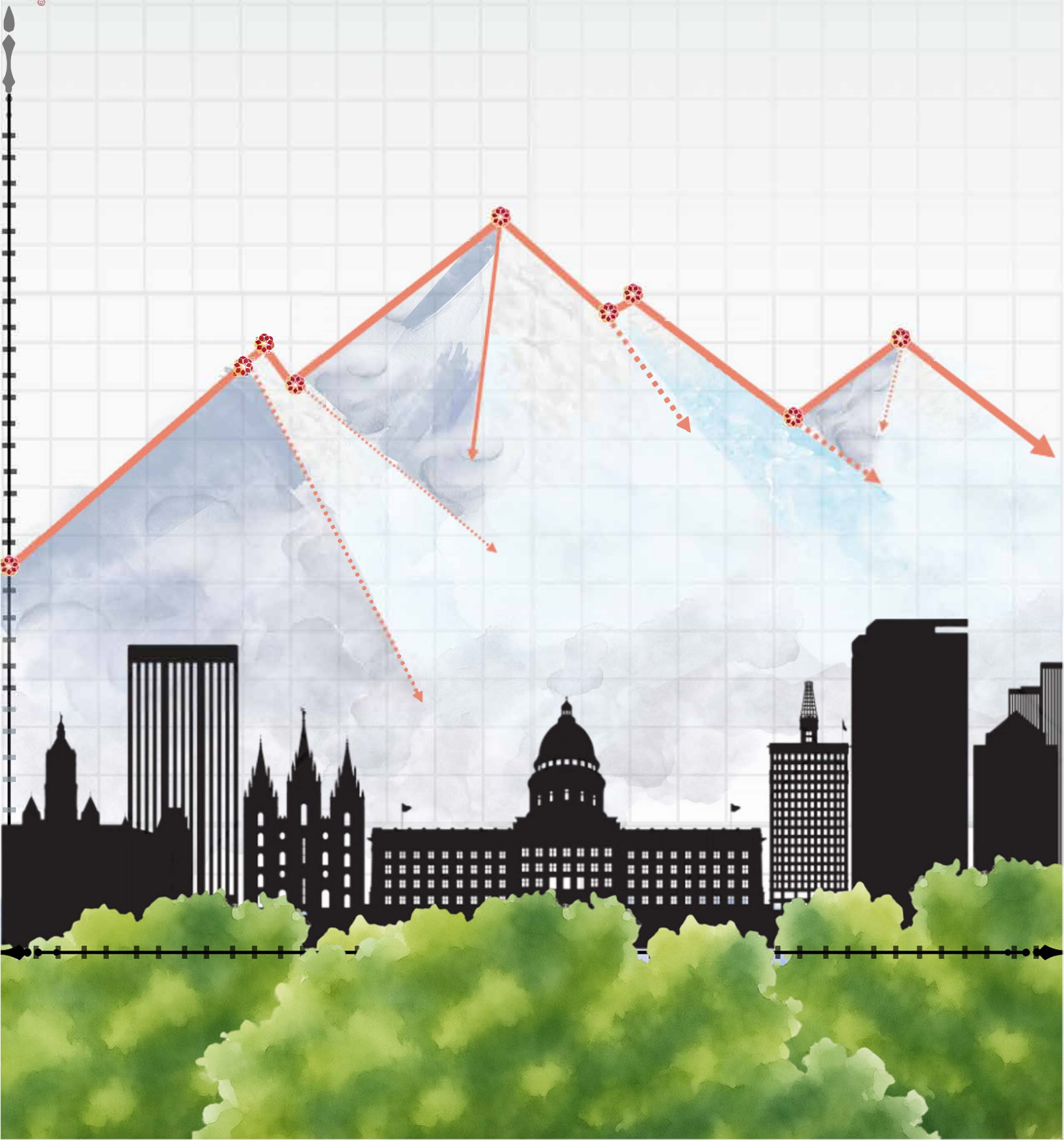


UWHR 2025

 THE UTAH WOMEN'S HEALTH REVIEW



Masthead

Volume 5 Number 1 May 2026

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Letter from the Editor

It is an honor to present the 2024–2025 issue of the Utah Women's Health Review, my inaugural edition as Editor-in-Chief.

I assumed this role with tremendous gratitude to Dr. Karen Schliep, who balanced the responsibilities of Editor-in-Chief for the past five years while continuing her work as a leading researcher in reproductive epidemiology. Her research on endometriosis and the increasing attention being paid to this condition offers a fitting example of the transformation we are witnessing in women's health. Conditions once viewed primarily through a reproductive or gynecologic lens are increasingly understood as having broader implications for a woman's health.

This transformation in how we understand women's health is happening across the field. Perimenopause and menopause are finally receiving the attention, research, and clinical care they deserve. We are increasingly recognizing pregnancy and perinatal conditions not as isolated and limited conditions, but as experiences that can shape a woman's health across her lifespan. Even the language we use to describe disease is evolving: polycystic ovary syndrome (PCOS) has recently been renamed polyendocrine metabolic ovarian syndrome (PMOS) to better reflect the condition's broader endocrine and metabolic features. These changes reflect a larger shift toward understanding women's health as interconnected across organ systems and throughout the lifespan.

I would also like to express my sincere gratitude to the entire team at the Center of Excellence in Women's Health, particularly Dr. Camille Moreno, Dr. Kathleen Digre, and Leanne Johnson. They work tirelessly to advance women's health knowl-

edge at the University of Utah and throughout the state of Utah. Their support extends far beyond this journal, encompassing the annual Center of Excellence Women's Health Conference, monthly virtual ECHO sessions that are open to all, and CRAM sessions designed to foster research collaboration and mentorship.

The 2024–2025 year brought two excellent women's health symposia to our community. The first is the Stillbirth Symposium which had a focus on health equity, both locally and nationally. Experts focused on patient-centered care and evidence-based medicine with an introduction to the toolkit from the American College of Obstetrics and Gynecology. We also celebrated the Center of Excellence Women's Health Conference, themed Innovations in Women's Health. Our keynote speaker, Dr. Missy McNeil, a renowned women's health physician and educator from Brown University, provided an engaging overview of important advances in women's health. She is a personal mentor and friend, and it was my privilege to introduce her to my new women's health community. Her presentation highlighted the latest evidence surrounding issues such as menopausal hormone therapy, osteoporosis management, and breast cancer screening, reminding us of the importance of continually translating new evidence into clinical practice.

The UWHR itself continues to grow. During this year, we published four research articles and eight data snapshots, providing opportunities to highlight both original research and important data relevant to women's health in Utah. We have also begun accepting clinical vignettes, one of the oldest and most enduring forms of medical education. In addition, we have expanded our Associate

Editor board with six new members. I am delighted to welcome Drs. Gomez-Lumbreras, Clifton, Cioletti, Neal, Jhawer, and Kroencke. The expertise and commitment of our Associate Editors, editorial team, and peer reviewers, strengthen the quality and breadth of the work we publish.

As the field of women's health continues to evolve, so too does the Utah Women's Health Review. I am grateful to everyone who has contributed to this journal and to the broader community of women's health researchers, clinicians, educators, trainees, and advocates who make this work possible.

With these exciting changes in women's health and at the Review, I invite you not only to explore this edition, but also to consider contributing your scholarship, perspectives and innovations as we continue advancing women's health together!

Vidya V. Gopinath, MD, FACP
Utah Women's Health Review
Editor-in-Chief

Women, Disrupted: Environmental, Endocrine, Emotional, Equity, & Economic Impacts on Women's Health

Symposium 2025

Visit the symposium archive at <https://uwhr.utah.edu/innovations-in-womens-health-full-recording-2025/> for video presentations and posters.

Menopause, if it's not your problem it will be: Exploring the impact of menopause on disease onset, which models we can use and why we need to study sex differences

Heddwen L. Brooks, PhD

Morning Panel Discussion

Heddwen Brooks, PhD; Erin Rothwell, PhD; & Alton Swennes, DVM

Sex-related Outcomes in Erythropoietin-Mediated Angiogenesis in an Experimental Model of Age-related Macular Degeneration

Mary Hartnett, MD

Evolutionary Responses to Environmental Change: Examples from Vertebrate History

Colleen Farmer, PhD

PRDM16 Associated cardiomyopathy: Biological Sex Matters

Sihem Boudina, PhD

Sex differences in asthma; how this disease presents differently in males versus females, and the immunology that contributes to those changes

Kristi Warren, PhD

Panel Discussion: A Changing Landscape for Obesity: Clinical and Pharmacologic Advances

Kathleen Digre, MD (Moderator);
Juliana S. Simonetti, MD; Tanya Halliday, PhD, RD;
Hanna Raber, PharmD, BCACP; & Ware Branch, MD

A New Era of Obesity Treatment

Juliana S. Simonetti, MD

New Thinking on Diet and Exercise

Tanya Halliday, PhD, RD

GLP1s for Obesity Management: Worth the Hype?

Hanna Raber, PharmD, BCACP

Overweight-Obesity: A Leading Threat to Reproduction & Health

Ware Branch, MD

Innovations in Cervical Cancer: Primary HPV Testing and Self-Collection

Deanna Kepka, PhD, MPH & Kathryn A. Maurer, MD

Utilization of Transcranial Magnetic Stimulation (TMS) in Perinatal Mood & Substance Use Disorder

Rana Jawish, MD

Innovations in Sleep

Kelly Glazer Baron, PhD, MPH, DBSM

Individualizing Menopausal Hormone Therapy (MHT): Principles and Practice

Camille Moreno, DO, MSCP

Risks vs. Benefits of MH

Makenzie Kay Daniels, PHARMD, PGY2

Clinical Utility and Safety of Compounded Bioidentical Hormone Therapy (cbHT)

Venkata (Kash) Yellepeddi, PhD

Panel Discussion: Innovations in Hormonal Care: Individualizing Your Approach

Kirtly Parker-Jones, MD (Moderator);
Camille Moreno, DO, MSCP; Makenzie Kay Daniels, PHARMD, PGY2;
Venkata (Kash) Yellepeddi, PhD

What's New in Women's Health 2025

Melissa McNeil MD MPH MACP

Stillbirth Symposium: Closing the Gaps

Symposium 2025

Visit the symposium archive at <https://uwhr.utah.edu/stillbirth-symposium-closing-the-gaps-full-record-ing-2025/> for video presentations and posters.

Introductions: What is your Why?	Susannah Leisher, PhD & Stacey Fletcher (facilitator)
Why Stillbirth Matters for Health Equity	Susannah Leisher, PhD
Impact on Parents and the Need for Equitable Bereavement Care	Stacey Fletcher
Why Health Inequities Continue in America	Richard Ferguson, MD
Introducing Some Tools for Equitable Bereavement Care	Sunayna Wahi; Naomi Riches, PhD; & Melannie Green
Case study of successful stillbirth prevention research and links to health equity and bereavement care	Ware Branch, MD
Unacknowledged Grief: Closing the Gaps in Stillbirth Bereavement Care	Dr. Kathleen Massmann
Introducing the ACOG Toolkit for Stillbirth Bereavement Care	Dr. Michael Belmonte & Sheila Reynoso, MPH
Overview of Global Bereavement Care Pathways	Susannah Leisher, PhD; Keelin O'Donoghue; Siobhan Loughnan; & Vicki Flenady
Small group work: Needs and Gaps, Resources and Strengths	Susannah Leisher PhD (facilitator)
Reporting back: Next Steps Toward Equitable Bereavement Care for Stillbirth	Bob Silver, MD
Annual Award and Closing Words	Bob Silver, MD
Closing the Gaps: Moments of Reflection	Stacey Fletcher (facilitator) & Hayley Fletcher (singer)

Background

Stillbirth, sometimes called fetal mortality, is a public health issue that spans many of the seven domains of health. However, stillbirth remains relatively undiscussed and unexplored. Even the definition is not widely agreed upon across states and nations.¹ In Utah, stillbirth is defined as a baby of at least 20 weeks gestational age being born without a heartbeat.¹

Stillbirth is particularly impactful on the emotional, social, and physical domains of health. People who experience stillbirth are at a much higher risk for depression, PTSD, and many other mental health disorders.² This decline in mental health can also result in a decrease in social well-being.² Many women who experience stillbirth report feeling isolated, as if friends and family are afraid to talk with them because they would need to confront the reality that stillbirths happen and could easily happen to us or someone we know.³ Women who experience stillbirth are also more at risk for several physical ailments later in life as well, including end-stage renal disease, hypertension, and future stillbirths.⁴⁻⁶ Stillbirth, while an outcome of pregnancy, is also a gateway to future health problems that span the physical, social, and emotional domains of health.

Worldwide, stillbirths appear to be an issue faced primarily by low-income countries, and, as might be expected, can be explained by many conditions that are prevalent in those areas (malaria, HIV, syphilis, etc.).⁷ Prevention for stillbirths includes proper nutrition, vaccination, and proper and attentive prenatal care. However, the US experiences a higher rate of stillbirths than other high-income countries, so there must undoubtedly be causes yet unexplored and unexplained that contribute to this disparity.⁷ Possible theories for

common causes of stillbirth include umbilical cord abnormalities, fetal malnutrition, and placental abnormalities.⁸⁻¹⁰ It is important to note that the definitive cause for about half of all stillbirths continues to go unexplained.¹

This data snapshot looks at critical statistics and trends affecting stillbirth and how Utah compares with the United States.

Data

One of the most interesting trends in stillbirth is the lack of decline over time. Medicine has improved immensely over the past two decades, and essential advancements continue each year. However, stillbirth rates in the United States and Utah have remained relatively stagnant over the last twenty years, seemingly unaffected by breakthroughs in medical innovation. Figure 1 compares stillbirth rates in Utah and the United States since 2000. Notably, rates in Utah have begun to fluctuate substantially since 2014 – perhaps even starting to increase despite the great variability. Though there have been significant advancements in prenatal care practices, including improved imaging, the invention of the Non-Invasive Pregnancy Test (NIPT) and other blood tests for identifying chromosomal and other genetic anomalies, and improved fetal monitoring techniques, the fact that stillbirth rates continue to plateau around six stillbirths per 1,000 births shows us that there are other more important factors at play that contribute to stillbirth.

Another interesting trend can be seen in the distribution of stillbirths across Utah, as shown in Figure 2. While Salt Lake County and Utah County have comparatively low rates of fetal mortality, the more rural

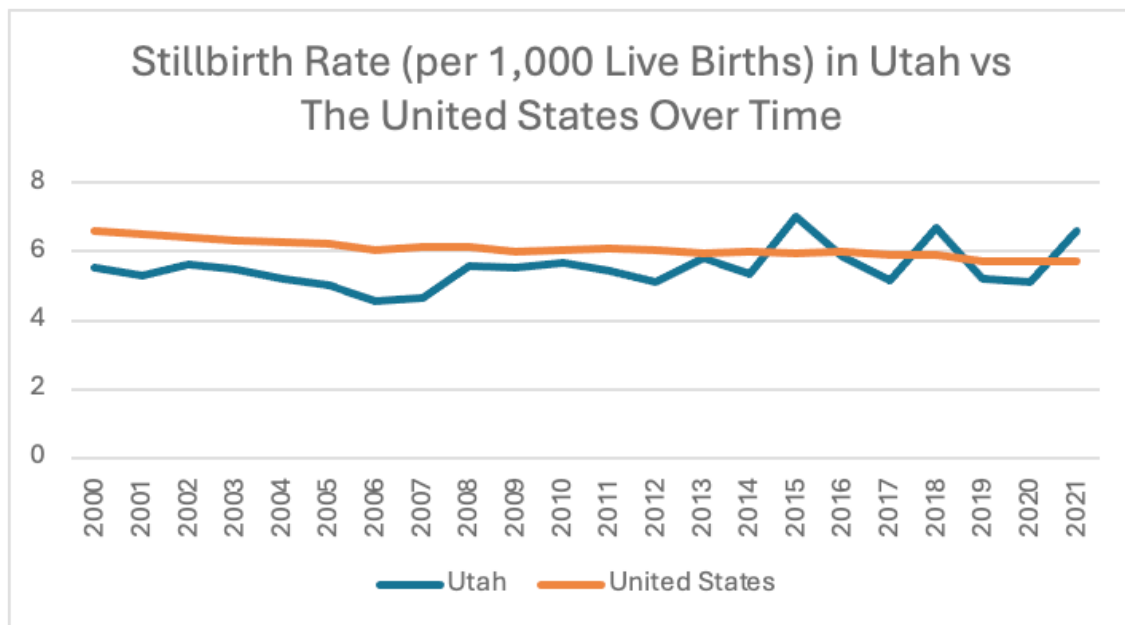


Figure 1. Trend in stillbirth rate over time in Utah (increasing) and the United States (decreasing). Data from IBIS Utah¹¹ and the CDC.¹²

areas, such as TriCounty, tend to have much higher rates of fetal mortalities. While no study defines the relationship between rurality and stillbirth rates/risk, there is a breadth of research explaining and hypothesizing the health disparities faced in rural communities. Current explanations include access to healthcare

and hospitals and a higher general incidence of disease.¹³ This trend would certainly help explain disparities in stillbirth in Utah, with many of these health areas not having any OB/GYN providers, hospitals, or birthing centers. One final but critically important trend in stillbirths is the disparity in stillbirth rates

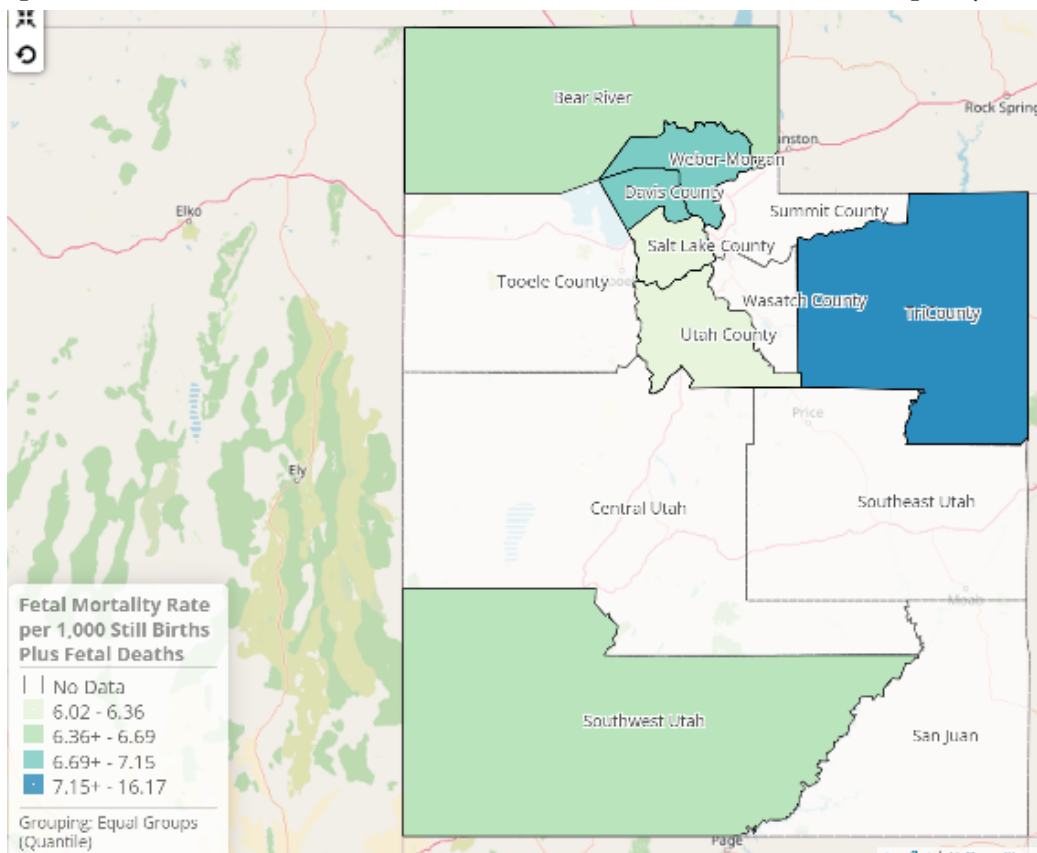


Figure 2. 2023 Fetal mortality rate per 1,000 still births plus fetal deaths in Utah separated by health district.¹¹ This is the rate of fetal mortalities per 1,000 births of any kind.

between different races. In Utah, black women are nearly three times as likely to have a stillborn baby as white women. This statistic is surprising and alarming, highlighting the effect of social determinants of health on pregnancies for black women. While this disparity has been known by researchers since 2009, to date, no studies have adequately closed this gap.¹⁴

Table 1. 2022 Stillbirth rates per 1,000 births.

	Utah	United States
Black	14.94	9.94
White	5.41	4.68
American Indian/Alaskan Native*	N/A	6.22
Asian*	N/A	3.96
Native Hawaiian or Other Pacific Islander*	N/A	10.18
>1 Race*	N/A	4.01
Not black or white (AIAN, NHOPI, Asian, or >1 Race)	4.20	4.57
Total	5.48	5.48

* <10 reported stillbirths in Utah. "Not black or white" category created to represent these races with certainty.

Calculated using stillbirth and live birth counts from CDC Wonder.¹⁵

Conclusion

The existence of disparities in stillbirth rates emphasizes that they do not happen randomly. Thus, there must be a way to prevent stillbirths – although we currently lack the knowledge to do so. Based on the data presented in this snapshot, it is apparent that the issue of stillbirth needs more research and attention.

The most significant gaps in stillbirth research are evident in the data trends presented in this snapshot. The causes of stillbirth must be better understood before evidence-based prevention interventions can be implemented. If recent medical innovations and interventions were improving the care of women at risk for stillbirth, then there would not be a plateau in stillbirth rates over the last twenty years. The underly-

ing causes of demographic disparities in stillbirth rates are also crucial to understand. Identifying care practices and treatments that women in urban areas receive that women in rural areas do not could help refine the care provided for all pregnant women, especially those living in rural areas and with more risk for adverse pregnancy outcomes. We must also understand the cultural, social, and genetic determinants of pregnancy health that explain the higher rates of stillbirth in black and other racial minority women.

In 2024, The University of Utah launched a “Stillbirth Center of Excellence,” seeking to advance stillbirth research, advocate for stillbirth-related issues, and attain higher levels of clinical care for women who have experienced or are at high risk for pregnancy loss, especially stillbirth. Research efforts include free-of-charge fetal autopsies, placental exams, and other participation in over twenty active studies seeking to understand and explain stillbirth.¹ Brave women like Stacey Fletcher lead advocacy efforts, including open support for policies to prevent and reduce stillbirths, like the SHINE for Autumn Act, and seeking to normalize the discussion around stillbirth by establishing sensitivity training and resources for all that may interact closely with women that have experienced stillbirth.^{3,16} The standard for clinical care has also risen, with the key feature of this center being a specialized clinic for “Rainbow Pregnancies” – providing prenatal care for women who are pregnant after experiencing pregnancy loss, especially stillbirth. This clinic is provided by highly trained maternal-fetal medicine physicians and midwives and seeks to provide culturally competent care combined by connecting clinical care with bereavement and mental health support.¹ While the impact of this center is yet to be seen, it is an essential first step in improving prenatal care and reducing stillbirths in Utah.

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Systematic Analysis of Factors Contributing to the Prevalence of Depression Among Women in Utah, Compared to the National Average

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Background

This data snapshot presents a comparative analysis of the mental health of women in Utah relative to the national average for women across the United States. It explores the factors that contribute to the notably higher rates of depression among women in Utah compared to the national average. The study explores key questions, including why Utah ranks higher than the national average in depression rates among women and adults, which mental health disorders are more prevalent among women in Utah than among women nationwide, and what unique factors contribute to mental health challenges faced by women in Utah.

This topic intersects with the emotional health domain of the Utah Women's Health Review. This data snapshot decisively focuses on three significant mental health disorders: anxiety disorders, mood disorders, and depression among women in Utah. The rationale for selecting these specific mental health conditions lies in their shared underlying causes and the common environmental factors that contribute to their development. Understanding these connections is essential for addressing and mitigating the impact of these mental health challenges.¹

The World Health Organization (WHO) states that “mental health is essential to overall health”. It defines health not merely as the absence of disease, but as a state of complete physical, social, and mental well-being.²

Depression, also known as depressive disorder, is a prevalent mental disorder.³ According to a systematic review, roughly 280 million people in the world (1 in 40) are experiencing depression, and depression is 50%

more prevalent in women than men. Globally, women experience depression during pregnancy and after childbirth at a rate 10% higher than women who are peripartum or postpartum.⁴

The mental health of Utah women is an important issue to consider. The state of Utah consistently ranks above the national average for depression among women. It is known that chronic diseases like high blood pressure and diabetes often coexist with mental health problems and hence lead to worsening the overall health condition.⁵

Utah Women Stat, a research snapshot, stated that increasing access to effective treatments and a better understanding of the elements surrounding mental disorders and support will enhance the good mental health of Utah women.^{6,7}

Data

Prevalence of Mental Illness in Adults: Comparison in Utah vs. Other States (2023-2024)

According to Mental Health America, Utah ranked 46th in mental health in 2023 and maintained the same ranking in 2024, indicating consistent mental health challenges over the two years (Figures 1,2). Notably, the state has consistently reported the highest rates of adults experiencing any mental illness and serious suicidal thoughts for both years. Contributing factors to these poor rankings include a lack of insurance, unmet medical needs, and the high cost of care. States ranked 22nd to 26th in 2023 and 2024 for reduced access to care, indicating a higher prevalence of mental illness.^{8,9}

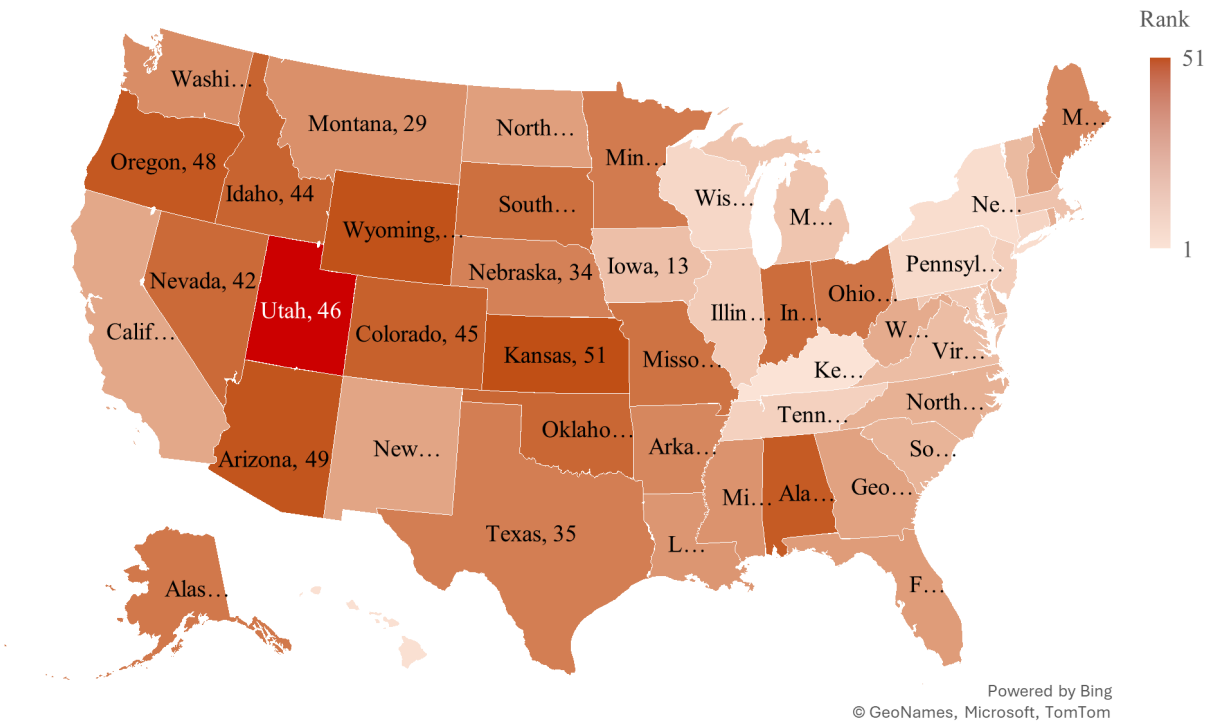


Figure 1. Prevalence of mental illness in adults by State in 2023
Source: Adapted from (Mental Health America 2023)⁷

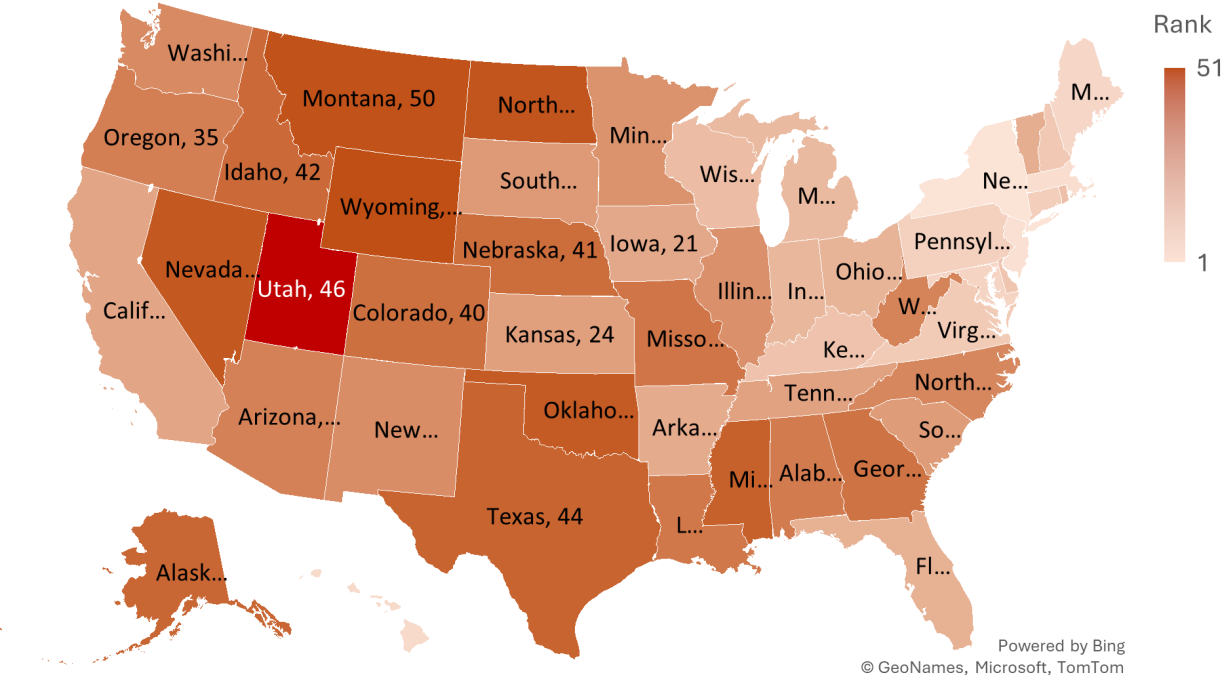


Figure 2. Prevalence of mental illness in adults by State in 2024,
Source: Adapted from (Mental Health America 2024)⁸

Note: 1. Any Mental Illness (AMI) refers to individuals who have experienced any mental, behavioral, or emotional disorders, not including developmental and substance use disorders, within the past year that aligned with DSM-IV criteria.

