrated no association or a reduction of risk for Native American women. For pregnancy-induced hypertension, one study identified that

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continuous smokeless tobacco use and cigarette smoking had no association. [37] A separate study determined that an age younger than 35 had a decreased risk of hypertensive disorders of pregnancy compared to those older than 35. [40] One study found no association between hypertensive disorders of pregnancy (e.g., preeclampsia) and BMI. [31] While one of the three studies that focused on genetic predisposition identified that having CRP_B, rs1205, (A allele dominant) decreased risk. [32] Native American race and rural residency were found to have no risk of severe maternal morbidity and/or mortality in three distinct studies. [10,39,41]. One study did not find an association between having a prior uterine incision and postpartum hemorrhage. [38] Another study found no association between uterine atony and having a gravidity greater than 5, induction augmentation, or chorioamnionitis. In contrast, a separate study found no association between disseminated intravascular coagulation and a rural residency. [10,40].

Reporting biases and certainty of evidence

All studies had a reliance on administrative data sources to assess outcomes and exposures simultaneously. All studies noted this to be a considerable limitation in their study design. Four studies noted concerns with small sample sizes, missing exposure and outcome data, and critical demographic information that may have led to misclassification bias. Two studies considered reporting bias in their study designs, while almost all studies (14/15 studies) referred to the misidentification of Native American women based on predetermined guidelines for race designation.

DISCUSSION

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This systematic review synthesized the current literature by conducting a broad search of outcomes associated with maternal morbidity and mortality and identifying their associated risk factors for Native American women in the US. A large number of studies identified risk factors at the individual level concerning maternal outcomes; of these, the majority suggested that an overweight or obese BMI, advanced maternal age, parity, and rural maternal residency are associated with Native American maternal morbidity or mortality. Few studies contradicted these findings and demonstrated no association with Native American race, rural maternal residency, or advanced maternal age. One study found no association with hypertensive disorders of pregnancy, including pregnancy-induced hypertension, preeclampsia, and severe preeclampsia with continuous smokeless tobacco use or continuous cigarette smoking. [37]

Studies assessing the relationship between genetic factors and preeclampsia or severe preeclampsia were completed in an Indian Reservation within a specific tribal health system. [32–34] This ensured that the findings were specific to supporting community initiatives with tribal support. These studies uncovered that there may not be evidence of an association between genetic expression and preeclampsia for Native American women. However, all these studies concurred that many of the risk factors, such as maternal age, nulliparity, and obesity, that are associated with preeclampsia and severe preeclampsia in other populations were also operative in Native American communities. [32–34] BMJ Open: first published as 10.1136/bmjopen-2024-08380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

Unfortunately, we identified a small number of risk factors at the community level of the socioecological model (i.e., maternal residency and Indian Health Service region). This limitation further indicates the need to expand research to identify and understand the role of community and society-level risk factors on maternal health among Native American women in the United States. Determinants of health such as access to behavioral and primary care services,

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housing, crime and violence, and health policies have been demonstrated to contribute directly to maternal mortality and morbidity in more extensive population studies. [44]

In addition, this review was only able to identify a minimal number of studies that examined risk factors for maternal morbidities. This low number of studies further limits our ability to correctly identify any level of agreement for these findings on the outcomes. Surprisingly, this review could not find any information on prenatal care utilization patterns and their association with maternal mortality or morbidity despite strong evidence supporting adequate prenatal care utilization in culturally informed healthcare institutions. Early and adequate prenatal care is thought to promote healthy pregnancies through screening and managing a woman's risk factors and health conditions and promote healthy behaviors during pregnancy. [6]

This study focused on a very clinical outcome in Native American women; however, it's critical to note that there were other risk factors and outcomes that did not necessarily manifest themselves during the delivery event that can also lead to morbidity and mortality, such as postpartum depression, substance use behavior, or exposure to infectious diseases. There continues to be a gap in the literature exploring the relationship between depression and maternal morbidity and mortality in Native American women. [45] In addition, the effects of historical trauma, discrimination, and racism were not considered in this study despite it being a significant determinant of health in the lives of Native American peoples. [17] These experiences have played a role in the weathering of health status for Native American women. The weathering hypothesis suggests that cumulative stress from racism and socioeconomically disadvantaged communities produce a weathering effect on health that can explain disparate outcomes. [13]

Appraisal

Most of the included studies were rated as "good" (13/15 studies), while two were rated as "fair" based. Despite this, we were able to highlight the methodological shortcomings of some of the studies, such as the failure to assess the exposure more than once over time, the inability to demonstrate that exposure was measured before outcome measurement, or not adjusting models to include potential confounders. Additionally, some studies failed to provide sample size justification or did not randomly select cases or controls from the eligible study population,

posing bias risks.

We identified additional shortcomings in the available evidence. Racial/ethnic misclassification on administrative databases leads to challenges with underreporting and further affects the selection of study participants. Given that the total population of Native American women of reproductive age (15-44 years) in the United States is 0.8%, small errors in misclassification can greatly affect data analyses [46]. Multiple studies in this review reported small sample sizes, making it difficult to determine if a particular outcome was a true finding, possibly allowing for type II errors. Among studies that included samples that were not fully Native American, the majority reported a Native American sample size of $\leq 1.35\%$. This is a long-standing concern in research with Native American communities. This lack of research in these communities, primarily inhibited by concerns about low sample sizes, prevents additional risk factors for morbidity and mortality that are particular to Native American women from being discovered. Measurement of maternal morbidity and mortality varied across the studies. The review used a broader definition of the outcomes and included others not listed by CDC as severe maternal morbidity such as postpartum hemorrhage, uterine atony, placental abruption, and ectopic pregnancy. Lastly, a heavy reliance on administrative data poses unique challenges in identifying risk factors not traditionally included in these datasets, given that their purpose is not always

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aligned with the study hypothesis. Improvements in the collection of social determinants of health in administrative databases have demonstrated a promising approach to further study the effects of these determinants on population health. [47] Studies also mentioned the lack of consistency in data quality, such as the accuracy of self-reported data or the level of detail collected, including missing data.

Strengths and limitations

Our systematic review face some limitations. The search terms in MeSH and other standardized language posed a unique challenge as the terms "maternal morbidity" and "maternal mortality" were non-existent. Therefore, this systematic review adopted an expansive search strategy informed by other published literature. [3,48] There is a possibility of missing articles, given that an adopted search strategy was used. Addiitonally not all MesH terms in PubMed translated into other standardized languages for other databases. There is a risk of publication bias and selective reporting of significant findings in the studies. Using NIH's quality assessment tools which are not independently published nor standardized may introduce bias due to the qualitative nature of the review. Despite this, other systematic reviews have built the evidence supporting the utility and practicality of utilizing this tool in critical review of published evidence. [3] Furthermore, the diverse methodologies prevented us from conducting a meta-analysis, so our findings are descriptive and guide future research on risk factors for maternal morbidity and mortality in Native American women.

Despite these limitations, this systematic review is one of the few that identifies risk factors for various outcomes indicating severe maternal morbidity and mortality among Native American women in the US. We comprehensively reviewed the current literature using multiple search strategies followed the CDC's list of procedural and diagnoses for SMM. This systematic review

utilized recommended language to identify research in Native American communities following the National Library of Medicine guidance. [49]

Implications for practice, policy, and future research

Our review demonstrates the lack of attention reflected in the scarcity of evidence available to understand this maternal and child health crisis among a population that is often ignored. The limited type of risk factors studied, the study designs, settings, and outcomes limit the ability of healthcare and public health organizations to properly design and implement tailored approaches to reduce disparities in this community further. More needs to be done to expand the research to reduce these inequities among Native American women in the US. μΨC

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OTHER INFORMATION

Registration and protocol: The registration and protocol information for this review can be accessed at: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=363405, identifier: CRD42022363405. No amendments were submitted during implementation of the protocol.

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Contributorship statement: MC and PM: developed the protocol objectives and design. MC wrote the protocol and is the submitting author unders supervision of PM and JM. MC and JM developed the search strategy. AZ, CR, AN, and AA reviewed abstrats and full-text articles, extracted data from included studies, and critically appraised the literature. AZ and AN co-wrote the introduction, CR and AA co-wrote the methods, and MC wrote the remaining sections

including results and discussion. PM, JE, CH, SP, VN, and LB reviewed and made corrections to the manuscript on multiple occasions that led to the final written manuscript.

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	id=doi:10.1007%2Fs11606-022-07653-8&atitle=TRENDS+IN+PRE-
	PREGNANCY+HYPERTENSION+AMONG+BIRTHING+INDIVIDUALS+BY+RACE
	+AND+ETHNICITY+IN+THE+UNITED+STATES%2C+1995-2019%3A+AN+AGE-
	PERIOD-
	COHORT+ANALYSIS&stitle=J.+Gen.+Intern.+Med.&title=Journal+of+General+Interna
	l+Medicine&volume=37&issue=&spage=S336&epage=S337&aulast=Cameron&aufirst=
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Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States



Appendix 1. Search Strategy by Database

PubMed Search Strategy

#1 birth[tiab] OR labor[tiab] OR delivery[tiab] OR mothers[tiab] OR maternal[tiab] OR "peripartum period"[mesh] OR peripartum[tiab] OR "labor, obstetric"[mesh] OR "obstetric*"[mesh] OR "obstetric*"[tiab] OR "pregnancy"[mesh] OR "pregnan*"[tiab] OR "perinatal"[tiab] OR "prenatal"[tiab] OR "parturition"[mesh] OR "parturition"[tiab]

#2 "tribal" OR "tribe" OR "first nations" OR "indigenous peoples"[mesh] OR indigenous OR "health services, indigenous"[mesh] OR "american indians or alaska natives"[mesh] OR "american indian*" OR "indians, north american"[mesh] OR "native American" OR "alaska native"

#3 "severe maternal morbidity" OR "near miss" OR "adverse maternal outcomes" OR "maternal mortality" OR "Near Miss, Healthcare"[Mesh] OR "Pregnancy/Adverse Effects"[Mesh] OR "Pregnancy/Injuries"[Mesh] OR "Pregnancy/Mortality"[Mesh] OR "Pregnancy/complications"[Mesh] OR "Obstetric Labor Complications"[Mesh] OR "Delivery, Obstetric/adverse effects"[Mesh] OR "Delivery, Obstetric/complications"[Mesh] OR "Delivery, Obstetric/mortality"[Mesh] OR "Maternal Mortality"[Mesh] OR "mortality"[mesh] OR "morbidity"[mesh] OR "pregnancy complications" OR mortality OR morbidity OR "labor complications" OR "delivery complications"

#4 Search (#1 AND #2 AND #3)

EMBASE Search Strategy

('delivery:ab,ti' OR 'birth:ab,ti' OR 'labor:ab,ti' OR 'mothers':ab,ti OR 'maternal':ab,ti OR 'peripartum':ab,ti OR 'obstetric':ab,ti OR 'pregnancy':ab,ti OR 'perinatal':ab,ti OR 'prenatal':ab,ti OR 'parturition':ab,ti OR 'perinatal period'/exp OR 'labor'/exp OR 'pregnancy'/exp OR 'birth'/exp)

AND

(tribe OR 'indian health service' OR indigenous OR tribal OR 'first nations' OR 'american indian' OR 'native american' OR 'alaska native' OR 'indigenous people'/exp OR 'indigenous health care'/exp OR 'american indian'/exp)

AND

('severe maternal morbidity' OR 'adverse maternal outcomes' OR 'maternal mortality' OR 'pregnancy complications' OR 'mortality' OR 'morbidity' OR 'labor complications' OR 'delivery complications' OR 'near miss (health care)'/exp OR 'near miss' OR 'pregnancy complication'/exp OR 'maternal mortality'/exp OR 'labor complication'/exp OR 'maternal outcome'/exp OR 'delivery complications'/exp OR 'maternal morbidity'/exp OR 'morbidity'/exp OR 'mortality'/exp)

CINAHL Search Strategy

((TI delivery OR AB delivery) OR (TI birth OR AB birth) OR (TI labor OR AB labor) OR (TI mothers OR AB mothers) OR (TI maternal OR AB maternal) OR (TI peripartum OR AB peripartum) OR (TI obstetrics OR AB obstetrics) OR (TI pregnancy OR AB pregnancy) OR (TI perinatal OR AB perinatal) OR (TI prenatal OR AB prenatal) OR (TI parturition OR AB parturition) OR (TI delivery OR AB delivery) OR MM "Perinatal Period" OR MM "Obstetric Patients" OR MM "Delivery, Obstetric+" OR MM "Pregnancy+" OR MM "Labor+" OR MM "Obstetrics+" OR MM "Childbirth+")

AND

(tribe OR "indian health service" OR Indigenous OR "native american" OR "american indian" OR Tribal OR "first nations people" OR "alaska native" OR MM "Indigenous Peoples+" OR MM "Health Services, Indigenous" OR MM "Native Americans+")

AND

("severe maternal morbidity" OR "near miss" OR "pregnancy complications" OR "obstetric complications" OR mortality OR morbidity OR "maternal mortality" OR "maternal morbidity" OR "delivery complications" OR MM "near-death experiences" OR MM "maternal mortality" OR MM "obstetric emergencies" OR MM "Pregnancy Complications+" OR MM "labor complications" OR MM "maternal mortality" OR MM "morbidity+" OR MM "mortality+")

SCOPUS Search Strategy

("severe maternal morbidity" OR "near miss" OR "pregnancy complications" OR mortality OR morbidity OR "labor complications" OR "delivery complications" OR "maternal mortality" OR "maternal morbidity" OR "obstetric complications")

AND

(indigenous OR "native american" OR "american indian" OR tribal OR "alaska native" OR "first nations" OR tribe OR "indian health service")

AND

(TITLE-ABS (mother) OR TITLE-ABS (maternal) OR TITLE-ABS (peripartum) OR TITLE-ABS (obstetric) OR TITLE-ABS (pregnancy) OR TITLE-ABS (perinatal) OR TITLE-ABS (prenatal) OR TITLE-ABS (parturition) OR TITLE-ABS (labor) OR TITLE-ABS (birth) OR TITLE-ABS (delivery))

Append	lix 2. Table	of inclu	ıded studie	es		RW1 C	Jpen		d by copy	mjopen-2	
Study #	Authors	Year	Study Design	Locatio n	Sample Size, Data Source	Native American subsample size (% of total sample)	Risk Factor (Social ecological level)	Outcome(s)	Covariat, including for use	Quality Rating	Key Findings ([9 Confidence Inte unless otherwise stated
Hypert	ensive Disord	ers of Pr	egnancy (8)						s relatec	aber 202	
1178	Cameron, N et al.	2022	Cross Sectional	Nationw ide	51,685,525 all live births in the US to individuals aged 15-44 years, birth vital records	492,771 (9.3%)	Maternal residence (C)	Pregnancy induced hypertension	to text and data mining, Al training, and similar technologies.	Good Good 24. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique	-The incidence of hypertensive diso of pregnancy diffe by racial and ethn identity within bo rural and urban ar The highest age- adjusted incidence hypertensive diso of pregnancy was observed among individuals who identify as Ameri- Indian/ Alaskan N -Significant increa- the incidence of hypertension diso of pregnancy amo Native American women in rural ar compared to those urban areas in 200 2014 (2017 RR= [1.11-1.33] and 20 RR=1.17, [1.08-1] -No significant in in the incidence of hypertension diso of pregnancy amo

						BMJ C	pen		6/bmjop cted by		Page 4
									en-2024-088380 on 28 copyright, including f		Native American women living in rural areas compared to those in urban areas was observed in 2019 (2019 RR=1.03, [0.96-1.11])
2230	England, L et al.	2013	Case Control	Anchora ge, AK	1,123 singleton deliveries from 1997- 2005 to AN women residing in western Alaska, hospital administrat ive database / 503 cases and 502 controls	1,123 (100%)	Continuous smokeless tobacco use (I) and continuous cigarette smoking (I)	Pregnancy associated hypertension, pre- eclampsia, and gestational hypertension	Parity, pregnange 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique orgess related to text and data mining, Al training, and similar technologies. BMI, materna age	Good	 -No significant associations were observed between smokeless tobacco use and pregnancy- associated hypertension (aOR 0.92, [0.56– 1.51]). -No significant associations were observed between smokeless tobacco use and pre-eclampsia (aOR 0.90, [0.52–1.56]). -No significant associations were observed between smokeless tobacco use and gestational hypertension (aOR 0.93, [0.42–2.03). -No significant associations were observed between continuous cigarette smoking and pregnancy-associated hypertension (aOR 0.65, [0.31–1.37]). -No significant associations were observed between

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1 2 3 4 5 6 7 8 9 10 11 12 13										en-2024-088380 on 28 November 2024 Enseignemei copyright, including for uses related t	continuous cigarette smoking and pre- eclampsia (aOR 0.69, [0.30–1.58]). -No significant associations were observed between continuous cigarette smoking and gestational hypertension (aOR 0.52, [0.14–1.90).
13 14 15 16 17 18 19 20 21 22 23 24 25 27 28 29 30 31 23 34 35 36 37 38 39 40 41 42 43	8141	Zamora- Kapoor, A et al.	2016	Cohort	Washin gton State	71,080 singleton live births from 2003- 2013 to Whit and AI/AN women, linked birth- hospital discharge records	7,189 (10.1%)	Maternal race (I), BMI (I)	Pre-eclampsia	Birth years for a constrained from burne age, and the form burne age, attainment (ABES)	-AI/ANs had an increased risk of pre- eclampsia compared to Whites after controlling for all covariates except BMI (OR 1.17 [1.06– 1.29]). After further adjustment for BMI, the racial disparity in pre- eclampsia risk was greatly attenuated (aOR 1.05, [0.95–1.16]). -AI/ANs who were underweight (OR 1.39, [0.64-3.02]), normal weight (OR 1.02, [0.83- 1.22]), overweight (OR 1.23, [0.93, 1.36]), or obese (OR 1.00, [0.86, 1.17]) generally had relative risks of pre- eclampsia comparable, or slightly (but not statistically significantly) greater than those of their White counterparts.
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1371	Chang, J et al.	2014	Cohort	Nationw ide	3,113,164 singleton births between 20-44 weeks gestation without major fetal anomalies in 2010, US natality file	34,348 (1.10%)	Cigarette use during pregnancy (I), maternal age (I)	Pregnancy induced hypertension (inclusive of pre-eclampsia and eclampsia)	Prenatalopyright care adequacy, including gain, uses related by marital status, ses related by chronic related by n, diabetes on, by percented by texts, and preecland by ia, eclamps tobacco data	Good Good An-2024-088380 on 28 November 2024 Downloaded fr	-The odds of pregnance induced hypertension was greater in non- Hispanic American Indian women 35 years or older who smoked during pregnancy (aOF 1.29, [0.88-1.89]). -A reduced odds of PII was evident in non- Hispanic American Indian women younger than 35 years old who smoked during pregnancy based (aOR 0.76, [0.66-0.87]).
7372	Tiwari, R et al.	2021	Cohort	Washin gton State	105,466 singleton live births from 22 facilities from 2018- 2018, hospital administrat ive database	978 (0.92%)	Pre- pregnancy BMI (I)	Pre-eclampsia	Maternabis age, parity, delivery Al hospital, tr governmän t health g insurance substance abuse, milar use, and te alcohol use	Good	-The strength of the association of overweight/obesity wi preeclampsia was muc greater among NH AI/AN women (aRR 5.24; [1.92–14.30]) an NH Native Hawaiian/Other Pacifi Islander women than among other race/ethnicities (aRR 5.88, [1.30-36.51]).
835	Best, L et al.	2012	Case Control	Belcourt , ND	299 women tribal members of the Turtle Mountain Band of Chippewa who sought care in an IHS	299 (100%)	Age at delivery (I), nulliparity (I), BMI (I), Single nucleotide polymorphi sms [NOS3, rs1799983	Pre-eclampsia	Nullipar ff y, BMI, age at delivery	Good	-Age at delivery (aOR 1.0823, [p=0.0185]), nulliparity (aOR 6.8628, [p<0.001]), an obesity (aOR 1.0951, [p<0.001]) show robus independent effects associated with preeclampsia.

Page 45 of 62				BMJ O	pen		/bmjop ;ted by		
2 3 4 5 5 6 7 3 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25			hospital or clinic from 2004-2009, electronic medical records / 101 cases and 198 matched controls		(G allele recess), NOS3, rs3918227 (A allele dom), GNB3, rs5442 (A allele dom), DDAH1, rs10158674 (C allele recess), DDAH1, rs233115 (A allele recess)] (I)		en-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.b Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, a		-There was no significant association between any of single nucleotide polymorphisms studied and pre-eclampsia. -NOS3, rs1799983 (G allele recess) (aOR 1.4087, [p=0.2354]) -NOS3, rs3918227 (A allele dom) (aOR 0.7356, [p=0.4611]) -GNB3, rs5442 (A allele dom) (aOR 0.9147, [p=0.8655]) -DDAH1, rs10158674 (C allele recess) (aOR 1.0165, [p=0.9898]) -DDAH1, rs233115 (A allele recess) (aOR 2.2227. [p=0.1578])
26 836 Best, L et 27 836 Best, L et 28 al. 29 30 30 31 32 33 33 34 35 36 36 37 38 39 40 41 42 43 44 44	2012 Case Control	Belcourt , ND	196 women tribal members of the Turtle Mountain Band of Chippewa who sought care in an IHS hospital or clinic from 2004-2009, electronic medical records / 66 cases and	196 (100%)	Age at delivery (I), nulliparity (I), BMI (I), single nucleotide polymorphi sms [CRP_A rs3093077 (T allele additive), CRP_B rs1205 (A allele dom), CRP_C rs1130864	Pre- eclampsia, severe pre- eclampsia	Nulliparty, weight and first ar prenatal tec visit, BMH, birthweight of infante, gestational diabetes, age at delivery	Good	-Age at delivery did not show a significant association with pre- eclampsia (aOR 1.036, [p=0.398]) and severe preeclampsia (aOR 1.027, [p=0.586]). -Nulliparity (aOR 4.274, [p=0.003] and aOR 4.520, [p=0.009])) and obesity (aOR 1.093, [p=0.002] and aOR 1.094, [p=0.007]) show robust independent associations with

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				130 matched controls		(T allele dom), MBL2 rs1800451 (T allele dom, IL1A rs3783550 (T allele dom), CTLA4 rs231775 (A allele dom)](I)		Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, A	an-2024 Dee2e0 on 29 November 2024 Downloaded from http://	preeclampsia and severe pre-eclampsia. -There was no significant association between any of single nucleotide polymorphisms studied with pre-eclampsia and severe pre-eclampsia except CRP_B, rs1205, (A allele dom). -CRP_B, rs1205, (A allele dom) was the only single nucleotide polymorphism that showed a significant association with severe pre-eclampsia (aOR 0.259, [p=0.020]).
837 Best, L et al.	2013	Case Control	Belcourt , ND	410 women tribal members of the Turtle Mountain Band of Chippewa who sought care at an IHS hospital or clinic from 2004-2012, electronic medical records / 140 cases and 270 matched controls	410 (100%)	Age at delivery (I), nulliparity (I), BMI (I), gestational diabetes (I), single nucleotide polymorphi sms [CRP rs3093068 (G allele add), CRP rs3093068 (G allele recess, CRP rs3093068 (G allele dom), CRP	Pre- eclampsia, severe pre- eclampsia	Nullipar ia y, weight an first g prenatal an visit, BM J , birthwei n diabetes hnologies	Good	-Age at delivery did not show a significant association with pre- eclampsia (aOR 1.053, [p=0.076]) and severe preeclampsia (aOR 1.052, [p=0.166]). -Gestational diabetes did not show a significant association with pre-eclampsia (aOR 1.684, [p=0.278]) and severe pre- eclampsia (aOR 2.241, [p=0.166]). -Independent effects of nulliparity (aOR 5.6, [p=0.001] and aOR 4.17, [p=0.001]) and

Page 4	7 of 62						BMJ C)pen		cted by	6/bmjop	
$1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \\ 7 \\ 8 \\ 9 \\ 10 \\ 11 \\ 12 \\ 13 \\ 14 \\ 15 \\ 16 \\ 17 \\ 18 \\ 19 \\ 20 \\ 21 \\ 22 \\ 23 \\ 24 \\ 25 \\ 26 \\ 27 \\ 28 \\ 29 \\ 30 \\ 31 \\ 32 \\ 33 $								rs876538 (C allele add), CRP , rs876538 (C allele recess), CRP rs876538 (C allele dom), rs3093068 (G dom) and rs876538 (C recess) add risk score] (I)		Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, and similar technologi	n-2024-088380 on 28 November 2024. Downloaded from <u>http://bmjopen.bmj.com/ on June 7, 20</u>	obesity (aOR 1.061, [p=0.002] and aOR 1.059, [p=0.001]) on pre-eclampsia and severe pre-eclampsia were observed. -There was no significant association between any of single nucleotide polymorphisms studied with pre-eclampsia and severe pre-eclampsia except CRP rs3093068 (G allele add) and CRP rs3093068 (G allele dom) with severe pre- eclampsia (aOR 2.587, [p=0.05] and aOR 2.587, [p=0.050]) -The rs3093068 (G dom) and rs876538 (C recess) additive risk score showed significant association with pre-eclampsia (aOR 1.779, [p=0.016]) and severe pre- eclampsia (aOR 2.035, [p=0.013]).
34 35		Severe Mater	rnal Mor	bidity and N	Iortality (4)					ies.	025 at A	
37 38 39 40 41 42 43 44	119	Admon, L et al.	2018	Cross Sectional	Nationw ide	2,523,528 all hospital deliveries that occurred between 2012-2015,	20,447 (0.810%)	No chronic conditions, any physical health condition (I), any	SMM	Age, income, payer, rural vs. urban residence, and	gence Bibliographique	-The incidence of severe maternal morbidity was significantly higher among deliveries to women in every racial and ethnic minatory
45					For peer	review only - h	ttp://bmjopen.l	bmj.com/site/al	bout/guidelines.x	html	de l	

