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Characteristics of Pregnancy-Related Deaths Due to Hemorrhage, 2017-2019

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Characteristics of Pregnancy-Related Deaths Due to Hemorrhage, 2017-2019

By

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B.S., West Chester University of Pennsylvania, 2021

Thesis Committee Chair: Michael Kramer, PhD

An abstract of

A thesis submitted to the Faculty of the
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Abstract

Characteristics of Pregnancy-Related Deaths Due to Hemorrhage, 2017-2019

By Alyssa Harvey

Background: Hemorrhage is a leading underlying cause of pregnancy-related death, and in a recent analysis of 1,018 pregnancy-related deaths from Maternal Mortality Review Committees (MMRCs) in 36 U.S. states, it accounted for 13.7% of pregnancy-related deaths. Postpartum hemorrhage, ectopic pregnancy, and placenta accreta spectrum have all been identified as important contributors to hemorrhage and pregnancy-related mortality. MMRCs are uniquely situated to identify contributing factors of pregnancy-related deaths due to hemorrhage as well as the context in which these deaths occurred.

Methods: This analysis examined a subset of aggregate Maternal Mortality Review Information Application (MMRIA) dataset of pregnancy-related deaths occurring from 2017-2019. Data was further restricted to preventable, pregnancy-related deaths due to hemorrhage when examining contributing factor classes, contributing factor levels, and recommendation levels, which are unique to deaths deemed preventable. All categorical variables were summarized quantitatively using percentages. Among the preventable pregnancy-related deaths with an underlying specific cause of ectopic rupture, a mixed inductive and deductive thematic analysis was performed on the committee-assigned contributing factors and recommendation free-text fields.

Results: There were 133 total pregnancy-related with an underlying cause of death of hemorrhage. Ruptured ectopic pregnancy accounted for 21.1% of cases. 90.1% of the 133 deaths were determined to be preventable. The most common contributing factor classes among the patient/family and provider levels was knowledge while clinical skill/quality of care was the most common class among the facility, systems, and community levels. Barriers to care, delay in identification, treatment, and transfer of care, clinical skill and quality of care (including assessment, continuity of care/care coordination, and policies/procedures), awareness, knowledge, and education, as well as reproductive health were identified as key findings from the thematic analysis.

Conclusion: The results of this analysis can be used to inform a variety of clinical, social, and epidemiological programs and research activities. While descriptive in nature, these results can be used to inform future association studies such as case-control and cohort studies. The qualitative findings can help guide prevention and clinical interventions geared toward pregnancy-related deaths due to ectopic rupture.

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Background

Hemorrhage as a Leading Cause of Maternal Mortality

The maternal mortality ratio (MMR), which is "the number of maternal deaths per 100,000 live births, [where] maternal death is the death of a woman while pregnant or within 42 days of termination of pregnancy," in the U.S. is high compared to other economically advanced nations and has not improved over the last several decades, despite technological advancements and increasing national healthcare expenditures.[1,2] The pregnancy-related mortality ratio in the United States has steadily increased from 7.2 deaths per 100,000 live births in 1987 to 17.3 deaths per 100,000 live births in 2018.[3] The Pregnancy Morality Surveillance System (PMSS) defines a pregnancy-related death as the death of a woman while pregnant or within 1 year of the end of pregnancy from any cause related to or aggravated by the pregnancy.[3] The pregnancy-related mortality ratio (PRMR) is the number of pregnancy-related deaths for every 100,000 live births.[3] Hemorrhage, including obstetric and postpartum hemorrhage, has been persistently ranked as one of the leading causes of pregnancy-related deaths despite advances in science and medicine which leads to efforts that explore the social and systematic factors, and changes in medical etiologies, that may contribute to the deaths of these individuals.[4-7] While the proportionate contribution of hemorrhage to pregnancy-related deaths declined from 28.7% to 18.2% between 1987 and 1997, over the ensuing 20 years, hemorrhage has persisted as a leading cause of pregnancy-related death ranking 4th overall at 11% of all pregnancy-related deaths with a cause of death determination from 2016-2018.[3,6] This change from a sharp decline over a 10-year period to almost no change over the last 20 years, may be indicative that the exisitng interventions are not addressing some of the key contribiting factors to preganncy-related deaths due to hemorrhage. Maternal Mortality Review Committees (MMRCs) are multi-disciplinary committees that convene at the state or local level to comprehensively review deaths of women

during or within a year of pregnancy to more fully understand the circumstances surrounding each death.[8] Among all deaths reviewed by Maternal Mortality Review Committees (MMRCs) in 14 states from 2008 to 2017, hemorrhage was identified as the second leading underlying cause of pregnancy-related death accounting for 13.1% of deaths.[7] Hemorrhage persists as the second leading underlying cause of pregnancy-related death in the most recent analysis of data from 36 state MMRCs from 2017-2019, accounting for 13.7% of pregnancy-related deaths with an identified underlying cause of death.[5]