Source: Substance Abuse and Mental Health Services Administration 2013¹⁰

Social determinants of health, such as education, income, housing, and access to healthcare facilities, account for nearly half of an individual’s health status.¹¹ Women in Utah, compared to other women in the nation, are experiencing one of the highest gender wage gaps, with white non-Hispanic women earning 61 cents for each dollar earned by white men.¹² Women in Utah who earn less than \$25000 yearly, belong to a minority, or have a high school education or less are more likely to have poor health outcomes.¹²

The safety and security of women are also contributing factors to depression in women in Utah. For example, the experiences of Indigenous women and girls in Utah highlight a significant need for increased safety and support. A recent report by the Urban Indian Health Institute, titled “Missing and Murdered Indigenous Women & Girls,” reveals that Salt Lake City ranks among the top ten U.S. cities with cases involving missing and murdered Indigenous women and girls.¹¹

This alarming statistic underscores the ongoing challenges that many Indigenous women face in Utah, including feelings of insecurity and threats to safety in their everyday lives. Such concerns can contribute to mental health issues, including depression and anxiety, particularly related to fear of violence and vulnerability when out alone at night.¹³ Highlighting these issues is crucial for fostering a safer and more supportive environment for Indigenous women and girls in Salt Lake City. By addressing the root causes of these fears and working towards a more inclusive and equitable community, we can help improve mental health outcomes and overall well-being for women in Utah. Together, we can advocate for policy changes and community

support that enhance mental health services, promote safer living conditions, and provide greater support for women affected by depression in Utah.

Data from the Utah Department of Health show that women are more likely to experience poor mental health at every age compared to men (Table 1).

Utah women report an average of 4.2 days of poor mental health each month, compared to a monthly average of 2.7 days reported by Utah men.¹⁵ This trend indicates a significant disparity in mental health experiences between genders. One-fourth of Utah women ages 18-34 years report poor mental health for more than seven days within the last month at higher rates than men, with approximately one-fourth of women aged 18 to 34 falling into this category.¹⁶

One possible explanation for this difference between genders is the mental health conditions that are more common among women during their reproductive years.⁶ Utah maintains the highest birth rate in the U.S. (13.9 live births per 1,000 women in Utah vs. 11.0 live births per 1,000 women in the U.S.). In 2021, Utah ranked fifth in the nation for the general fertility rate. In addition, Utah’s average family size is larger than the national average (3.51 vs 3.15).¹⁷

A higher number of pregnant women and mothers may contribute to comparatively higher rates of postpartum depression in Utah women than the national average.^{18,19} Given the birthrate and household size ranking for Utah among the nation, it is important to prioritize education for new mothers to understand

Table 1. Trends in Poor Mental Health (7 or More Days) in Adults in Utah by Sex and Age
Group for the years 2015 and 2023.

Year	2015		2023	
Age Group	Women (%)	Men (%)	Women (%)	Men (%)
18–34	24.1	16.4	44.6	30.2
35–49	18.2	12.1	26.9	18.2
50–64	18.8	9.4	18.7	12.3
65+	12.8	6.9	14	8.9

Source: Adapted from Utah Department of Health 2017¹⁶ & Utah Department of Health 2023¹⁴

peripartum and postpartum depression, symptoms, and management resources.

These statistics highlight some unique challenges that Utah women may face regarding mental health, potentially linked to a social trend in higher birth rates and family size. Recognizing these patterns can help inform better mental health support and resources tailored specifically for women in Utah.

Postpartum Depression: A Prevalent Mental Health Disorder Among Utah Women

Mental health conditions, such as postpartum mood disorders during and after pregnancy, can affect individuals after childbirth.⁶ It is reported that a condition called postpartum major depression is the “most prevalent complication of childbirth and also the most prevalent perinatal mental health disorder.”²⁰ Fifteen percent of mothers experience postpartum depression, a severe condition that is different from “baby blues,” which refers to temporary emotional distress and a period of mood swings that mostly resolve within in few days or weeks of childbirth.²¹

The data on postpartum depression rates in Utah has been cited in a more recent report that Utah was ranked second highest of 26 reporting sites, with 15.3% of women who report recurring symptoms of postpartum depression.^{22,6} The Pregnancy Risk Assessment Monitoring System reports that postpartum depression affects 1 in 8 women in Utah. Furthermore, one in three women in Utah will suffer from postpartum depression, anxiety during pregnancy, or depression during pregnancy.²³ The Public Health Indicator-Based Information System (IBIS) documented that in 2022, 15.0% of Utah women reported symptoms of postpartum depression. The most recent comparative data for postpartum depression symptoms among women in Utah is from 2020. The rate of postpartum depression among Utah women was 14.9%, compared to 12.9% in 46 states.⁷

Research indicates that women in Utah are experiencing higher rates of mental health issues compared with men in the state and compared with women across the nation. These challenges are reflective of ongoing gender disparities that women face throughout various stages of their lives in Utah. According to WalletHub’s report titled “Best & Worst States for Women’s Equal-

ity,” Utah has been ranked as the worst state for women’s equality in the United States for nine consecutive years. Utah has opportunities for improvement in several key areas, including workplace environment, education & health, and income gap.²⁴ Utah state also ranks low nationally for political empowerment of women and gaps in executive positions for women. These findings highlight the potential for growth and positive change in several different aspects of society.²⁴

Good mental health is a cornerstone of overall well-being, significantly impacting an individual’s ability to function effectively. In Utah, women are particularly vulnerable, experiencing a notably higher prevalence of mental health disorders, such as postpartum depression, anxiety, and depression. This increased vulnerability is further compounded by socioeconomic factors, including wage disparities with their male counterparts and persistent gender inequalities in various sectors.

The Behavioral Risk Factor Surveillance System reported that Utah adult women are more likely to experience clinically diagnosed depression in their lifetime (32.1%) than adult Utah men in the state (16.3%).⁶ Factors contributing to these mental health challenges in women may include societal pressures, lack of access to mental health resources, and the roles women often play within family dynamics. The mental health struggles of one family member can negatively affect the well-being of the entire household.

Given the complexities of mental health challenges in Utah, it is vital to address them proactively. A complete community-wide response is required, which includes expanding access to mental health services, implementing targeted programs for women, and launching initiatives that promote gender equity. By prioritizing mental health support, we can create a healthier environment for individuals and families, ultimately enhancing the overall quality of life in Utah.

No agency has funded this data snapshot.

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The Intersection of Smoking, Mental Health, and Social Well-Being Among Women in Utah: A Data Snapshot

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Abstract

Cigarette smoking remains a leading preventable source of morbidity and death among women in the United States. This data snapshot examines the intersection of smoking behavior, mental health, and social health among Utah women, a state with unique demographic and cultural influences on health behavior. While Utah's smoking prevalence is lower than that of the country as a whole, there are disparities, most strikingly among mentally ill women. The prevalence of smoking among Utah women aged 18-44 decreased significantly from 2013 through 2022, with the largest declines among younger age groups. However, Utah women's depression rates remain dramatically higher than national rates, increasing from 34.8% in 2017-2018 to 38.7% in 2021-2022. Tobacco is also closely associated with other risk indicators, including binge drinking, asthma, and chronic diseases such as obesity and high blood pressure. Although the contributors to this trend are not fully established, this positive shift in smoking rates underscores the importance of continued monitoring and sustained tobacco control efforts. At the same time, persistently high rates of depression among Utah women call for expanded investment in mental health care, behavioral interventions, and stronger social support systems to promote women's overall well-being.

Background

Cigarette smoking is the leading preventable cause of disease, death, and disability in United States, responsible for more than 480,000 deaths annually¹, including 201,770 women.² Smoking habits among women are embedded within mental health and social-emotional well-being, a multifaceted public health concern.³ In

Utah, this connection is particularly strong due to the fact that the demographic and cultural context of this state influences smoking behavior and psychological status.⁴

Utah's population demonstrates several public health strengths. Women in the state have some of the lowest rates of tobacco and alcohol use nationwide.⁴ While the national prevalence of smoking among women in the U.S. is 11.2%, 5.9% of Utah women aged 18-44 report having smoked at least 100 cigarettes in their lifetime and currently smoke daily or on some days.² However, research indicates that individuals with mental health conditions are significantly more likely to smoke than those without such conditions.⁵ Approximately 27.2% of U.S. adults with any mental illness are current smokers,⁶ compared to 11.2% of those without mental illness, highlighting the strong association between smoking and mental health disorders.⁷

Mental health is a unique concern among Utah women, with the state having consistently ranked above the national rate for depression. Mental illness is often comorbid with chronic diseases such as hypertension and diabetes, exacerbating poor health outcomes.⁴ Recent data shows that 39.8% of Utah women ages 18-44 have been diagnosed with a depressive disorder, including depression, major depression, minor depression, or dysthymia.⁸ This measure reflects a key component of mental health burden among younger women, specifically depression, but does not include other conditions such as anxiety or bipolar disorder.⁹ Younger women, particularly those aged 18-34, experience significantly higher rates of poor mental health than the state average, with the highest rates among those who smoke, binge drink, or have asthma.⁴ This bidirectional relationship suggests that while smoking may serve as a

Table 1. Smoking Trends Among Women by Age Group and Year

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Age Group	2013-2014	2017-2018	2021-2022
	n (%)	n (%)	n (%)
Ages 18-24	650 (5.2%)	438 (3.5%)	338 (2.7%)
Ages 25-34	1225 (9.8%)	988 (7.9%)	838 (6.7%)
Ages 35-44	1438 (11.5%)	1150 (9.2%)	962 (7.7%)

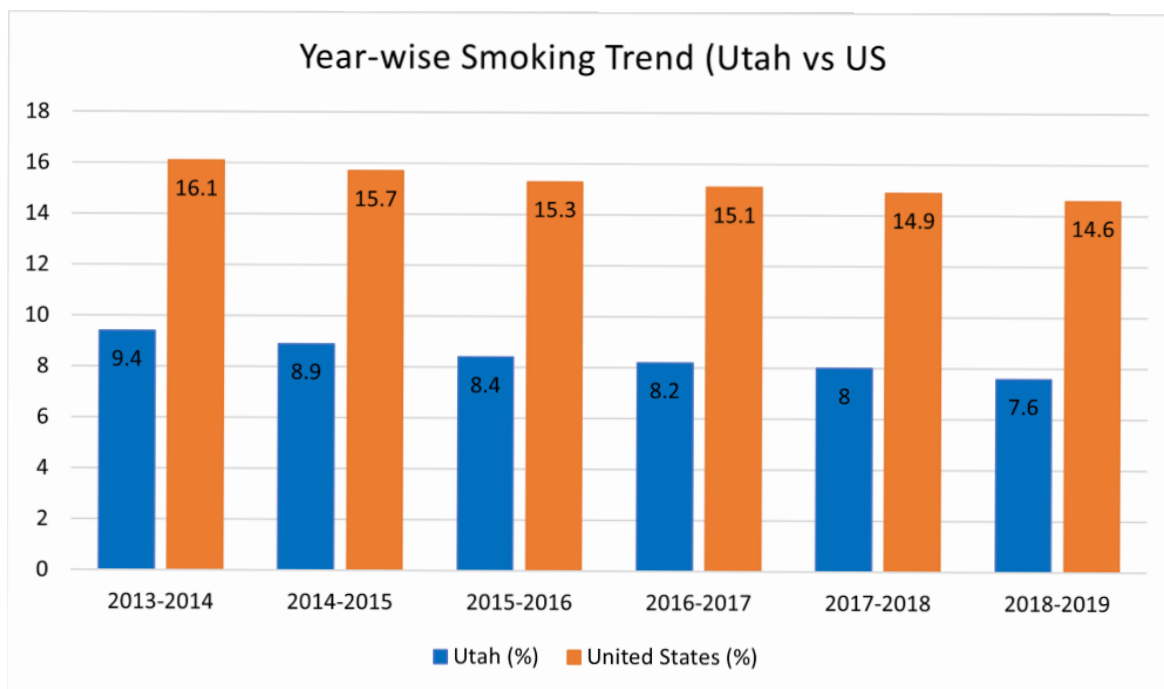


Figure 1. Year-wise Female Smoking Trends in Utah vs. the United States²

while the national rate decreased to 14.6%.

Figure 2 illustrates the trends in reported depression among women in Utah compared to the national average in the United States from 2017-2018 to 2021-2022. Depression rates among women increased steadily in both Utah and the U.S., with Utah consistently reporting higher rates than the national average. In 2017-2018, the prevalence of depression among Utah women was 34.8%, while that in the nation was 24.8%. This gap persisted as Utah's prevalence increased to 38.7%

in 2021-2022 and the national prevalence to 27.9%. Table 2 presents the prevalence of risk factors among women in Utah with poor mental health. Tobacco use was the most strongly associated factor (42.8%), followed by binge drinking (39.5%) and asthma (38.5%). Chronic conditions such as obesity (27.7%), arthritis (25.4%), diabetes (24.0%), heart disease (23.8%), hypertension (23.0%), and high cholesterol (21.1%) were also prevalent, highlighting the strong connection between mental health and chronic illness.

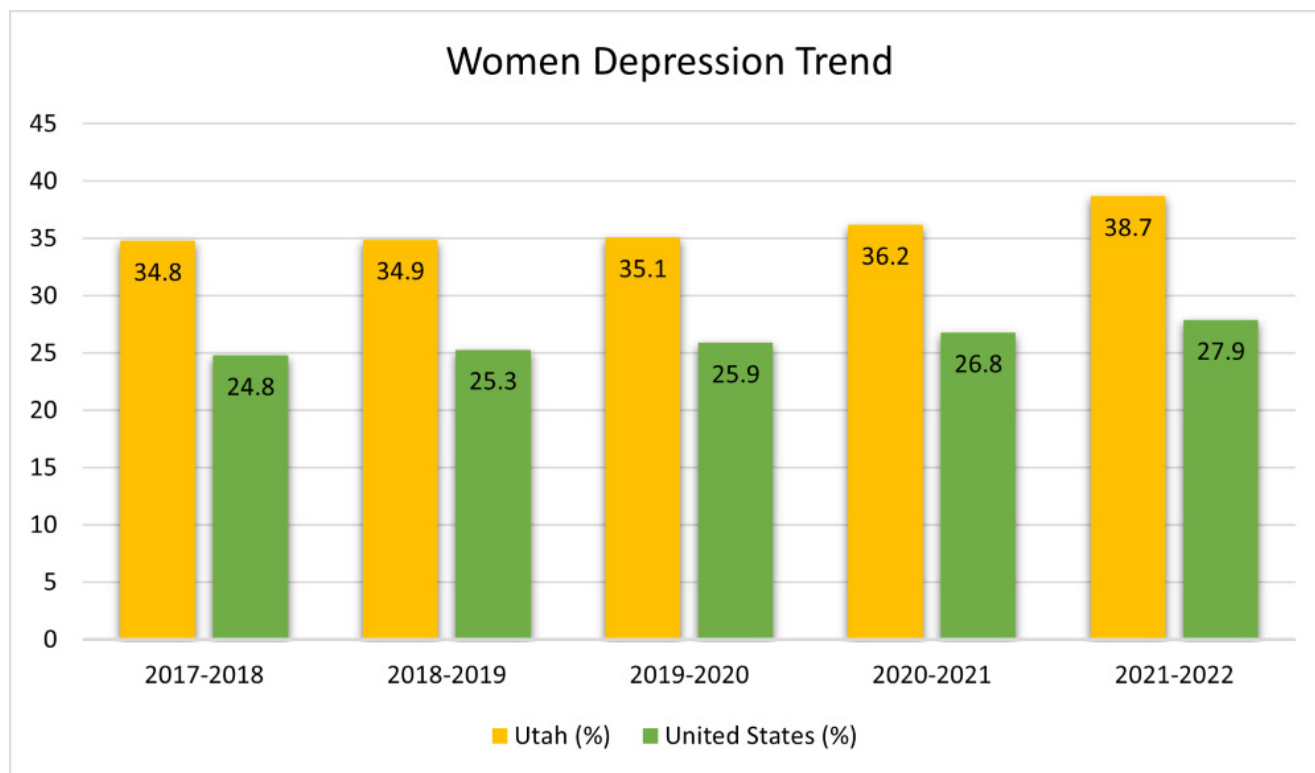


Figure 2. Year-wise Female Depression Trends in Utah vs. the United States⁸

Table 2. Risk Factors of Women with Poor Mental Health in Utah⁸

Table 2: Risk Factors of Women with Poor Mental Health in Utah ⁸

Category	Frequency	Percentage (%)
Tobacco Use	5350	42.8
Binge Drinking	4938	39.5
Asthma	4812	38.5
Obesity	3462	27.7
Arthritis	3175	25.4
Diabetes	3000	24
Heart Disease	2975	23.8
Hypertension	2875	23
High Cholesterol	2638	21.1

Conclusion & Recommendations

These findings suggest a positive trend in reduced smoking among younger women in Utah. While the causes of this decline are likely multifactorial, further investigation is needed to evaluate the potential influence of statewide tobacco control efforts. Utah's persistently elevated depression rates highlight the continued need for expanded mental health services and integrated support systems.

Recommendations:

- Expand mental health and smoking cessation programs by integrating behavioral therapy and stress management strategies tailored to women at high risk.

- Strengthen social support systems to address loneliness and chronic stress, which are linked to both smoking and poor mental health outcomes.

- Enhance targeted outreach efforts to vulnerable populations, including low-income women and those with mental health conditions, through culturally and linguistically appropriate interventions.

Funding & Conflict of Interest

No external funding was received for this study. The authors declare that there are no conflicts of interest associated with this study.

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Diabetes among American Indian/Alaska Native Utah Women

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More than 30 million Americans are currently living with diabetes—approximately 1 in every 10 people.¹ Of these cases, over 90% are classified as type 2 diabetes.² Diabetes is more prevalent within certain populations and age groups, with risk generally increasing with age. While about 10% of the overall adult population has diabetes, this figure rises to over 25% among adults aged 65 years and older.³ Historically, type 2 diabetes was most commonly diagnosed in individuals aged 45 and older. However, in recent years, it has become increasingly common among children, teens, and young adults.⁴

Type 2 diabetes is a chronic condition that affects the way the body processes glucose, the main source of energy from food. It develops when the body's cells become resistant to insulin—a hormone made by the pancreas that helps glucose enter cells to be used for energy.⁵ In response to insulin resistance, the pancreas initially produces more insulin to compensate. However, over time, the pancreas cannot keep up with the increased demand, leading to elevated blood sugar levels. Persistently high blood sugar can damage various organs and systems in the body, increasing risk of serious health problems such as heart disease, vision loss, and kidney disease.⁵

Symptoms of type 2 diabetes often develop gradually over several years and may go unnoticed for a long time. Because these symptoms can be subtle or easily mistaken for other conditions, it is important to be aware of your risk factors and consult a healthcare provider about getting your blood sugar tested. Common signs of type 2 diabetes include frequent urination, frequent and unsatisfied thirst, unexpected weight loss, uncontrolled hunger, blurry vision, numb or tingling hands or feet, unexplained fatigue, dry skin, sores that

heal slowly, and frequent infections.⁶

Type 2 diabetes is preventable through early identification of impaired glucose tolerance, healthy eating, and physical exercise.³ Better health outcomes are often achieved through close supervision and coordination of a multidisciplinary healthcare team and strong family and social support.⁷ Individuals with diabetes must also learn new habits to regulate their diabetes, including checking blood sugar regularly, injecting insulin (as needed), and monitoring blood pressure and cholesterol.

Type 2 diabetes has been a serious public health problem among American Indians and Alaska Natives for almost 40 years.⁸ Type 2 diabetes is a major cause of morbidity (such as blindness, kidney failure, lower-extremity amputation, and cardiovascular disease) among American Indian and Alaska Natives (AI/ANs) adults. Since the early 1960s, AI/ANs have been disproportionately affected by diabetes compared with other US populations.⁸

In the United States, 9.7% of adult women have been diagnosed with diabetes.¹ According to the most recent reports from the Utah Department of Health, more than 16.7% of Utah's AI/ANs population has diabetes, compared to 8.5% of all Utahns.⁹ In 2017, the Indian Health Service reported that 14.8% of AI/ANs women have diabetes.¹⁰ From 2015 through 2019, about 7.2% of female adults in Utah reported having diabetes (Table 1).¹¹ Utah AI/AN die from complications of type 2 diabetes at twice the rate of the general Utah Population (147.4 diabetes deaths per 100,000 Utah AI/ANs compared to 73.0 deaths per 100,000 Utah general Population).¹² Many of the poor health conditions that disproportionately affect the AI/ANs population are

attributed to poverty, lifestyle, genetics, and an inadequate healthcare delivery system.¹³

Utah public health agencies and local health departments partner with the National Diabetes Prevention Program (NDPP) to support diabetes prevention and management efforts across the state. NDPP offers evidence-based, low-cost community interventions designed for individuals with prediabetes, helping them reduce their risk of developing type 2 diabetes through lifestyle changes¹⁴ In addition to NDPP classes, agencies also work with primary care clinics to promote the Diabetes Self-Management Program (DSMP), known as “Living Well with Diabetes,” which provides education and support for individuals already diagnosed with diabetes. The NDPP’s mission is to help people with prediabetes to participate in affordable, high-quality lifestyle change programs to reduce their risk of type 2 diabetes and improve their overall health.

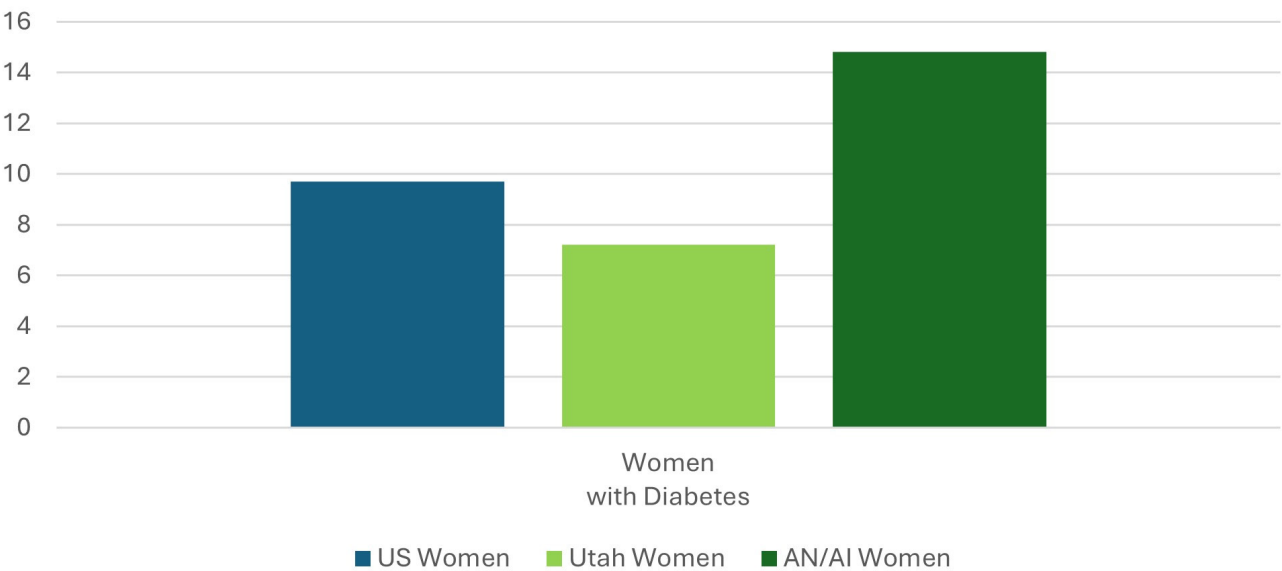
DSMP classes teach participants skills to manage their diabetes and other chronic conditions. Physical and emotional symptoms come with diabetes; this program aims to help participants effectively communicate with their healthcare providers and make healthy day-to-day decisions. DSMP has been shown to improve

hypoglycemia, depression, diet, communication with physicians, and diabetes management self-efficacy.¹⁵

Local DSMP workshops provide two trained instructors and meet once a week for six weeks. During the workshop, the topics covered include pain, fatigue, and stress management; monitoring blood sugar and managing hyper/hypoglycemia; creating an action plan to set and achieve attainable goals; problem-solving; dealing with difficult emotions and complications; physical activity and exercise; healthy eating; communication skills and working with your health care professional; and foot care.¹⁶

In conclusion, type 2 diabetes remains a major public health concern in the United States and disproportionately affecting AI/ANs women. NDPP and DSMP programs play a crucial role in helping individuals to delay or properly manage their diabetes. These programs provide tools and support to educate participants about healthy lifestyle changes. It is critical to address the social of determinants health in this population. Addressing what is known about social determinants of health can help reduce the burden of type 2 diabetes and improve the quality life among AI/ANs women.

Table 1: Percentage of Diabetes in US and Utah among Women



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HPV Vaccination and Cervical Cancer Rates – How Utah is doing compared to the rest of the US

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Abstract

Human papillomavirus (HPV) is the most common sexually transmitted infection, with nearly all sexually active individuals exposed to it at some point in their lives. While most HPV infections resolve on their own, persistent infections with high-risk strains, particularly HPV-16 and HPV-18, can lead to cervical cancer. The HPV vaccine is highly effective in preventing infections from the most dangerous strains of the virus and can reduce the risk of cervical cancer by up to 90%. Despite such convincing evidence for cancer prevention, the uptake of HPV vaccination in the US and Utah still lags behind other vaccines. As of 2023, in Utah teens ages 13-17, 61.2% of males and females are up-to-date with their HPV vaccination, increased substantially from 30.5% in 2016. Utah now matches the average percentage of up-to-date in teens in the US (61.4%). While this improvement in up-to-date status of HPV vaccination in Utah adolescents is encouraging uptake still significantly lags behind when compared to other common childhood vaccinations which have an estimated coverage percentage of >90%. Utah has many resources and initiatives aimed at improving our HPV vaccination rate.