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National	behavioral	hospital 6	category compared wi
Inpatient	health	region T.	deliveries among non-
Sample	condition	icgion. igh	Hispanic white wome
Sample	(I) multiple	t, 188	Thispanie white wohie
	(I), indutiple	ncl 38	-American
	chionic	ud Do	Indian/Alaska Native
	conditions		women are at increase
	(1),	fo	risk of severe matern
	maternal		morbidity compared
	race (1)	Seg Eng	non-Hispanic white
		s re	women (aRR 1.5 [1
		slat 2	1.71) This is not
		ed 102	i./j). This is not
			significant when bloc
		te Sup	transitusions are not
			included in severe
		nd Prie	maternal morbidity
		da Űr Ge	(aRR 0.90, [0.68-1.2
			-Among deliveries to
			women with comorb
		nin S)	women with comorb
		<u> 9</u>	physical and behavio
			health conditions,
			significant difference
		l Ei Ka	in severe maternal
		g, <mark>p</mark>	morbidity were
		an an	identified among rac
		S S	and ethnic minority
		i <u>e</u>	compared with non-
		lar or	Hispanic white wom
		t t	and the largest
			disparities were
			identified among
		ogi 20	women with multiple
		es. 125	chronic conditions.
		₩	
		A g	-In comparing
			deliveries among
		l ě	American
			Indian/Alaskan Nativ
		l E	women with non-
		l đ	Hispanic white wom
			the rate difference fo
		<u>5</u>	severe maternal

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 22										an-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, and similar technc	morbidity incidence increased from 66.6 [95% CI 39.9-93.3] to 101.3 [95% CI -41.0- 243.5] per 10,000 delivery hospitalizations, respectively, in comparing deliveries in which no and multiple chronic conditions were identified. -American Indian/Alaskan Native women compared to non-Hispanic white women are at increased risk for severe maternal morbidity when any physical health condition is present (aRR 1.5, [1.3-1.7]), any behavioral health condition is present (aRR 1.2, [0.90-1.6]), and having multiple (2 or more) chronic conditions (aRR 1.4, [0.93-2.20]).
32 33 34 35 36 37 38 39 40 41 42 43 44	3421	Interrante, J et al.	2022	Cross Sectional	Nationw ide	6,357,796 maternal records from childbirth hospitalizat ions from 2007-2015, National Inpatient Sample	43,929 (0.691%)	Primary payer type (I), maternal residence (C), maternal race (I)	SMM and Mortality (SMMM)	Maternal race and s ethnicity, maternal residence, maternal age, childbirth year, bottom quartile of	 -Rural Indigenous Medicaid-funded births had the highest adjusted predicted rate of SMMM (224.9 per 10,000 births, [187.0- 262.9]). -Among rural residents, births by Indigenous people had the greatest differences in rates
45 46 47					For peer	review only - h	ttp://bmjopen.l	omj.com/site/a	bout/guidelines.x	ntml de	

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1 2 3 4 5 6 7 8 9 10 11 2 13 4 5 6 7 8 9 10 11 2 13 4 5 6 7 8 9 10 11 2 13 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2				income, pyright hospital region, t , cesareanincludi use disorder, depressions HIV or relation hypertension hypertension systemic and disease, pulmonad hypertension sus, chronic training, disease, Al training, upus erythemata mining, disease, chronic heart disease, diabetes chronic respirato y disease chronic respirato hypertension hype	between Medicaid- funded and privately insured births (aRD, 97.8, [50.4–145.3]). -When examining the intersection of rurality and race and ethnicity, births among Indigenous rural residents had significant additive interaction, with 40% (aAP 0.40, [0.11-0.69]) of SMMM cases in that population owing to the interaction. -When examining the intersection of urban status and race and ethnicity, births among Indigenous urban residents did not have an additive interaction (aAP 0.06, [-0.20- 0.32]). -If the excess risk of SMMM associated with Medicaid could be mitigated (i.e., if the risk of SMMM among Medicaid-funded births could be decreased to the risk among the privately insured), this would not only prevent the 23 cases per 10,000 births that occur among white urban residents, but an additional 98 cases per 10,000 births	t
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1 2 3										copyright	en-2024-0	among Indigenous rural residents.
4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	952	Booker, W et al.	2018	Cohort	Nationw ide	1,724,694 delivery hospitalizat ions from women aged 40-54 years between 1998-2014, National Inpatient Sample	7,107 (0.412%)	Maternal race (I)	SMM, SMM excluding blood transfusions	Year, be size, be insurance status, for location, s related to text hospital to text teaching status, aff race to text tatus, aff teaching tatus, aff tatus, aff teaching tatus, aff teaching	Good 88380 on 28 November 2024 Downloaded from	 The incidence of SMM was greater among Native American women but not significant compared to Non-Hispanic white women (aRR 1.08, [0.93-1.25]). Risk for severe morbidity excluding transfusion among Native Americans is not demonstrated because of small denominators.
20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	4010	Kozhiman nil, K et al.	2020	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (I)	SMMM, SMMM excluding blood transfusion	Age, in , insuranc A payer, in income, in hospital region and similar technologies .	Good Good http://bmionen.hmi.com/ on June 7 2025 at Agence Ribliographique 1	-The incidence of SMMM was greater among indigenous women compared with white women (aRR 1.8, [1.6–2.0]). -Within each racial group, incidence of SMMM was higher among rural compared with urban residents (2.3% for rural indigenous women vs 1.8% for urban indigenous women) (a RR 1.3, [1.0–1.6]); (1.3% for rural white women vs 1.2% for urban white women) (aRR 1.1, [1.1–1.2]). -Within indigenous women, the incidence
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									n-2024-088380 on 28 l opyright, including fo	of SMM (excluding transfusions) among rural compared to urb residents was not significant (aRR 0.7, [0.4-1.0)].
J	Blood Transf	fusions (2	2)						r use	
3421	Interrante, J et al.	2022	Cross Sectional	Nationw ide	6,357,796 maternal records from childbirth hospitalizat ions from 2007-2015, National Inpatient Sample	43,929 (0.691%)	Primary payer type (I), maternal residence (C), maternal race (I)	Blood transfusions	Maternal Good race and Good residence age, data Ministry age, data Ministry year, ministry outrile Gr income, Al monistry vear, and substance income, Al monistry region, income, Al monistry operation birth, and substance use milistry disorder, and substance income, Al monistry region, for a lune disorder, and substance income, Al monistry on, cesare and on depression, HIV or monistry hypertensi on, systemic lupus erythemato sus, chronic kidney disease, chronic	 -Rural residents had greater odds of blood transfusion for both Medicaid-funded (aO 1.15, [1.06-1.25]) and privately insured (aOI 1.20, [1.11-1.31]) hospital births compared to urban residents. -Medicaid-funded (aO 1.71, [1.39-2.11]) and privately insured hospital (aOR 1.42, [1.05-1.92]) indigeno births had the second highest odds of blood transfusions compare to other racial/ethnic groups. This yielded a additive interaction pvalue of 0.006.

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								heart by right disease, give the search of t	
Kozhiman nil, K et al.	2020	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (I)	Blood transfusions	Age, aten 2024. Good insurance to text and from http://bmjopen.b hospital and data mining, Al training, a	-The incidence of blood transfusions was greate among indigenous women compared with white women (aRR 1.8 [1.5–2.0]). -The incidence of blood transfusion among rura indigenous women compared to urban indigenous women was statistically greater (aRR 1.6, [1.2-2.0]).
Postpartum H	Hemorrh	age (PPH) (2	2)					mj.com	
Chalouhi, S et al	2015	Cohort	Gallup, NM	1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records	751 (70.7%)	Maternal race (I), age (I), parity (I), gravidity (I), birthweight (I), retained placenta (I), magnesium sulfate use (I), induction augmentati on (I),	Postpartum hemorrhage	None 7, 2025 at Agence Bibliographique	-A significantly higher proportion of Native Americans than non- native women developed PPH (11.6% vs 7.0%, [p= 0.02]). -In multivariable logistic regression analysis, the significar predictors of PPH wer Native American ethm origin (OR 1.8, [1.1- 3.0]), decreased gravidity of fewer than
P (?	Kozhiman nil, K et al. ostpartum I Chalouhi, S et al	Kozhiman nil, K et al.2020ostpartumHemorrhChalouhi, S et al2015	Kozhiman nil, K et al.2020Cross Sectional alostpartum Hemorrhage (PPH) (2Chalouhi, S et al2015Cohort	Cozhiman ii), K et i.2020Cross SectionalNationw ideSectionalVation SectionalVation SectionalVation Sectionalostpartum Hemorrbage (PPH) (2)Chalouhi, S et al2015CohortGallup, NMSet al2015CohortGallup, NMSet al2015CohortFor peer	Cozhiman nil, K et l.2020Cross SectionalNationw ide7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sampleostpartum Hemorrhage (PPH) (2)Chalouhi, S et al2015CohortGallup, NM1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical recordsFor peer review only - h	Cozhiman iil, K et al.2020Cross SectionalNationw ide7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample101,943 (1.35%)ostpartum Hemorrhage (PPH) (2)Chalouhi, S et al2015CohortGallup, NM1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, nedical records751 (70.7%)	Cozhiman iil, K et i.2020Cross SectionalNationw ide7,561,729 hospital live births from white and ndigenous women between 2012-2015, National Inpatient Sample101,943 (1.35%)maternal residence (C), maternal race (I)ostpartum Hemorrhage (PPH) (2)Chalouhi, S et al2015CohortGallup, NM1,062 women who delivered vaginally at the 	Sozhiman il, K et l.2020Cross SectionalNationw ide7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample101,943 (1.35%)maternal residence (C), maternal race (I)Blood transfusionsostpartum Hemorrhage (PPH) (2)Chalouhi, S et al2015CohortGallup, NM1,062 women who delivered vaginally at he Rehoboth McKinley Hospital indigenous sume751 (70.7%)Maternal race (I), age (I), parity (I), retained placenta (I), magersium sulfate use (I), induction augmentati or (I),Postpartum hemorrhage	Cozhiman 2020 Cross Nationw 7,561,729 101,943 maternal residence Blood Age, Blood Goodinations Age, Goodinations Goodinations Age, Blood Insurance Opposition Goodinations Age, Blood Insurance Core Core <t< td=""></t<>

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					chorioamni onitis (I)		n-2024-088380 on 28 Novemb Ense copyright, including for uses r		5 (OR 1.2, [1.1-1.4]), increased birth weight greater than 4500 grams (OR 1.1, [1.0-1.0]), retained placenta (OR 51.0, [9.8-288.2]), and use of magnesium sulfate (OR 3.5, [1.4- 9.0]).
2944 Hadley, M et al 20	021 Case Control	Anchora ge, AK	384 deliveries between 2018-2019 at the Alaska Native Medical Center, medical records / 128 cases and 256 controls	384 (100%)	BMI (I), antepartum bleeding (I), routine aspirin used prescribed (I), prior uterine incision (I), prior uterine incision and vaginal delivery (I), parity (I), macrosomi a, pre- eclampsia without severe features with magnesium sulfate during labor (I), pre- eclampsia with severe features and use of	Postpartum hemorrhage	er 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique ignement Superieur (ABES) . elated to text and data mining, Al training, and similar technologies. Not reported	Fair	-In the bivariate analysis, the following risk factors were significantly associated with a higher likelihood of postpartum hemorrhage: BMI of 40 or more (OR 2.6, [1.4- 4.5]), antepartum bleeding (OR 6.3, [1.2- 31.6]), previous postpartum hemorrhage (OR 5.0, [2.6-9.8]), suspected macrosomia with estimated fetal weight of 4000 g or more (OR 2.7, [1.4- 5.3]), pre-eclampsia with severe features and use of magnesium sulfate during labor (OR 4.7, [2.4-9.2], length of third stage labor longer than 20 min (OR 2.2, [1.1-4.4]), and use of oxytocin for more than 12 h (OR 5.0, [2.3-10.6]). -Residence in a rural community (OR 2.2, [1.4-3.6]) and vitamin

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	For peer rev	view only - http://bl	magnesium sulfate (I), previous postpartum hemorrhage (I), length of 2nd stage of labor (I), length of 3rd stage of labor (I), rural residence (C), and oxytocin (I), and inpatient induction length (I)	en-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on_lune 7, 2025 at Agence Bibliographique Enseignement Superieur (ABES) . Copyright, including for uses related to text and data mining, Al training, and similar technologies.	D supplementation (OR 1.7, [1.1-2.6]) were also significantly associated with postpartum hemorrhage. -Multivariate condition logistic regression analyses found that antepartum bleeding (OR 8.8, [1.6-48.5]), pre-eclampsia with severe features and use of magnesium sulfate (OR 5.3, [2.4-11.9]), previous postpartum hemorrhage (OR 2.7, [1.2-6.1]), third stage of labor of 20min or more (OR 2.9, [1.2-6.9]), rural residence (OR 2.0, [1.2-3.5]), fetal macrosomia (OR 4.0, [2.1-7.5]), and oxytocin use for more than 12h (OR 3.0, [1.1-8.0]) all remained significantly associated with an increased risk of hemorrhage in Native American women. -Routine aspirin use (OR 1.7, [0.9-3.4]), prior uterine incision (OR 1.0, [0.52-2.1]), prior uterine incision and vaginal delivery (OR 1.6, [0.58-4.4]), a parity of 5 or more (OR 1.8, [0.87-3.9]), pre- eclampsia without severe features without

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	Misc. Outco	mes (5)								en-2024-088380 on 28 November 2024. Downloa ded Enseignement Superieur (copyright, including for uses related to text and dat	use of magnesium sulfate (OR 2.1, [0.98- 4.4]), length of second stage of labor grater or equal to 1 hour (OR 1.6 [0.88-3.0]), and an inpatient induction length of greater or equal to 36 hours (OR 2.3, [0.4-12.8]) were not significantly associated with a higher likelihood of postpartum hemorrhage.
1331	Chalouhi, S et al	2015	Cohort	Gallup, NM	1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records	751 (70.7%)	Maternal race (I), age (I), parity (I), gravidity (I), birthweight (I), retained placenta (I), magnesium sulfate use (I), induction augmentati on (I), chorioamni onitis (I)	Uterine atony	None	G fro m http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliograp ABES) . a mining, Al training, and similar technologies.	Dod-Uterine atony was recorded in a significantly higher proportion of Native Americans than non- native patients (9.6% vs 4.8%; [p=0.01])In univariate analysis, factors predicting uterine atony were native race (p=0.01), decreasing gravidity (p=0.02), induction augmentation (p=0.1), increasing birthweight (p=0.07), and chorioamnionitis (p=0.08)In multivariable logistic regression analysis, Native

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1 2 3 4 5 6										copyright, includin	2024-088380 on	(OR 2.0, [1.1–3.7]) and increasing birthweight (OR 1.0, [1.0 1.0]) were significant predictors of uterine atony.
7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	1861	deRavello, L et al	2015	Cross Sectional	Nationw ide	229,986 American Indian and Alaska Native (AI/AN) women aged 15–44 years seeking care at Indian Health Service (IHS), Tribal, and urban Indian health facilities during 2002–2009, Indian Health Service National Patient Informatio n Reporting System	229,986 (100%)	Maternal age (I), IHS region (C)	Ectopic pregnancy	g for uses related to text and data mining, Al training, and similar technologies.	irr Fa 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographiqu Enseignement Superieur (ABES) .	 The ectopic pregnancy (EP) rate among AI/AN women was lowest in the 15–19 years age group (5.5 EPs per 1,000 pregnancies) and highest among 35–39 year old (18.7 EPs per 1,000 pregnancies). Compared to AI/AN women aged 15-18 years, women aged 35- 39 years were 3.4 times more likely to have an EP (RR 3.4, [2.90- 4.03]). Compared to AI/AN women aged 15- 18 years, the risk of an EP increased with age from 1.56-3.42, except in women aged 40-44 years were the risk was less at 2.62 times (RR 2.62, [2.02-3.36]). EP rates varied by geographic region, ranging between 6.9 and 24.4 per 1,000 pregnancies in the Northern Plains East and the East region, respectively. Compared to AI/AN women who received

							BMJ (Open		5/bmjop cted by	Page 5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36										n-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Ag Enseignement Superieur (ABES) . :opyright, including for uses related to text and data mining, Al training, and similar technologies.	care in the Northern Plains East region, women who received care in the East region were 3.55 times more likely to have an EP (RR 3.55, [2.75-4.57]), in the Alaska region the risk was 2.17 times (RR 2.17, [1.73-2.72]), in the Southern plains region the risk was 1.56 times (RR 1.57, [1.25- 1.95]), in the West region the risk was 1.39 times (RR 1.39, [1.09- 1.77]), in the Norther Plains West region the risk was 1.36 times (1.36, [1.08-1.71]), and in the Southwest region the risk was lowest at 1.33 times (RR 1.33, [1.07-1.65]). -We found relatively stable annual rates of EP among AI/AN women receiving care at IHS-affiliated facilities during 2002– 2009, but considerable variation by age group and geographic region.
37 38 39 40 41 42 43 44	2230	England, L et al.	2013	Case Control	Anchora ge, AK	1,123 singleton deliveries from 1997- 2005 to AN women residing in	1,123 (100%)	Continuous smokeless tobacco use (I) and continuous cigarette smoking (I)	Placental abruption, placental abruption expanded definition	Parity, pre- pregnancy BMI, maternal age BMI , B B B B B B B B B B	-Thirty-nine percent of case deliveries were also preterm (compared with 7% of controls, [p<0.001]), and 9.8% were also complicated by pregnancy
45 46	L	1	1	I	For peer	review only - h	ttp://bmjopen.	bmj.com/site/al	bout/guidelines.>	khtml 🛓	1

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29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47	Iar technologies. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37	4010	Kozhiman nil, K et al.	2020	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (C)	Disseminated intravascular coagulation (DIC), hysterectomy	Age, insurance, including for uses related to text and data mining, Al training, and similar technologies.	Good m-2024-088380 on 28 November 2024. Downloaded from http://bmianen.hmi.com/ on_lune 7, 2025 at Agento	DIC -The incidence of DIC was greater but not significant among indigenous woman compared with white women (1.6% vs 0.9%, respectively) (aRR 1.1, [0.8-1.5]). -Within indigenous women, there was no difference between rural women and urban women (0.2% vs 0.2%, respectively) (aRR 0.8, [0.3-1.3]). Hysterectomy -The incidence of a hysterectomy was greater among indigenous woman compared with white women (0.1% vs 0.1%, respectively) (aRR 1.8, [1.0-2.6]). -Within indigenous women, there was a marginal increased risk but not significant of hysterectomy among rural women (aRR 1.3, [0.3-2.3]).
38 39 40 41 42 43 44					For peer	review only - h	ttn://hmionen	hmi com/cita/a	hout/auidelines v	r - -	e Bibliographique d	

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Appendix 3. Results of NIH Quality Assessments for Included Studies

For observational cohort and cross-sectional studies:

ID#	Authors	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	G12	Q13	Q13	Rating
119	Admon L, et al.	2018	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	NA	Yes	nseignen e <u>s</u> relater N	mber 20	Yes	Good
952	Booker W, et al.	2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	nent Sup Yog text a	24. Down	Yes	Good
1178	Cameron, N. et al.	2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	erieur (A N <mark>R</mark> d data	oaded fr	No	Good
1331	Chalouhi, S. et al.	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	BES). Y®ning, .		No	Good
1371	Chang, J et al	2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yerai	NR	Yes	Good
1861	deRavello, L. et al.	2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	nking, and	Den NA	No	Fair
3421	Interrante, J. et al.	2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Y ⊛ milar	NA 9	Yes	Good
4010	Kozhimannil, K et al.	2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	teshnolo	June 7,	Yes	Good
7372	Tiwari, R. et al	2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Y & S	2025 at <i>F</i>	Yes	Good
8141	Zamora- Kapoor A., et al	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Agence Biblic	Yes	Good
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Quality of included studies was assess Studies (https://www.nhlbi.nih.gov/hes Q1. Was the research question or objec Q2. Was the study population clearly s Q3. Was the participation rate of eligit Q4. Were all the subjects selected or ra- being in the study prespecified and app Q5. Was a sample size justification, po Q6. For the analyses in this paper, wer Q7. Was the timeframe sufficient so th Q8. For exposures that can vary in amo or exposure measured as continuous va Q9. Were the exposure (c) assessed mo	ed using the National Institutes of Health (NIH) Quality Assessment tool for Observational alth-topics/study-quality-assessment-tools). ctive in this paper clearly stated? specified and defined? ble persons at least 50%? ecruited from the same or similar populations (including the same time period)? Were in plied uniformly to all participants? ower description, or variance and effect estimates provided? re the exposure(s) of interest measured prior to the outcome(s) being measured? nat one could reasonably expect to see an association between exposure and outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if if the study examine different levels of the exposure as related to the outcome if the study examples is the study example. The study examples is
Q10. was the exposure(s) assessed mo Q11. Were the outcome measures (dep Q12. Were the outcome assessors blim Q13. Was loss to follow-up after basel Q14. Were key potential confounding	be than once over time? bendent variables) clearly defined, valid, reliable, and implemented consistently across a ded to the exposure status of participants? line 20% or less? variables measured and adjusted statistically for their impact on the relationship betweet training, and similar technic in the second of the
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For case	e-control studies:											ight, inc	27-08838		
ID#	Authors	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Ç10	Q11	Q12	R
835	Best, L. et al	2012	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes A	Yes	Yes	G
836	Best, L. et al.	2012	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	uses Lens	Yes	Yes	G
837	Best, L et al.	2013	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes		Yes	Yes	G
2230	England L, et al	2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	ied to	Yes	Yes	G
2944	Hadley, M et al	2021	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yest of	No	Yes	Fa
 Q6. Were the cases clearly defined and differentiated from controls? Q7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls random by selected from those eligible as the end of concurrent controls? Q9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event the period) across all study participants? Q11. Were the assessors of exposure/risk blinded to the case or control status of participants? Q12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did get a participant as a control study analysis? 															
participar Q11. Wei Q12. Wei matching	nts? re the assessors of exp re key potential confou during study analysis?	osure/risk unding var ?	blinded to iables me	o the case asured an	e or contr nd adjust	rol status ed statisti	of partici ically in t	pants? he analys	ses? If ma	atching w	as used, o	ichnolegies.	vestigato	rs accoun	as a dy it for
participar Q11. Wei Q12. Wei matching Q, quest	nts? re the assessors of exp re key potential confor during study analysis tion; CD, cannot be	osure/risk unding var ? determir	blinded to iables me	o the case asured an , not app	e or contr nd adjust	ol status ed statisti	of partici ically in t	pants? he analys ed; N, n	ses? If ma	atching w	as used, o	ichnol e gies. did	Nyvestigato	rs accoun	as a dy tt for

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Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States: A systematic review

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Secondary Subject Heading:	Epidemiology, Public health
Keywords:	Mortality, OBSTETRICS, PUBLIC HEALTH, Maternal medicine < OBSTETRICS, Systematic Review, Pregnant Women

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TITLE

Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States: A systematic review

AUTHORS AND AFFILIATION

Martín F. Celaya^{1,2}, Alaa I. Zahlan², Chelsea Rock³, Akshay Nathan⁴, Aishwarya Acharya²,

Purnima Madhivanan², John Ehiri², Chengcheng Hu², Sydney Pettygrove², Velia Leybas Nuño²

1. Arizona Department of Health Services, Phoenix, Arizona, United States

2. Mel & Enid Zuckerman College of Public Health, University of Arizona, Tucson, Arizona,

United States

3. College of Health Solutions, Arizona State University, Phoenix, Arizona, United States

4. Boston University, Boston, Massachusetts, United States

AUTHORS' E-MAIL ADDRESSES

Martín F. Celaya, martin.celaya@azdhs.gov; Alaa I Zahlan, azahlan@arizona.edu; Chelsea

Rock, <u>chelsea.rock@azdhs.gov</u>; Akshay Nathan, <u>shayaknathan@gmail.com</u>; Aishwarya

Acharya, aishwaryaacharya@arizona.edu; Purnima Madhivanan, pmadhivanan@arizona.edu;

John Ehiri, jehiri@arizona.edu; Chengcheng Hu, hucc@arizona.edu; Sydney Pettygrove,

sydneyp@arizona.edu; Velia Leybas Nuño, vleybas@arizona.edu

SUBMITTING AND CORRESPONDING AUTHOR

Martín F. Celaya, martin.celaya@azdhs.gov

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Main text: 3988 (excluding title page, abstract, references, figures, tables, and other required content)

- Table 1. Outcomes of interest
- Table 2. PubMed search strategy
- Table 3. Summary of risk factors and outcomes by risk/association category

NUMBER OF FIGURES: 1

Figure 1. PRISMA flow diagram

NUMBER OF APPENDICES: 4

- Appendix 1. Search strategy by database
- Appendix 2. Risk factors and outcomes by volument of studies
- Appendix 3. Table of included studies
- Appendix 4. Results of NIH Quality Assessments for included studies

KEYWORDS: American Indian or Alaska Native, Mothers, Morbidity

ABSTRACT

Introduction and objective

Maternal morbidity and mortality (MMM) is a public health concern in the US, with Native American women experiencing higher rates than non-Hispanic White women. However, research on risk factors for MMM outcomes among Native American women is limited. This systematic review comprehensively synthesizes and critically appraises the literature on risk factors for MMM experienced by Native American women.