Racial and Ethnic Disparities

Racial and ethnic disparities in pregnancy-related mortality are also persistent, with significantly higher PRMRs among Black and American Indian/Alaskan Native (AI/AN) women than among White, Asian/Pacific Islander, and Hispanic women.[6,9,10] Surveillance data has shown that non-Hispanic Black, American Indian, and Alaskan Native women are 2-3 times more likely to die as a result of pregnancy-related causes than non-Hispanic white women.[11] In the most recent data from 36 MMRCs, hemorrhage was the leading underlying cause of death among non-Hispanic Asian persons (at 31.3%), and the second leading underlying cause, below mental health conditions, among all American Indian or Alaska Native persons.[5,12]

Etiologies of Pregnancy-Related Mortality with an Underlying Cause of Hemorrhage

Pregnancy-related mortality due to hemorrhage may be attributed to three broad etiologies: abnormal formation or location of the placenta, trauma during labor and delivery, and failure of uterine contraction after delivery.[13,14] When Maternal Mortality Review Committees review a pregnancy-related death, they assign an underlying cause of death. More specific causes of pregnancy-related deaths due to hemorrhage can be further categorized into the following: uterine rupture, placental abruption, placenta previa, ruptured ectopic, uterine atony/postpartum

hemorrhage, placenta accreta/increta/percreta, retained placenta, and laceration/intra-abdominal bleeding.[15] Postpartum hemorrhage, ectopic pregnancy and placenta accreta spectrum have all been identified as important contributors to hemorrhage and pregnancy-related mortality.[16-18] Ruptured ectopic pregnancy is one cause of pregnancy-related deaths due to hemorrhage that remains largely unchanged as a top cause of not only obstetric hemorrhage, but pregnancy-related mortality in general. In fact, from 2011-2013, ruptured ectopic pregnancies were the top cause of hemorrhage related mortality.[13] A recently published population-based study in Washington examined temporal trends in maternal mortality and severe morbidity associated with hospitalization due to ectopic pregnancy from 1987 to 2014. While hospitalizations due to ectopic pregnancy decreased over the time period, severe maternal morbidity and mortality among hospitalized women increased and these trends were independent of changes in maternal ages, type of health insurance, and underlying chronic morbidity.[19]

Preventability of Pregnancy-Related Deaths

Most pregnancy-related deaths with an underlying cause of hemorrhage are preventable.[20,21] Common contributing factors have been identified at provider and facility levels and include delayed response to clinical warning signs, ineffective care, inadequate staff knowledge, systems issues (ie, lack of massive transfusion protocols), and coordination of care (ie, delays in blood product administration).[22] The frequency of pregnancy-related mortality due to hemorrhage and the high degree of preventability led to regional and national efforts to better equip providers, facilities and hospital systems with screening tools, toolkits/bundles, and other prevention measures to reduce the morbidity and mortality due to obstetric hemorrhage.[23,24] State and national organizations suggest that risk assessment for obstetric hemorrhage be conducted antenatally as well as upon admission and over the course of labor and delivery as other risk

factors emerge.[14] Many deliveries occur in hospitals located in rural or small communities and these centers often do not have the capacity to deal with an obstetric emergency such as hemorrhage.[14] In order to ensure appropriate management of patient care, these facilities should have policies and procedures in place to assess when it is necessary to transfer an individual to a facility with a higher level of care.[14] While strides have been taken to improve outcomes, obstetric hemorrhage remains a leading cause of pregnancy-related mortality.[5,8,23,24] Changes in the spectrum of etiologies, definitions, and disparities in access to care may explain the lack of significant progress made in reducing pregnancy-related deaths due to hemorrhage.[25]

Research Gaps and Purpose of this Analysis

Recent surveillance has shown that over four-fifths of pregnancy-related deaths are preventable.[5] Maternal mortality review committees are uniquely situated to identify contributing factors of pregnancy-related deaths due to hemorrhage as well as the context in which these deaths occurred. MMRCs make determinations on pregnancy-relatedness, preventability, identify contributing factors, and create recommendations that address the contributing factors and inform future care.[1,7] There are three national surveillance systems for pregnancy-related mortality within the Centers for Disease Control and Prevention. The National Vital Statistics System (NVSS) is run by the National Center for Health Statistics (NCHS). Within the National Center for Chronic Disease Prevention and Health Promotion, the Division of Reproductive Health is responsible for the Pregnancy Mortality Surveillance System (PMSS), and the ERASE MM Program with participating states using the Maternal Mortality Review Information Application (MMRIA). Data collected by MMRCs from reviews of pregnancy-associated deaths are entered into MMRIA for further analysis and reporting at the jurisdiction and national level.[7]