Background

Human papillomavirus (HPV) is the most common sexually transmitted infection, with nearly all sexually active individuals exposed to it at some point in their lives. While most HPV infections resolve on their own, persistent infections with high-risk strains, particularly HPV-16 and HPV-18, can lead to cervical cancer. HPV is responsible for more than 90% of cervical cancer cases in the US.¹ Cervical cancer is the fourth most common cancer among women, with

an estimated 600,000 new cases and 340,000 deaths globally each year.² The HPV vaccine is highly effective in preventing infections from the most dangerous strains of the virus and can reduce the risk of cervical cancer by up to 90%. First available in 2006, it has been administered over 270 million times globally and has been proven to be safe and effective. The first version of the vaccine, Gardasil 4, provided protection against 4 strains of HPV. In 2014, Gardasil 9 was approved by the FDA and now covers 9 major strains of HPV and the trials leading to its approval found it to be nearly 100% effective in preventing the 6 HPV cancers.³ A recent retrospective analysis of cervical cancer mortality found an overall 62% reduction in cervical cancer mortality among women under the age of 25, corresponding with the first cohort of women for whom HPV vaccination was available.⁴ Despite such convincing evidence for cancer prevention, the uptake of HPV vaccination in the US and Utah still lags behind other vaccines. The HPV vaccine is currently recommended for all children and teens between the ages of 9 and 29, with the typical practice to start the vaccination at age 11. The vaccine is given in a 2 or 3 shot series depending on the age at which the first dose was given.⁵ This data snapshot will compare Utah's HPV vaccine rate among adolescents to that of the US as well as look at cervical cancer rates in Utah and the US.

Data

As of 2023, in Utah teens ages 13-17, 61.2% of males and females are up-to-date with their HPV vaccination. This has increased substantially from 30.5% in 2016. Utah now matches the average percentage of up-to-date in teens in the US (61.4%)⁶ (Figure 1a). While this improvement in up-to-date status of HPV vaccination in Utah adolescents is encouraging, as shown in

Figure 1b, HPV vaccine uptake still significantly lags behind when compared to other common childhood vaccinations, including meningococcal conjugate (MenACWY), tetanus, diphtheria, pertussis (Tdap),

measles, mumps, rubella (MMR), varicella, hepatitis A and hepatitis B, all of which have an estimated coverage percentage of >90%.⁶

A)

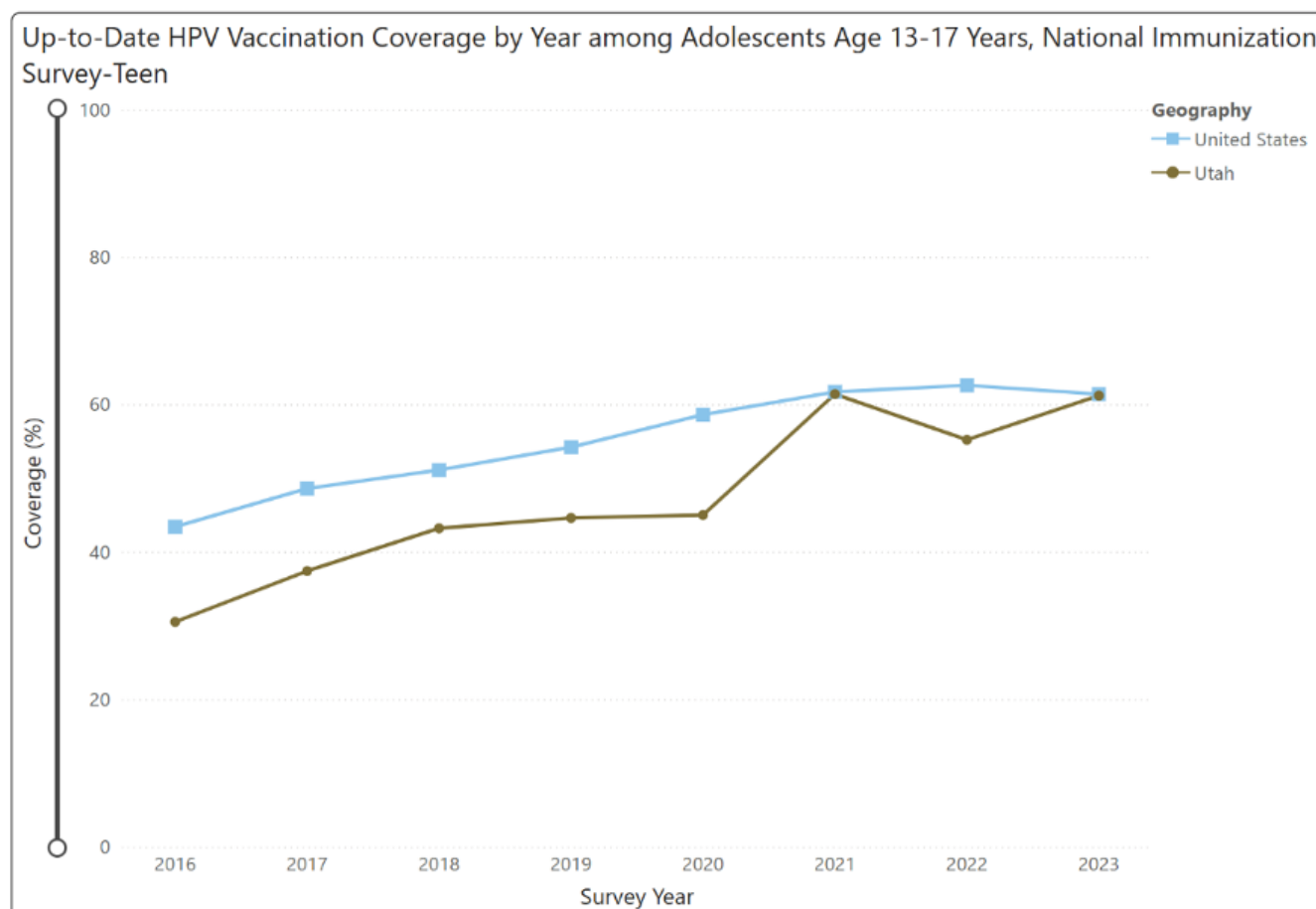


Figure 1. A) Up-to-date HPV vaccination among adolescents aged 13-17 in the US and Utah from 2016 – 2023. B) Vaccination coverage of most common childhood vaccines in Utah adolescents aged 13-17 compared to HPV Data
Source: <https://www.cdc.gov/teenvaxview/interactive/index.html> Accessed on 3/3/2025.

Given that HPV is the primary cause of cervical cancer and recent retrospective studies demonstrating an overall decrease in cervical cancer mortality in the population for whom HPV vaccination has been available⁴, it makes sense to compare cervical cancer incidence in Utah and across the United States as compared to HPV vaccination coverage. As seen in

the heat maps in Figure 2, there is generally a higher incidence of cervical cancer (darker blue) in states in which HPV vaccination coverage is lower (lighter blue). Though Utah is near the national average for HPV vaccination coverage (61.2%), it has a low incidence of rate of cervical cancer (6 cases per 100,000).^{6,7}

B)

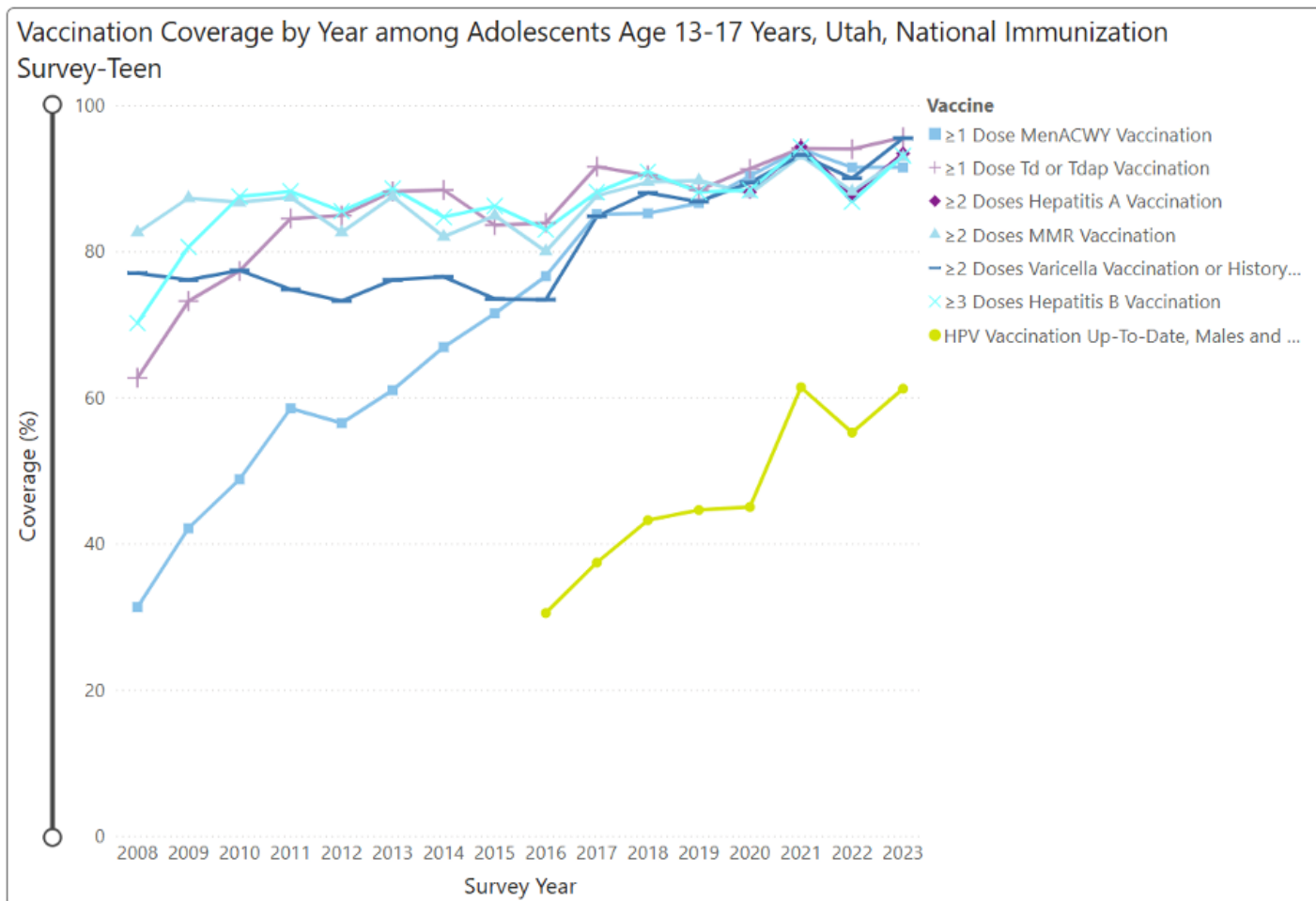
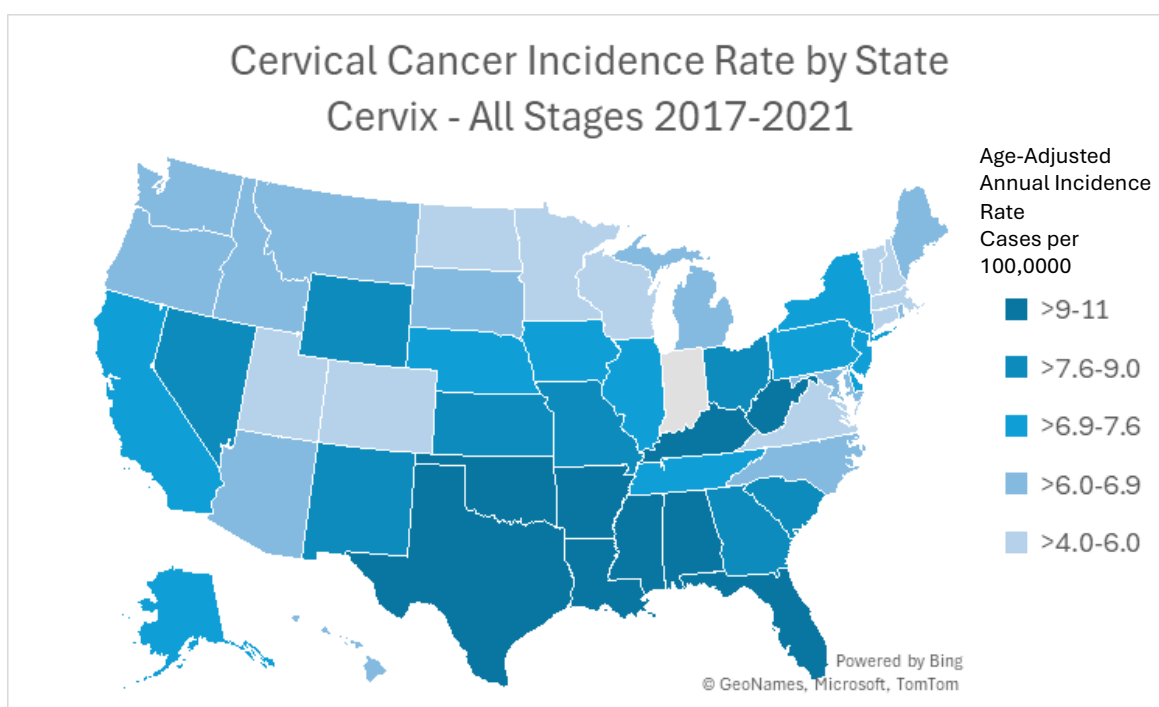


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Data Source: <https://www.cdc.gov/teenvaxview/interactive/index.html> Accessed on 3/3/2025.



Up-to-Date HPV Vaccination Coverage among Adolescents Age 13 - 17 Years, 2023, National Immunization Survey-Teen

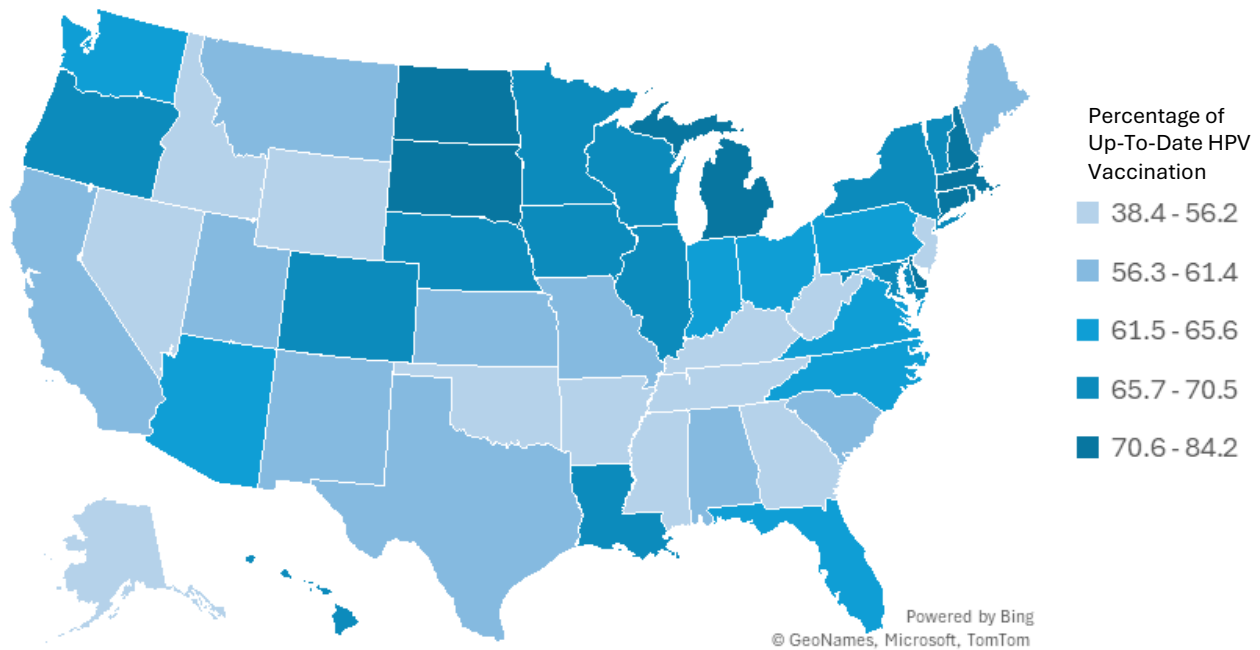


Figure 2. Comparison of state by state cervical cancer incidence rate (top) to up-to-date HPV vaccination coverage (bottom). As expected, there is an inverse correlation between cervical cancer incidence and HPV vaccination coverage. Cervical cancer incidence data obtained from National Program of Cancer Registries and Surveillance, Epidemiology, and End Results SEER*Stat Database - United States Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute. Based on the 2023 submission⁷. HPV Vaccination Coverage Data obtained from <https://www.cdc.gov/teenvaxview/interactive/index.html> Accessed on 3/3/20256.

What is Being Done?

Utah has implemented several initiatives to improve HPV vaccination rates among adolescents. Below you will find resources shared in the “Complete Health Indicator Report of Immunizations: HPV, adolescents” from the Utah Department of Health and Human Services,⁸ as well as some additional resources and research currently being done in Utah.

- **Public Media Campaigns:** The state has launched extensive media campaigns to educate the public about the benefits of HPV vaccination and its role in cancer prevention. <https://cancer.utah.gov/cancers/hpv/>

- **Intermountain West HPV Vaccination Coalition:** This coalition, encompassing members from 20 states, meets regularly to identify barriers to HPV vaccination, build partnerships, and discuss related policy priorities and research efforts. <https://healthcare.utah.edu/huntsmancancerinstitute/about-us/hpv-coalition>

- **Healthcare Provider Education:** The Utah Department of Health and Human Services, in collaboration with organizations like Utah Area Health Education Centers (AHEC), the American Cancer Society, and the Huntsman Cancer Institute, has formed a statewide workgroup focused on educating physicians about HPV vaccination and associated diseases. <https://immunize.utah.gov/hpv-information-for-the-public/> The CDC also provides toolkits and resources for physicians on talking to parents about HPV vaccinations, encouraging healthcare providers to discuss it similar to all other routine childhood vaccinations - <https://www.cdc.gov/vaccines/vpd/hpv/hcp/index.html>

- **Targeted Pilot Programs:** From July 2021 to May 2022, efforts were made to increase HPV vaccination rates in Utah’s lowest-performing health districts. Primary care clinics in regions such as Bear River, Southeast, Southwest, Tri County, and Utah County participated in tailored, evidence-based interventions to boost vaccination rates. <https://utahafp.org/how-you-can-help-increase-hpv-vaccination-rates-in-utah/>

- **Research and Grants:** The Huntsman Cancer Institute, in partnership with the American Cancer Society North Region, has been involved in initiatives aimed at increasing adolescent HPV vaccination rates across five Mountain West states, including Utah. <https://uofuhealth.utah.edu/huntsman/labs/kepka/research/grants>

Now more than ever, it is important for medical providers, public health students and employees, and defenders of women and children's health to arm themselves with evidence-backed data to share with family, friends, and representatives to keep increasing the rate of this life-saving vaccine.

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Climate change and the role of disseminated coccidioidomycosis in at-risk populations, including pregnant people

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Background

The soil-dwelling pathogenic fungus *Coccidioides* is native to the Southwestern United States and parts of South America. *Coccidioides* causes coccidioidomycosis in humans, or Valley fever (VF), through inhalation of airborne fungal spores.¹ VF is predominantly a respiratory disease, but can manifest in any organ system.² About 60% of cases are asymptomatic.³ The remaining 40% of cases present as generic respiratory symptoms that are reminiscent of other respiratory diseases (like CAP – community-acquired pneumonia), such as cough, shortness of breath, night sweats, and chest pain.^{1,3-5} In a minority of cases, VF can have more serious complications such as pneumonia or death.¹ Severe VF cases can be characterized by disseminated (extrathoracic) involvement or serious respiratory complications, posing a serious risk of morbidity and mortality to immunocompromised and pregnant patients.^{3,6,7} Disseminated conditions involving the skin, bones, joints, and central nervous system, such as meningitis, have been documented.⁸

While *Coccidioides* has been historically associated with regions in the Southwestern United States, recent research linked the fungus and its ability to flourish in a specific geographic area with the changing climate. *Coccidioides* grows well in wet soil and can quickly break into easily inhaled spores once that soil dries and becomes airborne. *Coccidioides* is very susceptible to changing climate patterns involving increased precipitation followed by significant dry periods.^{9,10,11} These trends are reflected by climate change, and in real-time, the fungus has been able to migrate and extend its range of endemicity further north. Recent studies have started to document this phenomenon, including outbreaks in Northern Utah, Washington,

and Oregon, beyond the traditionally associated area of endemicity.^{12,13,14,15} The changing endemic range will inevitably expose novel hosts to a pathogenic fungus that can cause serious death and disease.

The concerns indicated by modeled predictions of the extension of *Coccidioides*'s endemic range are also reflected in the changing incidence of the disease Valley fever. The CDC reported only 2,271 cases in 1998. However, 21,171 cases were reported in 2023 (Figure 1).^{16, 17, 18} Though only 20,000 cases are reported annually in the US on average, this case burden is likely a severe underrepresentation of the true caseload.²⁰ The CDC reported the true estimated burden of VF in the US is likely 206,000 – 360,000 symptomatic cases annually.^{1,19, 20} This value is roughly “10-18 times higher than reported”, and the CDC also estimates the true death burden to be “5-6 times higher than reported.”²⁰ As the endemic zone for this fungus spreads, novel hosts will suffer undue consequences. Populations with a disproportionate risk of developing disseminated disease will suffer irreversible effects, and therefore, resources should be directed toward understanding not only the changing ecology of the fungus but also the clinical manifestation of the disease, and factors that complicate receiving a diagnosis.

VF can be mild, but for those who have an immunocompromised status, such as HIV, recent organ transplant patients, or pregnancy status (and others), the risk of acquiring the severe disseminated disease is heightened. The heightened risk of severe disseminated disease in pregnant women is relatively poorly understood but may involve the role of Th2 (type 2 helper T cells) and immunity required for a healthy fetus.^{16,21} In geographic areas where *Coccidioides* is endemic, the fungus may impact as many as 1 in 1,000 pregnant

patients, according to several reports, although this trend can vary depending on geographic region.²²⁻²⁴ Recent studies have reported that pregnant people who develop the disease later in their pregnancy are at higher risk, including the postpartum period.^{6,16,25-27} Pregnant people are not regularly screened for Valley fever, even in endemic areas. Clinical guidance does not suggest a need for regular screening during prenatal care.⁶ However, some experts suggest incorporating serologic screening for pregnant patients in endemic areas.²⁸ Additionally, VF can reactivate and progress to disseminated disease upon novel immunocompromised status, even if the initial infection was mild.¹ The primary treatment against the fungal infection, specifically Triazoles, can be teratogenic and increase the risk of spontaneous abortion, although it's only traditionally avoided during the first trimester.^{6,8,26} Infrequently, VF has also been reported to impact the fetus via disease transmission from the mother.^{24,29} Therefore, due to the imposing risks of a changing climate and a potentially severe pathogenic fungus, the detection process and effect of VF in pregnant women should be studied to reduce detriment to the physical and envi-

ronmental health of pregnant women in the Western United States.

Data

The previously established endemic region of *Coccidioides* only extended to southern Utah. However, due to a recent outbreak in Dinosaur National Monument (Northern Utah) and modeled predictions of the impact of climate change on *Coccidioides*, concerns for an increase in underreported incidence in Utah are well-founded. In an attempt to understand how Valley fever incidence may be changing in Utah, the NNDSS (National Notifiable Diseases Surveillance System) was accessed for Utah Valley fever case rates. This data only ranges from 2016 to 2022; however, the CDC published case reports for combined states, including Nevada, New Mexico, and Utah, which are represented in Figure 2. Figure 3 further elucidates the shorter trend for each separate state but does not include numbers for 2023. It is clear that US cases are increasing, and there is a significant case burden in New Mexico, Nevada, and Utah. Any fluctuations over the course

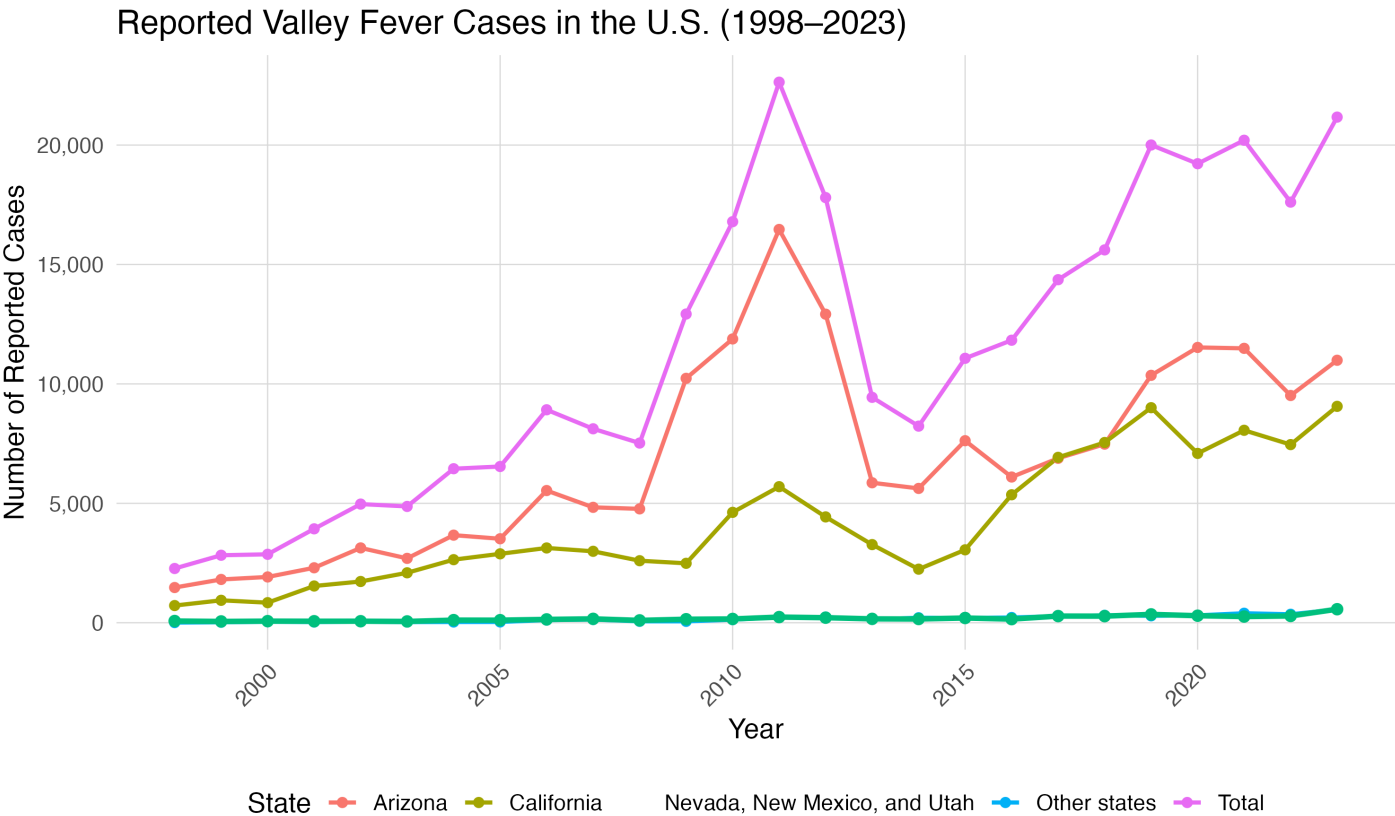


Figure 1. Valley fever case numbers from 1998 – 2023, graph created and published by the CDC²⁰

of time could be attributable to the impact of the COVID-19 pandemic on Valley fever case reporting, and previously described environmental fluctuations related to precipitation. Despite this limited data, based on previous reports from the literature, it is likely that Figure 2 is an underrepresentation of the true case burden of Coccidioidomycosis in Utah, as well as Nevada and New Mexico. Further analysis should be undertaken to examine the true case burden of Valley fever in Utah, with a specific emphasis on pregnant and other immunocompromised individuals due to the increased

risk of severe disease to that patient population.