Methods and analysis

A systematic search was conducted on 10 October 2022 in PubMed, Embase, CINAHL, and Scopus for articles published since 2012. Selection criteria included observational studies set in the US, involving Native American women in the perinatal period, and examining the relationship between risk factors and MMM outcomes. Three reviewers screened and extracted data from the included studies, with risk of bias assessed using National Institutes of Health quality assessment tools. Data were analyzed descriptively.

Results

Fifteen studies were analyzed, with Native American women as the primary study population in seven studies. All studies utilized administrative databases, with settings including nationwide (7 studies), statewide (4 studies), and Indian reservations (4 studies). Nine MMM outcomes were identified. The majority of studies focused on hypertensive disorders of pregnancy (8 studies) and severe maternal morbidity (SMM) (4 studies). Twenty-six risk factors were identified at the individual level (24 factors) and community level (2 factors). Key risk factors included Native American race (6 studies), rural maternal residency (4 studies), overweight/obese body mass

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index (2 studies), maternal age (2 studies), nulliparity (2 studies), and preexisting medical conditions (1 study).

Conclusion

The findings highlight the scarcity of research on MMM risk factors for Native American women, limiting the ability of healthcare and public health organizations to develop and implement tailored approaches to reduce disparities. More focused research is needed to better understand and address these risk factors.

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PROSPERO registration number CRD42022363405.

ARTICLE SUMMARY

Strengths and limitations of this study

- The review searched a variety of scientific databses to identify a wide range of studies on maternal morbidity and mortality in Native American women in the United States.
- The review incorporated studies conducted on Indian reservations and within specific tribal health systems, providing insights tailored to the unique contexts and experiences of Native American women.
- The review synthesizes and critically appraises the limited existing literature on risk factors for maternal morbidity and mortality specifically among Native American women in the United States.
- Many included studies had small sample sizes or low percentages of Native American women, limiting the generalizability of the findings to this specific population.
- Included studies relied on administrative databases (i.e., hospital discharge database, vital recods registries, or electronic health records), which introduce potential reporting biases and misclassification issues, especially concerning the racial categorization of Native American participants.
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INTRODUCTION

Maternal morbidity and mortality (MMM) are alarming public health problems in the United States (US). The Centers for Disease Control and Prevention (CDC) defines maternal mortality as the death of a woman during pregnancy, at delivery, or soon after delivery. [1] Severe maternal morbidity (SMM) refers to complications during labor and delivery with short- and long-term health consequences (e.g., sepsis, blood transfusion, preeclampsia, or hysterectomy). [2,3] The US has one of the highest maternal mortality ratios of any high-income country, reporting 26.4 maternal deaths per 100,000 live births.[4] The SMM rate surged 75% from 1998-1999 to 129 per 10,000 delivery hospitalizations in 2008-2009.[2] Rising rates of blood transfusions, acute renal failure, shock, and other adverse outcomes primarily drove this increase.[2] The rising MMM rates involve complex interactions of factors at patients and families, providers or facilities, overall systems, and within the community at various points in a woman's reproductive life cylee. [5]

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Significant racial and ethnic health inequities persist in maternal health. [6–9] Native American women are three to four times more likely to die than non-Hispanic White women from pregnancy-related complications and are three to five times more likely to experience SMM than non-Hispanic White women. [6,10,11] Historical trauma, racism, colonization, genocide, forced migration, reproductive coercion, and cultural erasure contribute to these adverse outcomes. [12–14] Native American women experience unique prolonged systemic barriers that create inequitable social conditions compared to other groups. [14–16] Some systemic barriers include limited access to providers and birthing facilities. [14,17,18] In addition, a history of forced sterilization and forced infant and child separations has led to a strong distrust of the healthcare systems and providers, including the Indian Health Service. [19–21]

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Rationale

A scoping review on Native American women and the leading causes of maternal mortality in the US identified risk factors like historical trauma, inequities in healthcare availability, access and utilization, preexisting health conditions, and rurality. [22] A separate review of social determinants on pregnancy-related mortality and morbidity identified that race was a significant factor. [3] However, the review did not provide a list of risk factors specific to Native American women, nor did it identify a study that evaluated maternal deaths among Native American women. [3] There is a need to explore further and assess the quality of research specific to MMM risk factors experienced by Native American women. Identifying this information can help identify areas for prevention focused on Native American communities.

Objective

To assess and critically appraise individual and community-level risk factors for pregnancyrelated morbidity and mortality experienced by Native American women in the US.

METHODS

This systematic review follows a protocol previously published, which provides a comprehensive framework for examining pregnancy-related mortality and morbidity among Native American women. [23] Adhering to this pre-established protocol ensures methodological rigor and transparency, facilitating reproducibility and reliability in the findings presented.

Patient and public involvement

Patients and the public were not involved in the design, conduct, reporting, or dissemination of this research.

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Eligibility criteria

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Mata-Analyses (PRISMA) guidelines. [24] Inclusion criteria for studies were: 1) observational study design; 2) study set in the United States; 3) population was Native American women in the perinatal (i.e., the time surrounding childbirth) or puerperium period (i.e., the time after childbirth up to 6 weeks); 4) outcomes focused on measures of pregnancy-related mortality and morbidity; 5) examined the relationship between a risk factor/exposure and stated outcomes. Studies focusing on a different population were included if they offered a stratified analysis by race and contained a racial category for Native Americans. Studies were excluded if: 1) studies focused only on birth, neonatal, or infant outcomes; 2) studies that did not examine the relationship between a risk factor/exposure and stated outcomes; 3) studies with settings outside of the United States; 4) studies that did not include findings for Native American women; and 5) studies that focus on the preconception or postpartum phases.

Information sources and search strategy

The search was carried out on 10 October 2022. The review searched scientific databases (PubMed, Embase, CINAHL, and Scopus) from 1 January 2012 to 10 October 2022. This timeframe was chosen to align with a new standard for identifiying severe maternal morbidity published on 12 November 2012. [2] With technical assistance from a health sciences librarian, the team used search tools and strategies, including shortening keywords where appropriate, using thesaurus terms, and using database-specific controlled vocabulary (e.g., Medical Subject Headings, MeSH). The search strategy combined terms and search strings with the appropriate Boolean operators. The complete search strategy is available in Appendix 1. Covidence was used

to manage every stage of the systematic review, including screenings, data extractions, and risk of bias assessments. [25]

Selection process

Two independent reviewers screened titles and abstracts based on the eligibility criteria. If any disagreement occurred, a third reviewer arbitrated. After the titles and abstracts were screened, two independent reviewers screened full-text articles. The reasons for exclusion were noted at the full-text article stage.

Data collection process

Two independent reviewers extracted study details such as location, study design, eligibility criteria, methods, year of the article, year(s) of study, data source, objectives, sample size and population, independent (risk factors) and dependent (outcomes) variables, key findings, measures of effect/association with p-values and confidence intervals, and limitations. If there were disagreements between the reviewers, a third reviewer arbitrated. For any missing information, the lead author contacted the corresponding authors thrice via email or phone to request information. Any discrepancies within data extraction were reviewed and discussed in a team setting.

Data items

Primary outcomes of interest were maternal morbidity and mortality, including severe maternal morbidity (SMM) based on the CDC's list of 21 diagnoses and procedures (Table 1). [26]

Table 1Outcomes of interest

Mortality and near-misses

Severe maternal morbidity diagnostic or	Acute myocardial infarction
procedural outcomes	Acute renal failure
	Adult respiratory Distress Syndrome
	Amniotic fluid embolism
	Aneurysm
	Cardiac arrest
	Disseminated intravascular coagulation
	Eclampsia
	Heart failure
	Puerperal cerebrovascular disorders
	Pulmonary edema
	Sepsis
	Severe anesthesia complications
	Shock
	Sickle cell anemia with crisis
	Thrombotic embolism
	Blood transfusion
	Conversion of cardiac rhythm
	Hysterectomy
	Temporary tracheostomy
	Ventilation
Additional morbidity outcomes	Postpartum hemorrhage
	Ectopic pregnancy
	Placental abruption
	Uterine atony

This list was used to identify additional articles that did not utilize a composite outcome of severe maternal morbidity or mortality. Given the scope of this review, the terms "pregnancy complications," "obstetric complications," "labor complications," and "near-miss" were added to the list of outcomes to increase the sensitivity of the review. The search strategy was pilot-tested in PubMed, finalized, and adapted to other databases (Table 2). The complete search strategy is available in Appendix 1. The results from each database-specific search strategy were downloaded from the respective databases and uploaded to the EndNote version 20 reference manager software. [27] After removing the duplicates, the citations were imported into Covidence.

Table 2PubMed search strategy

#1 birth[tiab] OR labor[tiab] OR delivery[tiab] OR mothers[tiab] OR maternal[tiab] OR
"peripartum period"[mesh] OR peripartum[tiab] OR "labor, obstetric"[mesh] OR
"obstetric*"[mesh] OR "obstetric*"[tiab] OR "pregnancy"[mesh] OR "pregnan*"[tiab] OR
"perinatal"[tiab] OR "prenatal"[tiab] OR "parturition"[mesh] OR "parturition"[tiab]
#2 "tribal" OR "tribe" OR "first nations" OR "indigenous peoples"[mesh] OR indigenous OR
"health services, indigenous"[mesh] OR "american indians or alaska natives"[mesh] OR
"american indian*" OR "indians, north american"[mesh] OR "native American" OR "alaska native"

#3 "severe maternal morbidity" OR "near miss" OR "adverse maternal outcomes" OR "maternal mortality" OR "Near Miss, Healthcare"[Mesh] OR "Pregnancy/Adverse Effects"[Mesh] OR "Pregnancy/Injuries"[Mesh] OR "Pregnancy/Mortality"[Mesh] OR "Pregnancy/complications"[Mesh] OR "Obstetric Labor Complications"[Mesh] OR "Delivery, Obstetric/adverse effects"[Mesh] OR "Delivery, Obstetric/complications"[Mesh] OR "Delivery, Obstetric/mortality"[Mesh] OR "Maternal Mortality"[Mesh] OR "mortality"[mesh] OR "morbidity"[mesh] OR "pregnancy complications" OR mortality OR morbidity OR "labor complications" OR "delivery complications"

#4 Search (#1 AND #2 AND #3)

Study risk of bias assessment and certainty assessment

Risk of bias was assessed using the NIH's Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies and Case-Control Studies to examine critical concepts for each study's validity. [28] Two independent reviewers assessed articles using the tool's criteria and

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rated them as "good," "fair," or "poor" quality. This rating was based on the percentage of "Yes" responses out of the total applicable questions in each tool. A study will be rated as "good" if it receives a "Yes" response for \geq 80% of the applicable NIH critical appraisal questions, "fair" for 50%-79%, and "poor" for \leq 49%. A "good" rating meant there was the least risk of bias, and the results were considered valid. [28] A "fair" rating indicated susceptibility to some bias but was insufficient to invalidate its results and would vary in their strengths and weaknesses. [28] A "poor" rating indicated a significant risk of bias and invalidated its results. [28] When the ratings differed, a third reviewer arbitrated an article's rating.

Effect measures

Measures of effect such as risk and odds ratios with 95% confidence intervals were extracted. Descriptive statistics like prevalence and incidence were also included.

Potential overlap in cohorts

Given the research scarcity on the population of interest and topic mentioned in this article, we attempted to manage for potential overlap in populations across different cohorts in the included studies. Several strategies were used to manage any potential overlap and ensure the integrity and accuracy of the findings: 1) data sources for cohorts were meticulously documented, including specific populations covered by each study; 2) cohorts were often segmented by geographic regions and demographic characteristics relevant to Native American women and; 3) assessed study periods to identify and address any potential overlap in cohorts.

Synthesis methods

A description of the findings for each study included in the review is provided in Appendix 2. This table includes the risk factors, outcomes of interest, and study characteristics. A descriptive

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synthesis of the results was the most appropriate for this review since there was a large diversity of study designs, risk factors, and outcomes. The heterogeneity of the studies in this review hindered any quantitative synthesis of the identified risk factors' effect sizes. The identified risk factors are also organized into socioecological levels (i.e., individual, family, community, society, or systems).[29] Risk factors were grouped by outcome examined. The information that was reported for each risk factor included 1) the number of studies that analyzed the risk factor, 2) the number of studies that had a measure of effect for a risk factor and was reported to be statistically significant, and 3) the number of studies that had a measure of effect for a risk factor, and was not statistically significant.

[INSERT FIGURE 1]

RESULTS

Study Selection and study characteristics

A total of 8,220 articles were identified, of which 357 duplicates were removed, resulting in 7,863 articles for screening (Figure 1). During the screening process, there were 6,967 agreements for inclusion and 896 conflicts resolved by an arbitrator, for an overall percent agreement of 88.6%. The selection process yielded 145 articles, of which 15 were included in the review. [10,11,30–39] The most common reasons for study exclusion were: the wrong patient population (41 studies), the wrong setting (22 studies), and the wrong type of publication (21 studies). Most (80.0%) studies used secondary data sources (i.e. hospital discharge records, vital records, as such) to examine associations between risk factors and outcomes. There was an equal number of studies across three study designs (5 studies each). The sample size across all studies ranged from 196 to 51,685,525 with a mean sample size of 4,479,962, a median of 72,697, a

standard deviation of 12,732,821.6, and an interquartile range of 2,123,375.0. Seven studies focused primarily on Native American women (i.e., the study sample comprised mainly of Native American women).[32–34,36–38,40] The remaining eight studies included Native American women as a subgroup in their sample.[10,11,30,31,35,39,41,42] Of these eight studies, the percentage of Native American women that were part of the overall sample ranged from 0.4% to 10.1%, and six of these studies had a proportion of Native American women in their sample that was \leq 1.4%. The total number of Native American participants across all studies ranged from 196 to 492,771 with a mean of 57,266.5, a median of 7,107, a standard deviation of 129,234.2, and an interquartile range of 26,817.0. Study settings included nationwide (7/15 studies) [10,11,35,36,39,41,42], statewide (4/15 studies) [30,31,37,38], and on Indian reservations (4/15 studies) [32–34,40].

Risk of bias in studies

Fourteen studies were rated as "good" and one was rated as "fair" according to the NIH's Study Quality Assessment Tools. See Appendix 4 for individual assessments of quality. All cohort and cross-sectional studies were rated "good." [11,30,31,35,36,39–43] Most studies did not assess the exposure more than once over time (7/10 studies). [30,31,35,39–41,43] A smaller proportion were unable to demonstrate that the exposure of interest was measured before the outcome being measured (5/10 studies) [11,36,39,42,43] or did not adjust models to include potential confounders to assess their impact on the relationship between exposure(s) and outcome(s) (3/10 studies).[36,40,42] The reviewers were unable to find evidence in some studies if the outcome assessors were blinded to the exposure status of participants (3/10 studies) [11,36,42] or whether there was a loss to follow-up amongst the cohort studies (3/5 studies). [30,35,40] Amongst the case-control studies, four were rated as "good" [32–34,37] while one was rated as "fair." [38] The reviewers ascertained that some studies failed to provide a sample size justification (3/5 studies) [32–34] or did not randomly select cases and/or controls from the eligible study population (2/5 studies). [33,38]

Results of individual studies and syntheses

Nine outcomes were identified in the studies: hypertensive disorders of pregnancy (preeclampsia, severe preeclampsia, gestational hypertension, and hypertensive disorders of pregnancy), blood transfusions, postpartum hemorrhage, disseminated intravascular coagulation (DIC), hysterectomy, ectopic pregnancy, uterine atony, placental abruption, and SMM with mortality as a composite outcome. Twenty-six risk factors were identified, 24 of these were individual risk factors while two were community risk factors. No studies examined interpersonal/relationship or societal levels risk factors.

Appendix 2 lists the frequency by which each risk factor and outcome was studied in the literature. A majority of studies examined "hypertensive disorders of pregnancy" (8/15 studies) [30–35,37,42] and "severe maternal morbidity and/or mortality" (4/15 studies) [10,11,39,41] as outcomes. A majority of studies examined body mass index (BMI) (6/15 studies) [30–34,38], maternal age (6/15 studies) [32–36,40], maternal race (5/15 studies) [10,31,39–41], and parity (5/15 studies) [32–34,38,40] as risk factors for various outcomes. Table 3 is a summary table that reports the number of studies grouped by outcome, the risk factors examined for associations, and the direction of those associations. Appendix 3 summarizes additional details on study design, sample size, and data sources, exposures and outcome variables, covariates, key findings, including the measures of effect and study quality ratings.

Table 3. Summary of risk factors and outcomes by risk/association category*

Outcome	↑Increased risk or positive association	—No association	↓Decreased risk or negative association	
Hypertensive disorders of pregn	ancy (8 studies)			
Pregnancy-induced hypertension	Rural maternal residency ¹¹⁷⁸ Maternal age 35 years or older and smoked during prepnancy ¹³⁷¹	Continuous smokeless tobacco use ²²³⁰ Continuous cigarette smokino ²²³⁰	Maternal age<35 years and smoked during pregnancy ¹³⁷¹	
Pre-eclampsia	Native American maternal race ⁸¹⁴¹ Overweight/obese BMI ^{7372, 835, 836, 837 Age at delivery^{835, 836} Nulliparity^{835, 836, 837} Gestational diabetes⁸³⁷ Genetic factors $CRP_A, rs3093077,$ (T allele additive)⁸³⁶ MBL2, rs1800451, (T allele dominant) ⁸³⁶ IL1A, rs3273550, (T allele dominant)⁸³⁶ CTLA4, rs21775, (A allele dominant)⁸³⁶ CRP, rs3093068, (G allele additive)⁸³⁷ CRP, rs876538, (C allele additive)⁸³⁷ CRP, rs876538, (C allele recessive)⁸³⁷}	Continuous smokeless tobacco use ²²³⁰ Continuous cigarette smoking ²²³⁰ Age at delivery ⁸³⁷ BMI ^{\$141}	Genetic factors CRP_B, rs1205, (allele dom) ⁸³⁶ CRP_C, rs113086 (T allele dom) ⁸³⁶ CRP, rs876538, ((allele dominant) ⁸³	
Severe pre-eclampsia	Nulliparity ^{836, 837} Obese BMI ^{836,837} Age at delivery ⁸³⁶ Gestational diabetes ⁸³⁷ Genetic factors MBL2, rs1800451, (T allele dominant) ⁸³⁶ IL1A, rs3273550, (T allele dominant) ⁸³⁶ CTLA4, rs21775, (A allele dominant) ⁸³⁶ CRP, rs3093068, (G allele additive) ⁸³⁷ CRP, rs876538, (C allele additive) ⁸³⁷ CRP, rs876538, (C allele recessive) ⁸³⁷	Age at delivery ⁸³⁷	Genetic factors CRP_A, rs309307 (T allele additive) <i>CRP_B, rs1205, (t allele dom)⁸³⁶</i> CRP_C, rs113086 (T allele dom) ⁸³⁶ CRP, rs876538, (t allele dominant) ⁸³⁷	

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Severe Maternal Morbidity and	/or Mortality (4 studies)		
Severe maternal morbidity (SMM) with transfusions	Native American maternal race ¹¹⁹ Any physical health condition ¹¹⁹ Any behavioral health condition ¹¹⁹ Multiple chronic conditions ¹¹⁹	Native American maternal race ⁹⁵²	
Severe maternal morbidity without transfusions		Rural maternal residency ⁴⁰¹⁰	
Severe maternal morbidity and mortality (SMMM)	Rural maternal residency ³⁴²¹ Native American race ⁴⁰¹⁰ Medicaid funded births ³⁴²¹	Urban maternal residency ³⁴²¹	
Blood Transfusions (2 studies)			
Blood transfusions	Rural maternal residency ^{3421,} 4010 Medicaid-funded births ³⁴²¹ Native American maternal race ⁴⁰¹⁰		
Postpartum Hemorrhage (2 stuc	lies)		
Postpartum hemorrhagePostpartum hemorrhage	Native American Maternal race ¹³³¹ Gravidity<5 ¹¹³¹ Birthweight>4500g ¹¹³¹ Retained placenta ¹¹³¹ Magnesium sulfate use ^{1131, 2944} Antepartum bleeding ²⁹⁴⁴ Previous postpartum hemorrhage ²⁹⁴⁴ Third stage of labor>20m ²⁹⁴⁴ Maternal rural residence ²⁹⁴⁴ Fetal macrosomia ²⁹⁴⁴ Oxytocin use>12h ²⁹⁴⁴ Routine aspirin use ²⁹⁴⁴ Prior uterine incision and vaginal delivery ²⁹⁴⁴ Pre-eclampsia without severe features without use of magnesium sulfate ²⁹⁴⁴ Prenty 52 ²⁹⁴⁴ Length of second stage of labor> lh ²⁹⁴⁴ Inpatient induction length≥ to 36h ²⁹⁴⁴	Prior uterine incision ²⁹⁴⁴	
Other Outcomes (4 studies)			
Uterine atony	Native American maternal race ¹³³¹ Birthweight>4500g ¹³³¹	Gravidity<5 ¹³³¹ Induction augmentation ¹³³¹ Chorioamnionitis ¹³³¹	
Ectopic pregnancy	Maternal age>19 years ¹⁸⁶¹ IHS region ¹⁸⁶¹		
Placental abruption	Continuous use of smokeless tobacco ²²³⁰ Continuous cigarette smoking ²²³⁰		
Disseminated intravascular coagulation	Native American race ⁴⁰¹⁰	Rural maternal residency ⁴⁰¹⁰	
Hysterectomy	<i>Native American race⁴⁰¹⁰</i> Rural maternal residency ⁴⁰¹⁰		
*BMI body mass index: h bours: n	n minutes: significant associations at	e italicized and bolded significant	association in the same direction as

*BMI, body mass index; h, hours; m, minutes; significant associations are italicized and bolded, significant association in the same direction as categorized

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Specific to hypertensive disorders of pregnancy, having a rural residency (1/1 studies), an overweight or obese BMI (4/5 studies), age above 35 years also referred to as "advanced maternal age" (1/4 studies), and nulliparity (3/3 studies) were significantly associated with increased risk. [30,32–34,42] Genetic predispositions to hypertensive disorders of pregnancy were not significantly associated with increased risk (3/3 studies). [32–34] Studies that focused on SMMM identified being of Native American race (2/3 studies), having a physical health condition (1/1 study), a rural residency (1/2 studies), and births primarly paid by Medicaid (i.e., public government insurance) (1/1 study) as significantly associated with increased risk. The risk of blood transfusions was significantly associated with Native American race (1/1 study), rural residency (2/2 studies), and Medicaid-funded births (1/1 study). [10,11,39] Postpartum hemorrhage risk was significantly associated with being of Native American race when compared to other racial/ethnic groups, a gravidity ≤ 5 , a birthweight of 4500g, having a retained placenta, magnesium sulfate use (2/2 studies), antepartum bleeding, previous postpartum hemorrhage, being in third stage labor greater than 20 minutes, maternal rural residency, fetal macrosomia, and oxytocin use for longer than 12 hours. [38,40] Other outcomes are further described in Appendix 3.

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This systematic review identified factors that demonstrated no association or a reduction of risk for Native American women. For pregnancy-induced hypertension, one study identified that continuous smokeless tobacco use and cigarette smoking had no association. [37] A separate study determined that those younger than 35 had a decreased risk of hypertensive disorders of pregnancy compared to those older than 35. [40] One study found no association between hypertensive disorders of pregnancy (e.g., preeclampsia) and BMI. [31] One of the three studies that focused on genetic predisposition identified that having CRP B, rs1205, (A allele dominant)

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decreased risk. [32] Native American race and rural residency were found to have no risk of severe maternal morbidity and/or mortality in three distinct studies. [10,39,41]. One study did not find an association between having a prior uterine incision and postpartum hemorrhage. [38] Another study found no association between uterine atony and having a gravidity greater than 5, induction augmentation, or chorioamnionitis. In contrast, a separate study found no association between disseminated intravascular coagulation and a rural residency. [10,40].

Reporting biases and certainty of evidence

All studies relied on administrative data sources to assess outcomes and exposures simultaneously, and all noted this as a considerable limitation in their study design. Four studies noted concerns with small sample sizes, missing exposure and outcome data, and critical demographic information that may have led to misclassification bias. Two studies considered reporting bias in their study designs, while almost all studies (14/15 studies) referred to the misidentification of Native American women based on predetermined guidelines for race designation.