Valley fever is hard to diagnose because it consistently masquerades as other common respiratory disorders, and patients are unlikely to seek medical care if their symptoms are mild. Additionally, because this disease is environmentally acquired, knowledge of VF prevalence and, therefore, clinical intent to test for VF decreases as the distance from traditionally endemic areas increases.

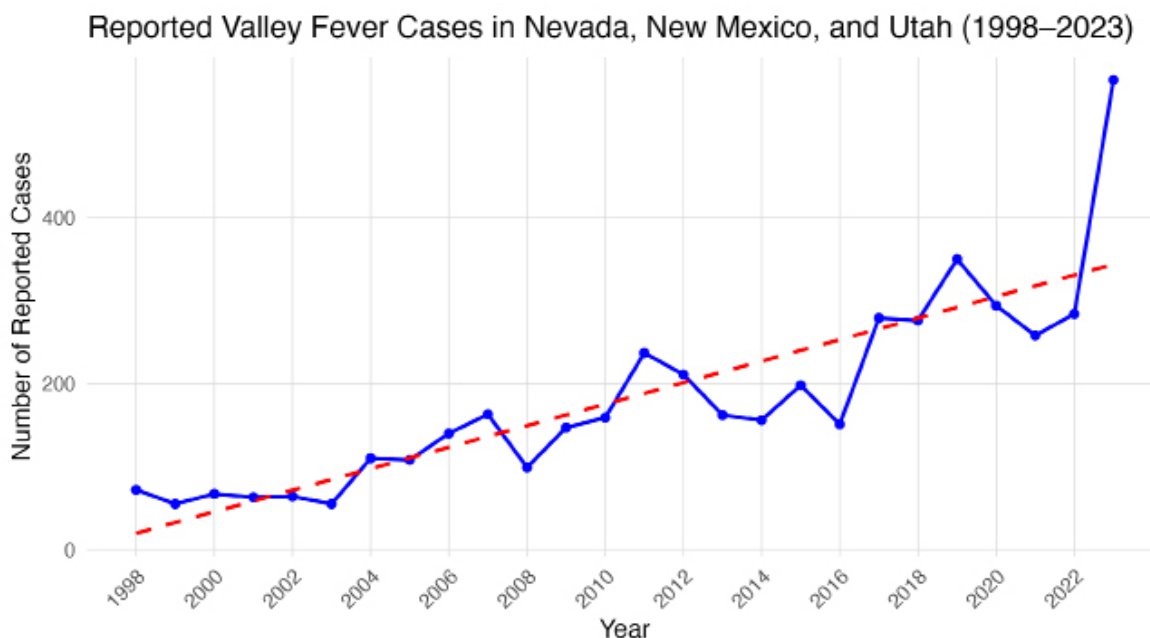


Figure 2. A comparison between the US and Utah VF cases from 2016 to 2022³⁴

*Data was pulled from the NNDSS and analyzed using SAS.

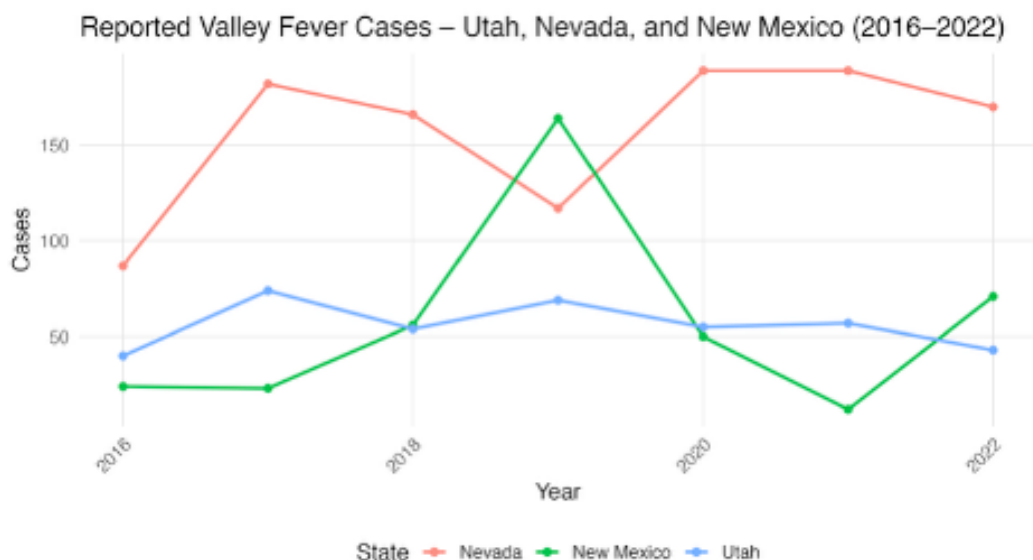


Figure 3. Valley fever case numbers from 2016 – 2022, data accessed from the CDC NNDSS.³⁷

One study reported that a high number of VF cases present in clinics outside of the area where the disease was initially acquired.²² This highlights the need to investigate issues with diagnosis, such as delayed or missed diagnosis, in the light of at-risk populations like pregnant people. The increased susceptibility of pregnant patients, the potential for delayed or misdiagnosis, and the adverse effects of treatment makes this population important to study with regard to this disease.

An important first step for overcoming diagnostic delay is to quantify that delay and identify geographic areas where it occurs most frequently for targeted interventions. There have been few efforts to quantify diagnostic delay, especially outside of endemic areas. Table 1 describes several papers published between 2001 and 2023 that directly quantified diagnostic delay or made an important commentary. Interestingly, only 1 of these studies actively mentioned pregnancy, high-

lighting the need to further investigate not only the role of diagnostic delay in VF cases but also how this coincides with pregnant VF patients.

Without future research attempting to quantify the spread of disease and a greater understanding of how VF may impact pregnant patients and others, the consequences will continue to unfold in a disproportionate manner in at-risk populations. This problem is best addressed by first determining where VF cases are being underreported. This can be recognized by understanding locations with the highest burden of diagnostic delay. Miller 2023 presents a framework for understanding the frequency, duration, and risk factors for diagnostic delay.³⁰ This approach could be used on Valley fever with a focus on disseminated cases and VF in pregnant patients. Finally, this information should be utilized to improve treatment methods for VF patients and reduce the diagnostic delay that costs extreme disseminated cases their lives.

Table 1. A review of 6 studies that studied the diagnostic delay in Coccidioidomycosis (2001 - 2023)

*RA = Retrospective analysis of patient reports.

Study ID	Time period	State	Delay definition	Delay quantified	Pregnancy mentioned?
1 GINN 2019 (31)	2011–2014	Phoenix, AZ	“Time between seeking care for cocci and receiving diagnosis”	46% received diagnosis within 1 month of seeking care; 54% within 1–6 months	No
2 DONOVAN 2019 (32)	2015–2017	Tucson, AZ	“Time between initial evaluation and diagnosis date (diagnostic delay)”	246 had delayed diagnosis >1 day; median delay 23 days (43% of patients)	No
3 BENEDICT 2018 (33)	2016	14 states	“Time from seeking healthcare to diagnosis”	Median 38 days (range 1–1,654 days)	No
4 DESAI 2001 (34)	1975–1998	Cleveland, OH	“Delay between presentation and diagnosis”	Median 3 months from symptom onset (range 4 weeks–14 months)	Yes
5 CHI 2020 (35)	2011	Southern CA	“Antibiotic received prior to cocci diagnosis date (as a marker of pre-diagnosis treatment)”	70% received antibiotics in the 3 months before 1st positive test; 36% received antibiotics in the 3 months after	No
6 POLICEPA TIL 2023 (36)	2010–2022	Central Valley CA	“Time from symptom onset to diagnosis”	Mean 12 weeks (IQR 8–16 weeks)	No

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The Impact of Maternal Race and Ethnicity on Adverse Birth Outcomes: A Data Snapshot

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Introduction

Infant mortality in the US is frequently caused by adverse birth outcomes, particularly by low-birth-weight (LBW) and preterm births (PTBs).¹ In 2021, the United States (US) recorded its highest PTB, accounting for 10.5% of all live births, which was only 4% in 2007.² These outcomes are shaped by a complex interplay of maternal risk factors, including health behaviors, exposures to acute and chronic stress, access to healthcare, and the availability of financial and societal resources.³

Importantly, substantial disparities in LBW and PTB persist across racial and ethnic.⁴⁻⁹ PTB rates among non-Hispanic Black women have been reported to be approximately 50% higher compared to non-Hispanic white (NHW) women.² Notably, well-educated and high-income Black women in the US still experience two-fold adverse birth outcomes comparable to or worse than those of white women with fewer resources, underscoring how deeply race and social status are intertwined in shaping maternal and infant health.^{10,11} American Indian/Alaska Native populations also experience disproportionately high rates (13%) of PTB compared to the US national average (11.4%).¹²

Preterm delivery was linked to 68% of newborn fatalities between 2017 and 2021, which continues to be the major cause of infant mortality and is linked to increased risks of long-term illness.¹³ In 2022, conditions associated with LBW and short gestation were responsible for 14.0% of baby deaths.¹⁴ Even while there is clear evidence of significant differences between states, limited research has looked at how these patterns show up in states with different racial and ethnic groups, like Utah. To create focused, culturally relevant interven-

tions that address the underlying causes of unfavorable outcomes, it is imperative to comprehend Utah-specific trends. Given prior evidence of the influence of race and ethnicity on PTB/LBW, this study set out to describes Utah's unique race/ethnicity makeup in comparison to the US as a whole, as well as in relation to adverse pregnancy outcomes experienced by Utah mothers. Findings from this data snapshot can inform future work in Utah investigating the multiple risk factors associated with adverse pregnancy outcomes, such as lifestyle and socioeconomic status, taking into consideration race and ethnicity as potential effect modifiers.

Methods

Data accessed for this analysis included PTB, defined as deliveries prior to the 37th week of pregnancy, and LBW, defined as a newborn weighing less than 2,500 gm.¹ The US data source was: National Vital Statistics System, National Center for Health Statistics, U.S. Centers for Disease Control and Prevention. Additionally, the Utah data source was the Utah Birth Certificate Database, Office of Vital Records and Statistics, Utah Department of Health and Human Services. Both of the data sources were obtained from the Utah Department of Health and Human Services' Indicator-Based Information System for Public Health (IBIS-PH).¹³ These publicly available platforms provide standardized, population-level health data for the state of Utah in addition to the US as a whole. PTB by mother's race/ethnicity and LBW by mother's race were accessible and utilized for comparisons at the state and federal levels for the year 2023. On the other hand, due to limited availability, LBW by mother's ethnicity data were taken from the year 2020 for Utah and 2019 for the US.

Results

Overall, Utah’s PTB rate in 2023 was 9.4% compared to the US PTB rate of 10.4% (Table 1). PTB rates varied across racial groups in Utah. Native Hawaiian/Pacific Islander and Black/African American individuals experienced the highest rates, at 11.5% and 11.1%, respectively, while White individuals had the lowest rate at 9.1%. Other groups, including American Indian/Alaska Native (10.5%), Asian (10.4%), and those of

multiple races (9.6%), fell in between.

Regarding ethnicity, the US national preterm birth rate was 10.4%, while Utah Hispanic/Latino mothers had a PTB rate of 10.3%, and Utah non-Hispanic/Latino mothers had a slightly lower rate of 9.1%. Moreover, those with unknown ethnicity had the highest PTB rate at 14.2% (Figure 1).

Table 1. Preterm Birth by Maternal Race among Utah and the US Population in IBIS-PH 2023 Data

Utah Maternal Race	Preterm Birth (%)
American Indian/Alaska Native	10.5
Asian	10.4
Black, African American	11.1
Native Hawaiian, Pacific Islander	11.5
White	9.1
Other	10.6
Two or more races	9.6
All races	9.4
US	10.4

Figure 1. Preterm Birth by Maternal Ethnicity among Utah and the US Population in IBIS-PH 2023 Data

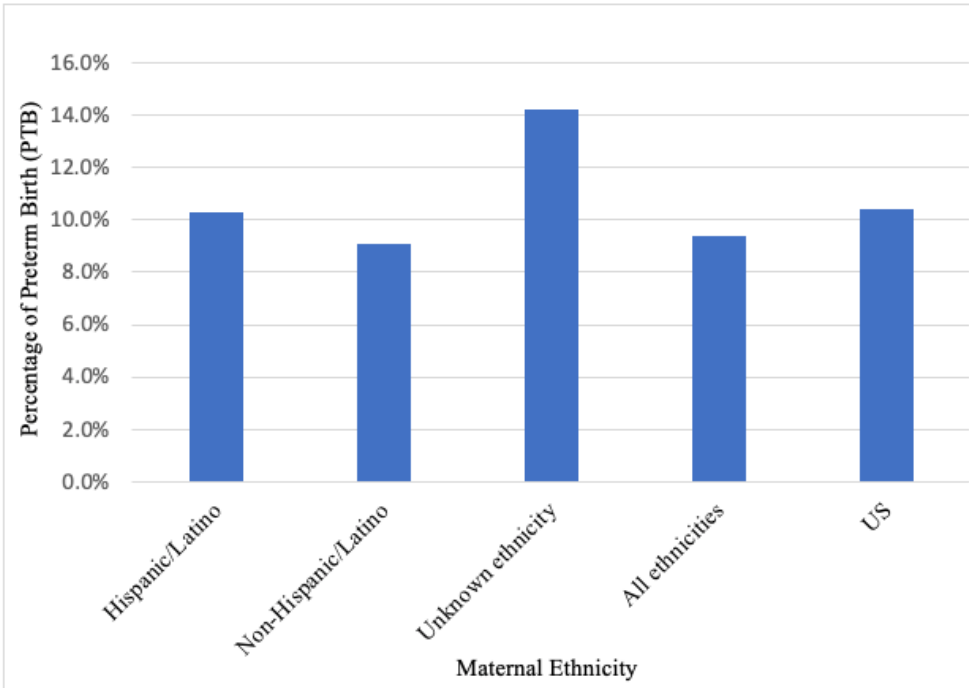


Table 2. Low Birth Weight by Maternal Race among the Utah Population in IBIS-PH 2023 Data

Utah Maternal Race	Low Birth Weight (%)
White	7.0
Black or African American	11.8
American Indian or Alaska Native	8.7
Asian	11.3
Native Hawaiian/Pacific Islander	6.9
More than one race	7.0
Other racial entries	8.6

Figure 2. Low Birth Weight by Maternal Ethnicity among Utah (2020) and the United States (2019) in IBIS-PH Data

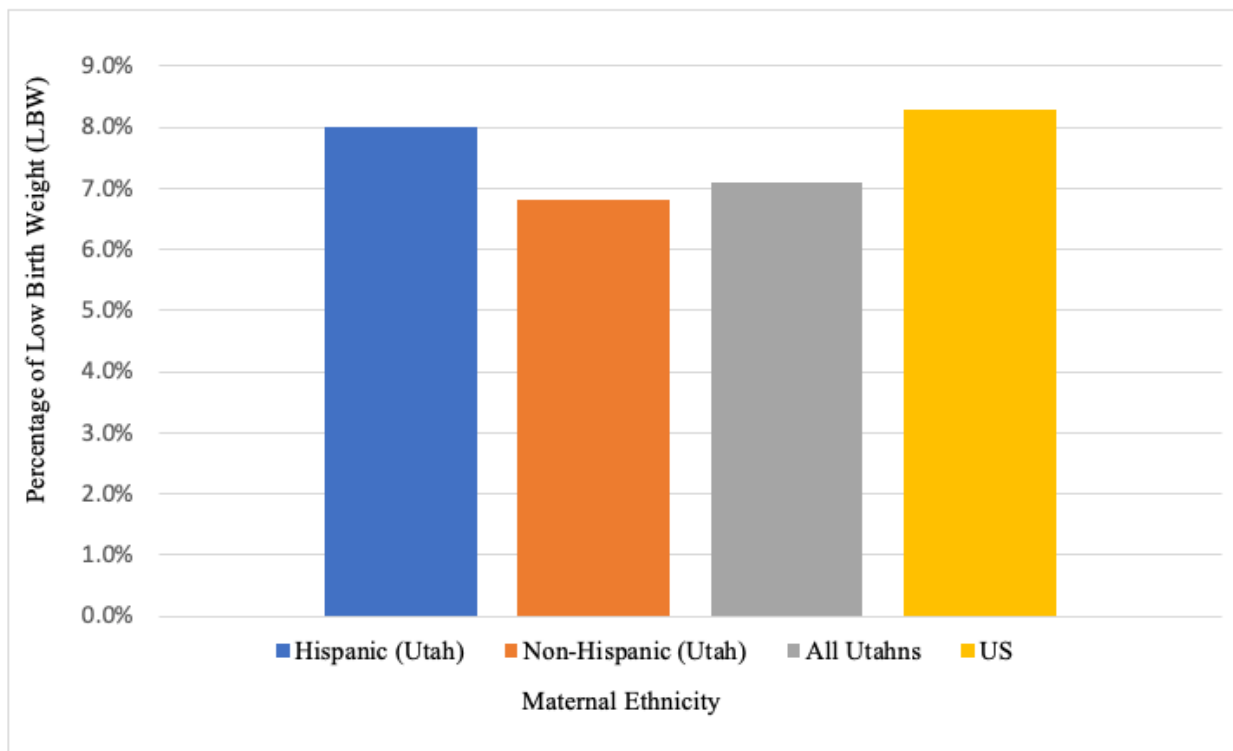


Table 2 identified that Black or African American and Asian individuals in Utah experienced the highest rates of low birth weight (11.8% and 11.3% respectively), while Native Hawaiian/Pacific Islander individuals had the lowest rate (6.9%). American Indian or Alaska Native mothers also showed an elevated rate at 8.7%, as did those categorized under “Other racial entries” at 8.6%. White mothers reported 7.0% and mothers identified as “More than one race” experienced a similar

LBW rate of 7.0%.

The overall LBW rate for all Utah mothers was 7.1% in 2020, which was lower than the US national rate of 8.3% in 2019 (Figure 2). Utah Hispanic mothers had a low-birth-weight rate of 8.0%, which was higher than the 6.8% observed among Utah non-Hispanic mothers.

Conclusion

This study highlighted notable disparities in PTB and LBW across racial and ethnic groups in Utah. Black, African American, and Native Hawaiian/Pacific Islander mothers experienced higher rates of PTB compared to White mothers, who had the most favorable outcomes. PTB rates also varied by ethnicity, with the group classified as having unknown ethnicity showing the highest rate, while non-Hispanic/Latino mothers had the lowest.

Overall, Utah's LBWs were better than the national average. Nonetheless, compared to their non-Hispanic counterparts, Hispanic mothers had somewhat greater rates of low birth weight, highlighting persistent inequalities.

These trends imply that a wide range of factors, such as socioeconomic status, maternal education, access to healthcare, and the cumulative consequences of racism and discrimination, may affect birth outcomes. Targeted public health measures are urgently required, as evidenced by the increased risks of PTB and LBW and their severe consequences for infant survival and long-term health. Improving mother and child health requires addressing persistent inequalities through better housing, education, and culturally competent prenatal care. Additionally, data specific to Utah highlight the value of local surveillance as well as tailored approaches to meet the particular requirements of varied populations and lessen avoidable differences in birth outcomes.

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Epilepsy Folklore Belief is Prevalent in Hispanic/Latinx Patients with Epilepsy, Though May Not Be a Barrier to Accessing Care

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Abstract

Objectives: To investigate whether epilepsy folklore, the belief that epilepsy is caused by supernatural phenomena, is a barrier to accessing neurologic care in the Hispanic/Latinx community and, if so, to what degree.

Methods: In this single-center cross-sectional study, adults were selected who self-identified as Hispanic/Latinx with a diagnosis of epilepsy as determined by an epileptologist at our center and ICD-10 code. Participants were approached during their scheduled visits and consented to complete a unique survey in Spanish or English. Study survey measures included assessment of belief in epilepsy folklore, barriers to healthcare, standard clinical data, Epilepsy Stigma Scale, and Medication Adherence Rating Scale.

Results: A total of 43.3% of the 30 participants enrolled in the study endorsed a belief in epilepsy folklore. 13.3% of all participants indicated that a belief in folklore was an important or very important factor in their decision whether to establish care with a neurologist. Although prevalent, folklore belief did not appear to cause a delay in accessing care. The top two barriers to care were “lack of health insurance” and “stigma.”

Conclusions: While generalized conclusions cannot be made due to the small sample size and self-report bias, these findings suggest that a belief in epilepsy folklore is common in Hispanic/Latinx patients with epilepsy; however, lack of insurance may be a larger barrier to care.

Implications: It is imperative for healthcare providers to recognize and address healthcare disparities, devel-

op educational initiatives, and provide more culturally informed care to patients in their preferred language.

Introduction

Epilepsy is a chronic and socially-isolating neurologic condition that affects an estimated 2.3 – 4 million people in the United States alone.¹⁻³ Although data is limited, there are approximately 363,000 Hispanic/Latinx persons in the United States with a diagnosis of active epilepsy, defined as current use of an anti-seizure medication (ASM) and/or who have had a seizure within the last 12 months.³ There are an estimated total of 605,000 Hispanic/Latinx persons living in the United States who have ever been diagnosed with epilepsy.³

Not only is epilepsy a very prevalent disorder, but it is also associated with increased mortality. The consequences of untreated seizures can be devastating, including structural damage to the brain, accidental death, suicide, sudden unexpected death in epilepsy (SUDEP), and respiratory failure.^{4,5} As such, it is important to diagnose patients who meet criteria for epilepsy as soon as possible. Since approximately 70% of patients with epilepsy will respond to an ASM, it is critical to avoid delays and initiate treatment immediately.⁶

In the Hispanic/Latinx community, there are multiple barriers for patients to receive appropriate medical care, thereby resulting in treatment delays. Lack of health insurance, inability to take time off from work, language barriers, and difficulties navigating the complex medical system, particularly specialty services such as Neurology, all impede one's ability to access appropriate medical care.⁷⁻⁹ Another barrier for Hispanic/Latinx persons to receive appropriate medical care for epilepsy is a lack of understanding of the disorder.

Studies have shown that many Spanish-speaking adults report no familiarity with epilepsy.⁹ This lack of familiarity with the disorder alone creates a barrier, as one would not seek treatment for a condition that they do not recognize. Even if patients do accurately identify the medical condition, shame and fear of providers' potential lack of understanding of culturally complex topics like stigma may also influence their decision whether to seek care.

Studies have shown that a sizable portion of Spanish-speaking adults agree that appropriate treatment options for epilepsy include avoiding stress, eating healthy meals, exercising, taking vitamins, and using herbal remedies.⁹ While these lifestyle modifications are important for any person, they are not included in recommended practice guidelines.^{10,11}

Another potential barrier to accessing neurologic care in the Hispanic/Latinx community, which has not been well-studied, is epilepsy folklore. Epilepsy folklore is the belief that epilepsy is caused by supernatural forces. Based on the current literature, paranormal beliefs about epilepsy that exist in the Hispanic/Latinx community may hinder one's ability to establish care with a neurologist, which is further complicated by the stigma associated with the condition.^{6,9,12} Bolstering these results, the Epilepsy Foundation of San Diego (EFSD) pilot survey illustrated that the majority of Hispanic/Latinx persons misattributed the causes of epilepsy, believing that spiritual forces or moralistic failings were responsible.⁸ A belief in epilepsy folklore has been correlated with decreased adherence to an ASM regimen.¹³ However, the degree to which epilepsy folklore acts as a barrier to accessing neurologic care, especially when compared to other known barriers to care, has never been directly assessed.

This pilot study sought to determine the extent to which epilepsy folklore acts as a barrier to accessing neurologic care for Hispanic/Latinx persons with epilepsy. Thus, the first aim of this project was to quantitatively determine the extent to which a belief in epilepsy folklore influences the decision of a Hispanic/Latinx person with epilepsy to seek medical treatment for their epilepsy, defined as establishing care with a neurologist and initiating an ASM. Moreover, the second aim of this project was to qualitatively determine the role that epilepsy folklore plays in how individuals with epilepsy are perceived.

Methods

This study was approved by the Institutional Review Board of the University of Utah, IRB_00149212 on 10/10/2022. In this cross-sectional pilot study, we identified adults aged 18-65 years old at the University of Utah through an electronic data pull who self-identified as Hispanic/Latinx with a diagnosis of epilepsy, which was determined by an epileptologist at our center and ICD-10 codes in patients' medical records. Exclusion criteria included cognitive impairment or mental illness that would impair one's ability to provide informed consent to participate in the study, non-Latinx or non-Hispanic heritage, and/or a diagnosis of psychogenic non-epileptic seizures without a concurrent diagnosis of epilepsy. The data pull identified all patients meeting these inclusion criteria that were already established in the university system. Participants were approached during their regularly scheduled clinic visits with their epileptologist. Patients were consented and enrolled on site to complete a unique 50-question survey that was available in Spanish and English, designed through REDCap. Informed consent was documented in REDCap.

The first aim of the study to quantitatively determine the extent to which a belief in epilepsy folklore influences the decision of a Hispanic/Latinx person with epilepsy to seek medical treatment for their epilepsy. A belief in epilepsy folklore was determined based on participant responses to multiple choice questions about causes of epilepsy and appropriate treatments for epilepsy. The survey also included Likert scale questions where participants graded the importance of various factors in their decision whether to establish care with a neurologist, including the belief that epilepsy was caused by supernatural phenomena. To determine how influential epilepsy folklore belief was as a barrier to care, the time between first seizure and establishment with a neurologist and the time between first seizure and/or initiation of ASM were compared between those with and without folklore beliefs.

The second aim of the project was to qualitatively determine the role that epilepsy folklore plays in how individuals with epilepsy are perceived. This was assessed through open-ended questions inquiring about participants' knowledge of epilepsy folklore and its influence on their perception of individuals with epilepsy. These responses were analyzed for common themes and

sentiments. Given the stigmatization of epilepsy in the Hispanic/Latinx community, which potentially was perpetuated by epilepsy folklore, the survey also contained the Epilepsy Stigma Scale (ESS).

Study survey measures included standard of care clinical data, open-ended questions about participants' experiences with epilepsy, assessment of belief in epilepsy folklore, and barriers to accessing healthcare. These questions were developed specifically for this study in consultation with our neuropsychologist, who performs epilepsy pre-surgical neuropsychological evaluations in English and Spanish. Formal survey measures included the ESS and Medication Adherence Rating Scale (MARS). The ESS is a 10-item questionnaire designed to assess the degree to which a person believes that epilepsy is perceived as negative and interferes with relationships with others.¹⁴ Utilizing a Likert scale, participants indicate the extent they agree or disagree with each statement, ranging from strongly disagree (score of 1) to strongly agree (score of 7).¹⁴ The higher a person's response score on the ESS, the more stigmatized they feel because of their epilepsy. While this tool does not sum the total of participants' responses to have an objective measure of stigma, it allows providers to qualitatively assess why a patient may be feeling stigmatized because of their epilepsy. The MARS is a 10-item questionnaire that evaluates a patient's medication adherence behavior, attitude toward taking their medications, and negative side effects.^{15,16} The MARS is not numerically scored, as it assesses behaviors. While the tool was initially developed to assess adherence to psychoactive medications, iterations of it have been shown to be reliable for the assessment of medication adherence in other medical conditions.¹⁶ The higher someone scores on the MARS, the more compliant they are with medication.

Regarding barriers to care, participants were asked about the importance of various known barriers to care, such as lack of health insurance, in their decision whether to establish care with a neurologist. Using a Likert scale, participants selected whether each barrier was "very unimportant," "unimportant," "neutral," "important" or "very important" in their decision.

Data analysis was performed by dividing participants into two groups based on their belief in epilepsy folklore or lack thereof. The Shapiro test was performed on each group's data to determine if the values were

normally distributed. The non-parametric Wilcoxon test was employed if no normality could be confirmed at the 0.05 level. The T-test was used if normality of the data was confirmed.

Results

Given the stigma associated with an epilepsy diagnosis in the Hispanic/Latinx community, it was initially unclear how many patients would elect to participate in this pilot study. An enrollment goal of 30 patients was felt to be achievable given the total number of Hispanic/Latinx patients established in the healthcare system. Of the 30 patients enrolled in the study, 70% were male and 30% were female. Twenty-two participants elected to take the survey in English, and eight elected to take it in Spanish. The mean age of enrolled participants was 36.3 years (standard deviation 14.6), with participants ranging from 19 years old to 65 years old. The mean number of years of education of enrolled patients was 11.9, ranging from 4 years to 17 years. The most common country of origin for a participant's parents was Mexico, with 53.3% of participants' mothers and 50% of participants' fathers originating from Mexico (Table 1).

Study participants were asked various open-ended questions to assess their experiences with epilepsy and the views of their family, community, and church. These responses were qualitatively analyzed for common themes. When asked what they knew about seizures prior to having their first seizure, 70% of participants answered that they did not have any prior knowledge. When asked what their family's reaction was the first time they had a seizure, 76.7% of participants indicated their family was scared or unprepared. When asked about the views of seizures held in their community, 40% of participants indicated there were no specific views, 13.3% indicated people in their community thought seizures were caused by demons, and the responses of the remaining 46.7% of participants were classified as "other," given the lack of overlapping themes. 86.7% of participants indicated there was no information about seizures available in their community. 80% of participants noted their church did not provide any information about seizures, 10% of participants indicated their church associated demons with seizures, and 10% indicated they were not religious.

To assess their understanding of epilepsy, participants were asked to select all causes of epilepsy from a predetermined list. Out of the twenty-two participants who completed the survey in English, the most selected answer choice was “head injury,” selected by 81.8% of participants. Out of the eight participants who completed the survey in Spanish, the most selected answer choice was a tie between “head injury” and “migraine headaches,” with 50% of participants selecting each option (Table 2). Participants were also asked to select appropriate treatments for epilepsy from a predetermined list. For both the English and Spanish survey

responses, the top three responses were “anti-seizure medication” (96.7%), “adequate sleep” (63.3%), and “healthy diet” (53.3%) (Table 3).

Based on the Likert scale questions for participants who completed the survey in English, the most important barrier to care was a tie between “inability to take time off from work” and “lack of health insurance.” For participants who completed the survey in Spanish, the most important barrier to care was “stigma.” Overall, the most important barrier was “lack of health insurance” (Table 4).

Table 1. Demographic and Clinical Characteristics of the 30 participants enrolled in the study

	English Survey Responses (n=22)	Spanish Survey Responses (n=8)	Total Participants (n=30)
Male gender	15 (68.2%)	6 (75%)	21 (70%)
Female gender	7 (31.8%)	2 (25%)	9 (30%)
Age in years (minimum to maximum)	19 years old to 65 years old	24 years old to 61 years old	19 years old to 65 years old
Mean age in years +/- standard deviation	34.6 +/- 14.5	40.9 +/- 14.5	36.3 +/- 14.6
Number of years of schooling (minimum to maximum)	4 to 17	6 to 16	4 to 17
Mean number of years of schooling +/- standard deviation	12.4 +/- 2.7	10.8 +/- 4	11.9 +/- 3.1
Most common country of origin for participants' mothers	Mexico (50%)	Mexico (62.5%)	Mexico (53.3%)
Most common country of origin for participants' fathers	Mexico (n=10, 45.5%)	Mexico (n=5, 62.5%)	Mexico (n=15, 50%)
Number of current ASMs (minimum to maximum)	0 to 3	0 to 2	0 to 3
Mean number of current ASMs +/- standard deviation	1.6 +/- 0.8	1.3 +/- 0.7	1.5 +/- 0.8
Most commonly used current ASM (number of participants)	Levetiracetam (14)	Oxcarbazepine (3)	Levetiracetam (16)

Table 1, continued. Demographic and Clinical Characteristics of the 30 participants enrolled in the study

Number of past ASMs (minimum to maximum)	0 to 5	0 to 5	0 to 5
Mean number of past ASMs +/- standard deviation	1.4 +/- 1.4	1.8 +/- 2.0	1.5 +/- 0.8
Most commonly used past ASM (number of participants)	Levetiracetam (6)	Levetiracetam (3)	Levetiracetam (9)
Number of self-reported psychiatric disorders (minimum to maximum)	0 to 4	0 to 2	0 to 4
Mean number of psychiatric disorders +/- standard deviation	0.6 +/- 1.1	0.9 +/- 0.8	0.7 +/- 1.1
Most commonly reported psychiatric disorder (number of participants)	Depression (6)	Depression (4)	Depression (10)

A belief in folklore was defined by at least one of the following: selection of “possession by an evil spirit or demon,” “lack of spiritual faith” or “sins” as causes of epilepsy, selection of “exorcism” or “prayer” as treatment options, and/or grading of “epilepsy is caused by a supernatural phenomenon” as an important or very important factor in their decision whether to establish care with a neurologist. A total of 43.3% of participants indicated a belief in epilepsy folklore (40.9% of those who completed the survey in English and 50% of those who completed the survey in Spanish).

Results from the MARS found that the majority of participants (63.3%) forget to take their medication. Regarding questions from the ESS where patients selected that they slightly agree, moderately agree, or strongly agree with a given statement, most participants (53.3%) indicated people treat them differently because of their epilepsy. Nearly half of all study participants (46.7%) endorsed each of the following sentiments: feeling like they always need to prove themselves, feeling like there is a stigma attached to having a seizure condition, and feeling different from other adults.

The Shapiro test showed that the difference in years

between the time of first seizure and establishment of care with a neurologist and/or initiation of an ASM for patients with or without a belief in folklore was not a normally distributed data set. Therefore, the Wilcoxon test was utilized and yielded a p-value of 0.3128, indicating that folklore belief did not serve as a statistically significant barrier to care (p-value > 0.05). The Shapiro test showed that ESS data was normally distributed. Therefore, the T-test was utilized to analyze the data from the two groups (folklore belief and lack thereof) and yielded a p-value of 0.4225, indicating folklore did not have a statistically significant impact on stigma (p-value > 0.05).

Discussion

Given the morbidity of untreated seizures, it is imperative to identify potential barriers to care to reduce the time it takes to establish care with a neurologist and start treatment. Interestingly, a 2014 study found that the death rate among persons in the Hispanic/Latinx community, where epilepsy was cited as a contributing cause, had noticeably increased over nearly one decade.¹⁷ It is unclear why the number of deaths related to epilepsy may be increasing. One theory may be that

Table 2. Causes of Epilepsy

	English Survey Responses (n=22)	Spanish Survey Responses (n=8)	Total Participants (n=30)
Brain tumors	15 (68.2%)	3 (37.5%)	18 (60%)
Anxiety	13 (59.1%)	3 (37.5%)	16 (53.3%)
Lack of oxygen at birth	10 (45.5%)	2 (25%)	12 (40%)
Possession by an evil spirit or demon	2 (9.1%)	1 (12.5%)	3 (10%)
Lack of spiritual faith	1 (4.5%)	1 (12.5%)	2 (6.7%)
Meningitis	5 (22.7%)	2 (25%)	7 (23.3%)
Eating undercooked pork	2 (9.1%)	0	2 (6.7%)
Sins	1 (4.5%)	0	1 (3.3%)
Head injury	18 (81.8%)	4 (50%)	22 (73.3%)
Migraine headaches	13 (59.1%)	4 (50%)	17 (56.7%)

To assess knowledge of epilepsy, participants were asked, "Which of the following are causes of epilepsy? Select all that apply." The most selected choice was "head injury," chosen by 73.3% of participants overall. Note: this question did not inquire about the cause of each participant's specific epilepsy.

Table 3. Treatments for Epilepsy

	English Survey Responses (n=22)	Spanish Survey Responses (n=8)	Total Participants (n=30)
Exorcism	0	0	0
Anti-seizure medication	22 (100%)	7 (87.5%)	29 (96.7%)
Vitamin supplementation	6 (27.3%)	3 (37.5%)	9 (30%)
Healthy diet	12 (54.5%)	4 (50%)	16 (53.3%)
Adequate sleep	14 (63.6%)	5 (62.5%)	19 (63.3%)
Prayer	8 (36.4%)	3 (37.5%)	11 (36.7%)
Herbal remedies	5 (22.7%)	0	5 (16.7%)

Participants were asked, "Which of the following are appropriate treatments for epilepsy? Select all that apply." The most selected option was "anti-seizure medication," chosen by 96.7% of participants overall.

Table 4. Barriers to Accessing Neurologic Care

	English Survey Responses (n=22)	Spanish Survey Responses (n=8)	Total Participants (n=30)
The stigma of seeing a doctor for seizures	10 (45.5%)	8 (100%)	18 (60%)
Potential language barrier between you and your doctor	8 (36.4%)	6 (75%)	14 (46.7%)
Lack of transportation between your home and appointments	11 (50%)	4 (50%)	15 (50%)
Inability to take time off from work to attend appointments	13 (59.1%)	4 (50%)	17 (56.7%)
Lack of health insurance	13 (59.1%)	7 (87.5%)	20 (66.7%)
Belief that epilepsy was caused by a supernatural phenomenon	2 (9.1%)	2 (25%)	4 (13.3%)

Using a Likert scale, patients graded the importance of various barriers to care in their decision whether to establish care with a neurologist as “very unimportant,” “unimportant,” “neutral,” “important” or “very important.” Participants who marked that a barrier was “important” or “very important” were included in this table. Overall, the most commonly selected barrier to care was “lack of health insurance” followed by “stigma.”

more deaths related to the disorder are simply being reported. It is important, however, to scrutinize all potential barriers to accessing appropriate medical care to address them. Acculturation may also influence providers’ ability to provide culturally informed care, although it is uncommon for this to be directly explored in the healthcare setting.

The results of this study add to the existing literature that while epilepsy folklore beliefs are prevalent (43.3% of study participants), they may not pose an obstacle to accessing neurologic care. However, lack of health insurance and stigma were significant barriers, coinciding with the current literature.⁷⁻⁹

It is important to acknowledge the limitations of this study, namely that Hispanic/Latinx persons with epilepsy who were not established with a neurologist were unable to be included in this study, as there were no mechanisms for identifying these individuals. Therefore, it is possible their survey responses would be

different from those captured in this study. To try and address this limitation, the Likert scale questions that asked participants to grade the importance of various barriers to accessing care specifically inquired about the importance of these obstacles prior to each participant’s establishment with a neurologist. However, their responses still may differ from those who have not overcome barriers to accessing care.

Our study was also limited by a small sample size, a higher level of education, and potential inaccuracy of self-reported data. Regarding education level, folklore is utilized by communities to pass down moral lessons, beliefs, and values to younger generations. Individuals who seek higher education are exposed to other worldviews, which may shift their perspectives on these traditions. Since the survey was available in English and Spanish, it does not appear that language barriers affected the results of the study. However, given that the majority of individuals who completed this survey preferred the English version, it is possible that this

study group was more acculturated. Language is closely tied to culture, and one's primary language speaks to their cultural beliefs. While the level of acculturation was not assessed, participants who chose to take the survey in Spanish may be less assimilated to the culture of the United States than those who chose to take it in English. Patients who are less assimilated may be less likely to seek western medical treatments and may hold different epilepsy folklore beliefs.

Health Implications and Future Implications

While generalized conclusions cannot be made due to this study's small sample size, our findings suggest that a belief in epilepsy folklore is common amongst Hispanic/Latinx patients with epilepsy. Lack of insurance and stigma, however, may be larger barriers to care. These findings may be utilized by healthcare providers to develop initiatives to provide education, increase access to care for Hispanic/Latinx patients with epilepsy, and provide more culturally informed care to members of this community in their preferred language.

Future iterations of this work will include a larger

study population and chart review of standard clinical data to corroborate the self-reported information, such as the date of first seizure. With a larger sample size, future iterations of this work will aim to analyze differences in folklore beliefs and barriers to care based on country of origin, background, and degree of acculturation. Future iterations of this work will also seek to include Hispanic/Latinx patients with epilepsy seen by primary care providers to eliminate barriers that may exist to accessing subspecialty care.

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Statements and Declarations

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Endometriosis and hypertriglyceridemia: Why do we care about severity and typology?

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Abstract

Background: While plausible mechanisms exist for an association between endometriosis and hypertriglyceridemia, prior studies have shown inconsistent findings, possibly due to the inability to assess endometriosis severity or subtypes.

Objectives: Among 473 premenopausal individuals undergoing gynecologic laparoscopy, the present study assessed the association between incident endometriosis and non-fasting serum triglycerides.

Methods: Participants were recruited (2007–2009) among women undergoing diagnostic or therapeutic laparoscopy or laparotomy (for any indication) and who had no prior endometriosis diagnosis. Endometriosis was categorized using American Society for Reproductive Medicine staging (I–IV). Typology was defined as superficial endometriosis [SE], ovarian endometrioma [OE], and deep infiltrating endometriosis [DE]. We collected biospecimens, anthropometrics, and self-reported sociodemographics at enrollment, prior to surgery. We evaluated the association between endometriosis diagnosis, stage, typology, and triglyceride concentrations using non-fasting female cutpoints (normal <175mg/dL vs hypertriglyceridemia ≥175mg/dL) via generalized linear models. We also evaluated whether the association differed by menstrual cycle phase.

Results: Among the cohort, 108 women (23%) had hypertriglyceridemia > 175 mg/dL. Overall, endometriosis was not associated with prevalence of hypertri-

glyceridemia (adjusted prevalence ratio (aPR): 1.24, 95% CI: 0.87, 1.77), after accounting for baseline age, race/ethnicity, marital status, BMI, income, and serum cotinine. However, this varied by stage and type. Women with moderate to severe stage endometriosis had a higher aPR for hypertriglyceridemia, 1.74 (95% CI: 1.03, 2.95), compared to those without endometriosis. DE combined with OE was associated with a 3.59 higher aPR (95% CI: 2.33, 5.54) for hypertriglyceridemia. A pattern emerged showing stronger associations in the follicular phase compared to the luteal phase.

Conclusions: In summary, while no association was observed for overall endometriosis and hypertriglyceridemia, we observed moderate to severe stage endometriosis as well as DE and OE endometriosis was associated with prevalence of hypertriglyceridemia.

Background

Endometriosis is a chronic gynecologic condition without an established causal pathway.¹ It is considered a major reproductive health concern in the US, severely impacting more than 6.5 million women ages 15–44.^{2,3} Endometriosis may also lead to debilitating symptoms that can severely impact quality of life such as chronic pelvic pain, dysmenorrhea, and infertility.^{4,5}

Prior research has suggested that endometriosis may be linked to cardiovascular disease event. In particular, women with endometriosis are at an increased risk of coronary heart disease, cerebrovascular disease, and stroke.⁶ Therefore, the impact of endometriosis on

lipid profiles such as triglycerides is of great interest. This is partly due to conditions such as elevated triglycerides also regarded as a risk factor for heart disease and stroke.⁷

Research on the associations between endometriosis and elevated triglyceride levels is currently limited, with very few studies exploring hypertriglyceridemia (defined as triglyceride levels of 150 mg/dl or higher). In the limited existing research, studies have been inconsistent.⁸⁻¹³ Melo et al.⁸ observed that triglyceride levels were higher in women with endometriosis (105.3 mg/dl) compared to women without endometriosis (83 mg/dl). Similarly, Li et al.¹² reported higher mean triglyceride levels in women with endometriosis (1.87 mmol/L) compared to a control group (1.38 mmol/L). In contrast to Melo et al.⁸ and Li et al.¹² research, Zheng et al.⁹ observed higher triglycerides levels in women with no endometriosis (1.23 mmol/L) compared to 1.12 mmol/L in women with endometriosis. This conflict could be attributed to its use of a study sample from a single health center, having a predominantly Asian participant demographic, and study participants with no endometriosis being older and having a higher Body Mass Index (BMI).

However, Zheng et al.⁹ did observe in women with endometriosis, higher staging was associated with higher triglyceride concentrations (moderate 0.96 mmol/L vs severe endometriosis 1.26 mmol/L).⁸ The pattern of higher concentrations among higher staged endometriosis was also observed by Verit et al.¹¹ However, most studies have not been able to include data on stage and no prior studies we are aware of have considered endometriosis typology.

In addition to not assessing severity or type of endometriosis, prior studies have not accounted for triglyceride fasting status and phase of menstrual cycle (follicular vs luteal). Epidemiological research has suggested that non-fasting vs fasting triglycerides better predict health outcomes, such as cardiovascular disease.¹⁴ Additionally, detailed within-in woman assessments have shown high variability in lipid levels by menstrual cycle phase, with higher levels documented in the follicular phase.¹⁵ Further, current research has not accounted for multiple confounding factors that can impact the relationship between endometriosis and hypertriglyceridemia. In particular, the role of physical activity, alcohol and caffeine consumption,

and smoking.

The present study aims to address prior gaps in the literature by assessing the association between endometriosis diagnosis, staging or severity, typology, and the occurrence of hypertriglyceridemia, considering fasting status, menstrual cycle phase, and multiple confounding factors assessed prior to incident endometriosis diagnosis.

Methods

Cohort Selection

The present study utilized data from the Endometriosis, Natural History, Diagnosis and Outcomes (ENDO) study (2007–2009).² The ENDO study was designed to 1) examine the scope and magnitude of endometriosis by diagnostic method and choice of comparison group; and 2) investigate the relationship between endocrine disrupting chemicals (EDCs) and occurrence of gynecologic pathology, including endometriosis. Eligibility criteria for enrollment in the ENDO study includes: 18–44 years of age, currently menstruating, no breast feeding ≥ 6 months, no cancer history other than nonmelanoma skin cancer, and no injectable hormonal treatment within the past 2 years.

Participants included 473 premenopausal women undergoing diagnostic or therapeutic laparoscopy or laparotomy regardless of clinical indication (pelvic pain, pelvic mass, menstrual irregularities, suspected fibroids, tubal ligation, and infertility) from clinical centers in Salt Lake City, UT and San Francisco, CA. The University of Utah Institutional Review Board (IRB) approved the study (IRB #00021614), and all participants gave written informed consent before enrollment and data collection.

Data Collection

Standardized data collection included a baseline personal interview, collection of biospecimens (blood, urine, peritoneal fluid, omental fat, and endometriosis implants when available), and in-person anthropometric assessment.² The baseline questionnaire, anthropometric assessment, and specimen collection occurred before surgery. Socio-demographics, reproductive and medical history, and lifestyle information were self-reported. For the anthropometric assessment, height

was measured with a portable stadiometer and weight with electronic scales. Body Mass Index (BMI) was calculated from height and weight measurements (weight [kg] / height [m]²). BMI was categorized according to the Centers for Disease Control and Prevention classification <18.5 kg/m²; 18.5-24.99 kg/m²; 25.0-29.99 kg/m²; and ≥ 30.0 kg/m²). Serum cotinine (ng/mL) was measured and used to evaluate smoking.

Outcome: hypertriglyceridemia

Hypertriglyceridemia was defined as non-fasting triglyceride concentration level ≥175mg/dL, as this has been determined in prior research to be the optimal non-fasting cut-point for mid-life women.¹⁶ A sensitivity analysis was conducted using the standard cut-point of ≥150 mg/dL.¹⁷

Exposure: endometriosis diagnosis, staging, & typology

The exposure of interest was visualized endometriosis diagnosis (yes/no) along with endometriosis stage and typology. For endometriosis, all surgeons participating in the ENDO study were trained in the diagnosis and staging of endometriosis. The surgeons completed a standardized operative report immediately after surgery to capture the degree of endometriosis and gynecologic and pelvic pathology.^{2,18} Endometriosis staging was categorized using the revised American Society for Reproductive Medicine (rASRM) disease stage. The rASRM uses a weighted point score to categorize endometriosis staging: stage I, minimal (scores 1-5); stage II, mild (scores 6-15); stage III, moderate (scores 16-40); and stage IV, severe (scores >40).¹⁹ Endometriosis typology was assessed using the rASRM form. Women with only superficial lesions on the ovary or peritoneum were considered to have superficial endometriosis (SE), women with deep lesions (>5mm invasion) noted in the peritoneum or with obliteration of the posterior cul-de-sac were considered to have deep infiltrating endometriosis (DE), and women with deep lesion of any size noted in the ovary were considered to have ovarian endometrioma (OE). Women who had deep ovarian and peritoneal lesions were considered to have OE and DE.^{20,21}

Due to sample size limitations, endometriosis staging was reclassified into minimal to mild (stage I/II) and moderate to severe (stage III/IV) endometriosis. Typology was also classified into SE only, OE or DE, and

OE and DE. “No endometriosis” served as the comparison for diagnosis, staging, and typology. Women with “No endometriosis” is also defined as women with no endometriosis but with other gynecological conditions and women with no endometriosis with normal pelvis.

Covariates

Confounders were determined via literature review and the use of directed acyclic graphs.²² Our primary models adjusted for baseline age (continuous), race and ethnicity (Hispanic vs non-Hispanic; non-white vs white), marital status (not-married vs married), BMI (continuous, kg/m²), income (Below poverty Line, ≤180% of poverty Line, vs > 180% of poverty line) and serum cotinine (continuous, ng/ml). Additional covariates considered included level of physical activity (low, moderate, high), history of alcohol consumption (yes, no), and average daily caffeine consumption (continuous). We also include models adjusted for self-reported parity, prior to laparoscopy/laparotomy. While endometriosis impacts infertility and consequently parity, parity is known to impact endometriosis.

Statistical Analysis

We used modified Poisson regression with robust standard errors to calculate adjusted prevalence ratios (aPRs) and 95% CIs for the association between endometriosis diagnosis, staging, and typology and hypertriglyceridemia.^{23,24} Given that triglyceride levels have been shown to vary by stage of menstrual cycle (follicular and luteal),²⁵ stratified results were presented. Geometric mean concentrations of triglycerides by endometriosis diagnosis, stage, and typology were generated overall and by menstrual cycle phase. We formally assessed whether the association between endometriosis and hypertriglyceridemia may be modified by menstrual cycle phase via the Wald test.

Sensitivity Analysis

We assessed potential non-linearity of triglycerides in relation to endometriosis using restricted cubic splines, adjusting for age, race/ethnicity, marital, categorical BMI, and log serum cotinine variables. Tests for non-linearity used the likelihood ratio test, comparing the adjusted model with only the linear term to the adjusted model with the linear and the cubic spline terms. Further, we conducted an additional analysis using

the standard hypertriglyceridemia cutpoint of ≥ 150 mg/dL vs less for comparability with past and future studies.¹⁷ Finally, we considered alternative models adjusting for additional potential confounders including physical activity, caffeine and alcohol consumption, and parity.

Ethics Approval

Study participants were remunerated for their time and travel. Full human subjects approval was obtained for the conduct of this study; each of the women provided informed consent before any data collection.²

Results

Descriptive analyses

Among 473 women in the study, 108 (22.8%) had hypertriglyceridemia (≥ 175 mg/dL) and 190 (40.2%) had endometriosis. Women with endometriosis were more likely to be younger, $>180\%$ of the poverty line, and have a lower BMI compared to women without endometriosis (Table 1). Women with hypertriglyceridemia had a higher BMI compared to those without hypertriglyceridemia. Further, women with moderate to severe endometriosis had a higher prevalence of hypertriglyceridemia (35.2%) than women with minimal to mild endometriosis (18.7%) and those with no endometriosis diagnosis (22.6%).

Differences were also observed by endometriosis subtype, and women with combined OE and DE endometriosis had the highest prevalence of hypertriglyceridemia (50.0%) (Table 1). In addition, women with combined OE and DE endometriosis had higher mean (169 ± 81 mg/dl) and median [25%, 75%] (179 [99, 215] mg/dl) triglycerides compared to women with no endometriosis (mean= 147 ± 101 ; median [25%, 75%] 121 [90, 166] mg/dl).

Association between endometriosis and hypertriglyceridemia

Overall, women with diagnosed endometriosis had a 1.24 (95% CI 0.87, 1.77) higher prevalence of hypertriglyceridemia after adjusting for age at baseline, race/ethnicity, marital status, BMI, income, and serum cotinine compared to women without endometriosis

(Table 2). This pattern varied by endometriosis severity and typology. Compared to women with no endometriosis, women with moderate to severe endometriosis had a 1.74 (95% CI 1.03, 2.95) higher adjusted prevalence of hypertriglyceridemia; while there was no association observed with minimal to mild (Stage I/II) endometriosis (aPR: 1.06, 95% CI: 0.70, 1.59).

When we investigated endometriosis typology, we observed that women with combined OE and DE experienced a 3.59 (95% CI 2.33, 5.54) higher adjusted prevalence of hypertriglyceridemia compared to those without endometriosis.

Role of menstrual cycle

On average, among everyone in the cohort, there was little difference in hypertriglyceridemia prevalence between women assessed in the follicular phase (22.0%) versus the luteal phase (21.9%) (Table 1). However, among women diagnosed with endometriosis, hypertriglyceridemia prevalence was higher in the follicular phase (26.7%) versus the luteal phase (20.6%). (Table 3). While there was no clear pattern for staging (Table 3), we found the highest prevalence of hypertriglyceridemia among women with OE and DE in the follicular phase (70.0%) versus the luteal phase (33.3%) (Table 3). Indeed, after adjustment, women with OE and DE were 4.38 times more likely to have hypertriglyceridemia (95% CI: 2.36, 8.12) in the follicular phase compared to 2.92 (95% CI: 1.06, 8.04) in the luteal phase (Table 3). Continuous assessment of geometric mean concentrations of serum triglyceride indicated a pattern of higher concentrations in the follicular phase, versus luteal phases, for women with endometriosis, severe staging, and most notably typology as evidenced by the non-overlapping 95% CIs (Supplementary Table 2). Restricted cubic splines revealed a linear relationship between endometriosis and serum triglycerides; however, precision was low due to limited power in our study (Supplementary Figure 1). Results were slightly attenuated when evaluating hypertriglyceridemia at the level of ≥ 150 mg/dL vs less (Supplementary Table 1). Results did not appreciably change when considering other confounding factors (Supplementary Table 3).