DISCUSSION

This systematic review synthesized the current literature by conducting a broad search of outcomes associated with maternal morbidity and mortality and identifying their associated risk factors for Native American women in the US. Despite the importance of understanding these outcomes for this population, we found a limited number of studies addressing these critical issues. All fifteen studies identified risk factors at the individual level, suggesting that an overweight or obese BMI, advanced maternal age, parity, and rural maternal residency are associated with Native American maternal morbidity or mortality. Few studies contradicted these

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findings and demonstrated no association with Native American race, rural maternal residency, or advanced maternal age. One study found no association with hypertensive disorders of pregnancy, including pregnancy-induced hypertension, preeclampsia, and severe preeclampsia with continuous smokeless tobacco use or continuous cigarette smoking. [37]

One notable finding is that age does not appear to be a substantial risk factor, contrasting with findings in other populations where advanced maternal age is often linked to higher risks.[44] This could be attributed to potential protective factors or differences in health profiles among Native American women that merit further investigation. Two studies found no significant association between age at delivery and preeclampsia among Native American women.[33,34] Conversely, the higher risk of morbidities among public governmental health insurance (i.e., Medicare or Medicaid) recipients is concerning and suggests a need for targeted interventions within this subgroup. Studies showed that rural Native American Medicaid-funded births had the highest adjusted rate of severe maternal morbidity and mortality, indicating potential disparities in healthcare quality and access.[39,45]

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Studies assessing the relationship between genetic factors and preeclampsia or severe preeclampsia were completed in an Indian Reservation within a specific tribal health system.[32– 34] These studies uncovered that there is no association between genetic expression and preeclampsia for Native American women. However, all these studies concurred that many of the risk factors, such as maternal age, nulliparity, and obesity, that are associated with preeclampsia and severe preeclampsia in other populations were also operative in Native American communities.[32–34]

At the community level, our review identified four studies that included risk factors such as maternal residency and the Indian Health Service Region. This limitation further indicates the

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need to expand research to identify and understand the role of community and society-level risk factors. Social determinants of health, such as access to behavioral and primary care services, housing, crime and violence, and health policies, have been demonstrated to contribute directly to maternal mortality and morbidity in more extensive population studies.[46] Studies highlighted the higher incidence of SMM and mortality among rural Native American women compared to their urban counterparts, emphasizing the critical impact of geographic and systemic disparities. [38,40,43]

This review did not find any information on prenatal care utilization and its association with maternal morbidity or mortality despite strong evidence supporting adequate prenatal care utilization in culturally competent healthcare institutions.[15,47,48] Early and adequate prenatal care is thought to promote healthy pregnancies through screening and managing a woman's risk factors and health conditions and promote healthy behaviors during pregnancy.[6]

It's important to recognize that other risk factors, like postpartum depression, substance use, and behavioral health challenges, can also lead to morbidity and mortality, even if they don't occur during delivery.[49] This study didn't consider the effects of historical trauma, discrimination, and racism, which are significant health determinants for Native Americans.[17] These experiences contribute to health deterioration over time, as explained by the weathering hypothesis, which suggests that cumulative stress from racism and socioeconomic disadvantages leads to worse health outcomes.[13]

Appraisal

Most studies were rated as "good" (14/15 studies), while one was rated as "fair." Despite this, we were able to highlight the methodological shortcomings of some of the studies, such as the

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failure to assess the exposure more than once over time, the inability to demonstrate that exposure was measured before outcome measurement, or not adjusting models to include potential confounders. Additionally, some studies failed to provide sample size justification or did not randomly select cases or controls from the eligible study population, posing bias risks. We identified additional shortcomings in the available evidence. Racial/ethnic misclassification on administrative databases leads to challenges with underreporting and further affects the selection of study participants. Given the small percentage of Native American births in the United States, which is only 0.7%, minor errors in misclassification can significantly impact data analysis.[50] Multiple studies in this review reported small sample sizes, making it difficult to determine if a particular outcome was a true finding, possibly allowing for type II errors. Among studies that included samples that were not fully Native American, most reported a Native American sample size of $\leq 1.4\%$. The limited research in these communities hinders the identification of additional risk factors for morbidity and mortality specific to Native American women.[51] The measurement of maternal morbidity and mortality varied across the studies. This review used a broader definition of these outcomes, including conditions not listed by the CDC as severe maternal morbidity. This approach aimed to provide a complete understanding of the risk factors and health outcomes specific to Native American women. Lastly, relying heavily on administrative data presents unique challenges in identifying risk factors not traditionally included in these datasets, as their primary purpose may not align with the study's hypothesis.[52]

Strengths and limitations

Our systematic review faced some limitations despite our use of an expansive search strategy informed by other published reviews.[3,53] We were unable to translate all MesH terms from

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PubMed into indexed language for other databases. There is also a risk of publication bias and selective reporting of significant findings in the studies. Using NIH's quality assessment tools, which are not independently published nor standardized may introduce bias due to the qualitative nature of the review. Despite this, other systematic reviews have built the evidence supporting the utility and practicality of utilizing this tool. [3] Furthermore, the review revealed significant variation in the risk factors and outcomes across different studies. This highlights the complexity and heterogeneity of maternal health issues among Native American women. This variation presents a challenge in drawing definitive conclusions.

Despite these limitations, this systematic review is one of the few that identifies risk factors for various outcomes indicating severe maternal morbidity and mortality among Native American women in the US. The review addresses a critical gap in the literature by focusing on this historically marginalized and underserved population, providing valuable insights for targeted public health interventions and policies. Including various study designs allows for a more comprehensive understanding of the associated risk factors and outcomes. We comprehensively reviewed the current literature using multiple search strategies incorporating the CDC's list of procedural and diagnoses for SMM. This systematic review utilized recommended language to identify research in Native American communities following the National Library of Medicine guidance. [54] Rigorous quality assessment tools were employed to evaluate the methodological quality of the included studies, ensuring that the findings are based on reliable and valid evidence. Additionally, organizing the identified risk factors into socioecological levels provides a structured approach to understanding the complex interplay of factors influencing maternal health in Native American communities.

Implications for practice, policy, and future research

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Our review demonstrates the lack of attention reflected in the scarcity of evidence available to understand this public health crisis among a population that is often ignored. The limited type of risk factors studied, the study designs, settings, and outcomes limit the ability of healthcare and public health organizations to properly design and implement tailored approaches to reduce disparities in this community further. Public health initiatives must prioritize culturally competent care and address the unique challenges faced by Native American women to mitigate the risks of maternal morbidity and mortality. By acknowledging and addressing these gaps in the literature, public health can better inform policy, enhance clinical practices, and ultimately improve health outcomes for Native American mothers and their families.

OTHER INFORMATION

Registration and protocol: The registration and protocol information for this review can be accessed at: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=363405, identifier: CRD42022363405. No amendments were submitted during implementation of the protocol.

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Competing interests: None declared by all authors.

Data statement: The original contributions presented in the study are included in the article's supplemental material, further inquiries can be directed to the corresponding author.

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Contributorship statement: MC is responsible for the overall content as the guarantor. MC and PM: developed the protocol objectives and design. MC wrote the protocol and is the submitting author unders supervision of PM.. MC developed the search strategy. AZ, CR, AN, and AA reviewed abstracts and full-text articles, extracted data from included studies, and critically appraised the literature. AZ and AN co-wrote the introduction, CR and AA co-wrote the methods, and MC wrote the remaining sections, including results and discussion. PM, JE, CH, SP, and VN reviewed and made corrections to the manuscript on multiple occasions, leading to the final written manuscript.

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22	Figure Legend: Figure 1 - PRISMA flow diagram
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Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States



Appendix 1. Search strategy by database

PubMed Search Strategy

#1 birth[tiab] OR labor[tiab] OR delivery[tiab] OR mothers[tiab] OR maternal[tiab] OR
"peripartum period"[mesh] OR peripartum[tiab] OR "labor, obstetric"[mesh] OR
"obstetric*"[mesh] OR "obstetric*"[tiab] OR "pregnancy"[mesh] OR "pregnan*"[tiab] OR
"perinatal"[tiab] OR "prenatal"[tiab] OR "parturition"[mesh] OR "parturition"[tiab]

#2 "tribal" OR "tribe" OR "first nations" OR "indigenous peoples"[mesh] OR indigenous OR "health services, indigenous"[mesh] OR "american indians or alaska natives"[mesh] OR "american indian*" OR "indians, north american"[mesh] OR "native American" OR "alaska native"

#3 "severe maternal morbidity" OR "near miss" OR "adverse maternal outcomes" OR "maternal mortality" OR "Near Miss, Healthcare"[Mesh] OR "Pregnancy/Adverse Effects"[Mesh] OR "Pregnancy/Injuries"[Mesh] OR "Pregnancy/Mortality"[Mesh] OR "Pregnancy/complications"[Mesh] OR "Obstetric Labor Complications"[Mesh] OR "Delivery, Obstetric/adverse effects"[Mesh] OR "Delivery, Obstetric/complications"[Mesh] OR "Delivery, Obstetric/mortality"[Mesh] OR "Maternal Mortality"[Mesh] OR "morbidity"[mesh] OR "Delivery, complications" OR "Maternal Mortality"[Mesh] OR "morbidity"[mesh] OR "complications" OR mortality OR "norbidity OR "labor complications" OR "delivery complications"

#4 Search (#1 AND #2 AND #3)

EMBASE Search Strategy

('delivery:ab,ti' OR 'birth:ab,ti' OR 'labor:ab,ti' OR 'mothers':ab,ti OR 'maternal':ab,ti OR 'peripartum':ab,ti OR 'obstetric':ab,ti OR 'pregnancy':ab,ti OR 'perinatal':ab,ti OR 'prenatal':ab,ti OR 'perinatal period'/exp OR 'labor'/exp OR 'pregnancy'/exp OR 'birth'/exp)

AND

(tribe OR 'indian health service' OR indigenous OR tribal OR 'first nations' OR 'american indian' OR 'native american' OR 'alaska native' OR 'indigenous people'/exp OR 'indigenous health care'/exp OR 'american indian'/exp)

AND

('severe maternal morbidity' OR 'adverse maternal outcomes' OR 'maternal mortality' OR 'pregnancy complications' OR 'mortality' OR 'morbidity' OR 'labor complications' OR 'delivery complications' OR 'near miss (health care)'/exp OR 'near miss' OR 'pregnancy complication'/exp OR 'maternal mortality'/exp OR 'labor complication'/exp OR 'maternal outcome'/exp OR 'delivery complications'/exp OR 'maternal morbidity'/exp OR 'morbidity'/exp OR 'mortality'/exp)

CINAHL Search Strategy

((TI delivery OR AB delivery) OR (TI birth OR AB birth) OR (TI labor OR AB labor) OR (TI mothers OR AB mothers) OR (TI maternal OR AB maternal) OR (TI peripartum OR AB peripartum) OR (TI obstetrics OR AB obstetrics) OR (TI pregnancy OR AB pregnancy) OR (TI perinatal OR AB perinatal) OR (TI prenatal OR AB prenatal) OR (TI parturition OR AB parturition) OR (TI delivery OR AB delivery) OR MM "Perinatal Period" OR MM "Obstetric Patients" OR MM "Delivery, Obstetric+" OR MM "Pregnancy+" OR MM "Labor+" OR MM "Obstetrics+" OR MM "Childbirth+")

AND

(tribe OR "indian health service" OR Indigenous OR "native american" OR "american indian" OR Tribal OR "first nations people" OR "alaska native" OR MM "Indigenous Peoples+" OR MM "Health Services, Indigenous" OR MM "Native Americans+")

AND

("severe maternal morbidity" OR "near miss" OR "pregnancy complications" OR "obstetric complications" OR mortality OR morbidity OR "maternal mortality" OR "maternal morbidity" OR "delivery complications" OR MM "near-death experiences" OR MM "maternal mortality" OR MM "obstetric emergencies" OR MM "Pregnancy Complications+" OR MM "labor complications" OR MM "maternal mortality" OR MM "morbidity+" OR MM "mortality+")

SCOPUS Search Strategy

("severe maternal morbidity" OR "near miss" OR "pregnancy complications" OR mortality OR morbidity OR "labor complications" OR "delivery complications" OR "maternal mortality" OR "maternal morbidity" OR "obstetric complications")

AND

(indigenous OR "native american" OR "american indian" OR tribal OR "alaska native" OR "first nations" OR tribe OR "indian health service")

AND

(TITLE-ABS (mother) OR TITLE-ABS (maternal) OR TITLE-ABS (peripartum) OR TITLE-ABS (obstetric) OR TITLE-ABS (pregnancy) OR TITLE-ABS (perinatal) OR TITLE-ABS (prenatal) OR TITLE-ABS (parturition) OR TITLE-ABS (labor) OR TITLE-ABS (birth) OR TITLE-ABS (delivery))

Appendix 2.	Risk Factors	and Outcomes	by Volume	of Studies
Typenuix 2.	INISK I actors	and Outcomes	by volume	of Studies

					Ou	tcome*				
Risk Factor	SMMM	HDP [†]	BT	РРН	DIC	Hyst	EP	UA	РА	No. of Studies Examining Each Risk Factor ^a
Body mass index		5		1			1	1		7
Age		4		1			1	1		6
Maternal race	3	1	2	1	1	1		1		5
Parity		3		1				1		5
Maternal residence	2	1	2		1	1				3
Gene expressions		3								3
Fobacco use		2							1	2
Birth primary payer type	1		1							1
Magnesium Sulfate use				2				1		2
Inpatient induction				2				1		2
Augmentation				1				1		1
Birthweight				1				1		1
Physical health/ Phronic health status	1									1
Gestational diabetes		1								1
Behavioral health status (depression or substance use disorder)	1									1
Indian Health Service region							1			1
Gravidity					1			1		1
Routine aspirin use				1						1
Prior uterine incision or vaginal birth after cesarean				1						1
Macrosomia				1						1
Antepartum Bleeding				1						1
Previous PPH				1						1
Length of labor				1						1
Oxytocin use				1						1
Chorioamnionitis				1				1		1
Retained placenta				1				1		1
No. of Studies Examining Each Outcome ^a	4	8	2	2	2	1	1	1	1	15

*Severe maternal morbidity and mortality (SMMM), hypertensive disorders of pregnancy (HDP), blood transfusion (BT), postpartum hemorrhage (PPH), disseminated intravascular coagulation (DIC), hysterectomy (Hyst), ectopic pregnancy (EP), uterine atony (UA), and placental abruption (PA), blank cells represent no studies found. † The HDP category includes pre-eclampsia, severe pre-eclampsia, gestational hypertension, and hypertensive disorders of pregnancy. α Row and column figures do not represent totals since a study can include multiple risk factors or outcomes.

1	Append	ix 3. Table	of iı
2	Study	Authors	Ye
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11	Hyperte	ensive Disorde	ers o

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Append	ix 3. Table	of inclu	ıded studie	S		BMJ C	Dpen			5/bmjopen-2 cted by cop		Page 4
Study #	Authors	Year	Study Design	Locatio n	Sample Size, Data Source	Native American subsample size (% of total sample)	Risk Factor (Social ecological level)	Outcome(s)	Covari	924-088380 on 28 Novem Ens yrigat, including for uses	Quality Rating	Key Findings ([95% Confidence Intervals] unless otherwise stated
Hypert	ensive Disordo	ers of Pro	egnancy (8)							ber 202 eignen related		
1178	Cameron, N et al.	2022	Cross Sectional	Nationw ide	51,685,525 all live births in the US to individuals aged 15-44 years, birth vital records	492,771 (9.3%)	Maternal residence (C)	Pregnancy induced hypertension	None	24. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique of ent Superieur (ABES) . I to text and data mining, AI training, and similar technologies.	Good	-The incidence of hypertensive disorders of pregnancy differed by racial and ethnic identity within both rural and urban areas. The highest age- adjusted incidence of hypertensive disorders of pregnancy was observed among individuals who identify as American Indian/ Alaskan Native. -Significant increase in the incidence of hypertension disorders of pregnancy among Native American women in rural areas compared to those in urban areas in 2007 and 2014 (2017 RR=1.21, [1.11-1.33] and 2014 RR=1.17, [1.08-1.13]) -No significant increase in the incidence of hypertension disorders of pregnancy among

Page 4	1 of 61						BMJ C	pen		6/bmjop	
1 2 3 4 5 6 7										an-2024-088380 on 28 copyright, including f	Native American women living in rural areas compared to those in urban areas was observed in 2019 (2019 RR=1.03, [0.96-1.11])
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	2230	England, L et al.	2013	Case Control	Anchora ge, AK	1,123 singleton deliveries from 1997- 2005 to AN women residing in western Alaska, hospital administrat ive database / 503 cases and 502 controls	1,123 (100%)	Continuous smokeless tobacco use (I) and continuous cigarette smoking (I)	Pregnancy associated hypertension, pre- eclampsia, and gestational hypertension	November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographiq pregnanses related to text and data mining, Al training, and similar technologies. age	 -No significant associations were observed between smokeless tobacco use and pregnancy- associated hypertension (aOR 0.92, [0.56– 1.51]). -No significant associations were observed between smokeless tobacco use and pre-eclampsia (aOR 0.90, [0.52–1.56]). -No significant associations were observed between smokeless tobacco use and gestational hypertension (aOR 0.93, [0.42–2.03). -No significant associations were observed between continuous cigarette smoking and pregnancy-associated hypertension (aOR 0.65, [0.31–1.37]). -No significant associations were observed between

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									S P	continuous cigare
									2024-088380 on 28 November 2024 Enseigneme yright, including for uses related t	smoking and pre- eclampsia (aOR 0 [0.30–1.58]). -No significant associations were observed between continuous cigaret smoking and gesta hypertension (aOF 0.52, [0.14–1.90).
8141	Zamora- Kapoor, A et al.	2016	Cohort	Washin gton State	71,080 singleton live births from 2003- 2013 to Whit and AI/AN women, linked birth- hospital discharge records	7,189 (10.1%)	Maternal race (I), BMI (I)	Pre-eclampsia	Birth years of Good maternal age, Good attainment (ABES) . Medicaid from status, mining status, mining . Medicaid All insurance and on June 7, 2025 at Agence Bibliograp WIC participation n, prenatal smoking similar technologies. BMI milar technologies.	 -AI/ANs had an increased risk of preclampsia compared Whites after control for all covariates end BMI (OR 1.17 [1.0] 1.29]). After further adjustment for BM racial disparity in preclampsia risk wass greatly attenuated 1.05, [0.95–1.16]). -AI/ANs who were underweight (OR 1.02, [1.22]), overweight (OR 1.02, [1.22]), overweight 1.23, [0.93, 1.36]), obese (OR 1.00, [0] 1.17]) generally harelative risks of preclampsia compara or slightly (but not statistically significantly) great than those of their White counterparts

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Page 4	l3 of 61						BMJ C	pen		cted by	20hm ion	
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18	1371	Chang, J et al.	2014	Cohort	Nationw ide	3,113,164 singleton births between 20-44 weeks gestation without major fetal anomalies in 2010, US natality file	34,348 (1.10%)	Cigarette use during pregnancy (I), maternal age (I)	Pregnancy induced hypertension (inclusive of pre-eclampsia and eclampsia)	Prenatal care adequact, including gain, parity, including gain, parity, diabetes marital status, ses related hypertenated to text hypertenated to text hyper	Good Good An-2024-088380 on 28 November 2024 Downloaded fr	-The odds of pregnancy induced hypertension was greater in non- Hispanic American Indian women 35 years or older who smoked during pregnancy (aOR 1.29, [0.88-1.89]). -A reduced odds of PIH was evident in non- Hispanic American Indian women younger than 35 years old who smoked during pregnancy based (aOR 0.76, [0.66-0.87]).
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	7372	Tiwari, R et al.	2021	Cohort	Washin gton State	105,466 singleton live births from 22 facilities from 2018- 2018, hospital administrat ive database	978 (0.92%)	Pre- pregnancy BMI (I)	Pre-eclampsia	Maternability, age, partity, delivery A hospital, tra governmin t health g insurance abuse, milar use, and te alcohol the olog	Good	-The strength of the association of overweight/obesity with preeclampsia was much greater among NH AI/AN women (aRR 5.24; [1.92–14.30]) and NH Native Hawaiian/Other Pacific Islander women than among other race/ethnicities (aRR 5.88, [1.30-36.51]).
34 35 36 37 38 39 40 41 42 43 44 45	835	Best, L et al.	2012	Case Control	Belcourt , ND For peer	299 women tribal members of the Turtle Mountain Band of Chippewa who sought care in an IHS review only - h	299 (100%) ttp://bmjopen.l	Age at delivery (I), nulliparity (I), BMI (I), Single nucleotide polymorphi sms [NOS3, rs1799983 comj.com/site/al	Pre-eclampsia	Nullipar ff y, BMI, age at delivery	Good	-Age at delivery (aOR 1.0823, $[p=0.0185]$), nulliparity (aOR 6.8628, $[p<0.001]$), and obesity (aOR 1.0951, [p<0.001]) show robust independent effects associated with preeclampsia.
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					hospital or		(G allele		op		-There was no
					hospital or clinic from 2004-2009, electronic medical records / 101 cases and 198 matched controls		(G allele recess), NOS3, rs3918227 (A allele dom), GNB3, rs5442 (A allele dom), DDAH1, rs10158674 (C allele recess), DDAH1, rs233115 (A allele recess)] (I)		Enseignement Superieur (ABES) . pyright, including for uses related to text and data mining,	-2024_088380 on 28 November 2024. Downloaded from bitto	 There was no significant association between any of single nucleotide polymorphisms studie and pre-eclampsia. NOS3, rs1799983 (G allele recess) (aOR 1.4087, [p=0.2354]) NOS3, rs3918227 (A allele dom) (aOR 0.7356, [p=0.4611]) GNB3, rs5442 (A allele dom) (aOR 0.9147, [p=0.8655]) DDAH1, rs10158674 (C allele recess) (aOR 1.0165, [p=0.9898])
836	Best, L et al.	2012	Case Control	Belcourt , ND	196 women tribal members of the Turtle Mountain Band of Chippewa who sought care in an IHS hospital or clinic from 2004-2009, electronic medical records / 66 cases and	196 (100%)	Age at delivery (I), nulliparity (I), BMI (I), single nucleotide polymorphi sms [CRP_A rs3093077 (T allele additive), CRP_B rs1205 (A allele dom), CRP_C rs1130864	Pre- eclampsia, severe pre- eclampsia	Nulliparty, weight and first ar prenatal to visit, BMA, birthweight of infante, gestational diabetes, age at delivery	Good	-DDAH1, rs233115 (allele recess) (aOR 2.2227. [p=0.1578]) -Age at delivery did n show a significant association with pre- eclampsia (aOR 1.030 [p=0.398]) and severa preeclampsia (aOR 1.027, [p=0.586]). -Nulliparity (aOR 4.274, [p=0.003] and aOR 4.520, [p=0.009] and obesity (aOR 1.0 [p=0.002] and aOR 1.094, [p=0.007]) sho robust independent associations with

Page 4	5 of 61						BMJ O	pen		cted by	2 hmion	
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21						130 matched controls		(T allele dom), MBL2 rs1800451 (T allele dom, IL1A rs3783550 (T allele dom), CTLA4 rs231775 (A allele dom)](I)		Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, A	en-2024-088380 on 28 November 2024 Downloaded from http:/	preeclampsia and severe pre-eclampsia. - There was no significant association between any of single nucleotide polymorphisms studied with pre-eclampsia and severe pre-eclampsia except CRP_B, rs1205, (A allele dom). - CRP_B, rs1205, (A allele dom) was the only single nucleotide polymorphism that showed a significant association with severe pre-eclampsia (aOR 0.259, [p=0.020]).
22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	837	Best, L et al.	2013	Case Control	Belcourt , ND	410 women tribal members of the Turtle Mountain Band of Chippewa who sought care at an IHS hospital or clinic from 2004-2012, electronic medical records / 140 cases and 270 matched controls	410 (100%)	Age at delivery (I), nulliparity (I), BMI (I), gestational diabetes (I), single nucleotide polymorphi sms [CRP rs3093068 (G allele add), CRP rs3093068 (G allele recess, CRP rs3093068 (G allele dom), CRP	Pre- eclampsia, severe pre- eclampsia	Nulliparty, weight and first g prenatal and visit, BMJ, birthweight of infanty gestation diabetes mologies.	Good Good Maionan hai com on lune 7 2025 at Agence Ribliographique	-Age at delivery did not show a significant association with pre- eclampsia (aOR 1.053, [p=0.076]) and severe preeclampsia (aOR 1.052, [p=0.166]). -Gestational diabetes did not show a significant association with pre-eclampsia (aOR 1.684, [p=0.278]) and severe pre- eclampsia (aOR 2.241, [p=0.166]). -Independent effects of nulliparity (aOR 5.6, [p=0.001] and aOR 4.17, [p=0.001]) and