Table 1. Population characteristics by hypertriglyceridemia and endometriosis among ENDO Study participants (n=473)

Population Characteristics	Overall N (%)	Hypertriglyceridemia n (%)		Endometriosis n (%)	
		Yes	No	Yes	No
Overall, N (%)	473	108 (22.8)	365 (77.2)	190 (40.2)	283 (59.8)
Endometriosis					
Yes	190 (40.2)	44 (23.2)	146 (76.8)	-	-
No	283 (59.8)	64 (22.6)	219 (77.4)	-	-
Age at visit (yrs.), Mean (SD)	32.9 (6.9)	33.3 (6.9)	32.9 (7.0)	31.9 (6.8)	33.6 (7.1)
Race/Ethnicity					
Hispanic	63 (13.3)	17 (26.9)	46 (73.0)	24 (38.1)	39 (61.9)
Non-Hispanic White	354 (74.8)	80 (22.6)	274 (77.4)	142 (40.1)	212 (59.9)
Non-Hispanic Black	8 (1.7)	0 (0.0)	8 (100.0)	1 (12.5)	7 (87.5)
Non-Hispanic Other	48 (10.2)	11 (22.9)	37 (77.1)	23 (47.9)	25 (52.1)
Income					
Below Poverty Line	54 (11.4)	12 (22.2)	42 (77.8)	17 (31.5)	37 (68.5)
≤180% of Poverty Line	53 (11.2)	15 (28.3)	38 (71.7)	12 (22.6)	41 (77.4)
> 180% of Poverty Line	359 (75.9)	81 (22.6)	278 (77.4)	158 (44.0)	201 (55.9)
Marital Status					
Married	331 (69.9)	81 (24.5)	250 (75.5)	140 (42.3)	191 (57.7)
Single, Living as married	25 (5.3)	3 (12.0)	22 (88.0)	9 (36.0)	16 (64.0)
Other	113 (23.9)	24 (21.2)	89 (78.8)	40 (35.4)	73 (64.6)
BMI (Kg/m²), Mean (SD)	28.0 (8.0)	32.5 (9.4)	26.7 (7.0)	26.3 (7.2)	29.2 (8.4)
<18.5	18 (3.8)	0	18 (4.9)	9 (4.7)	9 (3.2)
18.5-24.99	190 (40.2)	24 (22.2)	166 (45.5)	97 (51.1)	93 (32.9)
25-29.99	109 (23.0)	24 (22.2)	85 (23.3)	39 (20.5)	70 (24.7)
Obese ≥ 30.0	156 (33.0)	60 (55.6)	96 (26.3)	45 (23.7)	111 (39.2)
Serum Cotinine, Median (IQR)	0.03 (0.18)	0.05 (17.17)	0.03 (0.11)	0.02 (0.08)	0.03 (0.61)
25 th Percentile	0.01	0.01	0.13	0.01	0.01
75 th Percentile	0.19	0.01	17.18	0.09	0.63
Serum Triglycerides, Median (IQR)	121.0 (77.0)	222.0 (89.0)	106.0 (47.0)	119.0 (82.0)	121.0 (76.0)
25 th Percentile	90.0	191.0	84.0	90.0	90.0
75 th Percentile	167.0	280.0	131.0	172.0	166.0
Menstrual Cycle					
Follicular	209 (44.2)	46 (22.0)	163 (77.9)	90 (43.1)	119 (56.9)
Luteal	187 (39.5)	41 (21.9)	146 (78.1)	73 (39.0)	114 (60.9)
Endometriosis Staging					
Minimal to Mild (Stage I/II)	139 (29.4)	26 (18.7)	113 (81.3)	-	-
Moderate to Severe (Stage III/IV)	51 (10.8)	18 (35.3)	33 (64.7)	-	-
Endometriosis Typology					
SE	116 (24.5)	25 (21.6)	91 (78.5)	-	-
OE or DE	52 (10.9)	8 (15.4)	44 (84.6)	-	-
OE & DE	22 (4.7)	11 (50.0)	11 (50.0)	-	-

Table 2. Endometriosis diagnosis, staging, and typology and hypertriglyceridemia among ENDO Study participants (n=473)

Endometriosis	Hypertriglyceridemia n (%)		Unadjusted PR (95% CI)	Adjusted ¹ PR (95% CI)
	Yes	No		
No	64 (22.6)	219 (77.4)	REF	REF
Yes	44 (23.2)	146 (76.8)	1.02 (0.73, 1.43)	1.24 (0.87, 1.77)
Endometriosis Stage				
No endometriosis	64 (22.6)	219 (77.4)	REF	REF
Minimal to Mild	26 (18.7)	113 (81.3)	0.83 (0.55, 1.25)	1.06 (0.70, 1.59)
Moderate to Severe	18 (35.3)	33 (64.7)	1.56 (1.02, 2.40)	1.74 (1.03, 2.95)
Endometriosis Subtype				
No endometriosis	64 (22.6)	219 (77.4)	REF	REF
SE	25 (21.6)	91 (78.4)	0.95 (0.63, 1.42)	1.18 (0.78, 1.77)
OE or DE	8 (15.4)	44 (84.6)	0.68 (0.35, 1.33)	0.75 (0.36, 1.57)
OE & DE	11 (50.0)	11 (50.0)	2.21 (1.38, 3.54)	3.59 (2.33, 5.54)

Abbreviations: prevalence ratio (PR), superficial peritoneal endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE)

¹Adjusted for age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine.

Commentary

Principal findings

In this study, we observed a higher prevalence of hypertriglyceridemia among women with moderate to severe (III/IV) endometriosis and women with combined OE and DE endometriosis typology, compared to women with no endometriosis diagnosis, after taking into account multiple confounding factors. The results also showed that triglyceride levels and hypertriglyceridemia risk estimates were higher in the follicular phase compared to the luteal phase among women with endometriosis but no difference in women without endometriosis.

Strengths of the study

The present study is novel in that it is one of a few studies that directly assessed the associations between endometriosis diagnosis, staging, typology, and risk of hypertriglyceridemia. The ENDO study had very few exclusion criteria, making our results generalizable to other women undergoing laparoscopy/laparotomy for multiple indications.

Limitations of the data

A limitation of this study is that it does not include fasting blood draws. This limitation may impact the strength of the association of hypertriglyceridemia. However, research has shown that non-fasting

Table 3. The association between hypertriglyceridemia and endometriosis among ENDO Study participants (n=473) stratified by menstrual cycle phase

1. Endometriosis Diagnosis

Exposure	Hypertriglyceridemia	Hypertriglyceridemia	Prevalence Ratio	
	Yes, N (%)	No, N (%)	Unadjusted PR	Adjusted PR ¹
Overall	108 (22.8)	365 (77.2)		
Endometriosis				
No	64 (22.6)	219 (77.4)	Ref	Ref
Yes	44 (23.2)	146 (76.8)	1.02 (0.73, 1.43)	1.24 (0.87, 1.77)
Follicular Phase	46 (22.0)	163 (78.0)		
Endometriosis				
No	22 (18.5)	97 (81.5)	Ref	Ref
Yes	24 (26.7)	66 (73.3)	1.44 (0.87, 2.40)	1.50 (0.86, 2.62)
Luteal Phase	41 (21.9)	146 (78.1)		
Endometriosis				
No	26 (22.8)	88 (77.2)	Ref	Ref
Yes	15 (20.6)	58 (79.4)	0.90 (0.51, 1.58)	1.35 (0.71, 2.57)

2. Endometriosis Staging

Exposure	Hypertriglyceridemia	Hypertriglyceridemia	Prevalence Ratio (PR)	
	Yes, N (%)	No, N (%)	Unadjusted PR	Adjusted PR
Overall	108 (22.8)	365 (77.2)		
Endometriosis				
No	64 (22.6)	219 (77.4)	Ref	Ref
Minimal to Mild	26 (18.7)	113 (81.8)	0.83 (0.55, 1.25)	1.06 (0.70, 1.59)
Moderate to Severe	18 (35.3)	33 (64.7)	1.56 (1.02, 2.40)	1.74 (1.03, 2.95)
Follicular Phase				
Endometriosis				
No	22 (18.5)	97 (81.5)	Ref	Ref
Minimal to Mild	16 (23.9)	51 (76.1)	1.29 (0.73, 2.28)	1.32 (0.75, 2.32)
Moderate to Severe	8 (34.8)	15 (65.2)	1.88 (0.96, 3.69)	1.97 (0.84, 4.61)
Luteal Phase				

Table 3, cont. The association between hypertriglyceridemia and endometriosis among ENDO Study participants (n=473) stratified by menstrual cycle phase

Endometriosis				
No	26 (22.8)	88 (77.2)	Ref	Ref
Minimal to Mild	7 (13.7)	44 (86.3)	0.60 (0.28, 1.30)	0.97 (0.43, 2.18)
Moderate to Severe	8 (34.8)	15 (65.2)	1.59 (0.83, 3.05)	2.29 (1.08, 4.87)

3. Endometriosis Typology				
	Hypertriglyceridemia			
Exposure	Yes, N (%)	No, N (%)	Prevalence Ratio (PR)	
Overall	108 (22.8)	365 (77.2)	Crude PR	Adjusted PR
Endometriosis				
No	64 (22.6)	219 (77.4)	Ref	Ref
SE	25 (21.6)	91 (78.4)	0.95 (0.63, 1.42)	1.18 (0.78, 1.77)
OE or DE	8 (15.4)	44 (84.6)	0.68 (0.35, 1.33)	0.75 (0.36, 1.57)
OE & DE	11 (50.0)	11 (50.0)	2.21 (1.38, 3.54)	3.59 (2.33, 5.54)

Follicular Phase				
Endometriosis				
No	22 (18.5)	97 (81.5)	Ref	Ref
SE	12 (22.6)	41 (77.4)	1.22 (0.66, 2.29)	1.38 (0.74, 2.58)
OE or DE	5 (18.5)	22 (81.5)	1.00 (0.42, 2.41)	0.73 (0.26, 2.08)
OE & DE	7 (70.0)	3 (30.0)	3.79 (2.18, 6.59)	4.38 (2.36, 8.12)
Luteal Phase				
Endometriosis				
No	26 (22.8)	88 (77.2)	Ref	Ref
SE	10 (22.7)	34 (77.3)	0.99 (0.52, 1.89)	1.45 (0.74, 2.84)
OE or DE	2 (10.0)	18 (90.0)	0.44 (0.11, 1.70)	0.74 (0.18, 2.97)
OE & DE	3 (33.3)	6 (66.7)	1.46 (0.55, 3.91)	2.92 (1.06, 8.04)

Abbreviations: prevalence ratio (PR), superficial endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE).

¹Adjusted for age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine

triglyceride levels are a better predictor of cardiovascular risk than fasting triglycerides.²⁶ Further, due to the small sample sizes, we lacked precision in some of our estimates, notably when looking at typology and in our spline analyses assessing potential non-linear relationships. Finally, while our study had few exclusion criteria, our sample was made up predominately

of white non-Hispanic women of higher socioeconomic status. Future studies assessing the relationship between endometriosis and triglycerides should make sure to include women of underrepresented minorities and of varying socioeconomic classes for more generalizability.

Commentary

Interpretation

Endometriosis staging and hypertriglyceridemia

We observed that moderate to severe (III/IV) endometriosis was more strongly associated with hypertriglyceridemia than minimal to mild (I/II) endometriosis. Prior studies have reported associations between elevated triglyceride levels and endometriosis staging.^{8,9,11,12} To illustrate, Verit et al.¹¹ and Zheng et al.⁹ both reported increasing triglycerides levels by increasing endometriosis severity. In the Verit et al. study, mean triglyceride levels were 135.0 mg/dL in women with no endometriosis, 157.3 mg/dL in women with minimal to mild endometriosis, and 189.0 mg/dL in women with moderate to severe endometriosis. Importantly, our study is also unique in that it is the only one that includes a multivariable assessment on the risk of hypertriglyceridemia or triglyceride levels ≥ 175 mg/dL.

Poor lipid metabolism in women with endometriosis is a potential clinical pathway for hypertriglyceridemia occurrence.¹² Sphingomyelin, a class of phospholipids and a critical component of the plasma membranes, is an important determinant of lipoprotein metabolism.^{27,28} While sphingomyelin is essential for cellular integrity, its accumulation—potentially exacerbated by endometriosis—can disrupt lipid metabolism and signaling pathways, contributing to elevated lipid levels in the bloodstream and tissues. Beyond lipid handling, sphingolipids more broadly are implicated in generalized inflammatory processes, which may explain why chronic inflammation from endometriosis, or indeed from other conditions, can contribute to increased cardiovascular risk.²⁷ Notably, research has associated higher-stage endometriosis with elevated sphingomyelin levels, supporting our finding that hypertriglyceridemia risk was highest in women with moderate to severe endometriosis compared to those with minimal to mild disease or no endometriosis. Thus, both lipid-specific and inflammation-mediated pathways may be relevant in linking endometriosis to cardiometabolic risk.^{27,28}

Endometriosis typology and hypertriglyceridemia

The present study also showed an association between endometriosis typology and hypertriglyceridemia. We

observed that combined ovarian and deep infiltrating endometriosis (OE and DE) had a higher risk of hypertriglyceridemia than SE or OE alone. Importantly, we found no study that has directly assessed hypertriglyceridemia risk by endometriosis typology.

The study of Vouk et al.,²⁹ however, documented elevated concentrations of sphingomyelins in women with ovarian endometriosis. As previously described, elevated levels of sphingomyelin disrupt lipid metabolism, which likely results in an abnormal increase in lipid uptake in the cells and tissue. Further, the study of Bedin et al.³⁰ examined lipid nanoparticle concentrations, an analogue to low density lipoprotein (LDL) receptors, in deep endometriotic tissues. The results suggest increased LDL uptake by endometriotic tissue. Although the study focuses on LDL, it is worth noting that LDL and triglycerides share similar clinical implications.

Role of the menstrual cycle phase

When we investigated whether cycle phase influenced the association between endometriosis and triglycerides, we found that the prevalence of hypertriglyceridemia and geometric mean triglyceride concentrations in women with endometriosis was higher in the follicular phase than in the luteal phase. Estrogen concentration, also associated with lipid metabolism, is known to rise with ovulation, possibly leading to higher lipid levels.¹⁵ The effect is more pronounced in the follicular phase as estrogen levels peak. The fact that we only found triglycerides to be higher in the follicular versus luteal phase among women with endometriosis may be related to women with endometriosis having higher estrogen levels,³¹ however further research is needed to confirm these novel findings. Additionally, while our findings collaborate the positive association between estrogen and lipoprotein cholesterol,^{15,32} more research looking specifically at triglycerides is needed.

Conclusions

Hypertriglyceridemia has far-reaching consequences for women's health, requiring increased attention. The condition is associated with an increased risk of all-cause mortality and incident cardiovascular disease events.³² There are also documented associations with pregnancy-related complications such as preeclampsia,

gestational diabetes, and fetal macrosomia.^{33,34} It may also be important for health professionals to inquire about the menstrual cycle phase during routine metabolic panels, as there is variability in triglyceride levels observed across different phases of the menstrual cycle, which can impact the interpretation of the test results. More research is also needed on the impact of endometriosis severity and localization endometriosis (staging vs typology) on triglycerides across the menstrual cycle phase.

In summary, while overall we found that women with,

compared to without endometriosis, had a null association with hypertriglyceridemia, when looking at typology, we found women with ovarian endometrioma combined with deep infiltrating had a four-fold higher prevalence of hypertriglyceridemia. Additionally, women with moderate to severe staging had a two-fold higher prevalence. We also observed differences by menstrual cycle phase. Although research is extensive on the effects of endometriosis on women's health, few studies exist assessing hypertriglyceridemia risk as an outcome, and even fewer studies specifically focusing on endometriosis staging and typology.

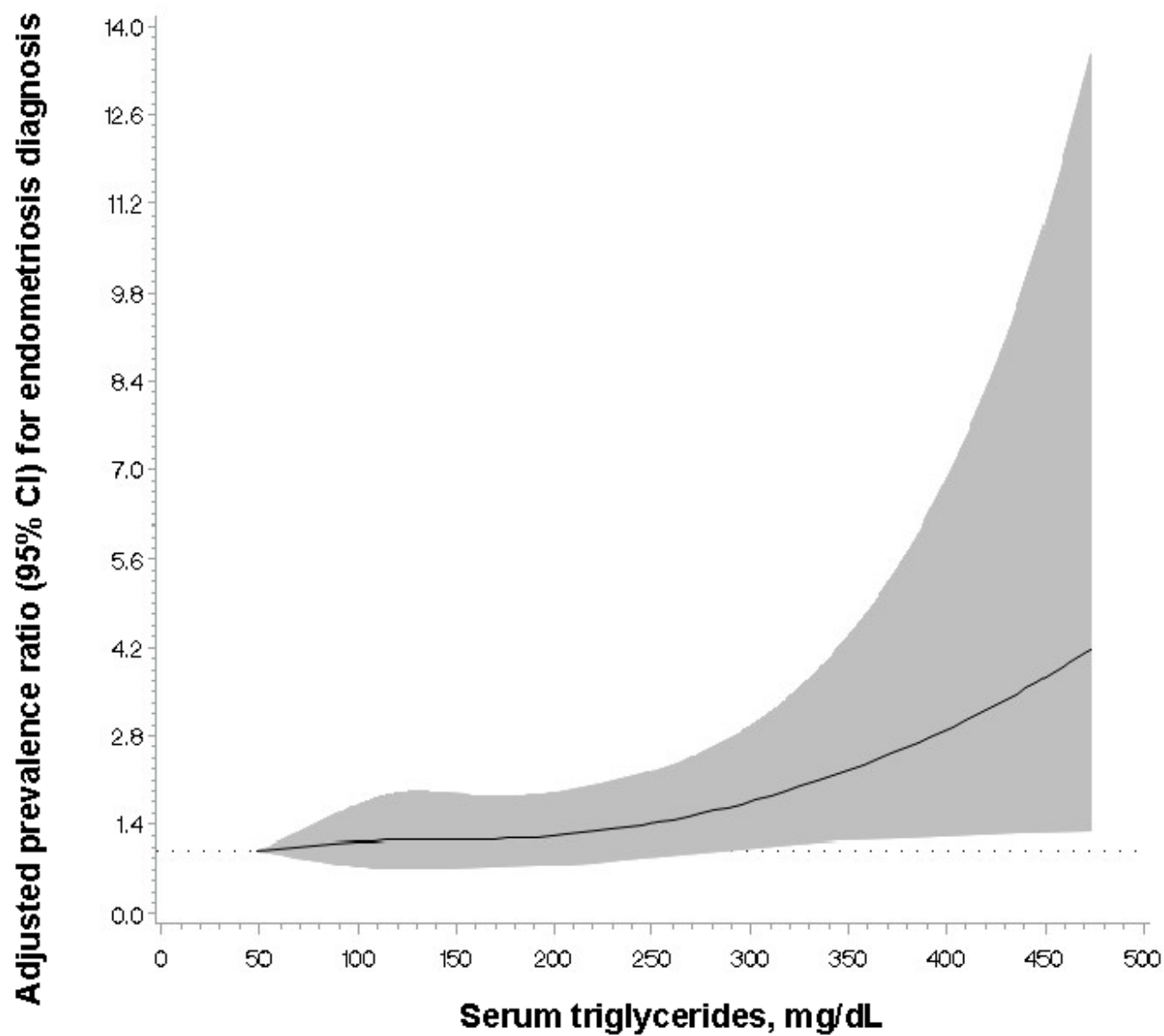
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Supplementary Figure 1: Restricted cubic spline regression assessing potential non-linear adjusted relationship between triglycerides and log triglycerides and endometriosis diagnosis. Spline was modeled with knots at 2.5, 50, 75 and 97.5 percentiles of serum triglycerides, which correspond to 58, 121, 167, and 336 mg/dL. Likelihood ratio test P=0.08



Supplementary Table 1: Endometriosis diagnosis, staging, and typology and risk of hypertriglyceridemia (defined as ≥ 150) among ENDO Study participants (n=473)

Endometriosis	Hypertriglyceridemia n (%)	Unadjusted PR (95% CI)	Adjusted ¹ PR (95% CI)
No	94 (33.2)	REF	REF
Yes	61 (32.1)	0.97 (0.74, 1.26)	1.14 (0.86, 1.52)
Endometriosis Stage			
No endometriosis	94 (33.2)	REF	REF
Minimal to Mild	38 (27.3)	0.82 (0.60, 1.13)	1.03 (0.73, 1.43)
Moderate to Severe	23 (45.1)	1.36 (0.96, 1.92)	1.49 (0.99, 2.24)
Endometriosis Subtype			
No endometriosis	94 (33.2)	REF	REF
SE	38 (32.8)	0.99 (0.72, 1.34)	1.23 (0.89, 1.68)
OE or DE	10 (19.2)	0.58 (0.32, 1.04)	0.61 (0.31, 1.18)
OE & DE	13 (59.1)	1.78 (1.21, 2.61)	2.49 (1.66, 3.73)

Abbreviations: prevalence ratio (PR), superficial peritoneal endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE)

¹ Adjusted for age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine.

Supplementary Table 2: Unadjusted Geometric mean concentration (mg/dL) of serum triglyceride levels by menstrual cycle phase and endometriosis status among ENDO Study participants (n=473)

	Overall	Menstrual Phase	
		Follicular	Luteal
Serum Triglycerides (mg/dl)	126.0 (120.6, 131.6)	126.9 (119.3, 135.0)	123.6 (116.1, 131.6)
Endometriosis			
Yes	122.7 (114.7, 131.2)	126.9 (114.6, 140.6)	114.9 (103.6, 127.4)
No	128.3 (121.1, 135.9)	126.9 (117.5, 137.1)	128.1 (118.5, 138.5)
Endometriosis Staging			
Minimal to Mild (I/II)	118.3 (110.1, 127.2)	122.8 (110.3, 136.8)	112.9 (99.5, 128.1)
Moderate to Severe (III/IV)	134.9 (116.1, 156.8)	139.2 (108.2, 179.1)	128.8 (103.8, 159.9)
Endometriosis Subtype			
SE	123.5 (113.9, 134.0)	127.4 (113.1, 143.5)	122.7 (105.7, 142.4)
OE or DE	110.6 (97.0, 126.1)	105.9 (86.9, 129.0)	108.7 (89.3, 132.3)
OE & DE	150.9 (123.0, 185.1)	203.0 (158.2, 260.5)	113.7 (86.0, 150.3)

Abbreviations: prevalence ratio (PR), superficial peritoneal endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE)

Supplementary Table 3: Endometriosis Diagnosis, Staging, and Typology and Hypertriglyceridemia [Other Confounding Factors]

Endometriosis	Hypertriglyceridemia n (%)	Adjusted* PR (95% CI)	Adjusted* PR (95% CI)	Adjusted ^b PR (95% CI)	Adjusted ^c PR (95% CI)	Adjusted ^d PR (95% CI)
No	64 (22.6)	REF	REF	REF	REF	REF
Yes	44 (23.2)	1.24 (0.87, 1.77)	1.46 (1.00, 2.13)	1.27 (0.90, 1.80)	1.31 (0.92, 1.88)	1.25 (0.89, 1.78)
Endometriosis Staging						
No Endometriosis	64 (22.6)	REF	REF	REF	REF	REF
Minimal to Mild	26 (18.7)	1.06 (0.70, 1.59)	1.21 (0.78, 1.88)	1.06 (0.70, 1.61)	1.09 (0.72, 1.67)	1.06 (0.70, 1.61)
Moderate to Severe	18 (35.3)	1.74 (1.03, 2.95)	2.16 (1.28, 3.65)	1.88 (1.16, 3.04)	1.92 (1.19, 3.09)	1.83 (1.12, 2.97)
Endometriosis Typology						
No Endometriosis	64 (22.6)	REF	REF	REF	REF	REF
SE	25 (21.6)	1.18 (0.78, 1.77)	1.27 (0.81, 1.99)	1.16 (0.77, 1.74)	1.18 (0.77, 1.79)	1.15 (0.77, 1.74)
OE or DE	8 (15.4)	0.75 (0.36, 1.57)	1.17 (0.55, 2.46)	0.85 (0.40, 1.82)	0.92 (0.43, 1.94)	0.84 (0.40, 1.77)
OE & DE	11 (50.0)	3.59 (2.33, 5.54)	3.22 (1.98, 5.25)	3.31 (2.16, 5.09)	3.29 (2.09, 5.16)	3.22 (2.09, 4.96)

Abbreviations: prevalence ratio (PR), superficial peritoneal endometriosis (SE), ovarian endometriomas (OE), deep infiltrating endometriosis (DE)

*Adjusted for age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine.

^aAdjusted for level of physical activity, age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine.

^bAdjusted for history of alcohol consumption, age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine.

^cAdjusted for average caffeine consumption per day, age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine.

^dAdjusted for parity (#of live births), age at baseline, race/ethnicity, marital status, BMI, income (poverty level), and serum cotinine.

Can Utah Tell a National Story? Evaluating External Validity in Maternal Health Research

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Background

Assessing the generalizability of a study population—also referred to as external validity—is essential in epidemiologic research because it determines the extent to which findings from a specific sample can be applied to broader populations. While internal validity refers to the accuracy of a study’s results within the sample studied (i.e., whether the observed associations are free from bias, confounding, or measurement error), external validity addresses whether those findings hold true across different groups, settings, or times.¹ Without careful attention to generalizability, interventions or policy recommendations may be ineffective or even harmful when applied outside the study context, especially in populations with differing sociodemographic or clinical characteristics.² In studies of maternal and reproductive health, this is particularly important given the wide variability in risk factors, access to care, and outcomes across geographic and racial/ethnic populations. Preterm birth (PTB), a leading cause of infant morbidity and mortality in the United States³, serves as an especially important lens for examining maternal health equity and risk factors.

To better understand the commonalities and differences among Utah women of reproductive age compared to the national population, we leveraged the Pregnancy Risk Assessment Monitoring System (PRAMS), a population-based surveillance project conducted by the Centers for Disease Control and Prevention (CDC) and state health departments.⁴ Specifically, the objective of our study was to use the PRAMS Phase 8 questionnaire to compare Utah state versus United States (US) national population characteristics overall, and by preterm birth status, among women who participated in PRAMS between 2016 and 2022.

Methods

Study Population

We utilized data from the US national PRAMS Phase 8 questionnaire (2016–2022). A detailed description of the PRAMS surveillance system methodology and protocols can be found elsewhere.⁴ In brief, the PRAMS sample is stratified so that subpopulations of particular public health interest can be oversampled. Stratification variables vary by state and may include Medicaid status, birth weight, maternal race/ethnicity, geographic area, and smoking status. Utah oversamples women of lower education levels and infant birth weight to purposely capture data on a known high-risk population. Each participating site draws a stratified random sample of 100 to 250 new mothers (2–6 months postpartum) every month from a frame of eligible birth certificates. New mothers are contacted via mailed questionnaire (available in English and Spanish) multiple times and telephone follow-up. The expected response rate according to the CDC is 50% nationwide. An informed consent document is included within each survey packet. Consent is implied if the survey is completed. A total of 249,970 women, reflecting an estimated population of 12,275,282 women, completed the PRAMS questionnaire 2016–2022 and were included in the present study.

For the questionnaire, women report on various health, lifestyle, psychosocial, and reproductive related factors that occurred before, during, and after their index birth. Sociodemographic and birth outcome information is captured via linked birth records.

Statistical Analysis

Descriptive statistics (frequencies for categorical variables and means [standard error] for continuous variables) were used to explore differences in PRAMs participant characteristics, overall and by preterm birth status (<37 weeks vs ≥37 weeks), between the Utah and US national study populations. Stata (StataCorp, College Station, TX) was used for the analyses. All analyses accounted for the complex sampling designs.⁴

Ethics Approval

The University of Utah Institutional Review Board deemed the survey and administration procedures as surveillance and hence not human research.

Results

Utah's maternal population, while sharing some similarities with national trends, also displayed notable demographic and behavioral differences. For example, women giving birth in Utah, compared to the US population, were more likely to be white (88.9% vs. 69.7%), privately insured (59.3% vs. 49.6%), have received infertility treatment (6.9% vs 2.3%), wanted their pregnancy then or sooner (67.6% vs 60.6%), and have depression (19.6% vs 15.0%) or anxiety (30.2% vs 24.3%). Women giving birth in Utah, compared to the US population, were less likely to live in a rural area (9.5% vs 15.6%), be nulliparous (35.1% vs. 39.0%), smoke (7.2% vs. 15.0%) or consume alcohol (28.2% vs. 57.5% nationally) prior to pregnancy (Table 1). Utah women, compared to the nation, also tended to have higher educational attainment (72.1% vs 63.9% with some college or above) and household income levels (63.5% vs 55.1% at \$40,000 or above annually) compared to the national average.

Nationally, PTB affected approximately 9% of births between 2016 and 2022, which was slightly less prevalent in Utah (8%). Subgroup analyses suggest that many of the risk factors for PTB are similarly associated with PTB in both Utah and the broader U.S. population (Table 2). For example, women who have a preterm labor, compared to those without preterm labor, are more likely to be older, black, Hispanic, of lower income and education, and more likely to have an unintended pregnancy. However, a few notable differences between the PRAMs national and Utah samples were observed. Among women diagnosed with dia-

betes or hypertension, 17.1% and 21.3%, respectively, had a preterm birth for PRAMs index pregnancy in the nation, compared to 20.6% and 25.5% respectively in Utah. Among women who experienced physical abuse in the year prior to pregnancy, 13.2% had a preterm birth for PRAMs index pregnancy in the nation, compared to 18.8% in Utah. Finally, among women with a prior preterm birth, 27.5% had a preterm birth reported for the PRAMs pregnancy, compared to 23.9% in Utah.

Conclusions

Overall, we found that while the relationship between population characteristics and prevalence of preterm birth was consistent in direction and magnitude between Utah and the US population of women of reproductive age, there are notable differences in socio-demographics and lifestyle factors that could impact external validity of Utah-based studies. Specifically, Utah's relatively low prevalence of Black birthing individuals limits the state's capacity to explore racial disparities in maternal and perinatal outcomes—one of the most pressing public health challenges nationwide.⁵ For instance, while prevalence of preterm labor was similar in Utah compared to the US, our and prior research has shown that Black women experience a significantly higher rate of PTB compared to white women, a disparity that may be largely driven by structural racism and chronic stress.⁶ In Utah, the small proportion of Black births (1.6%) precludes robust stratified analyses, necessitating cautious interpretation of generalizability in racially diverse contexts.