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						rs876538 (C allele add), CRP , rs876538 (C allele recess), CRP rs876538 (C allele dom), rs3093068 (G dom) and rs876538 (C recess) add risk score] (I)		Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, and similar technolog	n-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 20	obesity (aOR 1.061, [p=0.002] and aOR 1.059, [p=0.001]) on pre-eclampsia and severe pre-eclampsia were observed. -There was no significant association between any of single nucleotide polymorphisms studied with pre-eclampsia and severe pre-eclampsia except CRP rs3093068 (G allele add) and CRP rs3093068 (G allele dom) with severe pre- eclampsia (aOR 2.587, [p=0.05] and aOR 2.587, [p=0.050]) -The rs3093068 (G dom) and rs876538 (C recess) additive risk score showed significant association with pre-eclampsia (aOR 1.779, [p=0.016]) and severe pre- eclampsia (aOR 2.035, [p=0.013]).
Severe Mat	ernal Mo	rbidity and M	Iortality (4)					es.)25 at /	
119 Admon, L et al.	2018	Cross Sectional	Nationw ide	2,523,528 all hospital deliveries that occurred between 2012-2015,	20,447 (0.810%)	No chronic conditions, any physical health condition (I), any	SMM	Age, income, payer, rural vs. urban residence, and	gence Bibliographiqu	-The incidence of severe maternal morbidity was significantly higher among deliveries to women in every racial and ethnic minatory

Page 47 of 61		BMJ Open	6/bmjop cted by	
1 1 2 3 3 4 5 6 7 8 9 9 10 1 11 1 12 1 13 1 14 1 15 1 16 1 17 1 18 1 19 20 21 1 22 1 23 1 24 1 25 1 26 1 27 1 28 1 29 1 30 1	National Inpatient Sample	BMJ Open behavioral health condition (I), multiple chronic conditions (I), maternal race (I)	6/bmjop en-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on Jun Enseignement Superieur (ABES) . .cted by copyright, including for uses related to text and data mining, Al training, and similar tech hereion.	category compared with deliveries among non- Hispanic white women. -American Indian/Alaska Native women are at increased risk of severe maternal morbidity compared to non-Hispanic white women (aRR 1.5, [1.3- 1.7]). This is not significant when blood transfusions are not included in severe maternal morbidity (aRR 0.90, [0.68-1.2]). -Among deliveries to women with comorbid physical and behavioral health conditions, significant differences in severe maternal morbidity were identified among racial and ethnic minority compared with non- Hispanic white women and the largest disparities were
30 31 32 33 34			1 June 7, 2025 ; technologies.	and the largest disparities were identified among women with multiple chronic conditions.
35 36 37 38 39 40 41 42			at Agence Bibliograph i	-In comparing deliveries among American Indian/Alaskan Native women with non- Hispanic white women, the rate difference for
45 44 45	For peer review only - http://bmi	open.bmi.com/site/about/quide	elines.xhtml	Severe maternar

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morbidity incidence increased from 66.6 [95% CI 39.9-93.3] t 101.3 [95% CI -41.0- 243.5] per 10,000 delivery hospitalizations, respectively, in comparing deliveries which no and multipl chronic conditions w identified. -American Indian/Alaskan Natiw women compared to non-Hispanic white women are at increas risk for severe matern morbidity when any physical health condition is present (aRR 1.5, [1.3-1.7]), any behavioral health condition is present (aRR 1.2, [0.90-1.6]) and having multiple or more) chronic conditions (aRR 1.4, [0.93-2.20]).	-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7 Enseignement Superieur (ABES) . pyright, including for uses related to text and data mining, Al training, and similar techno										
 -Rural Indigenous Medicaid-funded birthad the highest adjust predicted rate of SMMM (224.9 per 10,000 births, [187.0 262.9]). -Among rural resident births by Indigenous people had the greated differences in rates 	rna bo and is: city, at rnal ence, Part Agence rnal birth birth ile of que	Mat race ethr mat resid mat age, chil year bott quar	SMM and Mortality (SMMM)	Primary payer type (I), maternal residence (C), maternal race (I)	43,929 (0.691%)	6,357,796 maternal records from childbirth hospitalizat ions from 2007-2015, National Inpatient Sample	Nationw ide	Cross Sectional	2022	Interrante, J et al.	3421

Page 49 of 61	BMJ Open	6/bmjop
1 2 3 4 5 6 7 8 9 10 11 1 12 1 13 1 14 15 15 1 16 1 17 1 18 1 19 20 21 1 22 1 23 1 24 1 25 1 26 1 27 28 29 1 30 1 31 1 32 1 33 1 34 1 35 1 36 1 37 1 38 1 39 1 40 1 41 42 43 44	For peer review only - http://bmiopen.bmi.com/site/about/quidelines.xhtml	 between Medicaid-funded and privately insured births (aRD, 97.8, [50.4–145.3]). -When examining the intersection of rurality and race and ethnicity, births among Indigenous rural residents had significant additive interaction, with 40% (aAP 0.40, [0.11-0.69]) of SMMM cases in that population owing to the interaction. -When examining the intersection of urban status and race and ethnicity, births among Indigenous urban residents did not have an additive interaction (aAP 0.06, [-0.20-0.32]). -If the excess risk of SMMM associated with Medicaid could be mitigated (i.e., if the risk of SMMM among Medicaid-funded births could be decreased to the risk among the privately insured), this would not only prevent the 23 cases per 10,000 births that occur among white urban residents, but an additional 98 cases per 10,000 births
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									copyright	an-2024-0	among Indigenous residents.
952	Booker, W et al.	2018	Cohort	Nationw ide	1,724,694 delivery hospitalizat ions from women aged 40-54 years between 1998-2014, National Inpatient Sample	7,107 (0.412%)	Maternal race (I)	SMM, SMM excluding blood transfusions	Year, ber size, ber insurance status, for uses status, for uses location. ucation ses quartile, and hospital to text and teaching and teaching and teaching and tatus, and tatus, and tatus, and teaching and tatus, and teaching	Good 88380 on 28 November 2024 Downloaded from	-The incidence of was greater among Native American women but not significant compar Non-Hispanic whi women (aRR 1.08 [0.93-1.25]). -Risk for severe morbidity excludit transfusion among Native Americans demonstrated beca of small denomina
4010	Kozhiman nil, K et al.	2020	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (I)	SMMM, SMMM excluding blood transfusion	Age, insurance fraining, payer, income, ning, region region similar technologies.	Good	-The incidence of SMMM was greated among indigenous women compared white women (aRF [1.6–2.0]). -Within each racia group, incidence o SMMM was highed among rural comp- with urban residen (2.3% for rural indigenous womer 1.8% for urban indigenous womer RR 1.3, [1.0–1.6]) (1.3% for rural wh women vs 1.2% for urban white wome (aRR 1.1, [1.1–1.2] -Within indigenou women, the incide

l of 61					BMJ (Open		omjop ed by	
								an-2024-088380 on 28 copyright, including fo	of SMM (excludit transfusions) amo rural compared to residents was not significant (aRR ([0.4-1.0)].
Blood Trans	fusions (2)							Noven En or use	
3421 Interrante, J et al.	2022	Cross Sectional	Nationw ide	6,357,796 maternal records from childbirth hospitalizat ions from 2007-2015, National Inpatient Sample	43,929 (0.691%)	Primary payer type (I), maternal residence (C), maternal race (I)	Blood transfusions	Materna Leigner 2024 Materna Leigner 2024 maternal Coventioned of Formula age , ddu (ABES) residence Coventioned of Formula age , ddu (ABES) quartile Coventioned of Formula age , ddu (ABES) disorder 7 disorder 7 pulmonaev hypertensii on, systemic lupus erythemato sus, chronic coventioned of Formula age , ddu (ABES) chronic kidney disease , chronic	-Rural residents ha greater odds of blo transfusion for bo Medicaid-funded 1.15, [1.06-1.25]) privately insured (1.20, [1.11-1.31]) hospital births compared to urban residents. -Medicaid-funded 1.71, [1.39-2.11]) privately insured hospital (aOR 1.4: [1.05-1.92]) indig births had the secc highest odds of bl transfusions comp to other racial/ethn groups. This yield additive interactio value of 0.006.

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									heart disease, gri diabetes, chronic nc hypertengi on, and din chronic for respiratory disease		
4010	Kozhiman nil, K et al.	2020	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (I)	Blood transfusions	Age, dinsurance for the second	Good	-The incidence of the transfusions was gramong indigenous women compared with women (aRR [1.5–2.0]). -The incidence of the transfusion among indigenous women compared to urban indigenous women statistically greater (aRR 1.6, [1.2-2.0])
	Postpartum	Hemorri	nage (PPH) (2	2)					and sin		
1331	Chalouhi, S et al	2015	Cohort	Gallup, NM	1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records	751 (70.7%)	Maternal race (I), age (I), parity (I), gravidity (I), birthweight (I), retained placenta (I), magnesium sulfate use (I), induction augmentati on (I),	Postpartum hemorrhage	None Richard and Andrews	Good	-A significantly hig proportion of Nativ Americans than no native women developed PPH (11 vs 7.0%, [p= 0.02]) -In multivariable logistic regression analysis, the signif predictors of PPH Native American e origin (OR 1.8, [1. 3.0]), decreased gravidity of fewer

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2 3 4 5 6 7 8 9 10							chorioamni onitis (I)		en-2024-088380 on 28 Novemb Ense copyright, including for uses r	5 (OR 1.2, [1.1-1.4]), increased birth weight greater than 4500 grams (OR 1.1, [1.0-1.0]), retained placenta (OR 51.0, [9.8-288.2]), and use of magnesium sulfate (OR 3.5, [1.4- 9.0]).
11 2944 H 12 13 et 13 14 et 15 16 1 16 1 1 17 18 1 19 20 2 21 2 2 23 2 2 24 25 2 25 26 2 27 28 2 29 30 31 31 32 33 34 35 36 37 38 39 40 41 42 43 44 5	Hadley, M et al	2021	Case Control	Anchora ge, AK	384 deliveries between 2018-2019 at the Alaska Native Medical Center, medical records / 128 cases and 256 controls	384 (100%)	BMI (I), antepartum bleeding (I), routine aspirin used prescribed (I), prior uterine incision (I), prior uterine incision and vaginal delivery (I), parity (I), macrosomi a, pre- eclampsia without severe features with magnesium sulfate during labor (I), pre- eclampsia with severe features and use of	Postpartum hemorrhage	Not er 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique elated to text and data mining, Al training, and similar technologies.	 -In the bivariate analysis, the following risk factors were significantly associated with a higher likelihood of postpartum hemorrhage: BMI of 40 or more (OR 2.6, [1.4- 4.5]), antepartum bleeding (OR 6.3, [1.2- 31.6]), previous postpartum hemorrhage (OR 5.0, [2.6-9.8]), suspected macrosomia with estimated fetal weight of 4000 g or more (OR 2.7, [1.4- 5.3]), pre-eclampsia with severe features and use of magnesium sulfate during labor (OR 4.7, [2.4-9.2], length of third stage labor longer than 20 min (OR 2.2, [1.1-4.4]), and use of oxytocin for more than 12 h (OR 5.0, [2.3-10.6]). -Residence in a rural community (OR 2.2, [1.4-3.6]) and vitamin

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1 2 3 4 5 6 7 8 9 10 11 23 4 5 6 7 8 9 10 11 23 24 25 26 27 28 9 30 31 22 33 4 35 36 37 38 9 40 41 42 43 44 5		For peer review o	nly - http://bmjopen.br	magnesium sulfate (I), previous postpartum hemorrhage (I), length of 2nd stage of labor (I), length of 3rd stage of labor (I), rural residence (C), and oxytocin (I), and inpatient induction length (I)	pout/quidelines.xht	ben-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, and similar technologies.	 D supplementation (OR 1.7, [1.1-2.6]) were also significantly associated with postpartum hemorrhage. -Multivariate condition logistic regression analyses found that antepartum bleeding (OR 8.8, [1.6-48.5]), pre-eclampsia with severe features and use of magnesium sulfate (OR 5.3, [2.4-11.9]), previous postpartum hemorrhage (OR 2.7, [1.2-6.1]), third stage of labor of 20min or more (OR 2.9, [1.2-6.9]), rural residence (OR 2.0, [1.2-3.5]), fetal macrosomia (OR 4.0, [2.1-7.5]), and oxytocin use for more than 12h (OR 3.0, [1.1-8.0]) all remained significantly associated with an increased risk of hemorrhage in Native American women. -Routine aspirin use (OR 1.7, [0.9-3.4]), prior uterine incision (OR 1.0, [0.52-2.1]), prior uterine incision and vaginal delivery (OR 1.6, [0.58-4.4]), a parity of 5 or more (OR 1.8, [0.87-3.9]), pre-eclampsia without severe features without
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0 1 2 3 4 5 6 7										en-2024-088380 on 28 November 2024. Downloade Enseignement Superigur copyright, including for uses related to text and d	use of magnesium sulfate (OR 2.1, [0.98- 4.4]), length of second stage of labor grater or equal to 1 hour (OR 1.6, [0.88-3.0]), and an inpatient induction length of greater or equal to 36 hours (OR 2.3, [0.4-12.8]) were not significantly associated with a higher likelihood of postpartum hemorrhage.
8 9	Misc. Outcon	nes (5)								ed frou r (ABH ata m	
1331 1 1 1 1 2 3 4 5 6 7 8 9 0 1 2 3 4 5 6 7 8 9 0 1 2 3 4	Chalouhi, S et al	2015	Cohort	Gallup, NM	1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records	751 (70.7%)	Maternal race (I), age (I), parity (I), gravidity (I), birthweight (I), retained placenta (I), magnesium sulfate use (I), induction augmentati on (I), chorioamni onitis (I)	Uterine atony	None	Good m http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographiqu ES) . EN, Al training, and similar technologies.	-Uterine atony was recorded in a significantly higher proportion of Native Americans than non- native patients (9.6% vs 4.8%; [p=0.01]). -In univariate analysis, factors predicting uterine atony were native race (p=0.01), decreasing gravidity (p=0.02), induction augmentation (p=0.1), increasing birthweight (p=0.07), and chorioamnionitis (p=0.08). -In multivariable logistic regression analysis, Native American ethnic origin

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									copyright, includin	9n-2024-088380 on	(OR 2.0, [1.1–3.7]) and increasing birthweight (OR 1.0, [1.0 1.0]) were significant predictors of uterine atony.
1861	deRavello, L et al	2015	Cross Sectional	Nationw ide	229,986 American Indian and Alaska Native (AI/AN) women aged 15–44 years seeking care at Indian Health Service (IHS), Tribal, and urban Indian health facilities during 2002–2009, Indian Health Service National Patient Informatio n Reporting System	229,986 (100%)	Maternal age (I), IHS region (C)	Ectopic pregnancy	Enseignement Superieur (ABES) . g for uses related to text and data mining, Al training, and similar technologies. None	Fair Fair 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique	 -The ectopic pregnancy (EP) rate among AI/AN women was lowest in the 15–19 years age group (5.5 EPs per 1,000 pregnancies) and highest among 35–39 year old (18.7 EPs per 1,000 pregnancies). -Compared to AI/AN women aged 15-18 years, women aged 35- 39 years were 3.4 times more likely to have an EP (RR 3.4, [2.90- 4.03]). Compared to AI/AN women aged 15- 18 years, the risk of an EP increased with age from 1.56-3.42, except in women aged 40-44 years were the risk was less at 2.62 times (RR 2.62, [2.02-3.36]). -EP rates varied by geographic region, ranging between 6.9 and 24.4 per 1,000 pregnancies in the Northern Plains East and the East region, respectively. -Compared to AI/AN women who received

Page 5	57 of 61						BMJ C)pen		cted by	s/hmion	
$1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \\ 7 \\ 8 \\ 9 \\ 10 \\ 11 \\ 12 \\ 13 \\ 14 \\ 15 \\ 16 \\ 17 \\ 18 \\ 19 \\ 20 \\ 21 \\ 22 \\ 23 \\ 24 \\ 25 \\ 26 \\ 27 \\ 28 \\ 29 \\ 30 \\ 31 \\ 32 \\ 33 \\ 34 \\ 35 \\ 36 \\ 36 \\ 36 \\ 36 \\ 36 \\ 36 \\ 36$										Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, and similar technologies.	sp-2024-088380 on 28 November 2024. Downloaded from <u>bttp://bmionen.bmi.com/ on</u> _lune_7_2025 at 4	care in the Northern Plains East region, women who received care in the East region were 3.55 times more likely to have an EP (RR 3.55, [2.75-4.57]), in the Alaska region the risk was 2.17 times (RR 2.17, [1.73-2.72]), in the Southern plains region the risk was 1.56 times (RR 1.57, [1.25- 1.95]), in the West region the risk was 1.39 times (RR 1.39, [1.09- 1.77]), in the Norther Plains West region the risk was 1.36 times (1.36, [1.08-1.71]), and in the Southwest region the risk was lowest at 1.33 times (RR 1.33, [1.07-1.65]). -We found relatively stable annual rates of EP among AI/AN women receiving care at IHS-affiliated facilities during 2002– 2009, but considerable variation by age group and geographic region.
37 38 39 40 41 42 43 44	2230	England, L et al.	2013	Case Control	Anchora ge, AK	1,123 singleton deliveries from 1997- 2005 to AN women residing in	1,123 (100%)	Continuous smokeless tobacco use (I) and continuous cigarette smoking (I)	Placental abruption, placental abruption expanded definition	Parity, pre- pregnancy BMI, maternal age	Good Bibliographicus	-Thirty-nine percent of case deliveries were also preterm (compared with 7% of controls, [p<0.001]), and 9.8% were also complicated by pregnancy
45 46 47					For peer	review only - h	up://bmJopen.l	omj.com/site/al	ooul/guidelines.x		Þ	

6/bmjopon-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.dom/ on June 7, 2025 Enseignement Superieur (ABES) . cted by copyright, including for uses related to text and data mining, Al training, and similar technologies. **BMJ** Open Page 58 of 61 associated hypertension western (compared with 7% of Alaska, hospital controls. [p=0.38]). administrat -There were no ive significant associations database between placental abruption and continuous smokeless tobacco use (aOR 1.11, [0.53-2.33] and continuous cigarette smoking (aOR 1.19, [0.43-3.29). -An expanded definition of abruption did not change this finding. There were no significant associations between continuous smokeless tobacco use (OR 1.07, [0.63-1.83]) or continuous cigarette smoking (aOR 1.04, [0.48-2.23]). ONL om/ on June 7, 2025 at Agence Bibliographique de l For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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 39 40 41 42 43 44 45 46 47 					For peer	review only - h	ttp://bmjopen.	bmj.com/site/a	bout/guidelines.x	html	Bibliographique de l	

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Appendix 4. Results of NIH quality assessments for included studies

For observational cohort and cross-sectional studies:

ID#	Authors	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12 uses	28 . 213 Ovem	Q14	Yes %	Rating
119	Admon L, et al.	2018	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	NA	Yes	eigner relate	NA 20	Yes	82%	Good
952	Booker W, et al.	2018	Yes	No	Yes	No	Yes	d so te	Yes	Yes	93%	Good						
1178	Cameron, N. et al.	2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	NRan	NA Io	No	83%	Good
1331	Chalouhi, S. et al.	2015	Yes	No	Yes	Yedata		No	92%	Good								
1371	Chang, J et al	2014	Yes	No	Yes	Yendinii Yendinii	¶NR	Yes	100%	Good								
1861	deRavello, L. et al.	2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	NIR - A	NA	No	83%	Good
3421	Interrante, J. et al.	2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yean	NA	Yes	85%	Good
4010	Kozhimannil, K et al.	2020	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	NA	Yes	ng, and s	en.NA	Yes	90%	Good
7372	Tiwari, R. et al	2021	Yes	No	Yes	Yendlar	NR 9	Yes	92%	Good								
8141	Zamora-Kapoor A., et al	2016	Yes	No	Yes	Nochno	of Yes	Yes	86%	Good								

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A study will be rated as "Good" if it receives a "Yes" response for $\geq 80\%$ of the applicable NIH critical appraisal questions, "Fair" by r 50%-79%, and "Poor" for $\leq 50\%$. at

Quality of included studies was assessed using the National Institutes of Health (NIH) Quality Assessment tool for Observational Cross-Sectional Studies (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). nce Bibliographique de l

Q1. Was the research question or objective in this paper clearly stated?

Q2. Was the study population clearly specified and defined?

Q3. Was the participation rate of eligible persons at least 50%?

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Page 61 of 61 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41	 Dynamic and the subjects selected or recruited from the same or similar populations (including the same time period)? Were in being in the study prespecified and applied uniformly to all participants? (2). Was a sample size justification, power description, or variance and effect estimates provided? (3). For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? (3). For exposures that can vary in amount or level, did the study examine different levels of the exposure and outcome in a supersures (independent variables) clearly defined, valid, reliable, and implemented consistently across query of the outcome measures (idependent variables) clearly defined, valid, reliable, and implemented consistently across query was the to outcome measures (idependent variables) clearly defined, valid, reliable, and implemented consistently across query query estatus of participants? (2). Were the outcome measures (idependent variables) clearly defined, valid, reliable, and implemented consistently across query estatus of follow-up after baseline 20% or less? (2). Were the outcome measures (independent variables) clearly defined, valid, reliable, and implemented consistently across a query defined, valid, reliable, and implemented consistently across a query was to follow-up after baseline 20% or less? (2). Were the outcome measures (idependent variables) clearly defined, valid, reliable, and implemented consistently across a query estimation of the exposure status of participants? (3). Was loss to follow-up after baseline 20% or less? (4). Were the outcome assessors binded to the exposure status of participants? (4). Were the outcom measures (idependent variables measured and adjusted statistically for their impact on the relationship between the status of participants? 	Justic Barbon and exclusion criteria for Sector an
42 43 44 45 46 47	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	phique de l

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gies

For case-control studies:

														S S		
ID#	Authors	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11		Yes %	Rating
835	Best, L. et al	2012	Yes	Yes	No	Yes	gyes No	92%	Good							
836	Best, L. et al.	2012	Yes	Yes	No	Yes	u s es ∰nse	92%	Good							
837	Best, L et al.	2013	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	oer∠u eiĝne rælate	83%	Good
2230	England L, et al	2013	Yes	nj⊛nt nj⊛nt ⊧¢Hto ;	100%	Good										
2944	Hadley, M et al	2021	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Stip Stip	75%	Fair

A study will be rated as "Good" if it receives a "Yes" response for $\geq 80\%$ of the applicable NIH critical appraisal questions, "Fair for 50%-79%, and "Poor" for

Q1. Was the research question or objective in this paper clearly stated and appropriate? Q2. Was the study population clearly specified and defined? Q3. Did the authors include a sample size justification? Q4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?

Q5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls aligned in the select cases are cased to identify or select cases and controls aligned in the select case aligned in the select c consistently across all study participants? simi

Q6. Were the cases clearly defined and differentiated from controls?

Q7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomay selected from those eligible?

O8. Was there use of concurrent controls?

Q9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case? Q10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same tinge period) across all study

participants?

O11. Were the assessors of exposure/risk blinded to the case or control status of participants?

Q12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis? gence Bibliographique de l

Q, question; CD, cannot be determined; NA, not applicable; NR, not reported

Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States: A systematic review

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TITLE

Individual and community level risk factors for maternal morbidity and mortality among Native American women in the United States: A systematic review

AUTHORS AND AFFILIATION

Martín F. Celaya^{1,2}, Alaa I. Zahlan², Chelsea Rock³, Akshay Nathan⁴, Aishwarya Acharya²,

Purnima Madhivanan², John Ehiri², Chengcheng Hu², Sydney Pettygrove², Velia Leybas Nuño²

1. Arizona Department of Health Services, Phoenix, Arizona, United States

2. Mel & Enid Zuckerman College of Public Health, University of Arizona, Tucson, Arizona,

United States

3. College of Health Solutions, Arizona State University, Phoenix, Arizona, United States

4. Boston University, Boston, Massachusetts, United States

AUTHORS' E-MAIL ADDRESSES

Martín F. Celaya, martin.celaya@azdhs.gov; Alaa I Zahlan, azahlan@arizona.edu; Chelsea

Rock, <u>chelsea.rock@azdhs.gov</u>; Akshay Nathan, <u>shayaknathan@gmail.com</u>; Aishwarya

Acharya, aishwaryaacharya@arizona.edu; Purnima Madhivanan, pmadhivanan@arizona.edu;

John Ehiri, jehiri@arizona.edu; Chengcheng Hu, hucc@arizona.edu; Sydney Pettygrove,

sydneyp@arizona.edu; Velia Leybas Nuño, vleybas@arizona.edu

SUBMITTING AND CORRESPONDING AUTHOR

Martín F. Celaya, martin.celaya@azdhs.gov

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- Table 1. Outcomes of interest
- Table 2. PubMed search strategy
- Table 3. Summary of risk factors and outcomes by risk/association category

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Figure 1. PRISMA flow diagram

NUMBER OF APPENDICES: 3

- Appendix 1. Search strategy by database
- Appendix 2. Risk factors and outcomes by volume of studies
- Appendix 3. Table of included studies
- Appendix 4. Results of NIH Quality Assessments for included studies

KEYWORDS: American Indian or Alaska Native, Maternal Morbidity and Mortality, Risk Factors BMJ Open: first published as 10.1136/bmjopen-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de Enseignement Superieur (ABES)

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ABSTRACT

Introduction and objective

Maternal morbidity and mortality (MMM) is a public health concern in the US, with Native American women experiencing higher rates than non-Hispanic White women. Research on risk factors for MMM among Native American women is limited. This systematic review comprehensively synthesizes and critically appraises the literature on risk factors for MMM experienced by Native American women.