Moreover, Utah's higher rates of infertility treatment, depression, and anxiety, may signal differences in access to reproductive care and psychological distress that can influence maternal outcomes. These unique aspects position Utah as an important, albeit non-representative, case study in maternal health—a state where certain protective factors (e.g., higher SES, lower smoking and alcohol rates) as well as certain risk factors (e.g., depression/anxiety) may be more prevalent—can still offer key insights into prevention and intervention strategies relevant across the U.S.

Finally, in our preterm birth-stratified analyses, we observed that in Utah, compared to the rest of the nation, women with a prior preterm birth were less likely to

have a subsequent preterm birth reported in PRAMs. In contrast, Utah women—regardless of prior preterm birth status—who reported depression, anxiety, or physical abuse in the year prior to pregnancy were more likely to have a preterm birth reported in PRAMs.

In sum, leveraging PRAMS data from both Utah and the national sample allows researchers and policymakers to assess the degree to which Utah's maternal health trends align with or diverge from broader patterns. This comparative approach strengthens the evidence base for tailoring public health interventions while ensuring they remain responsive to both local and national needs.

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Table 1. Characteristics of Women (n) from National Pregnancy Risk Assessment Monitoring System 2016–2022. United States sample N = 249,970 women reflecting an estimated population of 12,275,282 women; Utah N=9824 women reflecting a population of 324,194 women.

Characteristic	United States (n=249,970)	Utah (n=9824)
Age at visit (yrs.), Mean (SE)	29.3 ± 0.02	28.7 ± 0.1
Race (%) ¹		
White	69.7	88.9
Black	16.5	1.6
Other	13.8	9.4
Ethnicity (%) ¹		
Hispanic	17.7	16.6
Non-Hispanic	82.3	83.4
Pre-pregnancy BMI (mean [SE]) (%)	27.4 ± 0.02	26.3 ± 0.08
<18.5	3.0	3.6
18.5-24.9	41.8	48.0
25.0-29.9	26.5	25.0
30+	28.7	23.4
Income Grouped		
≤20k	24.6	14.6
>20–40k	20.3	21.9
>40–60k	13.1	20.1
>60k	42.0	43.4
Insurance (%)		
Insurance paid by job	49.6	59.3
On Other Insurance (not including Medicaid)	15.9	21.2
On Medicaid	22.5	7.5
No insurance	12.0	12.0
Education		
0–8 years	3.1	1.2
9–11 years	8.2	6.3
12 years	24.8	20.4
13–15 years	26.1	33.1
16+	37.8	39.0
Urban/Rural Residence		
Urban	84.4	90.5
Rural	15.6	9.5
Previous Preterm Birth (%)	3.8	5.5
Prior Low Birth Weight	12.4	9.8
Received infertility treatment	2.3	6.9
Nulliparous	39.0	35.1
(continued on next page)		

Table 1(con't). Characteristics of Women (n) from National Pregnancy Risk Assessment Monitoring System 2016–2022. United States sample N = 249,970 women reflecting an estimated population of 12,275,282 women; Utah N=9824 women reflecting a population of 324,194 women.

Pregnancy Intentions (%)		
Later	18.0	15.9
Sooner	15.3	19.7
Then	45.3	47.9
Did not want	6.0	4.2
Was not sure	15.4	12.3
Pre-pregnancy Medical Condition (%)		
Diabetes	3.2	2.7
Hypertension	5.4	4.2
Depression	15.0	19.6
Asthma	10.9	9.6
Thyroid Problems	7.3	7.8
PCOS	6.8	7.9
Anxiety	24.3	30.2
Smoked Cigarettes 3 mo. before pregnancy (%)	15.0	7.2
Drank alcohol 3 mo. before pregnancy (%)	57.5	28.2
Financial Stress, had difficulty paying bills	14.6	13.1
Financial Stress, husband/partner lost job	9.0	8.7
Financial Stress, mother lost job	9.8	5.9
Financial Stress, had reduction in work or pay	16.5	17.5
Total Stress (mean, SE)	1.7 ± 0.01	1.6 ± 0.02
Experienced racial bias	7.1	NA
Abuse		
Before pregnancy (husband/partner)	1.5	1.2
Before pregnancy (someone else)	1.7	1.4

Table 2. Characteristics by Preterm Birth Status from National Pregnancy Risk Assessment Monitoring System 2016–2022. United States sample N = 249,970 women reflecting an estimated population of 12,275,282 women; Utah N=9824 women reflecting a population of 324,194 women.

Characteristic	United States (n=249,970)		Utah (n=9824)	
	PTB (<37 weeks)	No PTB (≥37 weeks)	PTB (<37 weeks)	No PTB (≥37 weeks)
	9%	91%	8%	92%
Age at visit (yrs.), Mean (SE)	29.6 ± 0.05	29.3 ± 0.02	29.2 ± 0.18	28.6 ± 0.07
Race (%)				
White	8.2	91.8	8.1	91.9
Black	13.0	87.0	12.8	87.2
Other	8.5	91.5	8.4	91.6
Ethnicity (%)				
Hispanic	9.1	90.9	9.4	90.6
Non-Hispanic	9.0	91.0	8.0	92.0
Maternal BMI prior to pregnancy, Mean (SE)	28.4 ± 0.07	27.3 ± 0.02	27.4 ± 0.22	26.2 ± 0.08
Income-grouped				
≤20k	11.1	89.0	10.6	89.5
>20–40k	9.4	90.6	7.8	92.2
>40–60k	8.6	91.4	8.2	91.8
>60k	7.5	92.5	7.6	92.4
Insurance				
On Other Insurance (not including Medicaid)	8.3	91.7	8.0	92.0
On Medicaid (%)	10.8	89.2	10.0	90.0
No insurance (%)	9.3	90.7	8.3	91.7

Table 2 (con't). Characteristics by Preterm Birth Status from National Pregnancy Risk Assessment Monitoring System 2016–2022. United States sample N = 249,970 women reflecting an estimated population of 12,275,282 women; Utah N=9824 women reflecting a population of 324,194 women.

Education (%)				
0–8 years	9.7	90.3	7.96	92.0
9–11 years	10.7	89.3	9.8	90.2
12 years	10.3	89.7	9.97	90.0
13–15 years	9.3	90.7	8.5	91.5
16+	7.5	92.5	8.3	91.7
Urban/Rural Category (%)				
Urban	9.0	91.0	8.3	91.7
Rural	9.0	91.0	7.8	92.2
Prior Preterm Birth (%)	27.5	72.5	23.9	76.1
Prior Live Birth	8.7	91.3	8.0	92.0
Diagnosed with infertility (%)	16.5	83.5	15.5	84.5
Intention to get pregnant				
Sooner	9.6	90.4	8.8	91.2
Later	9.2	90.8	8.4	91.6
Then	8	92	7.1	92.9
Did not want	11.5	88.5	11.6	88.4
Pre-existing Medical Condition (%)				
Diabetes	17.1	82.9	20.6	79.4
Hypertension	21.3	78.7	25.5	74.5
Depression	11.6	88.4	11.2	88.8
Asthma	10.1	89.9	9.1	90.9
Thyroid Problems	9.8	90.2	10.6	89.4
PCOS	11.0	89	12.2	87.8
Anxiety	10.5	89.5	10.2	89.8
Smoke 3 months prior to pregnancy (%)	11.0	89	11.4	88.6
Drink 3 months prior to pregnancy (%)	8.4	91.6	8.4	91.6
Experienced racial bias (%)	11.5	88.5	--	--
Stress, had difficulty paying bills (%)	10.5	89.5	10.4	89.6
Abuse 12 months before pregnancy (%)	13.2	86.8	18.8	81.2

The Utah Children's Project: Design, Enrollment and Measures for a Child and Family Cohort

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Abstract

Objectives: We describe the eligibility criteria, recruitment, and enrollment of the children and families in the Utah Children's Project. We describe the measurement components of the UCP, including questionnaire instruments, geographically based exposure assessment, direct environmental assessment (including home air quality), DNA extraction, RNA banking, microbiome biosamples, and blood and urine banking.

Methods: In 2014, the University of Utah School of Medicine, Woman and Child Institute, launched the Utah Children's Project, a child and family cohort study, to understand how genes and the environmental exposures around the time of conception, pregnancy, infancy, and early childhood act to influence health, growth, and development of children. The UCP enrolled participants from six prior cohorts that enrolled mothers and sometimes fathers in the preconception or prenatal period. We invited parents, children, and up to one sibling to enroll in the UCP for long-term follow-up of health of the children and their parents. In 2016, the UCP joined the Environmental Influences on Child Health Outcomes Program (ECHO) Consortium of the National Institutes of Health.

Results: We describe the participation of UCP in ECHO, which has added many additional instruments and measures. We elucidate our successful efforts with remote data collection, which were accelerated by the COVID-19 pandemic.

Conclusions: Longitudinal data collection, for our cohort of children and families, supports research at both a national and local level. The successful methodologies employed in the UCP may be useful to other researchers planning to establish long-term prospective cohort studies.

Implications: This data collection enables national and local researchers to capture trends in the environment that may be transformative to children's health.

Introduction

Environmental exposures around the time of conception and during pregnancy, infancy, and early childhood can have lasting effects on the health and well-being of children. The Developmental Origin of Health and Disease theory suggests that environmental exposures during these critical times may also play a role in the development of diseases in adulthood.^{1,2} Environmental exposures and behaviors may change a person's epigenetics which can impact future generations.³

Over the last 50 years, there has been a sharp increase in major childhood health problems, including prematurity, obesity, asthma, and autism.⁴ The University of Utah School of Medicine launched the Utah Children's Project (UCP) in 2014 to understand how genes interact with our surroundings to influence child health, growth, and development. This child and family

cohort was built upon prior NIH-funded cohorts, such as National Children's Study and Home Observation of Periconceptional Exposures studies, that enrolled pregnant mothers (and sometimes fathers) in prenatal or preconception period. In 2016, the UCP joined the Environmental Influences on Child Outcomes Program (ECHO) Consortium of the National Institutes of Health.⁵ As of this writing, there are 46 ECHO sites across the United States, including more than 50,000 children and mothers from diverse populations, funded to examine the impact of early environmental exposures on child health and development.^{5,6} The ECHO Program seeks to understand how environmental exposures from preconception through early childhood influence child health and development, with the ultimate goal of identifying strategies to reduce disease risk and promote optimal health and well-being. By joining this nationwide collaborative research initiative, UCP secured funding to continue its study and gained the opportunity to contribute meaningful data and scientific insights to advance understanding of child health trajectories.

The purpose of this article is to provide a detailed description of the Utah Children's Project, including enrollment and study procedures. We describe the participation of UCP in the ECHO consortium and described possible opportunities for future use of UCP data.

Methods

Utah Children's Project

There were two enrollment stages of the UCP. In the first enrollment stage, participants were recruited to join the Utah Children's Project between 2014 and 2019 if they had participated in one of the following NIH-funded prenatal and/or preconception cohorts: National Children's Study – Salt Lake County Initial Vanguard Site (NCS – SLC; Utah PI: Ed Clark; enrolled 2009-2012)⁷, National Children's Study – Cache County (NCS – Cache; Utah PI: Ed Clark; enrolled 2010-2012)⁸, Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be (nuMoM2b; Utah PI: Robert Silver; enrolled 2010-2013)⁹, Home Observation of Periconceptional Exposures (HOPE; PI: Christy Porucznik; enrolled 2011-2015)¹⁰, Baby Affect and Behavior Study (BABY; PI: Elisabeth Conradt; enrolled 2016-2018)¹¹, Time to Pregnancy in Couples of Proven Fecundity (TTP; PI: Joseph Stanford; enrolled 2003-

2005.¹² The key selection criteria for each of the source cohorts and their inclusion and exclusion criteria are described in **Table 1**, and details of their aims and recruitment are given in the Supplemental File 1. Participants were recruited to UCP by telephone, email, and mailers. Original consents into the UCP occurred between June 12, 2014, and September 27, 2019. The second enrollment stage occurred after UCP joined ECHO. During this stage, participants were enrolled in 2022-2023 through the Preconception to Perinatal Outcomes (PPO) component, described further below (**Table 1**). By enrolling through PPO, UCP increased the number of participants recruited in the preconception period. Participants who enrolled in PPO were offered enrollment in ECHO as the babies were born.

UCP Eligibility

The original eligibility criteria for enrolling into UCP were:

1. Index child (or children in the case of twins) from one of the preconception/prenatal cohorts described in this paper.
2. Index child less than 18 years of age at enrollment
3. Residence in Utah at the time of enrollment
4. Child and at least one biological parent willing to participate and provide blood (preferred) or saliva for DNA to be analyzed in the study. The other biological parent is encouraged to participate, but this is not required
5. One full biologic sibling (older or younger, but less than 18 years; could be two in the case of twins) may also participate, but this is not required

Preconception to Perinatal Outcomes component

In addition to the original UCP participants described above, the UCP has also enrolled additional pregnant persons and couples trying to conceive, with subsequent enrollment of the child and at least one parent (but no sibling) into the study. These participants are also described further in Table 1 and the Supplemental File 1.

UCP Initial Visit

The enrollment visit included the index child, at least one biological parent, and often also an additional biological parent and biological full sibling. Written informed consent was obtained from all adults (18 years and older); verbal assent from children 7 to 17 years, and parental written informed consent for all

Table 1. Comparison of key selection criteria and enrollment characteristics for source cohorts

Cohort	First enrollment stage						Second enrollment stage
	NCS - IVS (SLC)	NCS - ARS (Cache)	HOPE	nuMoM2b-Utah	TTP	BABY	PPO (UCP)
Years of enrollment	2009-2012	2010-2012	2011-2015	2010-2013	2003-2005	2016-2018	2022-2023
Woman only = W Woman + Optional Man = W(M), or Woman and Man = WM	W(M)	W(M)	WM	W	W	W	W(M)
Preconception (PC) only, Pregnancy only, or Either	Either	Either	PC only	Pregnancy only	PC only	Pregnancy only	Either
Type of preconception: trying, or any at risk of pregnancy	Any	Any	Trying	NA	Trying	NA	Trying
Gestational age at enrollment	Any	Any	NA	<14 weeks	NA	26 weeks or more	Any
Children enrolled and followed in original study (before UCP)	Yes	Yes	No	No	No	Yes	Yes
Residence	Salt Lake County	Cache County	~1 hour drive of UU	Plan to deliver at participating hospital	~1 hour drive of UU	Plan to deliver at participating hospital	~1 hour drive of UU or USU
Woman's age, years	18-49 (PC)	18-49 (PC)	18-35	>12	18-35	18-40	18-49 (PC)
Man's age, years	18 or older	18 or older	18-40	NA	NA	NA	18-49
Language for questionnaires, visits	English or Spanish	English or Spanish	English	English or Spanish	English	English or Spanish	English
Prior pregnancy	Any	Any	Any	None >20 weeks	At least one	Any	Any
Exclude multiple gestation	No	No	No	Yes	No	Yes	No
Exclude medical fertility treatment or indicators of subfertility	No	No	Yes	No	Yes	No	Yes
Exclude donor gametes	No	No	Yes	Yes	Yes	Yes	Yes
Exclude recent long-acting hormonal contraceptive use	No	No	Yes	NA	Yes	NA	Yes
Exclude pregnancy complications such as preeclampsia or gestational diabetes	No	No	No	No	No	Yes	No
Recruitment targeted women with high levels of emotional dysregulation	No	No	No	No	No	Yes	No
For subsequent UCP, sibling eligible to enroll	Yes	Yes	Yes	Yes	Yes	Yes	No

UU = University of Utah; USU = Utah State University; NA = not applicable; NCS – IVS = National Children's Study – Salt Lake County Initial Vanguard Site; NCS = ARS (Cache) = National Children's Study – Cache County; HOPE = Home Observation of Periconceptional Exposures; nuMoM2b = Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be; TTP = Time to Pregnancy in Couples of Proven Fecundity; BABY = Baby Affect and Behavior Study; PPO (UCP) = Preconception to Perinatal Outcomes study of the Utah Children's Project

participants less than 18 years. For most children, questionnaires were completed by a parent. All participating family members completed medical histories, which were reviewed and verified by a clinician, questionnaires about the pregnancy for each child, a physical exam, and biospecimen collection, including venous blood, blood spots on FTA cards, and saliva. Medical histories of the index pregnancies were reviewed and verified by a clinician. Biospecimens were collected to enable the analysis of biological markers that reflect environmental exposures and health outcomes over time. These samples are essential for understanding the mechanisms by which early-life exposures influence child development and long-term health. Participants also underwent anthropometric measures, including height, weight, waist, hip, blood pressure, and heart rate. For some very young children, venous blood draw, blood pressure measurement, and hip measurement were waived based on parental preference. These visits were conducted at the University of Utah, Center for Clinical and Translational Science, in Salt Lake City, and Utah State University, the Center for Persons with Disabilities, Logan, Utah.

UCP Follow-up Visit with Microbiome Assessment and Dental Exam

The initial UCP follow-up visit was designed to be completed around one year from the enrollment visit. Only mothers and participating children were invited to complete the visits (Fathers were not included). Medical history addenda were completed for each participant, with a particular focus on antibiotic history, and dental history. Biological samples collected from the mother included nasal and vaginal swabs, and urine. The children provided nasal and rectal swabs, and urine. In addition, both mothers and children, provided saliva if it had not been collected at the initial visit. Microbiome sample collection questionnaires were distributed to each participant. Anthropometrics were performed including height, weight, waist, hip, blood pressure, and heart rate. Dental examinations with full mouth high resolution photographs were performed by a dental hygienist for children four years and older.

UCP Home Air Quality Monitoring

One of the key environmental exposures with high health impact in Salt Lake County and Cache County is air pollution. For precision measurement of air quality for participants in UCP, Utah investigators em-

ployed locally-developed low-cost air quality monitors, deployed in participant homes. These focused on the home deployment of these home monitors, and their acceptability, utility, efficacy, and ability to estimate environmental exposures inside and outside the homes of UCP participants.¹³⁻¹⁶ Through 2019, fifty families were recruited per a convenience sample from our existing cohort. Due to covid pandemic restrictions, contact and home visits to maintain these monitors were severely restricted during 2020-2021. Retrieval of the sensors and their data, from the homes, finalized in 2023.

Environmental Influences and Child Health Outcomes (ECHO)

Beginning in late 2016, the ECHO Consortium brings together existing cohorts of child research participants with various physical, chemical, social, behavioral, and biological exposures assessed preconceptionally, prenatally, or up to 5 years of age. Children are followed to age 21. The standardized data collected by ECHO sites focus on the following outcomes: pre, peri, and postnatal outcomes; neurodevelopment; upper and/or lower airways; obesity and related conditions; and positive health. All ECHO sites collect standardized demographics, typical early health and development, genetic influences on child health and development, environmental factors, and person-reported outcomes (PROs). Instruments and data collection forms are implemented in a centralized REDCap database and can be completed by study personnel during a visit or virtual visit, or often, by the participant or parent directly. Some data forms are collected once; others are collected more than once at different life stages.

UCP Implementation of ECHO

UCP applied and was selected to join the ECHO Consortium. These secured funding for the continuation of the study and created a mechanism to contribute UCP data to a broader scientific community working to address critical longitudinal research questions. From July 12, 2019, to April 26, 2022, existing UCP participants consented again to join the ECHO-wide protocol. Participants could choose between two levels of consent. Level 1 consent permits de-identified data and biospecimens to be shared and used only within the ECHO consortium for approved studies. Level 2 consent includes these permissions but also allows sharing with qualified researchers outside of ECHO, including through NIH-designated repositories, for broader

scientific se.

Upon joining the ECHO Consortium, UCP modified existing data collection and added additional data collection to match the ECHO-wide consortium protocol. The existing data collection process was modified to support the development of the ECHO-wide Cohort data platform, which incorporates essential data elements from all ECHO Cohort Awardees and their respective cohorts, as well as recommended data elements from selected subsets of Cohort Awards. Key changes to the data collection approach include contacting participants annually around the time of their child(ren)'s birthday(s), replacing most clinic visits with online surveys, conducting in-person clinic visits for children every five years, and implementing a special one-time visit with a parent. The total number of data collection forms from the ECHO-wide protocol for Level 2 participants engaged by UCP participants is over 120 forms. These are detailed in Supplemental File 2. Yearly visits in UCP cover all the elements of the ECHO-wide protocol for each childhood life stage. Biospecimens (blood, urine, hair, toenails) are collected at visits around ages 5, 10, and 15 years. Primary deciduous teeth are collected between visits. We administer the ECHO-wide questionnaires to children and parents that cover a broad domain of exposures and health. The NIH Toolbox Cognition Battery, which assesses executive function, attention, episodic memory, language, processing speed, and working memory, is also administered.¹⁷ We retain the name, Utah Children's Project for our local participants, all of whom are also part of the national ECHO dataset. The UCP and ECHO studies, which share the same study design, aim to investigate environmental exposures that influence child health and development, beginning in the preconception and prenatal periods and continuing through birth, infancy, early and middle childhood, and adolescence. After joining ECHO, we began collecting data required by ECHO-wide protocol, while also continuing to collect data specific to UCP interest. For example, in-home air quality monitoring was a unique component of the UCP study. Challenges and adaptations to COVID pandemic. With the advent of the COVID-19 pandemic, UCP discontinued all in-person study visits as of March 11, 2020. We began conducting virtual visits on April 8, 2020, which included continued remote administration of ECHO questionnaires and remote biospecimen collection, including hair, toenails, urine, saliva, and deciduous

teeth. As of April 8, 2021, a nurse began phlebotomy visits at willing participants' homes. As of May 26, 2022, we resumed clinic visits, including anthropometric and blood pressure measurements, NIH Toolbox Cognition Battery, and biospecimen collection, including hair, toenails, urine, and saliva or blood.

Results

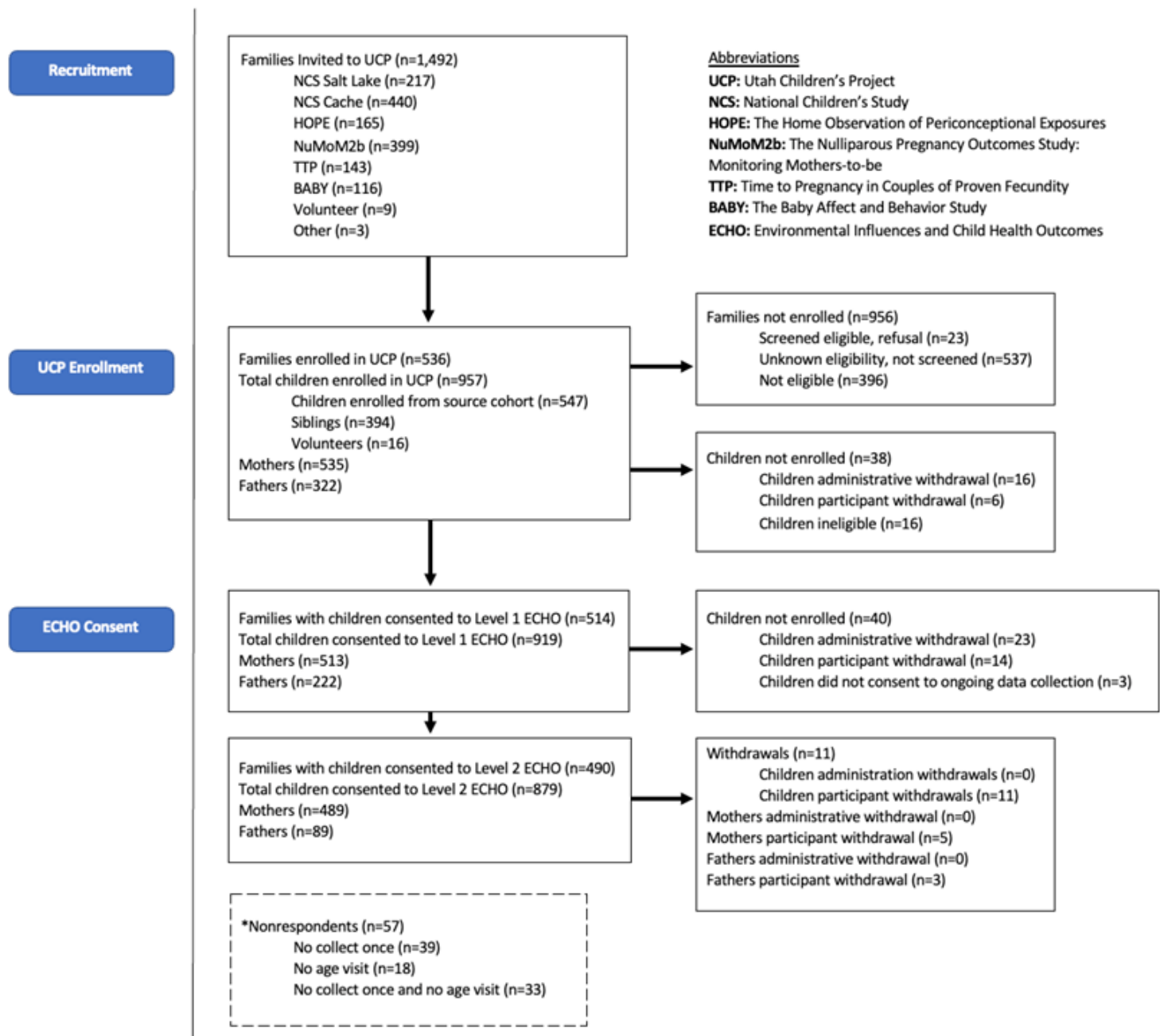
Across all original source cohorts, 1492 families were invited to participate in UCP. From these 536 families enrolled, including 957 children, 535 mothers, and 322 fathers. Completing further enrollment into the initial ECHO protocol (level 1 ECHO consent), there were 514 families, 919 children, 513 mothers, and 222 fathers. Completing further enrollment into ECHO (level 2 ECHO consent), there were 490 families, 879 children, 489 mothers, and 89 fathers. Details for each stage of enrollment and reasons not enrolled at age stage are detailed in **Figure 1**. Among all families invited to be screened for participation in ECHO, the participation rate for Level 2 was 32.8% (490/1492). Among all families screened for eligibility and found to be eligible (n=559), the participation rate for Level 2 was 87.7% (490/559).

At the time of consent and assent into ECHO (Level 1 or 2), 29 children were in infancy (age 0 to 11 months 30 days), 423 were in early childhood (age 1 to 5 years 11 months 30 days), 399 were in middle childhood (age 6 to 11 years 11 months 30 days), and 71 were adolescence (age 12 to 20 years 11 months 30 days).

Demographic characteristics of participants in ECHO Level 2 are detailed in **Table 2**. At the time of consent and assent into ECHO Level 2, the mean age of all children was 9.7 years, of mothers 39.1 years, and of fathers 40.5 years. The participants were predominantly white and Non-Hispanic. Most parents of the children were married, and the mean household size was 5.2 persons. Nearly half (46%) of families had a household income greater than \$100,000 yearly.

Many data collection components of UCP preceded the ECHO-wide protocol. These are detailed by number of participants completing each in **Table 3**. Although most were completed prior to receiving ECHO funding, many of these contributed data and specimens to ECHO. For example, extracted DNA was

Figure 1. Flow of recruitment, enrollment into UCP, and consent into ECHO



CONSORT Diagram. *Nonrespondents are still enrolled in the ECHO program but have yet to complete relevant study visits.

contributed to the ECHO biospecimen repository and included in ECHO analyses, as were nasal swabs, serum, and urine.

Other data collection components were completed as part of the ECHO-wide protocol. These are detailed in Table 4 by number of participants completing in each

life stage, as of June 2022. As noted above, because of the COVID-2019 pandemic, there were fewer specimens collected during 2020-2022 by in-person visits, which reduced the amount of blood, blood spots, saliva, and urine collected below what was planned. Remote biospecimen collection allowed for higher levels of collection of hair, toenails, and deciduous teeth.