Methods and analysis

A systematic search was conducted on 10 October 2022 in PubMed, Embase, CINAHL, and Scopus for articles published since 2012. Selection criteria included observational studies set in the US, involving Native American women in the perinatal period, and examining the relationship between risk factors and MMM outcomes. Three reviewers screened and extracted data from the included studies, with risk of bias assessed using National Institutes of Health quality assessment tools. Data were analyzed descriptively.

Results

Fifteen studies were included. All studies utilized administrative databases, with settings including nationwide (7 studies), statewide (4 studies), and Indian reservations (4 studies). The majority of studies focused on hypertensive disorders of pregnancy (8 studies) and severe maternal morbidity (SMM) (4 studies). Twenty-six risk factors were identified. Key risk factors included Native American race (6 studies), rural maternal residency (4 studies), overweight/obese body mass index (2 studies), maternal age (2 studies), nulliparity (2 studies), and preexisting medical conditions (1 study).

Conclusion

This review identified risk factors associated with MMM among Native American women, including rural residency, overweight or obesity, and advanced maternal age. However, the findings also reveal a scarcity of research specific to this population, limiting the ability to fully understand these risk factors and develop effective interventions. These results emphasize the need for further research and culturally relevant studies to inform public health and address disparities for Native American women, particularly those in rural areas. BMJ Open: first published as 10.1136/bmjopen-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

PROSPERO registration number CRD42022363405.

ARTICLE SUMMARY

Strengths and limitations of this study

- The review searched a variety of scientific databases to identify a wide range of studies on maternal morbidity and mortality in Native American women in the United States.
- The review incorporated studies conducted on Indian reservations and within specific tribal health systems, providing insights tailored to the unique contexts and experiences of Native American women.
- The review synthesizes and critically appraises the limited existing literature on risk factors for maternal morbidity and mortality specifically among Native American women in the United States.
- Many included studies had small sample sizes or low percentages of Native American women, limiting the generalizability of the findings to this specific population.
- Included studies relied on administrative databases (i.e., hospital discharge database, vital recods registries, or electronic health records), which introduce potential reporting biases and misclassification issues, especially concerning the racial categorization of Native American participants.

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INTRODUCTION

Maternal morbidity and mortality (MMM) are alarming public health problems in the United States (US). The Centers for Disease Control and Prevention (CDC) defines maternal mortality as the death of a woman during pregnancy, at delivery, or soon after delivery. [1] Severe maternal morbidity (SMM) refers to complications during labor and delivery with short- and long-term health consequences (e.g., sepsis, blood transfusion, preeclampsia, or hysterectomy). [2,3] The US has one of the highest maternal mortality ratios of any high-income country, reporting 26.4 maternal deaths per 100,000 live births.[4] In contrast, Finland has the lowest maternal mortality ratio of 3.8 deaths per 100,000 live births, a value nearly seven times lower that the U.S. [4] The SMM rate surged 75% from 1998-1999 to 129 per 10,000 delivery hospitalizations in 2008-2009.[2] Rising rates of blood transfusions, acute renal failure, shock, and other adverse outcomes primarily drove this increase.^[2] The rising MMM rates involve complex interactions of factors at patients and families, providers or facilities, overall systems, and within the community at various points in a woman's reproductive life cylce. [5] Significant racial and ethnic health inequities persist in maternal health. [6–9] Native American women are three to four times more likely to die than non-Hispanic White women from pregnancy-related complications and are three to five times more likely to experience SMM than BMJ Open: first published as 10.1136/bmjopen-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

non-Hispanic White women. [6,10,11] Historical trauma, racism, colonization, genocide, forced

migration, reproductive coercion, and cultural erasure contribute to these adverse outcomes. [12–

inequitable social conditions compared to other groups. [14–16] Some systemic barriers include limited access to providers and birthing facilities. [14,17,18] In addition, a history of forced

14] Native American women experience unique prolonged systemic barriers that create

sterilization and forced infant and child separations has led to a strong distrust of the healthcare systems and providers, including the Indian Health Service. [19–21]

Rationale

A scoping review on Native American women and the leading causes of maternal mortality in the US identified risk factors like historical trauma, inequities in healthcare availability, access and utilization, preexisting health conditions, and rurality. [22] A separate review of social determinants on pregnancy-related mortality and morbidity identified that race was a significant factor. [3] However, the review did not provide a list of risk factors specific to Native American women, nor did it identify a study that evaluated maternal deaths among Native American women. [3] There is a need to explore further and assess the quality of research specific to MMM risk factors experienced by Native American women. Identifying this information can help identify areas for prevention focused on Native American communities.

Objective

To assess and critically appraise individual and community-level risk factors for pregnancyrelated morbidity and mortality experienced by Native American women in the US.

METHODS

This systematic review follows a protocol previously published, which provides a comprehensive framework for examining pregnancy-related mortality and morbidity among Native American women. [23] Adhering to this pre-established protocol ensures methodological rigor and transparency, facilitating reproducibility and reliability in the findings presented.

Patient and public involvement

Patients and the public were not involved in the design, conduct, reporting, or dissemination of this research.

Eligibility criteria

This systematic review follows the Preferred Reporting Items for Systematic Reviews and Mata-Analyses (PRISMA) guidelines. [24] Inclusion criteria for studies were: 1) observational study design; 2) study set in the United States; 3) population was Native American women in the perinatal (i.e., the time surrounding childbirth) or puerperium period (i.e., the time after childbirth up to 6 weeks); 4) outcomes focused on measures of pregnancy-related mortality and morbidity; 5) examined the relationship between a risk factor/exposure and stated outcomes; and 6) had a publication date between 1 January 2012 and 10 October 2022. This timeframe aligns with a new standard for identifying severe maternal morbidity published on 12 November 2012. [2] Studies focusing on a different population were included if they offered a stratified analysis by race and contained a racial category for Native Americans. Studies were excluded if: 1) studies focused only on birth, neonatal, or infant outcomes; 2) studies that did not examine the relationship between a risk factor/exposure and stated outcomes, 3) studies with settings outside of the United States; 4) studies that did not include findings for Native American women; 5) studies that focus on the preconception or postpartum phases; and 6) studies were published outside of the specified time.

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Information sources and search strategy

The search was carried out on 10 October 2022. The review searched scientific databases (PubMed, Embase, CINAHL, and Scopus).. With technical assistance from a health sciences librarian, the team used search tools and strategies, including shortening keywords where

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appropriate, using thesaurus terms, and using database-specific controlled vocabulary (e.g., Medical Subject Headings, MeSH). The search strategy combined terms and search strings with the appropriate Boolean operators. The complete search strategy is available in Appendix 1. Covidence was used to manage every stage of the systematic review, including screenings, data extractions, and risk of bias assessments. [25]

Selection process

Two independent reviewers screened titles and abstracts based on the eligibility criteria. If any disagreement occurred, a third reviewer arbitrated. After the titles and abstracts were screened, two independent reviewers screened full-text articles. The reasons for exclusion were noted at the full-text article stage.

Data collection process

Two independent reviewers extracted study details such as location, study design, eligibility criteria, methods, year of the article, year(s) of study, data source, objectives, sample size and population, independent (risk factors) and dependent (outcomes) variables, key findings, measures of effect/association with p-values and confidence intervals, and limitations. For any missing information, the lead author contacted the corresponding authors thrice via email or phone to request information. Any discrepancies within data extraction were reviewed and discussed in a team setting.

Data items

Primary outcomes of interest were maternal morbidity and mortality, including severe maternal morbidity (SMM) based on the CDC's list of 21 diagnoses and procedures (Table 1). [26]

Table 1Outcomes of interest	
Mortality and near-misses	
Severe maternal morbidity diagnostic or	Acute myocardial infarction
procedural outcomes	Acute renal failure
	Adult respiratory Distress Syndrome
	Amniotic fluid embolism
	Aneurysm
	Cardiac arrest
	Disseminated intravascular coagulation
	Eclampsia
	Heart failure
	Puerperal cerebrovascular disorders
	Pulmonary edema
	Sepsis
	Severe anesthesia complications
	Shock
	Sickle cell anemia with crisis
	Thrombotic embolism
	Blood transfusion
	Conversion of cardiac rhythm
	Hysterectomy
	Temporary tracheostomy
	Ventilation
Additional morbidity outcomes	Postpartum hemorrhage
	Ectopic pregnancy
	Placental abruption
	Uterine atony

This list was used to identify additional articles that did not utilize a composite outcome of severe maternal morbidity or mortality. Given the scope of this review, the terms "pregnancy complications," "obstetric complications," "labor complications," and "near-miss" were added to the list of outcomes to increase the sensitivity of the review. Pregnancy, labor, and obstetric complications encompass conditions occurring during or after pregnancy, ranging from minor discomforts to severe diseases requiring medical intervention, including both pregnancy-related conditions and preexisting diseases in pregnant women.[27] A near-miss refers to a life-threatening event that does not result in death.[28] The search strategy was pilot-tested in

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PubMed, finalized, and adapted to other databases (Table 2). The complete search strategy is available in Appendix 1. The results from each database-specific search strategy were downloaded from the respective databases and uploaded to the EndNote software. [29] After removing the duplicates, the citations were imported into Covidence.

Table 2PubMed search strategy

#1 birth[tiab] OR labor[tiab] OR delivery[tiab] OR mothers[tiab] OR maternal[tiab] OR
"peripartum period"[mesh] OR peripartum[tiab] OR "labor, obstetric"[mesh] OR
"obstetric*"[mesh] OR "obstetric*"[tiab] OR "pregnancy"[mesh] OR "pregnan*"[tiab] OR
"perinatal"[tiab] OR "prenatal"[tiab] OR "parturition"[mesh] OR "parturition"[tiab]
#2 "tribal" OR "tribe" OR "first nations" OR "indigenous peoples"[mesh] OR indigenous OR
"health services, indigenous"[mesh] OR "american indians or alaska natives"[mesh] OR
"american indian*" OR "indians, north american"[mesh] OR "native American" OR "alaska native"

#3 "severe maternal morbidity" OR "near miss" OR "adverse maternal outcomes" OR "maternal mortality" OR "Near Miss, Healthcare"[Mesh] OR "Pregnancy/Adverse Effects"[Mesh] OR "Pregnancy/Injuries"[Mesh] OR "Pregnancy/Mortality"[Mesh] OR "Pregnancy/complications"[Mesh] OR "Obstetric Labor Complications"[Mesh] OR "Delivery, Obstetric/adverse effects"[Mesh] OR "Delivery, Obstetric/complications"[Mesh] OR "Delivery, Obstetric/mortality"[Mesh] OR "Maternal Mortality"[Mesh] OR "mortality"[mesh] OR "morbidity"[mesh] OR "pregnancy complications" OR mortality OR "labor complications" OR "delivery complications" #4 Search (#1 AND #2 AND #3)

Study risk of bias assessment and certainty assessment

Risk of bias was assessed using the NIH's Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies and Case-Control Studies to examine critical concepts for each study's validity. [30] Two independent reviewers assessed articles using the tool's criteria and rated them as "good," "fair," or "poor" quality. This rating was based on the percentage of "Yes" responses out of the total applicable questions in each tool. A study will be rated as "good" if it receives a "Yes" response for \geq 80% of the applicable NIH critical appraisal questions, "fair" for 50%-79%, and "poor" for \leq 49%. A "good" rating meant there was the least risk of bias, and the results were considered valid. [30] A "fair" rating indicated susceptibility to some bias but was insufficient to invalidate its results and would vary in their strengths and weaknesses. [30] A "poor" rating indicated a significant risk of bias and invalidated its results. [30] When the ratings differed, a third reviewer arbitrated an article's rating. BMJ Open: first published as 10.1136/bmjopen-2024-08380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

Effect measures

Measures of effect such as risk and odds ratios with 95% confidence intervals were extracted. Descriptive statistics like prevalence and incidence were also included.

Potential overlap in cohorts

Given the research scarcity on the population of interest and topic mentioned in this article, we attempted to manage for potential overlap in populations across different cohorts in the included studies. Several strategies were used to manage any potential overlap and ensure the integrity and accuracy of the findings: 1) data sources for cohorts were meticulously documented,

including specific populations covered by each study; 2) cohorts were often segmented by geographic regions and demographic characteristics relevant to Native American women and; 3) assessed study periods to identify and address any potential overlap in cohorts.

Synthesis methods

Appendix 2 provides a summary of study findings, including risk factors, outcomes, and study characteristics. A descriptive synthesis was used due to the diversity in study designs, risk factors, and outcomes, which precluded quantitative analysis. Risk factors were organized by socioecological levels (individual, family, community, society, or systems) and grouped by outcome. [31] For each risk factor, the table reports the number of studies analyzing it, and whether the effect was statistically significant.

[INSERT FIGURE 1]

RESULTS

Study Selection and study characteristics

A total of 8,220 articles were identified, of which 357 duplicates were removed, resulting in 7,863 articles for screening (Figure 1). During the screening process, there were 6,967 agreements for inclusion and 896 conflicts resolved by an arbitrator, for an overall percent agreement of 88.6%. The selection process yielded 145 articles, of which 15 were included in the review. [10,11,32–41] The most common reasons for study exclusion were: the wrong patient population (41 studies), the wrong setting (22 studies), and the wrong type of publication (21 studies). Most (80.0%) studies used secondary data sources (i.e. hospital discharge records, vital records, as such) to examine associations between risk factors and outcomes. There was an equal

number of studies across three study designs (5 studies each). The sample size across all studies ranged from 196 to 51,685,525 with a mean sample size of 4,479,962, a median of 72,697, a standard deviation of 12,732,821.6, and an interquartile range of 2,123,375.0. Seven studies focused primarily on Native American women (i.e., the study sample comprised mainly of Native American women).[34–36,38–40,42] The remaining eight studies included Native American women as a subgroup in their sample.[10,11,32,33,37,41,43,44] Of these eight studies, the percentage of Native American women that were part of the overall sample ranged from 0.4% to 10.1%, and six of these studies had a proportion of Native American women in their sample that was \leq 1.4%. The total number of Native American participants across all studies ranged from 196 to 492,771 with a mean of 57,266.5, a median of 7,107, a standard deviation of 129,234.2, and an interquartile range of 26,817.0. Study settings included nationwide (7/15 studies) [10,11,37,38,41,43,44], statewide (4/15 studies) [32,33,39,40], and on Indian reservations (4/15 studies) [34–36,42].

Risk of bias in studies

Fourteen studies were rated as "good" and one was rated as "fair" according to the NIH's Study Quality Assessment Tools. See Appendix 4 for individual assessments of quality. All cohort and cross-sectional studies were rated "good." [11,32,33,37,38,41–45] Most studies did not assess the exposure more than once over time (7/10 studies). [32,33,37,41–43,45] A smaller proportion were unable to demonstrate that the exposure of interest was measured before the outcome being measured (5/10 studies) [11,38,41,44,45] or did not adjust models to include potential confounders to assess their impact on the relationship between exposure(s) and outcome(s) (3/10 studies).[38,42,44] The reviewers were unable to find evidence in some studies if the outcome assessors were blinded to the exposure status of participants (3/10 studies) [11,38,44] or whether
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there was a loss to follow-up amongst the cohort studies (3/5 studies). [32,37,42] Amongst the case-control studies, four were rated as "good" [34–36,39] while one was rated as "fair." [40] The reviewers ascertained that some studies failed to provide a sample size justification (3/5 studies) [34–36] or did not randomly select cases and/or controls from the eligible study population (2/5 studies). [35,40]

Results of individual studies and syntheses

Nine outcomes were identified in the studies: hypertensive disorders of pregnancy (preeclampsia, severe preeclampsia, gestational hypertension, and hypertensive disorders of pregnancy), blood transfusions, postpartum hemorrhage, disseminated intravascular coagulation (DIC), hysterectomy, ectopic pregnancy, uterine atony, placental abruption, and SMM with mortality as a composite outcome. Twenty-six risk factors were identified, 24 of these were individual risk factors while two were community risk factors. No studies examined interpersonal/relationship or societal levels risk factors.

Appendix 2 lists the frequency by which each risk factor and outcome was studied in the literature. A majority of studies examined "hypertensive disorders of pregnancy" (8/15 studies) [32–37,39,44] and "severe maternal morbidity and/or mortality" (4/15 studies) [10,11,41,43] as outcomes. A majority of studies examined body mass index (BMI) (6/15 studies) [32–36,40], maternal age (6/15 studies) [34–38,42], maternal race (5/15 studies) [10,33,41–43], and parity (5/15 studies) [34–36,40,42] as risk factors for various outcomes. Table 3 is a summary table that reports the number of studies grouped by outcome, the risk factors examined for associations, and the direction of those associations. Appendix 3 summarizes additional details on study design, sample size, and data sources, exposures and outcome variables, covariates, key findings, including the measures of effect and study quality ratings.

Table 3. Summary of risk factors and outcomes by risk/association category*

Outcome	↑Increased risk or positive association	—No association	↓Decreased risk or negative association								
Hypertensive disorders of pregnancy (8 studies)											
Pregnancy-induced hypertension	Rural maternal residency ¹¹⁷⁸ Maternal age 35 years or older and smoked during pregnancy ¹³⁷¹	Continuous smokeless tobacco use ²²³⁰ Continuous cigarette smoking ²²³⁰	Maternal age<35 years and smoked during pregnancy ¹³⁷¹								
Pre-eclampsia	Native American maternal race ⁸¹⁴¹ Overweight/obese BMI ^{7372, 835, 836, 837 Age at delivery^{835, 836} Nulliparity^{835, 836, 837} Gestational diabetes⁸³⁷ Genetic factors (Single Neuclotide Polymorphisms, SNPs) CRP_A, rs3093077, (T allele additive)⁸³⁶ MBL2, rs1800451, (T allele dominant) ⁸³⁶ IL1A, rs3273550, (T allele dominant) ⁸³⁶ CTLA4, rs21775, (A allele dominant) ⁸³⁶ CRP, rs3093068, (G allele additive)⁸³⁷ CRP, rs876538, (C allele additive)⁸³⁷ CRP, rs876538, (C allele recessive)⁸³⁷ NOS3, rs1799983 (G allele recessive)⁸³⁵ DDAH1, rs203115 (A allele recessive)⁸³⁵}	Continuous smokeless tobacco use ²²³⁰ Continuous cigarette smoking ²²³⁰ Age at delivery ⁸³⁷ BMI ⁸¹⁴¹ Genetic factors (SNPs) GNB3, rs5442 (A allele dominant) ⁸³⁵	Genetic factors (SNPs) CRP_B, rs1205, (A allele dom) ⁸³⁶ CRP_C, rs1130864, (T allele dom) ⁸³⁶ CRP, rs876538, (C allele dominant) ⁸³⁷ NOS3, rs3918227 (A allele dominant) ⁸³⁵								

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Severe pre-eclampsia	Nulliparity ^{836, 837} Obese BMI ^{836,837} Age at delivery ⁸³⁶ Gestational diabetes ⁸³⁷ Genetic factors (SNPs) MBL2, rs1800451, (T allele dominant) ⁸³⁶ IL1A, rs3273550, (T allele dominant) ⁸³⁶ CTLA4, rs21775, (A allele dominant) ⁸³⁶ CRP, rs3093068, (G allele additive) ⁸³⁷ CRP, rs876538, (C allele additive) ⁸³⁷ CRP, rs876538, (C allele recessive) ⁸³⁷	Age at delivery ⁸³⁷	Genetic factors (SNPs) CRP_A, rs3093077, (T allele additive) ⁸³⁶ <i>CRP_B, rs1205, (A</i> <i>allele dom)⁸³⁶</i> CRP_C, rs1130864, (T allele dom) ⁸³⁶ CRP, rs876538, (C allele dominant) ⁸³⁷
Severe Maternal Morbidity and/	or Mortality (4 studies)		
Severe maternal morbidity (SMM) with transfusions	Native American maternal race ¹¹⁹ Any physical health condition ¹¹⁹ Any behavioral health condition ¹¹⁹ Multiple chronic conditions (2 or more) ¹¹⁹	Native American maternal race ⁹⁵²	
Severe maternal morbidity without transfusions		Native American maternal race ¹¹⁹ Rural maternal residency ⁴⁰¹⁰	
Severe maternal morbidity and mortality (SMMM)	Rural maternal residency ³⁴²¹ Native American race ⁴⁰¹⁰ Medicaid funded births ³⁴²¹	Urban maternal residency ³⁴²¹	
Blood Transfusions (2 studies)			
Blood transfusions	Rural maternal residency ^{3421,} ⁴⁰¹⁰ Medicaid-funded births ³⁴²¹ Native American maternal race ⁴⁰¹⁰		
Postpartum Hemorrhage (2 studi	les)		
Postpartum hemorrhagePostpartum hemorrhage	Native American Maternal race ¹³³¹ Gravidity<5 ¹¹³¹ Birthweight>4500g ¹¹³¹ Retained placenta ¹¹³¹ Magnesium sulfate use ^{1131, 2944} Antepartum bleeding ²⁹⁴⁴ Previous postpartum hemorrhage ²⁹⁴⁴ Third stage of labor>20m ²⁹⁴⁴ Maternal rural residence ²⁹⁴⁴ Fetal macrosomia ²⁹⁴⁴ Oxytocin use>12h ²⁹⁴⁴ Routine aspirin use ²⁹⁴⁴ Prior uterine incision and vaginal delivery ²⁹⁴⁴	Prior uterine incision ²⁹⁴⁴ BMI≥40 ²⁹⁴⁴ Vitamin D supplementation ²⁹⁴⁴	

	Pre-eclampsia without severe features without use of magnesium sulfate ²⁹⁴⁴ Parity \geq 5 ²⁹⁴⁴ Length of second stage of labor \geq 1h ²⁹⁴⁴ Inpatient induction length \geq to 36h ²⁹⁴⁴		
Other Outcomes (4 studies)			
Uterine atony	Native American maternal race ¹³³¹ Birthweight>4500g ¹³³¹	Gravidity<5 ¹³³¹ Induction augmentation ¹³³¹ Chorioamnionitis ¹³³¹	
Ectopic pregnancy	Maternal age≥19 years ¹⁸⁶¹ Indian Health Service region ¹⁸⁶¹		
Placental abruption	Continuous use of smokeless tobacco ²²³⁰ Continuous cigarette smoking ²²³⁰		
Disseminated intravascular coagulation	Native American race ⁴⁰¹⁰	Rural maternal residency ⁴⁰¹⁰	
Hysterectomy	<i>Native American race</i> ⁴⁰¹⁰ Rural maternal residency ⁴⁰¹⁰		

*BMI, body mass index; h, hours; m, minutes; significant associations are italicized and bolded, significant association in the same direction as categorized

Specific to hypertensive disorders of pregnancy, having a rural residency (1/1 studies), an overweight or obese BMI (4/5 studies), age above 35 years also referred to as "advanced maternal age" (1/4 studies), and nulliparity (3/3 studies) were significantly associated with increased risk. [32,34–36,44] Genetic predispositions to hypertensive disorders of pregnancy were not significantly associated with increased risk (3/3 studies). [34–36] Studies that focused on SMMM identified being of Native American race (2/3 studies), having a physical health condition (1/1 study), a rural residency (1/2 studies), and births primarly paid by Medicaid (i.e., public government insurance) (1/1 study) as significantly associated with increased risk. The risk of blood transfusions was significantly associated with Native American race (1/1 study), rural residency (2/2 studies), and Medicaid-funded births (1/1 study). [10,11,41] Postpartum hemorrhage risk was significantly associated with being of Native American race when compared to other racial/ethnic groups, a gravidity \leq 5, a birthweight of 4500g, having a retained

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placenta, magnesium sulfate use (2/2 studies), antepartum bleeding, previous postpartum hemorrhage, being in third stage labor greater than 20 minutes, maternal rural residency, fetal macrosomia, and oxytocin use for longer than 12 hours. [40,42] Other outcomes are further described in Appendix 3.

This systematic review identified several factors related to maternal health among Native American women, including some that did not align with findings from other populations. For example, continuous smokeless tobacco use and cigaerrete smoking were found to have no significant association with pregnancy-induced hypertension in one study. [39] A separate study identified that women under 35 had a decreased risk of hypertensive disorders of pregnancy compared to those older than 35. [42] One study found no association between hypertensive disorders of pregnancy (e.g., preeclampsia) and having an overweight/obese BMI. [33] Genetic factors also demonstrated varying outcomes. One study identified that the CRP B, rs1205 Single Nucleotide Polymophisms (SNPs) (A allele dominant) was associated with a decreased risk for pre-eclampsia while another study found the CRP rs3093068 SNP (G allele dominant) linked to an increased risk. [34,35] Other SNPs examined in these studies showed no sinigiifcant association with preeclampsia or other an increased risk while other SNPs showed no association or relationship. [34,35] In contrast to other studies, Native American race and rural residency were not assicated with severe maternal morbidity and/or mortality in three distinct studies. [10,41,43]. Another study found no significant association between uterine atony and factors such as high gravidity, induction augmentation, or chorioamnionitis. Interestingly, rural residency also did not appear to increase the risk of disseminated intravascular coagulation[10,40,42].

Reporting biases and certainty of evidence

All studies relied on administrative data sources to assess outcomes and exposures simultaneously, and all noted this as a considerable limitation in their study design. Four studies noted concerns with small sample sizes, missing exposure and outcome data, and critical demographic information that may have led to misclassification bias. Two studies considered reporting bias in their study designs, while almost all studies (14/15 studies) referred to the misidentification of Native American women based on predetermined guidelines for race

designation.

DISCUSSION

This systematic review synthesized the literature by conducting a broad search of outcomes associated with maternal morbidity and mortality and identifying their associated risk factors for Native American women in the US. Despite the importance of understanding these outcomes for this population, we found a limited number of studies addressing these critical issues. All fifteen studies identified risk factors at the individual level, suggesting that an overweight or obese BMI, advanced maternal age (35 years or older) in certain situations, parity, and rural maternal residency are associated with Native American maternal morbidity or mortality. Few studies contradicted these findings and demonstrated no association with Native American race, rural maternal residency, or advanced maternal age. One study found no association with hypertensive disorders of pregnancy, including pregnancy-induced hypertension, preeclampsia, and severe preeclampsia with continuous smokeless tobacco use or continuous cigarette smoking. [39]

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While advanced maternal age is often associated with higher risks for adverse maternal health otucomes in other populations, this review found both consistent and nuanced findings among Native American women. Specifically, advanced maternal age was associated with a higher risk of hypertensive disorders, including pregnancy-induced hypertension, especially among those

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who smoked during pregnancy. However, two studies found no significant association between age at delivery and preeclampsia in this population. These results suggest that while advanced age can be a risk factor for some outcomes, such as hypertension, it may not uniformly affect all maternal health conditions. This could also indicate the presence of potential protective factors or differences in health profiles among Native American women that merit further investigation. Conversely, the higher risk of morbidities among public governmental health insurance (i.e., Medicare or Medicaid) recipients is concerning and suggests a need for targeted interventions within this subgroup. Studies showed that rural Native American Medicaid-funded births had the highest adjusted rate of severe maternal morbidity and mortality, indicating potential disparities in healthcare quality and access.[41,46]

Studies assessing the relationship between genetic factors and preeclampsia or severe preeclampsia were completed in an Indian Reservation within a specific tribal health system.[34– 36] These studies uncovered that there were only two associations between genetic expression and preeclampsia for Native American women among those studies. These studies concurred that many of the risk factors, such as maternal age, nulliparity, and obesity, that are associated with preeclampsia and severe preeclampsia in other populations were also operative in Native American communities.[34–36]

At the community level, our review identified four studies that included risk factors such as maternal residency and the Indian Health Service Region. This limitation further indicates the need to expand research to identify and understand the role of community and society-level risk factors. Social determinants of health, such as access to behavioral and primary care services, housing, crime and violence, and health policies, have been demonstrated to contribute directly to maternal mortality and morbidity in more extensive population studies.[47] Studies

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highlighted the higher incidence of SMM and mortality among rural Native American women compared to their urban counterparts, emphasizing the critical impact of geographic and systemic disparities. [40,42,45]

This review did not find information on prenatal care utilization and its association with maternal morbidity or mortality despite strong evidence supporting adequate prenatal care utilization in culturally competent healthcare institutions.[15,48,49] Early and adequate prenatal care is thought to promote healthy pregnancies through screening and managing a woman's risk factors and health conditions and promote healthy behaviors during pregnancy.[6]

This review did not consider the effects of historical trauma, discrimination, and racism, which are significant health determinants for Native Americans.[17] These experiences contribute to health deterioration over time, as explained by the weathering hypothesis, which suggests that cumulative stress from racism and socioeconomic disadvantages leads to worse health outcomes.[13]

Appraisal

Most studies were rated as "good" (14/15 studies), while one was rated as "fair." Despite this, we were able to highlight the methodological shortcomings of some of the studies, such as the failure to assess the exposure more than once over time, the inability to demonstrate that exposure was measured before outcome measurement, or not adjusting models to include potential confounders. Additionally, some studies failed to provide sample size justification or did not randomly select cases or controls from the eligible study population, posing bias risks. We identified additional shortcomings in the available evidence. Racial/ethnic misclassification on administrative databases led to challenges with underreporting and further affected the

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selection of study participants. Given the small percentage of Native American births in the United States, which is only 0.7%, minor errors in misclassification can significantly impact data analysis.[50] Multiple studies in this review reported small sample sizes, making it difficult to determine if a particular outcome was a true finding, possibly allowing for type II errors. Among studies that included samples that were not fully Native American, most reported a Native American sample size of $\leq 1.4\%$. The limited research in these communities hinders the identification of additional risk factors for morbidity and mortality specific to Native American women.[51] The measurement of maternal morbidity and mortality varied across the studies. This review used a broader definition of these outcomes, including conditions not listed by the CDC as severe maternal morbidity. This approach aimed to provide a complete understanding of the risk factors and health outcomes specific to Native American women. Lastly, relying heavily on administrative data presents unique challenges in identifying risk factors not traditionally included in these datasets, as their primary purpose may not align with the study's hypothesis.[52]

Strengths and limitations

Our systematic review faced some limitations despite our use of an expansive search strategy informed by other published reviews.[3,53] We were unable to translate all MesH terms into indexed language for other databases. There is also a risk of publication bias and selective reporting of significant findings in the studies. Using NIH's quality assessment tools, which are not independently published nor standardized may introduce bias due to the qualitative nature of the review. Despite this, other systematic reviews have built the evidence supporting the utility and practicality of utilizing this tool. [3] Furthermore, the review revealed significant variation in the risk factors and outcomes across different studies. This highlights the complexity and

heterogeneity of maternal health issues among Native American women. This variation presents a challenge in drawing definitive conclusions.

Despite these limitations, this systematic review is one of the few that identifies risk factors for severe maternal morbidity and mortality among Native American women in the US. The review addresses a critical gap in the literature by focusing on this historically marginalized and underserved population, providing valuable insights for targeted public health interventions and policies. Including various study designs allows for a more comprehensive understanding of the associated risk factors and outcomes. We comprehensively reviewed the current literature using multiple search strategies incorporating the CDC's list of procedural and diagnoses for SMM. This systematic review utilized recommended language to identify research in Native American communities following the National Library of Medicine guidance. [54] Rigorous quality assessment tools were employed to evaluate the methodological quality of the included studies, ensuring that the findings are based on reliable and valid evidence. Additionally, organizing the identified risk factors into socioecological levels provides a structured approach to understanding the complex interplay of factors influencing maternal health in Native American communities.

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Implications for practice, policy, and future research

Our review demonstrates the lack of attention reflected in the scarcity of evidence available to understand this public health crisis among a population that is often ignored. The limited type of risk factors studied, the study designs, settings, and outcomes limit the ability of healthcare and public health organizations to properly design and implement tailored approaches to reduce disparities in this community further. Public health initiatives must prioritize culturally competent care and address the unique challenges faced by Native American women to mitigate the risks of maternal morbidity and mortality. By acknowledging and addressing these gaps in the literature, public health can better inform policy, enhance clinical practices, and ultimately improve health outcomes for Native American mothers and their families.
OTHER INFORMATION *Registration and protocol:* The registration and protocol information for this review can be accessed at: https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=363405, identifier: CRD42022363405. No amendments were submitted during implementation of the protocol. *Support:* This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors. *Competing interests:* None declared by all authors.

Data statement: The original contributions presented in the study are included in the article's supplemental material, further inquiries can be directed to the corresponding author.

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Contributorship statement: MC is responsible for the overall content as the guarantor. MC and PM: developed the protocol objectives and design. MC wrote the protocol and is the submitting author unders supervision of PM.. MC developed the search strategy. AZ, CR, AN, and AA reviewed abstracts and full-text articles, extracted data from included studies, and critically appraised the literature. AZ and AN co-wrote the introduction, CR and AA co-wrote the methods, and MC wrote the remaining sections, including results and discussion. PM, JE, CH, SP, and VN reviewed and made corrections to the manuscript on multiple occasions, leading to script. the final written manuscript.

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Figure Legend:

tor peet teriew only Figure 1 - PRISMA flow diagram

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Appendix 1. Search strategy by database

PubMed Search Strategy

#1 birth[tiab] OR labor[tiab] OR delivery[tiab] OR mothers[tiab] OR maternal[tiab] OR "peripartum period"[mesh] OR peripartum[tiab] OR "labor, obstetric"[mesh] OR "obstetric*"[mesh] OR "obstetric*"[tiab] OR "pregnancy"[mesh] OR "pregnan*"[tiab] OR "perinatal"[tiab] OR "prenatal"[tiab] OR "parturition"[mesh] OR "parturition"[tiab]

#2 "tribal" OR "tribe" OR "first nations" OR "indigenous peoples"[mesh] OR indigenous OR "health services, indigenous"[mesh] OR "american indians or alaska natives"[mesh] OR "american indian*" OR "indians, north american"[mesh] OR "native American" OR "alaska native"

#3 "severe maternal morbidity" OR "near miss" OR "adverse maternal outcomes" OR "maternal mortality" OR "Near Miss, Healthcare"[Mesh] OR "Pregnancy/Adverse Effects"[Mesh] OR "Pregnancy/Injuries"[Mesh] OR "Pregnancy/Mortality"[Mesh] OR "Pregnancy/complications"[Mesh] OR "Obstetric Labor Complications"[Mesh] OR "Delivery, Obstetric/adverse effects"[Mesh] OR "Delivery, Obstetric/complications"[Mesh] OR "Delivery, Obstetric/mortality"[Mesh] OR "Maternal Mortality"[Mesh] OR "morbidity"[mesh] OR "morbidity OR "labor complications" OR "delivery complications"

#4 Search (#1 AND #2 AND #3)

EMBASE Search Strategy

('delivery:ab,ti' OR 'birth:ab,ti' OR 'labor:ab,ti' OR 'mothers':ab,ti OR 'maternal':ab,ti OR 'peripartum':ab,ti OR 'obstetric':ab,ti OR 'pregnancy':ab,ti OR 'perinatal':ab,ti OR 'prenatal':ab,ti OR 'perinatal period'/exp OR 'labor'/exp OR 'pregnancy'/exp OR 'birth'/exp)

AND

(tribe OR 'indian health service' OR indigenous OR tribal OR 'first nations' OR 'american indian' OR 'native american' OR 'alaska native' OR 'indigenous people'/exp OR 'indigenous health care'/exp OR 'american indian'/exp)

AND

('severe maternal morbidity' OR 'adverse maternal outcomes' OR 'maternal mortality' OR 'pregnancy complications' OR 'mortality' OR 'morbidity' OR 'labor complications' OR 'delivery complications' OR 'near miss (health care)'/exp OR 'near miss' OR 'pregnancy complication'/exp OR 'maternal mortality'/exp OR 'labor complication'/exp OR 'maternal outcome'/exp OR 'delivery complications'/exp OR 'maternal morbidity'/exp OR 'morbidity'/exp OR 'mortality'/exp)

CINAHL Search Strategy

((TI delivery OR AB delivery) OR (TI birth OR AB birth) OR (TI labor OR AB labor) OR (TI mothers OR AB mothers) OR (TI maternal OR AB maternal) OR (TI peripartum OR AB peripartum) OR (TI obstetrics OR AB obstetrics) OR (TI pregnancy OR AB pregnancy) OR (TI perinatal OR AB perinatal) OR (TI prenatal OR AB prenatal) OR (TI perinatal OR AB perinatal) OR (TI prenatal OR AB perinatal) OR (TI delivery OR AB delivery) OR MM "Perinatal Period" OR MM "Obstetric Patients" OR MM "Delivery, Obstetric+" OR MM "Pregnancy+" OR MM "Labor+" OR MM "Obstetrics+" OR MM "Childbirth+")

AND

(tribe OR "indian health service" OR Indigenous OR "native american" OR "american indian" OR Tribal OR "first nations people" OR "alaska native" OR MM "Indigenous Peoples+" OR MM "Health Services, Indigenous" OR MM "Native Americans+")

AND

("severe maternal morbidity" OR "near miss" OR "pregnancy complications" OR "obstetric complications" OR mortality OR morbidity OR "maternal mortality" OR "maternal morbidity" OR "delivery complications" OR MM "near-death experiences" OR MM "maternal mortality" OR MM "obstetric emergencies" OR MM "Pregnancy Complications+" OR MM "labor complications" OR MM "maternal mortality" OR MM "morbidity+" OR MM "mortality+")

SCOPUS Search Strategy

("severe maternal morbidity" OR "near miss" OR "pregnancy complications" OR mortality OR morbidity OR "labor complications" OR "delivery complications" OR "maternal mortality" OR "maternal morbidity" OR "obstetric complications")

AND

(indigenous OR "native american" OR "american indian" OR tribal OR "alaska native" OR "first nations" OR tribe OR "indian health service")

AND

(TITLE-ABS (mother) OR TITLE-ABS (maternal) OR TITLE-ABS (peripartum) OR TITLE-ABS (obstetric) OR TITLE-ABS (pregnancy) OR TITLE-ABS (perinatal) OR TITLE-ABS (prenatal) OR TITLE-ABS (parturition) OR TITLE-ABS (labor) OR TITLE-ABS (birth) OR TITLE-ABS (delivery))

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No. of Studies Examining Each Risk Factor ^a	lished as 10. P
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Appendix 2. Risk Factors and Outcomes by Volume of Studies

					Out	tcome*				
Risk Factor	SMMM	HDP [†]	BT	РРН	DIC	Hyst	EP	UA	РА	No. of Studie Examining Each Risk Factor ^a
Body mass index		5		1			1	1		7
Age		4		1			1	1		6
Maternal race	3	1	2	1	1	1		1		5
Parity		3		1				1		5
Maternal residence	2	1	2		1	1				3
Gene expressions		3								3
Tobacco use		2							1	2
Birth primary payer type	1		1							1
Magnesium Sulfate use				2				1		2
Inpatient induction				2				1		2
Augmentation				1				1		1
Birthweight				1				1		1
Physical health/ chronic health status	1									1
Gestational diabetes		1								1
Behavioral health status (depression or substance use disorder)	1									1
Indian Health Service region							1			1
Gravidity					1			1		1
Routine aspirin use				1						1
Prior uterine incision or vaginal birth after cesarean				1						1
Macrosomia				1						1
Antepartum Bleeding				1						1
Previous PPH				1						1
Length of labor				1						1
Oxytocin use				1						1
Chorioamnionitis				1				1		1
Retained placenta				1				1		1
No. of Studies Examining Each Outcome ^a	4	8	2	2	2	1	1	1	1	15

*Severe maternal morbidity and mortality (SMMM), hypertensive disorders of pregnancy (HDP), transfusion (BT), postpartum hemorrhage (PPH), disseminated intravascular coagulation (DIC), h (Hyst), ectopic pregnancy (EP), uterine atony (UA), and placental abruption (PA), blank cells repr found. † The HDP category includes pre-eclampsia, severe pre-eclampsia, gestational hypertension hypertensive disorders of pregnancy. α Row and column figures do not represent totals since a stud multiple risk factors or outcomes.

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Study #	Authors	Year	Study Design	Locatio n	Sample Size, Data Source	Native American subsample size (% of total sample)	Risk Factor (Social ecological level)	Outcome(s)	Covariat, including for use	S Quality Rating	Key Findings ([9 Confidence Inte unless otherwise stated	
Hypert	ensive Disord	lers of Pro	egnancy (8)						s related	πber 202		
1178	Cameron, N et al.	2022	Cross Sectional	Nationw ide	51,685,525 all live births in the US to individuals aged 15-44 years, birth vital records	492,771 (9.3%)	Maternal residence (C)	Pregnancy induced hypertension	d to text and data mining, Al training, and similar technologies.	Good 24. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique nent Superieur (ABES) .	-The incidence of hypertensive diso of pregnancy diff by racial and ethn identity within bo rural and urban an The highest age- adjusted incidenc hypertensive diso of pregnancy was observed among individuals who identify as Ameri Indian/ Alaskan N -Significant incre the incidence of hypertension disc of pregnancy amo Native American women in rural an compared to thos urban areas in 20 2014 (2017 RR= [1.11-1.33] and 2 RR=1.17, [1.08-1] -No significant ir in the incidence of hypertension disc of pregnancy amo	

BMJ Open									Page 4		
								an-2024-088380 on 28 copyright, including f	Native American women living in rural areas compared to those in urban areas was observed in 2019 (2019 RR=1.03, [0.96-1.11])		
England, L et al.	2013	Case Control	Anchora ge, AK	1,123 singleton deliveries from 1997- 2005 to AN women residing in western Alaska, hospital administrat ive database / 503 cases and 502 controls	1,123 (100%)	Continuous smokeless tobacco use (I) and continuous cigarette smoking (I)	Pregnancy associated hypertension, pre- eclampsia, and gestational hypertension	Parity, pressure and data mining, Al training, and similar technologies.	 od -No significant associations were observed between smokeless tobacco use and pregnancy- associated hypertension (aOR 0.92, [0.56– 1.51]). -No significant associations were observed between smokeless tobacco use and pre-eclampsia (aOR 0.90, [0.52–1.56]). -No significant associations were observed between smokeless tobacco use and gestational hypertension (aOR 0.93, [0.42–2.03). -No significant associations were observed between continuous cigarette smoking and pregnancy-associated hypertension (aOR 0.65, [0.31–1.37]). -No significant associations were observed between 		

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							e n-2024-088380 on 28 November 2024 Enseigneme copyright, including for uses related t	continuous cigarette smoking and pre- eclampsia (aOR 0.69, [0.30–1.58]). -No significant associations were observed between continuous cigarette smoking and gestational hypertension (aOR 0.52, [0.14–1.90).
8141 Zamora- Kapoor, A et al.	2016 Coh	nort Washin gton State	71,080 singleton live births from 2003- 2013 to Whit and AI/AN women, linked birth- hospital discharge records	7,189 (10.1%)	Maternal race (I), BMI (I)	Pre-eclampsia	Birth year, Do Good maternal Superieur (ABES) education Hip marital marital Medicai (ABES) status, medicai (ABES) Medicai (ABES) wire annual status, medicai (ABES) marital mining status, medicai (ABES) wire annual status, medicai (ABES) wire annual status, medicai (ABES) wire annual status, medicai (ABES) wire annual status, medicai (ABES) marital mining wire annual status, medicai (ABES) milar technologies.	 -AI/ANs had an increased risk of preeclampsia compared to Whites after controlling for all covariates except BMI (OR 1.17 [1.06–1.29]). After further adjustment for BMI, the racial disparity in preeclampsia risk was greatly attenuated (aOR 1.05, [0.95–1.16]). -AI/ANs who were underweight (OR 1.39, [0.64-3.02]), normal weight (OR 1.02, [0.83-1.22]), overweight (OR 1.23, [0.93, 1.36]), or obese (OR 1.00, [0.86, 1.17]) generally had relative risks of preeclampsia comparable, or slightly (but not statistically significantly) greater than those of their White counterparts.

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Pag	bmion	ted by		pen	BMJ O						
 -The odds of pregnancy induced hypertension was greater in non- Hispanic American Indian women 35 year or older who smoked during pregnancy (aO 1.29, [0.88-1.89]). -A reduced odds of PI was evident in non- Hispanic American Indian women younge than 35 years old who smoked during pregnancy based (aOR 0.76, [0.66-0.87]). 	n-2024-088380 on 28 November 2024 Downloaded fr	Prenatal care copyright, including for uses related to text gain, parity, diabetes for uses related to text marital status, ses related to text hypertentiated t	Pregnancy induced hypertension (inclusive of pre-eclampsia and eclampsia)	Cigarette use during pregnancy (I), maternal age (I)	34,348 (1.10%)	3,113,164 singleton births between 20-44 weeks gestation without major fetal anomalies in 2010, US natality file	Nationw ide	Cohort	2014	Chang, J et al.	1371
-The strength of the association of overweight/obesity wi preeclampsia was muc greater among NH AI/AN women (aRR 5.24; [1.92–14.30]) an NH Native Hawaiian/Other Pacifi Islander women than among other race/ethnicities (aRR 5.88, [1.30-36.51]).	Good	Maternation age, parity, delivery A hospital, tr governman t health g insurance substances abuse, milar use, and te alcohol use	Pre-eclampsia	Pre- pregnancy BMI (I)	978 (0.92%)	105,466 singleton live births from 22 facilities from 2018- 2018, hospital administrat ive database	Washin gton State	Cohort	2021	Tiwari, R et al.	7372
-Age at delivery (aOR 1.0823, [p=0.0185]), nulliparity (aOR 6.8628, [p<0.001]), ar obesity (aOR 1.0951, [p<0.001]) show robu independent effects associated with preeclampsia.	Good Anonce Bibliographique	Nullipar ff y, BMI, age at delivery	Pre-eclampsia	Age at delivery (I), nulliparity (I), BMI (I), Single nucleotide polymorphi sms [NOS3, rs1799983	299 (100%)	299 women tribal members of the Turtle Mountain Band of Chippewa who sought care in an IHS	Belcourt , ND	Case Control	2012	Best, L et al.	835

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26						hospital or clinic from 2004-2009, electronic medical records / 101 cases and 198 matched controls		(G allele recess), NOS3, rs3918227 (A allele dom), GNB3, rs5442 (A allele dom), DDAH1, rs10158674 (C allele recess), DDAH1, rs233115 (A allele recess)] (I)		Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, a	n-2024-088380 on 28 November 2024. Downloaded from http://bmionen.bu	 There was no significant association between any of single nucleotide polymorphisms studied and pre-eclampsia. NOS3, rs1799983 (G allele recess) (aOR 1.4087, [p=0.2354]) NOS3, rs3918227 (A allele dom) (aOR 0.7356, [p=0.4611]) GNB3, rs5442 (A allele dom) (aOR 0.9147, [p=0.8655]) DDAH1, rs10158674 (C allele recess) (aOR 1.0165, [p=0.9898]) DDAH1, rs233115 (A allele recess) (aOR 2.2227. [p=0.1578])
26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	836	Best, L et al.	2012	Case Control	Belcourt , ND	196 women tribal members of the Turtle Mountain Band of Chippewa who sought care in an IHS hospital or clinic from 2004-2009, electronic medical records / 66 cases and	196 (100%)	Age at delivery (I), nulliparity (I), BMI (I), single nucleotide polymorphi sms [CRP_A rs3093077 (T allele additive), CRP_B rs1205 (A allele dom), CRP_C rs1130864	Pre- eclampsia, severe pre- eclampsia	Nulliparity, weight an first an prenatal to visit, BM, birthweight of infante gestational diabetes, age at delivery	Good Good Di Good Di Good	-Age at delivery did not show a significant association with pre- eclampsia (aOR 1.036, [p=0.398]) and severe preeclampsia (aOR 1.027, [p=0.586]). -Nulliparity (aOR 4.274, [p=0.003] and aOR 4.520, [p=0.009])) and obesity (aOR 1.093, [p=0.002] and aOR 1.094, [p=0.007]) show robust independent associations with

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22					130 matched controls		(T allele dom), MBL2 rs1800451 (T allele dom, IL1A rs3783550 (T allele dom), CTLA4 rs231775 (A allele dom)](I)		Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, A	en-2024-088380 on 28 November 2024. Downloaded from http://	preeclampsia and severe pre-eclampsia. - There was no significant association between any of single nucleotide polymorphisms studied with pre-eclampsia and severe pre-eclampsia except CRP_B, rs1205, (A allele dom). - CRP_B, rs1205, (A allele dom) was the only single nucleotide polymorphism that showed a significant association with severe pre-eclampsia (aOR 0.259, [p=0.020]).
23 83 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 44	Best, L o al.	2013 2013	Case Control	Belcourt , ND	410 women tribal members of the Turtle Mountain Band of Chippewa who sought care at an IHS hospital or clinic from 2004-2012, electronic medical records / 140 cases and 270 matched controls	410 (100%)	Age at delivery (I), nulliparity (I), BMI (I), gestational diabetes (I), single nucleotide polymorphi sms [CRP rs3093068 (G allele add), CRP rs3093068 (G allele recess, CRP rs3093068 (G allele dom), CRP	Pre- eclampsia, severe pre- eclampsia	Nulliparty, weight and first g prenatal and visit, BMi, birthweight of infanta gestational diabetes	Good Good biologen hini com/ on June 7, 2025 at Agence Bibliographique	-Age at delivery did not show a significant association with pre- eclampsia (aOR 1.053, [p=0.076]) and severe preeclampsia (aOR 1.052, [p=0.166]). -Gestational diabetes did not show a significant association with pre-eclampsia (aOR 1.684, [p=0.278]) and severe pre- eclampsia (aOR 2.241, [p=0.166]). -Independent effects of nulliparity (aOR 5.6, [p=0.001] and aOR 4.17, [p=0.001]) and