Table 2. Characteristics of UCP participants consented to Level 2 ECHO: children, parents, and families, as of date of Level 2 consent

Characteristic	Children N=879	Mother N=489	Father N=89	Families N=490
Age in years, mean (SD)	9.7 (3.4)	39.1 (5.5)	40.5 (6.4)	
Ethnicity, n (%)				
Hispanic	60 (6.8)	30 (6.0)	4 (4.2)	
	813	470		
Non-Hispanic	(91.9)	(93.6)	85 (89.5)	
Unknown	4 (0.5)	2 (0.4)	1 (1.1)	
Race, n (%)				
	813	462		
White	(92.0)	(92.0)	85 (89.5)	
Other	63 (6.2)	35 (5.98)	3 (2.1)	
Unknown	1 (0.1)	5 (1.0)	1 (1.1)	
Marital Status, n (%)				
		442		
Married		(88.0)	82 (86.3)	
Not Married		25 (5.0)	3 (3.2)	
Unknown		35 (7.0)	10 (10.5)	
Occupation, n (%)				
		131		
Professional		(26.1)	42 (44.2)	
Technical		11 (2.2)	12 (12.6)	
Clerical/Sales		19 (3.8)	6 (6.3)	
Skilled Laborer		6 (1.2)	5 (5.3)	
Unskilled Laborer		1 (0.2)	0 (0.0)	
		223		
Homemaker		(44.4)	1 (1.1)	
Student		9 (1.8)	4 (4.2)	
Educator		30 (6.0)	8 (8.4)	
Other		33 (6.6)	5 (5.3)	
Unknown		39 (7.8)	12 (12.6)	
Household persons, mean (SD)				5.2 (1.7)
Household income, n (%)				
Less than \$30,000				15 (4.1)
\$30,000-\$49,999				17 (4.6)
\$50,000-\$99,999				157 (42.8)
Greater than \$100,000				167 (45.5)
Unknown				11 (3.0)

Table 3. Completed evaluations and collected biospecimens for Utah Children's Project participants, prior to ECHO-wide protocol, as of June 10, 2021

Participant	Number Enrolled	Medical History	Physical Exam	Dental Exam	DNA	RNA	Serum	Nasal Swabs	Vaginal Swabs	Rectal Swabs	Urine
<i>Proband</i>	485	475	471	224	485	324	334	284	--	204	265
<i>Sibling</i>	377	370	368	159	372	12	226	253	--	168	218
<i>Mother</i>	489	474	474	--	483	464	467	286	261	--	284
<i>Father</i>	295	283	273	--	288	16	284				

Table 4. Biospecimens collected for Utah Children’s Project participants under the ECHO-wide protocol, by life stage at the time of collection, as of June 3, 2022

Sample Type	Life stage	Participants (N)
Blood	Middle Childhood	147
	Adolescence	45
Blood Spot	Middle Childhood	36
	Adolescence	10
Hair	Early Childhood	132
	Middle Childhood	402
	Adolescence	87
Saliva (for DNA)	Early Childhood	51
	Middle Childhood	48
	Adolescence	6
Toenails	Early Childhood	133
	Middle Childhood	396
	Adolescence	87
Tooth	Early Childhood	42
	Middle Childhood	345
	Adolescence	22
Urine	Early Childhood	119
	Middle Childhood	323
	Adolescence	76

Discussion

We believe that the UCP and broader ECHO projects will lead to significant discoveries in the fields of medicine and public health, similar to the Framingham Heart Health Study, the Nurses’ Health Study, and other longitudinal cohort studies. The data collected will be studied by researchers worldwide to improve children’s health for decades to come.

Ninety-eight percent of children enrolled in UCP who were eligible to enroll in ECHO choose to enroll. We enrolled 919 children, 115% of the planned enrollment into the ECHO program, and 513 mothers and 222 fathers.

UCP specimen collection pre-dated our entry into the nationwide ECHO cohort. The genetic value of trios (child and both parents) and expanded families (2 siblings, both parents) may be of high value in future studies that draw from available ECHO specimens.

The nation-wide ECHO project was originally funded from 2016-2023. A second cycle of ECHO is currently underway since 2023, and is planned to continue to 2030, as described at echochildren.org. This will ensure the continuation and expansion of the value of ECHO for future generations.

Conclusions and Implications

Longitudinal data collection, for our cohort of children and families, supports ongoing research at both a national and local level. UCP and the entire ECHO consortium demonstrate the ability to recruit and retain participants from established cohorts to assess the impact of exposures from preconception, during pregnancy, and early childhood on child health and development. The ECHO-wide Cohort allows investigators to explore various research questions across the five ECHO outcome domains.¹⁸ This approach allows a wider community of scientists to address critical longitudinal research questions that no single cohort, or even a few, could answer alone.

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The pelvic pain plot twist: malpositioned intrauterine devices are associated with acute presentation of pelvic pain

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Abstract

Background: Pelvic pain is a common and diagnostically challenging emergency department (ED) complaint. While intrauterine devices (IUDs) are widely used and generally safe, malpositioned IUDs can cause pain, bleeding, or other symptoms. Most research on IUD malposition comes from outpatient settings, leaving its prevalence and relevance in the ED poorly defined.

Methods: We performed a retrospective chart review of female patients aged eighteen to fifty-five who underwent radiologic pelvic ultrasound in a tertiary academic ED between January 1, 2020, and June 4, 2025. All pelvic ultrasounds ordered by the ED containing the term “IUD” were identified through radiology query. Patients were excluded for chronic (>6 wks) symptoms, absent IUDs, inadequate visualization, or insufficient documentation. Two independent reviewers coded exam indications and ultrasound findings. Descriptive statistics, and chi-square tests assessed frequencies and associations (significance $p < 0.05$).

Results: Of 751 ultrasound reports, 637 met inclusion criteria. Malpositioned IUDs were identified in 151 patients (23.63%), making it the most common abnormal ultrasound finding in patients with IUDs who had a pelvic US ordered in the ED, exceeding ruptured/hemorrhagic cysts (15.65%), intact cysts (13.46%), ovarian torsion (3.91%), ectopic pregnancy (3.60%), and fibroids (3.44%). Pain was the most common exam

indication overall (76.3%) and among patients with malpositioned IUDs (64.9%). Malposition showed significant associations with pain ($\chi^2=14.67$, $p=0.00013$), laterality of pain ($\chi^2=8.011$, $p<0.001$), bleeding ($\chi^2=5.196$, $p=0.022$), and concern for IUD position ($\chi^2=16.81$, $p<0.001$).

Conclusions: Malpositioned IUDs were the most frequent abnormal finding among reproductive age ED patients with an IUD undergoing pelvic ultrasound, occurring in nearly one in four cases. Given their prevalence and strong association with pain, malpositioned IUDs should be considered routinely in the ED differential for acute pelvic pain. Early identification may improve diagnostic accuracy and expedite appropriate management.

Introduction

Background

Pelvic pain is a common yet diagnostically challenging complaint in the emergency department (ED), encompassing a broad differential that ranges from infectious, structural, urological, gastrointestinal, and gynecological causes.^{1,2} The challenge associated with an accurate diagnosis is amplified by overlapping clinical symptoms across various conditions. Among the possible causes, and a potentially underrecognized etiology, are complications associated with intrauterine devices (IUD).³⁻⁵ With IUDs now widely used as a first-line contraceptive option, physicians are increasingly

encountering patients with device-related complaints, including acute pelvic pain.^{6,7}

While IUDs are typically safe and well-tolerated, malpositioning of IUDs can occur. When IUDs are displaced from their ideal position in the uterine fundus, they can provoke cramping, abnormal bleeding, or persistent pain.^{8,9} Malpositioning of the IUD can occur secondary to improper placement, spontaneous migration, or anatomical variations.^{8,10,11} In some patients the device may become embedded in the myometrium or partially perforated the myometrium causing an increase of the severity of symptoms.^{3,8,9} Despite these risks, the association between malpositioned IUDs and acute pelvic pain in emergency settings has not been extensively studied.⁴

The current research on IUD malposition mostly originates from outpatient gynecology or family medicine clinics, where symptoms tend to be evaluated in an elective, non-urgent environment.^{8,9,11-13} However, the emergency department often serves as the first point of contact for patients experiencing sudden-onset severe abdominal or pelvic pain that could be linked to IUD-related complications.¹⁴ Given that the clinical manifestations of a malpositioned IUD, especially pain, is non-specific, it may be underrepresented in the differential diagnosis during acute pelvic pain evaluations in the ED.^{1,2} While there remains a significant paucity of data regarding prevalence of IUD malpositioning, the existing literature that documents malpositioned IUDs in the emergency department does demonstrate full resolution of patient symptoms following removal of the malpositioned IUD.^{4,5}

Importance

Understanding the role of IUD malposition as an etiology of acute pelvic pain is essential for improving diagnostic accuracy and patient care in the emergency department setting. Despite increasing utilization of IUDs, and the documented rates of malposition, this complication is poorly studied within the ED context.

Goal of This Investigation

This study seeks to characterize the presence of malpositioned IUDs among patients who present to the ED with acute pelvic pain by examining how often this issue arises and how it is identified and managed.

Our overall aim is to determine the frequency of IUD malpositioning within reproductive age women presenting to our emergency department. As IUD usage continues to grow globally, understanding its acute complications in acute care environments like the ED becomes increasingly important for ensuring accurate and effective care.

Methods

Study Design & Setting

This is a retrospective chart review conducted at the University of Utah Health Department of Emergency Medicine, a tertiary academic medical center located in Salt Lake City, Utah. The study period was between January 1st, 2020 and June 4th, 2025.

Selection of Participants

The study cohort included female patients aged 18 to 55 years who underwent ultrasound imaging during an ED visit. Our institution utilizes a distinct identifier for imaging ordered by the ED allowing for query of all presenting complaints requiring US imaging. Cases were identified through a query performed by the Department of Radiology, which extracted all US reports that contained the term “IUD.” Patients were excluded if they had insufficient documentation in the radiology report to assess relevant variables, if the IUD was poorly visualized, or not present at time of exam, or if the exam indication was classified as chronic (present for greater than six weeks). The institutional review board at our institution reviewed and approved the study protocol (IRB_00184322). Informed consent was waived due to the retrospective nature of the study.

Outcomes Measured

Our primary outcome was determining the frequency of malpositioned IUDs found throughout the diagnostic evaluation for reproductive aged women presenting to the ED. Secondary outcomes included exam indications for patients found to have IUD malpositioning, frequency of other findings within this patient population, as well as correlations between exam indications and exam findings.

Data Abstraction

The data abstraction was performed in two phases; initial data abstraction, and subsequent data refinement. The initial data abstraction was performed utilizing a specialized radiology search engine and data analytics platform, Montage Search and Analytics (Montage Healthcare Solutions, Nuance/Microsoft). This software extracted unstructured radiology reports and clinical data. This software was utilized to complete case selection. We chose to utilize automatic data abstraction software as opposed to manual data abstraction, as automatic data abstraction has demonstrated similar or superior results, with decreased time and resource burden.¹⁵⁻¹⁸ Following this initial extraction/case selection process Microsoft Excel was utilized to automatically separate the report text into examination, examination findings, and examination impression.

Case Selection

At our institution, the emergency department imaging orders come under a specific identifiable code. This code is utilized for all imaging ordered by our institution's emergency department regardless of the patient's chief complaint, or other demographics. These codes also are separated based on imaging modalities which allowed us to identify all US imaging studies ordered by the emergency department. There were a total of 15,058 initial imaging studies. This included all US from the Emergency Department regardless of the specific type of US ordered.

Utilizing the Montage software, we queried all US imaging orders from the emergency department. The Montage software is a natural language processing model that scans all free-text radiology reports to identify specific words or phrasing. This natural language processing was applied to identify all patient imaging ordered by the emergency department that mentioned either "intrauterine device" or "IUD" within our study time period. This software identified 751 US imaging studies. We exported the imaging reports utilizing the software into a Microsoft Excel file. The data collected from Montage was anonymized and included exclusively the imaging report text.

Definition of Variables

Utilizing the imaging report text generated by the

Montage Software, the following data variables were collected, and subsequently isolated utilizing Microsoft Excel. Two primary variables were derived from each pelvic ultrasound report: (1) reason for the examination and (2) ultrasound findings/diagnosis. The reason for the examination was defined as the clinical indication documented in the radiology report at the time of ordering. Ultrasound findings were defined as imaging abnormalities described in the Findings and Impression sections of the report and were used to assign diagnostic categories. Examination indications were further categorized into predefined clinical groups based on the documented indication (e.g., pelvic pain, abnormal uterine bleeding, evaluation of adnexal mass). Ultrasound findings were categorized as normal or abnormal. Abnormal findings were further classified by diagnosis based on radiologist impression (e.g., ovarian cyst, uterine fibroid, pelvic free fluid). Diagnostic findings were abstracted from both the Findings and Impression sections of the radiology report, with priority given to the impression when discrepancies were present. An IUD was considered malpositioned if the device was described by the interpreting radiologist as low-lying, embedded, rotated, partially expelled, or not located in the uterine fundus (Figure 1).

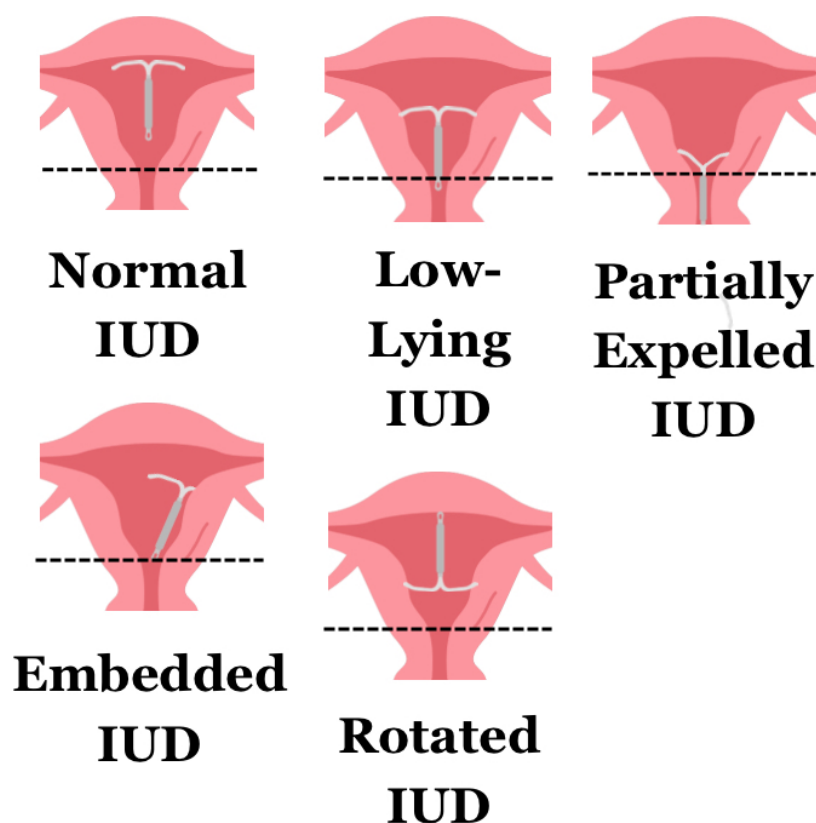
Abstraction Forms

Data abstraction was performed using a standardized manual abstraction form developed prior to data collection. The form included predefined fields for examination indication (reason for examination) and ultrasound findings/diagnosis, which were abstracted from the Findings and Impression sections of the radiology report. There were free-text fields available for reports that did not fit predefined categories.

Meetings

Prior to data abstraction, reviewers met to review study objectives, variable definitions, and abstraction procedures. Training included review of the standardized abstraction form and discussion of representative pelvic ultrasound reports. Any ambiguities in variable definitions were clarified prior to initiation of full data abstraction. Throughout this process the reviewers kept a collaborative log of any questions or ambiguities that were encountered throughout the coding process, and met regularly to review this log, and clarify any remaining coding questions, and reinforce standardized

Figure 1. Variations of Malpositioned IUDs



application of abstraction rules.

Monitoring

After independent abstraction by both reviewers, abstraction results were compared, and discrepancies were identified by a statistician who was not involved in the initial data abstraction. In cases of disagreement between reviewers, a third author independently reviewed the radiology report and adjudicated discrepancies while remaining blinded to both reviewers' original classifications.

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Blinding

Two independent reviewers manually abstracted data from radiology reports. Reviewers were blinded to each other's abstraction results throughout the data collection process.

Testing of Interrater Agreement

Interrater agreement was assessed on the independently abstracted dataset prior to adjudication to evaluate consistency of manual abstraction. Across 18,024 coding decisions, reviewers agreed on 17,893, yielding an overall observed agreement of 99.3%. A prevalence-adjusted kappa indicated near-perfect agreement ($\kappa=0.99$).

Data Analysis

Descriptive statistics were used to characterize the study population. Descriptive statistics were also performed to investigate frequencies of exam indications, as well as frequency of exam findings. Associations between clinical features and outcomes were analyzed using chi-square tests, and logistic regressions where appropriate. Specifically, chi-squared tests with Yates' continuity correction for 2x2 tables were used to evaluate for correlations between exam indications and findings. Statistical significance was defined as $p<0.05$.

Results

Characteristics of Study Subjects

A total of 751 ultrasound readings were included in the initial data extraction. During initial data analysis, 114 patients were excluded from the study due to not meeting inclusion criteria. In total, 637 participants were included in the study. All participants presented to the Emergency Department at the University of Utah Hospital. All participants received an ultrasound report by the University of Utah Hospital Radiology Department. The sample was drawn from a single academic institution and may not reflect broader geographic or cultural diversity.

Frequency of IUD Malpositioning

The primary outcome was determining the prevalence

of malpositioned IUDs within the patient population. Of the 637 ultrasounds obtained in the ED, 151 demonstrated a malpositioned IUD. This represents 23.63% of all participants demonstrating a malpositioned IUD. This is compared to 3.91% ($n=25$) of patients found to have ovarian torsion, 3.60% ($n=23$) found to have an ectopic pregnancy, 13.46% ($n=86$) found to have ovarian cysts, 15.64% ($n=100$) ruptured or hemorrhagic ovarian cysts, 3.44% ($n=22$) found to have uterine fibroids. The most common abnormal ultrasound finding in patients who received US imaging in the ED was malpositioned IUDs.

Figure 2. Prevalence of Malpositioned IUDs within the population

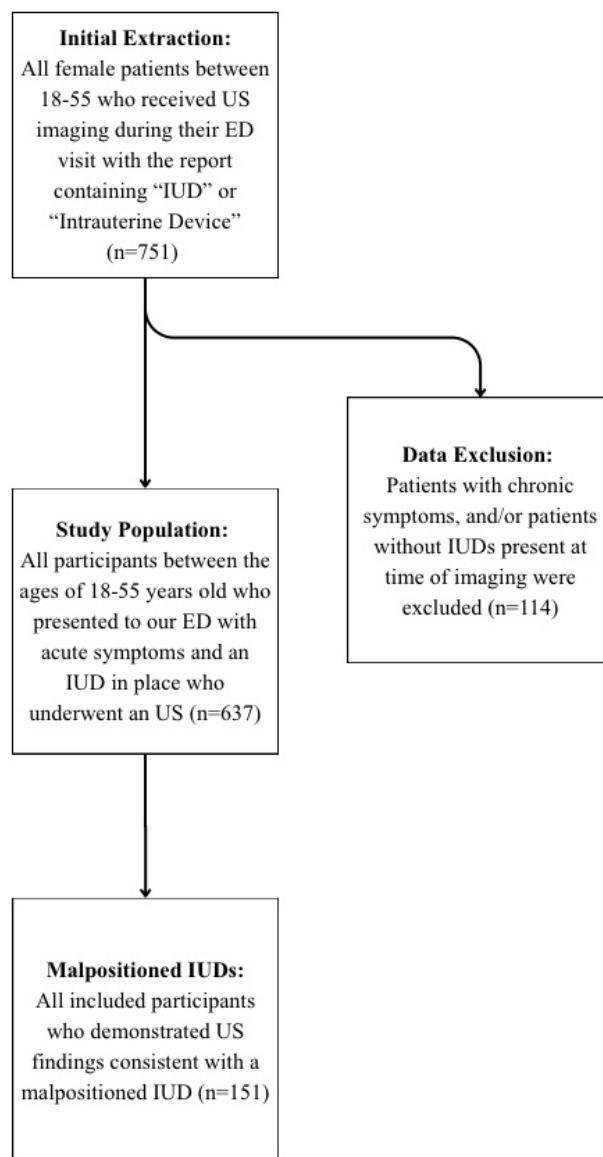


Table 1. Prevalence of Malpositioned IUDs within the population

Diagnosis	Quantity	Percentage
Normal	251	39.28%
Malpositioned or embedded	151	23.63%
Ruptured/Hemorrhagic cysts	100	15.65%
Cysts (Intact)	86	13.46%
Torsion/Suspected Torsion	25	3.91%
Ectopic	23	3.60%
Fibroid	22	3.44
Pregnancy (not ectopic)	10	1.56%
Adenomyosis	9	1.41%
Polyp	8	1.56%
Tubal ovarian	6	0.94%
Other	39	6.10%

Exam Indications

Within the population, the most common indication reported for the ultrasound was pain (n=486, 76.2%). This was further broken down by left sided pelvic pain (n=107, 16.74%), right sided pelvic pain (n=137, 21.44%), vaginal pain (n=3, 0.47%), and general abdominal pain (n=239, 37.40%). The next most common indication for the exam was bleeding or spotting, (n=135, 21.13%), followed by torsion evaluation (n=93, 14.55%). In total, 72 providers listed IUD placement evaluation or string concerns, representing 11.27% of the population.

Malpositioned IUDs & Exam Indications

Specifically within the subset of patients who were found to have a malpositioned IUD (n=151) the most common presenting symptom was once again pain (n=98, 64.9%). Broken down, this presented as 40.40% (n=61) with general pelvic/abdominal pain, 12.58% (n=19) with right sided pelvic pain, and 11.92% (n=18)

with left sided pelvic pain. The second most common presenting symptom for patients with malpositioned IUDs was bleeding (27.81% n=42), followed by IUD placement evaluation/string concerns (20.53% n=31). Torsion evaluation represented 9.93% (n=15) of exam indications within this subset.

Normal Positioned IUD & Exam Indications

Participants with normal positioned IUDs (n=486) were also most likely to have an exam indication of pelvic pain (79.84% n=388). This was further subdivided to be 36.63% (n=178) general pelvic/abdominal pain, 18.31% (n=89) left sided pelvic pain, 24.28% (n=118) right sided pelvic pain, and 0.62% (n=3) vaginal pain. Aside from pain, patients without malpositioned IUDs had exam indications including bleeding/spotting (19.14% n=93), torsion evaluation (15.84% n=77), and IUD placement evaluation or string problem (8.44% n=41).

Table 2. Indications for Exam

Indication	Quantity	Percentage
General Pain	486	76.30%
<i>Left Sided</i>	<i>107</i>	<i>16.74%</i>
<i>Right Sided</i>	<i>137</i>	<i>21.44%</i>
<i>Vaginal</i>	<i>3</i>	<i>0.47%</i>
<i>General abdominal/pelvic</i>	<i>239</i>	<i>37.40%</i>
Bleeding	135	21.13%
Torsion Evaluation	93	14.55%
IUD placement evaluation/String problem	72	11.27%
Pregnancy/pregnancy of unknown location evaluation	29	4.54%
Cramping	29	4.54%
Dysuria/hematuria	5	0.78%
Discharge related concern	5	0.78%
Other	22	3.44%
Unspecified	28	4.38%

Table 3. Malpositioned IUD & Exam Indications

Indication	Quantity	Percentage
General Pain	98	64.90%
<i>Left Sided</i>	<i>18</i>	<i>11.92%</i>
<i>Right Sided</i>	<i>19</i>	<i>12.58%</i>
<i>Vaginal</i>	<i>0</i>	<i>0.00%</i>
<i>General abdominal/pelvic</i>	<i>61</i>	<i>40.40%</i>
Bleeding	42	27.81%
IUD placement evaluation/String problem	31	20.53%

Table 3. Malpositioned IUD & Exam Indications (continued)

Indication	Quantity	Percentage
Torsion Evaluation	15	9.93%
Pregnancy/pregnancy of unknown location evaluation	14	9.27%
Cramping	10	6.62%
Dysuria/hematuria	2	1.32%
Discharge related concern	2	1.32%
Other	4	2.65%
Unspecified	9	5.96%

Table 4. Normal Positioned IUD & Exam Indications

Indication	Quantity	Percentage
General Pain	388	79.84%
<i>Left Sided</i>	<i>89</i>	<i>18.31%</i>
<i>Right Sided</i>	<i>118</i>	<i>24.28%</i>
<i>Vaginal</i>	<i>3</i>	<i>0.62%</i>
<i>General abdominal/pelvic</i>	<i>178</i>	<i>36.62%</i>
Bleeding	93	19.14%
Torsion Evaluation	77	15.84%
IUD placement evaluation/String problem	41	8.41%
Cramping	19	3.91%
Pregnancy/pregnancy of unknown location evaluation	15	3.09%
Dysuria/hematuria	3	0.62%
Discharge related concern	3	0.62%

Table 4. Normal Positioned IUD & Exam Indications (continued)

Indication	Quantity	Percentage
Other	18	3.70%
Unspecified	19	3.91%

Relationship between Exam Indications & Exam Findings

We performed chi-square tests of independence to evaluate associations between exam indications and malpositioned IUDs. Pelvic pain was significantly associated with IUD position ($\chi^2(1, N=637)=11.49$, $p=0.001$). Bleeding or spotting was also associated with malpositioned IUDs ($\chi^2(1, N=637)=4.64$, $p=0.031$), as was concern for IUD placement or string abnormality ($\chi^2(1, N=637)=15.55$, $p<0.001$). There was no statistically significant association between malpositioned IUDs and torsion evaluation ($\chi^2(1, N=637)=2.85$, $p=0.091$).

Discussion

Interpretation

Of all patients between the ages of 18-55 with IUDs in place who presented to a University of Utah emergency department within the last 5 years and had an ultrasound performed, nearly one in every four (23.63%) were found to have malpositioned IUDs. Malpositioned IUDs represented the most common abnormal ultrasound finding within this patient population. This is an important and substantial finding because currently, the diagnosis of IUD malpositioning is not typically on the differential for acute pelvic pain.

Previous Studies

Previous papers in the fields of gynecology and radiology have characterized the link between pelvic pain and malpositioned IUDs.^{1,3,6,9} Additionally, once identified IUDs are being removed safely in selected acute care settings and patients are reporting full resolution of their symptoms following the removal of their IUDs.^{4,5,12} However, this is the first report, to

our knowledge, which evaluates the intersection of malpositioned IUDs in an undifferentiated patient. Evaluating rates of malpositioned IUD in the acute setting, provides a framework including the increasing likelihood of encountering this diagnosis and the importance of maintaining malpositioned IUDs in their differential for other providers working in similar settings.

Limitations

The limitations of this study are centered around its structure. While it is a strong initial evaluation of the association of malpositioned IUDs and pelvic complaints, it is single centered. This may limit its external validity. The other limitation is the natural complexity of patient complaints, many ultrasounds demonstrate more than one pathologic finding. Without further research we cannot confidently link every malpositioned IUD as the primary source of a patient's pain. The studies retrospective nature further limits conclusions drawn as data pulled is limited to the quality of the documentation and the charting. This requires pain to be evaluated as a fixed binary rather than through the standardized pain scale.

Clinical Implications

A significant proportion of patients presenting to the emergency department with concerns of acute pelvic pain or other related complaints were identified on radiographic imaging to have malpositioned IUDs. While this is a commonly accepted source of pain in previous obstetrics and radiology literature, it has not been previously characterized in the acute setting. Our study demonstrates the importance of introducing malpositioned IUDs to providers' initial differential diagnosis on an undifferentiated patient with acute pelvic complaints. Understanding the prevalence of

malpositioned IUDs in patients with pelvic complaints, may help future providers identify this diagnosis more frequently and provide patients with definitive care. As medicine advances through evidence based practices, this research offers a path for our differential diagnosis to advance in the same manner.

Research Implications

Further research regarding a broader patient sample size at various institutions will further characterize the proportion of acute pelvic complaints and malpositioned IUDs. Research into the care and management of malpositioned IUD in the emergency department is additionally needed including but not limited to, proportion of malpositioned IUDs removed in the emergency department, complications, patient tolerance and symptom resolution. Further studies regarding

the evaluation of IUD position with bedside POCUS may additionally be beneficial as many critical access settings do not have access to sonographers and radiologists that are commonly available in tertiary centers.

Conclusion

Our retrospective chart review based study demonstrated malpositioned IUD as the most common abnormal ultrasound finding in the acute care setting. As IUD's have become the first line agent in contraception and rates of IUD use and duration are increasing, malpositioned IUDs have potential to increase in prominence. Including malpositioned IUD on the initial differential diagnosis of patients with acute pelvic concerns in the emergency department is vital to ensuring best patient care.

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