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pidity and Mortality (4)			rs876538 (C allele add), CRP , rs876538 (C allele recess), CRP rs876538 (C allele dom), rs3093068 (G dom) and rs876538 (C recess) add risk score] (I)		Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, and similar technologies.	en-2024-088380 on 28 November 2024 Downloaded from <u>http://bmionen.hmi.com/ on_lune</u> 7_2025 a	obesity (aOR 1.061, [p=0.002] and aOR 1.059, [p=0.001]) on pre-eclampsia and severe pre-eclampsia were observed. -There was no significant association between any of single nucleotide polymorphisms studied with pre-eclampsia and severe pre-eclampsia except CRP rs3093068 (G allele add) and CRP rs3093068 (G allele dom) with severe pre- eclampsia (aOR 2.587, [p=0.05] and aOR 2.587, [p=0.050]) -The rs3093068 (G dom) and rs876538 (C recess) additive risk score showed significant association with pre-eclampsia (aOR 1.779, [p=0.016]) and severe pre- eclampsia (aOR 2.035, [p=0.013]).
Cross Nationw Sectional ide	2,523,528 all hospital deliveries that occurred between 2012-2015,	20,447 (0.810%)	No chronic conditions, any physical health condition (I), any	SMM	Age, income, payer, rural vs. urban residence, and	Good Bibliographicule	-The incidence of severe maternal morbidity was significantly higher among deliveries to women in every racial and ethnic minatory
	vidity and Wortality (4) Cross Nationw Sectional Nationw ide	vidity and Wortality (4) Cross Sectional Nationw 2,523,528 all hospital deliveries that occurred between 2012-2015,	idity and Mortality (4) Cross Sectional Nationw ide 2,523,528 all hospital deliveries that occurred between 2012-2015, 20,447 (0.810%) For peer review only - http://bmjopent.	idity and Mortality (4) Cross Sectional Nationw ide 2,523,528 all hospital deliveries that occurred between 2012-2015, 20,447 (0.810%) No ehronic conditions, any physical health condition (1), any	bitUopen skille add), CRP rs876538 (Callele add), CRP rs876538 (Callele recess), CRP rs876538 (Callele down, rs876538 (Creess) add risk score] (I) score] (I) sidity and Mortality (4) Cross Sectional ide 2,523,528 all hospital deliveries that occurred poccurred cocurred poccurred pocurred pocurred pocurred pocurred pocured potwere	idity and Mortality (4) 2,523,528 that occurred 2012-2015, 20,447 (0,810%) No chronic (1), any SMM Age, pays, rural vs. urban residence, and	Bou Upen Ref Good Ref Str 2538 (C allele add), CRP ,rs876538 ,rs876538 ,rs876538 ,rs876538 (C allele dom), ns3093068 ,rs876538 ,rs876538 ,rs876538 ,rs876538 (C allele dom), nad ,rs876538 ,rs876538 ,rs876538 ,rs876538 (C allele dom, nad ,rs876538 ,rs876538 ,rs876538 ,rs876538

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category compared with	hospital e	behavioral	National		
deliveries among non-	region. Y. B	health	Inpatient		
Hispanic white women.	ght 6	condition	Sample		
1		(I), multiple	Ĩ		
-American		chronic			
Indian/Alaska Native	idi, e	conditions			
women are at increased	ng				
risk of severe maternal	for B	(1), maternal			
morbidity compared to	щ щ щ	race (I)			
non-Hispanic white	en ses	Tace (I)			
women (aRR 1.5, [1.3-	reic				
1.71). This is not	late r 2				
significant when blood	ed me D2				
transfusions are not	to ht F				
included in severe					
meternal morbidity	t a pe				
(a P P 0 0 0 [0.68, 1.2])	nd nd				
(aKK 0.90, [0.08-1.2]).	da la la				
-Among deliveries to					
women with comorbid	E E E E E E E E E E E E E E E E E E E				
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Indian/Alaskan Native	臣				
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Hispanic white women,	L L L L L L L L L L L L L L L L L L L				
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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 22										en-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June Enseignement Superieur (ABES) . copyright, including for uses related to text and data mining, Al training, and similar techno	morbidity incidence increased from 66.6 [95% CI 39.9-93.3] to 101.3 [95% CI -41.0- 243.5] per 10,000 delivery hospitalizations, respectively, in comparing deliveries in which no and multiple chronic conditions were identified. -American Indian/Alaskan Native women compared to non-Hispanic white women are at increased risk for severe maternal morbidity when any physical health condition is present (aRR 1.5, [1.3-1.7]), any behavioral health condition is present (aRR 1.2, [0.90-1.6]), and having multiple (2 or more) chronic conditions (aRR 1.4, [0.93-2.20]).
32 33 34 35 36 37 38 39 40 41 42 43 44	3421	Interrante, J et al.	2022	Cross Sectional	Nationw ide	6,357,796 maternal records from childbirth hospitalizat ions from 2007-2015, National Inpatient Sample	43,929 (0.691%)	Primary payer type (I), maternal residence (C), maternal race (I)	SMM and Mortality (SMMM)	Materna race and ethnicity, maternal residence, maternal age, childbirth year, bottom quartile of	 -Rural Indigenous Medicaid-funded births had the highest adjusted predicted rate of SMMM (224.9 per 10,000 births, [187.0- 262.9]). -Among rural residents, births by Indigenous people had the greatest differences in rates
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	income, by income, by income, by income, by insumed births (a cesarean for use for disorder, by HIV or selanement Superior AIDS, attement Superior by the selanement Superior chronic Composition by the selanement Superior chronic Downloaded disease, b chronic Downloaded disease, b chronic Downloaded disease, b chronic Downloaded disease, b chronic Downloaded disease b chronic Downloaded b b b b b b b b	id- ately RD, 3]). ag the urality nicity, mificant ion, 0.40, SMMM oulation ag the rban nd among n : have action 0- k of ted with be f the among d births sed to he i), this prevent 10,000 among dents, 198

e 51 of 62				BMJ Open								
								copyright	en-2024-0	among Indigenous rura residents.		
952 Booke et al.	, W 2018	Cohort	Nationw ide	1,724,694 delivery hospitalizat ions from women aged 40-54 years between 1998-2014, National Inpatient Sample	7,107 (0.412%)	Maternal race (I)	SMM, SMM excluding blood transfusions	Year, ber size, ber insurance status, for uses to spital uses location so related income related to text quartile, and to text hospital to text hospital to text hospital status, and the status, and the race ta mile	Good R8380 on 28 November 2024 Downloaded from	 The incidence of SMR was greater among Native American women but not significant compared t Non-Hispanic white women (aRR 1.08, [0.93-1.25]). Risk for severe morbidity excluding transfusion among Native Americans is nu demonstrated because of small denominators 		
4010 Kozhi nil, K al.	nan 2020 et	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (I)	SMMM, SMMM excluding blood transfusion	Age, g, insurance payer, and income, ning, region and similar technologies.	Good	-The incidence of SMMM was greater among indigenous women compared with white women (aRR 1.8 [1.6–2.0]). -Within each racial group, incidence of SMMM was higher among rural compared with urban residents (2.3% for rural indigenous women vs 1.8% for urban indigenous women) (a RR 1.3, [1.0–1.6]); (1.3% for rural white women vs 1.2% for urban white women) (aRR 1.1, [1.1–1.2]). -Within indigenous women, the incidence		
					BMJ	Open		//bmjopc	Рас			
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								2024-088380 on 28 copyright, including f	of SMM (excluding transfusions) among rural compared to urba residents was not significant (aRR 0.7, [0.4-1.0)].			
Blood	ransfusions	(2)						Noven En or use				
3421 Interra J et al.	nte, 2022	Cross Sectional	Nationw ide	6,357,796 maternal records from childbirth hospitalizat ions from 2007-2015, National Inpatient Sample	43,929 (0.691%)	Primary payer type (I), maternal residence (C), maternal race (I)	Blood transfusions	Maternalistic Good race and the Good residence to the Good age, data to	 -Rural residents had greater odds of blood transfusion for both Medicaid-funded (aOF 1.15, [1.06-1.25]) and privately insured (aOR 1.20, [1.11-1.31]) hospital births compared to urban residents. -Medicaid-funded (aO 1.71, [1.39-2.11]) and privately insured hospital (aOR 1.42, [1.05-1.92]) indigenous births had the second highest odds of blood transfusions compared to other racial/ethnic groups. This yielded ar additive interaction p-value of 0.006. 			

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								heart opyright disease, give the second seco	
Kozhiman nil, K et al.	2020	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (I)	Blood transfusions	Age, are 2024. Good insurance to text and to text and data mining, a	 The incidence of bloot transfusions was greated among indigenous women compared with white women (aRR 1.8 [1.5–2.0]). The incidence of bloot transfusion among rural indigenous women compared to urban indigenous women was statistically greater (aRR 1.6, [1.2-2.0]).
Postpartum I	Hemorrh	age (PPH) (2	2)					mj.cor nd sir	
Chalouhi, S et al	2015	Cohort	Gallup, NM	1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records	751 (70.7%)	Maternal race (I), age (I), parity (I), gravidity (I), birthweight (I), retained placenta (I), magnesium sulfate use (I), induction augmentati on (I),	Postpartum hemorrhage	None 7, 2025 at Agence Bibliographique	-A significantly higher proportion of Native Americans than non- native women developed PPH (11.6% vs 7.0%, [p= 0.02]). -In multivariable logistic regression analysis, the significar predictors of PPH wer Native American ethn origin (OR 1.8, [1.1- 3.0]), decreased gravidity of fewer than
	Kozhiman nil, K et al. Postpartum I Chalouhi, S et al	Kozhiman nil, K et al.2020Postpartum HemorrhChalouhi, S et al2015	Kozhiman nil, K et al.2020 Sectional SectionalPostpartum Hemorrhage (PPH) (2Chalouhi, S et al2015Cohort	Kozhiman nil, K et al.2020Cross SectionalNationw idePostpartum HemorrHet S et al2015CohortGallup, NMChalouhi, S et al2015CohortGallup, NM	Kozhiman nil, K et al.2020Cross SectionalNationw ide7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient SamplePostpartum Hemorrhage (PPH) (2)Chalouhi, S et al2015CohortGallup, NM1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records	Kozhiman nil, K et al.2020Cross SectionalNationw ide7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample101,943 (1.35%)Postpartum Hemorrhage (PPH) (2)Chalouhi, S et al2015CohortGallup, NM1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records751 (70.7%)	Kozhiman nil, K et al. 2020 Cross Sectional Nationw ide 7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample 101,943 (1.35%) maternal residence (C), maternal race (I) Postpartum Hemortbare (PPH) (2) Postpartum John (2) Sectional NM 1,062 women between 2012-2015, National Inpatient Sample 751 (70.7%) Maternal race (I), age (I), parity (I), gravidity (I), birthweight (I), retained placenta (I), magnesium sulfate use (I), induction augmentai on (I),	Kozhiman nil, K et al. 2020 Cross Sectional Nationv ide 7,561,729 hospital if we births and indigenous women between 2012-2015, National Inpatient Sample 101,943 (1.35%) maternal residence (C), maternal race (I) Blood transfusions Postpartum Veremositive 101,943 (1.35%) maternal residence (C), maternal race (I) Blood transfusions Postpartum Veremositive NM National Impatient Sample 101,943 (1.35%) maternal residence (C), maternal race (I) Blood transfusions Postpartum Veremositive Set al 2015 Cohort Gallup, NM 1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records 751 (70.7%) Maternal race (I), age (I), parity (I), parity (I), parity induction sulfate use (I), induction augmentati on (I), Postpartum hemorrhage	Kozhiman 2020 Cross Nationw 7,561,729 101,943 maternal Blood Age: Gooding Gooding nil, K et al. 2020 Sectional ide hospital live births from white and indigenous women (1,35%) Irasfrusions Irasfrusions Age: Gooding Gooding Kothiman 2012 Sectional Ide hospital live births from white and indigenous women (1,35%) Irasfrusions Irasfrusions Irasfrusions Age: Gooding Former equipation of the part of the p

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1 2 3 4 5 6 7 8 9 10							chorioamni onitis (I)		en-2024-088380 on 28 Novemb Ense copyright, including for uses I		5 (OR 1.2, [1.1-1.4]), increased birth weight greater than 4500 grams (OR 1.1, [1.0-1.0]), retained placenta (OR 51.0, [9.8-288.2]), and use of magnesium sulfate (OR 3.5, [1.4- 9.0]).
11 29 12 13 14 15 16 17 18 19 20 21 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44	Hadley, M et al	2021	Case Control	Anchora ge, AK	384 deliveries between 2018-2019 at the Alaska Native Medical Center, medical records / 128 cases and 256 controls	384 (100%)	BMI (I), antepartum bleeding (I), routine aspirin used prescribed (I), prior uterine incision (I), prior uterine incision and vaginal delivery (I), parity (I), macrosomi a, pre- eclampsia without severe features with magnesium sulfate during labor (I), pre- eclampsia with severe features and use of	Postpartum hemorrhage	er 2024. Downloaded from <u>http://hmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique</u> ignement Superieur (ABES) . elated to text and data mining, Al training, and similar technologies. Not reported	Fair	-In the bivariate analysis, the following risk factors were significantly associated with a higher likelihood of postpartum hemorrhage: BMI of 40 or more (OR 2.6, [1.4- 4.5]), antepartum bleeding (OR 6.3, [1.2- 31.6]), previous postpartum hemorrhage (OR 5.0, [2.6-9.8]), suspected macrosomia with estimated fetal weight of 4000 g or more (OR 2.7, [1.4- 5.3]), pre-eclampsia with severe features and use of magnesium sulfate during labor (OR 4.7, [2.4-9.2], length of third stage labor longer than 20 min (OR 2.2, [1.1-4.4]), and use of oxytocin for more than 12 h (OR 5.0, [2.3-10.6]). -Residence in a rural community (OR 2.2, [1.4-3.6]) and vitamin

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	Misc. Outco	mes (5)								e n-2024-088380 on 28 November 2024. Downloa ded Enseignement Superieur (copyright, including for uses related to text and dat	use of magnesium sulfate (OR 2.1, [0.98- 4.4]), length of second stage of labor grater or equal to 1 hour (OR 1.6 [0.88-3.0]), and an inpatient induction length of greater or equal to 36 hours (OR 2.3, [0.4-12.8]) were not significantly associated with a higher likelihood of postpartum hemorrhage.
1331	Chalouhi, S et al	2015	Cohort	Gallup, NM	1,062 women who delivered vaginally at the Rehoboth McKinley Hospital, medical records	751 (70.7%)	Maternal race (I), age (I), parity (I), gravidity (I), birthweight (I), retained placenta (I), magnesium sulfate use (I), induction augmentati on (I), chorioamni	Uterine atony	None	fro m http://bmjopen.bmj.com/ on June 7, 2025 at J ABES) . ABES, Al training, and similar technologies.	-Uterine atony was recorded in a significantly higher proportion of Native Americans than non- native patients (9.6% vs 4.8%; [p=0.01]). -In univariate analysis, factors predicting uterine atony were native race (p=0.01), decreasing gravidity (p=0.02), induction augmentation (p=0.1), increasing birthweight

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1 2 3 (OR 2.0 increasi (OR 1.0	2.0, [1.1–3.7]) and easing birthweight
4 5 6	ificant predictors of ine atony.
7 1861 deRavello, L et al 2015 Cross Sectional Nationv ide 229,986 Maternal age (1), IIS region (C) Maternal age (1), IIS region (C) Extopic pregnancy None 8 Print (IP) Print (IP) <td>e ectopic pregnancy) rate among AI/AN hen was lowest in 15–19 years age up (5.5 EPs per 0 pregnancies) and test among 35–39 old (18.7 EPs per 0 pregnancies). mpared to AI/AN hen aged 15-18 rs, women aged 35- rears were 3.4 times e likely to have an RR 3.4, [2.90-]). Compared to AN women aged 15- rears, the risk of an ncreased with age n 1.56-3.42, except romen aged 40-44 rs were the risk was at 2.62 times (RR c, [2.02-3.36]). rates varied by graphic region, ting between 6.9 24.4 per 1,000 mancies in the thern Plains East the East region, ectively. mpared to AI/AN hen who received</td>	e ectopic pregnancy) rate among AI/AN hen was lowest in 15–19 years age up (5.5 EPs per 0 pregnancies) and test among 35–39 old (18.7 EPs per 0 pregnancies). mpared to AI/AN hen aged 15-18 rs, women aged 35- rears were 3.4 times e likely to have an RR 3.4, [2.90-]). Compared to AN women aged 15- rears, the risk of an ncreased with age n 1.56-3.42, except romen aged 40-44 rs were the risk was at 2.62 times (RR c, [2.02-3.36]). rates varied by graphic region, ting between 6.9 24.4 per 1,000 mancies in the thern Plains East the East region, ectively. mpared to AI/AN hen who received

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									Enseignement Superieur (ABES) . opyright, including for uses related to text and data mining, AI training, and similar technologies.	a 2024 099390 on 29 November 2024 Downloaded from http://bmicoon.htmicoon.htmicoon.on.lune 7 2025 at A	care in the Northern Plains East region, women who receive care in the East regi were 3.55 times mo likely to have an EF (RR 3.55, [2.75-4.5 in the Alaska region risk was 2.17 times 2.17, [1.73-2.72]), i the Southern plains region the risk was times (RR 1.57, [1.2 1.95]), in the West region the risk was times (RR 1.39, [1.0 1.77]), in the Northe Plains West region risk was 1.36 times (1.36, [1.08-1.71]), in the Southwest reg the risk was lowest 1.33 times (RR 1.33 [1.07-1.65]). -We found relatively stable annual rates of EP among AI/AN women receiving ca at IHS-affiliated facilities during 200 2009, but considera variation by age groups and geographic regioned
2230	England, L et al.	2013	Case Control	Anchora ge, AK	1,123 singleton deliveries from 1997- 2005 to AN women residing in	1,123 (100%)	Continuous smokeless tobacco use (I) and continuous cigarette smoking (I)	Placental abruption, placental abruption expanded definition	Parity, pre- pregnancy BMI, maternal age	Good	-Thirty-nine percent case deliveries were also preterm (compa with 7% of controls, [p<0.001]), and 9.8% were also complicat by pregnancy

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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33	Sopyright, including for uses related to text and data mining, at training, and similar technologie	 associated hypertension (compared with 7% of controls. [p=0.38]). There were no significant associations between placental abruption and continuous smokeless tobacco use (aOR 1.11, [0.53-2.33] and continuous cigarette smoking (aOR 1.19, [0.43-3.29). An expanded definition of abruption did not change this finding. There were no significant associations between continuous smokeless tobacco use (OR 1.07, [0.63-1.83]) or continuous cigarette smoking (aOR 1.04, [0.48-2.23]).
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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 3 24 25 26 27 28 29 30 1 32 33 4 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 32 33 34 35 36 37 32 32 33 34 35 36 37 32 30 31 32 33 34 35 36 37 32 30 31 32 33 34 35 36 37 32 30 31 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 33 34 35 36 37 32 37 32 37 32 37 37 37 37 37 37 37 37 37 37 37 37 37	4010	Kozhiman nil, K et al.	2020	Cross Sectional	Nationw ide	7,561,729 hospital live births from white and indigenous women between 2012-2015, National Inpatient Sample	101,943 (1.35%)	maternal residence (C), maternal race (C)	Disseminated intravascular coagulation (DIC), hysterectomy	Age, insurancial for uses related to text and data mining, Al training, and similar technologies. hospital region	Good good pn-2024-088380 on 28 November 2024. Downloaded from http://bmjopen.bmj.com/ on June 7, 2025 at Ageno	DIC -The incidence of DIC was greater but not significant among indigenous woman compared with white women (1.6% vs 0.9%, respectively) (aRR 1.1, [0.8-1.5]). -Within indigenous women, there was no difference between rural women and urban women (0.2% vs 0.2%, respectively) (aRR 0.8, [0.3-1.3]). Hysterectomy -The incidence of a hysterectomy was greater among indigenous woman compared with white women (0.1% vs 0.1%, respectively) (aRR 1.8, [1.0-2.6]). -Within indigenous women, there was a marginal increased risk but not significant of hysterectomy among rural women (aRR 1.3, [0.3-2.3]).
39 40 41 42 43 44 45					For peer	review only - h	ittp://bmjopen.	bmj.com/site/a	about/guidelines.»	:html	Bibliographique de	

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Apper For ob	ndix 4. Results of I	NIH qu	ality a	nssess onal st	ments udies:	for iı	nclude	BMJ O ed stue	pen dies					ted by copyright, includi	/bmjopen-2024-088380 oi			
ID#	Authors	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q15 USES	28213	Q14	Yes %	Rati
119	Admon L, et al.	2018	Yes	Yes	Yes	Yes	Yes	No	Yes	NA	Yes	NA	Yes	NRate	NA	Yes	82%	Go
952	Booker W, et al.	2018	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yeg	Yes	Yes	93%	Go
1178	Cameron, N. et al.	2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	NRan	NA	No	83%	Go
1331	Chalouhi, S. et al.	2015	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yeo	ad NR	No	92%	Go
1371	Chang, J et al	2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yean		Yes	100%	Go
1861	deRavello, L. et al.	2015	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	NIR A	NA	No	83%	Go
3421	Interrante, J. et al.	2022	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Ye	NA	Yes	85%	Goo
4010	Kozhimannil, K et al.	2020	Yes	Yes	Yes	Yes	No	Yes	Yes	NA	Yes	NA	Yes	NR and s	NA NA	Yes	90%	Goo
7372	Tiwari, R. et al	2021	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yen		Yes	92%	Goo
8141	Zamora-Kapoor A., et al	2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Nochnol	n Yes	Yes	86%	Go
A study ≤50%. Quality Studies	v will be rated as "Good of included studies was (https://www.phlbi.pit	d" if it rec	ceives a d using	the Na	respon tional I	se for ≥	280% of He	f the ap	plicable IIH) Qu	e NIH o nality A	eritical ssessm	appraisa ent tool	l question for Obse	ns, "Feir"	"25 at Agenored	%-79%, and Cro	and "Po ss-Secti	or" fc onal

Q1. Was the research question or objective in this paper clearly stated?

Q2. Was the study population clearly specified and defined?

Q3. Was the participation rate of eligible persons at least 50%?

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Q4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were infoluses of the study prespecified and applied uniformly to all participants? Q5. Was a sample size justification, power description, or variance and effect estimates provided? Q6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured? Y7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if idexided? 8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the exposure measured as continuous variable? Were the exposure (independent variables) clearly defined to the outcome is the outcome measure (independent variables) clearly defined to the outcome (independent variables) clearly defined to the outcome measure (independent variables) clearly defined to

 Q10. Was the exposure(s) assessed more than once over time? Q11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across and outcome assessors blinded to the exposure status of participants? Q13. Was loss to follow-up after baseline 20% or less? Q14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between (s) and outcome(s)?

aded from http://bmjopen.bmj.com/ on June 7, 2025 at Agence Bibliographique de l ieur (ABES) . d data mining, Al training, and similar technologies.

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For case-control studies:

56	BMJ Open												6/bmjopen-2024-08838 .cted by copyright, inc				
	ID#	Authors	Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12 on	Yes %	Rating
	835	Best, L. et al	2012	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	28 No	92%	Good
	836	Best, L. et al.	2012	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	pvemi Prs USes	92%	Good
	837	Best, L et al.	2013	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	oer 2(eiĝne rælate	83%	Good
	2230	England L, et al	2013	Yes	Yes	Yes	Yes)24. E mg⊜nt ¢d⊣to:	100%	Good							
	2944	Hadley, M et al	2021	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Selp Selp	75%	Fair

A study will be rated as "Good" if it receives a "Yes" response for $\geq 80\%$ of the applicable NIH critical appraisal questions, "Fair for 50%-79%, and "Poor" for ided from pur (ABES i data min ≤50%.

Quality of included studies was assessed using the National Institutes of Health (NIH) Quality Assessment of Case-Control Study (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools): n bttp://bmjope S¥ .

Q1. Was the research question or objective in this paper clearly stated and appropriate? Q2. Was the study population clearly specified and defined? Q3. Did the authors include a sample size justification? Q4. Were controls selected or recruited from the same or similar population that gave rise to the cases (including the same timeframe)?

Q5. Were the definitions, inclusion and exclusion criteria, algorithms or processes used to identify or select cases and controls aligned in the select cases are cased to identify or select cases and controls aligned in the select case aligned in the select c consistently across all study participants? simi

O6. Were the cases clearly defined and differentiated from controls?

Q7. If less than 100 percent of eligible cases and/or controls were selected for the study, were the cases and/or controls randomay selected from those eligible?

Q8. Was there use of concurrent controls?

Q9. Were the investigators able to confirm that the exposure/risk occurred prior to the development of the condition or event that defined a participant as a case? Q10. Were the measures of exposure/risk clearly defined, valid, reliable, and implemented consistently (including the same tinge period) across all study

participants?

O11. Were the assessors of exposure/risk blinded to the case or control status of participants?

Q12. Were key potential confounding variables measured and adjusted statistically in the analyses? If matching was used, did the investigators account for matching during study analysis? gence Bibliographique de l

Q, question; CD, cannot be determined; NA, not applicable; NR, not reported

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