One significant existing gap in the literature is a close examination of maternal mortality due to hemorrhage from a holistic, public health lens. While many researchers and clinicians cite public health surveillance data systems such as NVSS and PMSS which are critical to understanding trends and knowing PRMRs, there is a need to supplement this data with Maternal Mortality Review Information Application (MMRIA) data to inform clinical recommendations. MMRCs offer more detailed accounts of pregnancy-related and pregnancy-associated deaths through diverse lenses. MMRIA data can be utilized to focus prevention efforts more effectively due to the ability of MMRCs to capture elements of the decedent's life that other surveillance systems do not. Maternal Mortality Reviews Committees synthesize information from a variety of sources such as maternal death certificates, birth and fetal death certificates, hospitalization and prenatal records, a social-environmental profile, as well as a community vital signs dashboard which provides context about the community in which the person lived. A key part of the information that is collected and entered into MMRIA are the contributing factors classes, contributing factor descriptions, and the recommendations put forth by the committee. This manuscript will shed light on the need for researchers and clinicians to consider the contributing factor descriptions and recommendations when formulating research studies as well as the creation and implementation of mitigation strategies in a clinical setting. Since ectopic rupture remains one of the leading causes of hemorrhage deaths, it is important to understand why existing intervention may not work for those who experience hemorrhage due to ectopic rupture. This may be because the points of intervention needed are outside of the hospital setting and are instead related to healthcare access and other social determinants of health. There are currently no publications that focus on content analysis of the contributing factor and recommendation free-text fields specifically for ectopic rupture, therefore this analysis will fill the existing gap

and provide a better understanding of how interventions can be altered to address the root causes of these deaths.

The purpose of the quantitative portion of the analysis is to synthesize the demographic and clinical characteristics as well as the current contributing and contextual factors and MMRC recommendations to describe with more detail the epidemiologic patterns of hemorrhage using this novel surveillance tool and to answer the questions: 1) *What are the demographic and clinical characteristics of pregnancy-related deaths with an underlying cause of hemorrhage? 2) W*hat *is the distribution of contributing factor classes among preventable pregnancy-related deaths with an underlying cause of hemorrhage, and what is the distribution of contributing factor levels and recommendation levels among preventable pregnancy-related deaths with an underlying cause of hemorrhage*? The results of the qualitative content analysis will be themes that arise from the contributing factor descriptions and recommendations which can be translated into actionable items for prevention, and answer the question: *Among the preventable deaths with an underlying cause of hemorrhage from ectopic rupture, what are the common themes of MMRC-identified contributing factors and recommendations based on free-text descriptions of each?*

Methods

Population and Data Source

This analysis used a subset of the pregnancy-related deaths in MMRIA (Maternal Mortality Review Information Application) from 36 states from 2017-2019. The analysis included only those who have experienced a pregnancy-related death with hemorrhage as the underlying cause of death that are residents of the included 36 U.S. states. Data was further restricted to preventable, pregnancy-related deaths due to hemorrhage when examining contributing factor

classes, contributing factor levels, and recommendation levels, which are unique to deaths deemed preventable. Preventable pregnancy-related deaths with a specific underlying cause of ectopic rupture were used for the qualitative analysis of contributing factor descriptions and recommendations.

Characterizing Pregnancy-Related Deaths with an Underlying Cause of Hemorrhage

The overarching goal of the quantitative summaries is to describe the patterns specific to pregnancy-related deaths with an underlying cause of hemorrhage. The variables used to characterize the hemorrhage deaths include race-ethnicity, age, education attainment, urbanicity, timing of death in relation to the end of pregnancy, and specific hemorrhage etiology. Consistent with prior methodology, the pregnancy-related deaths with an underlying cause of hemorrhage were described by the demographic and clinical characteristics as well as specific cause of death.[5] The percentage of the pregnancy-related hemorrhage deaths with a particular value for a variable (percentage of non-Hispanic Black individuals who experienced a pregnancy-related death with an underlying cause of hemorrhage).

The race-ethnicity variable was created based on a combination of availability of fields on the birth/fetal death certificate and death certificate of the decedent. The birth/fetal death certificate source of race and ethnicity was prioritized as this is more likely to be self-reported. The race-ethnicity variable is classified as: non-Hispanic American Indian or Alaska Native, non-Hispanic Asian, non-Hispanic Black, non-Hispanic Native Hawaiian and Other Pacific Islander, non-Hispanic White, Hispanic, non-Hispanic other/multiple races.

Age at death is based on information on the death record and is classified into the following categories: 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, ≥45 years.

Education attainment comes from the birth or fetal death record when available, and from the death records when a birth or fetal death record is available. If the death occurred during the postpartum period, and the death record indicated an education one level higher than the birth record, the higher education level from the death record was used. Education attainment is categorized into; 12th grade or less, no diploma, high school graduate or GED completed, some college credit, but no degree, associate or bachelor's degree, and advanced degree.

Timing in relation to the end of pregnancy is categorized as pregnant at time of death, death on the day of delivery, 1-6 days after end of pregnancy, 7-42 days after end of pregnancy, and 43 days to 1 year after end of pregnancy.

Geographic information was based on county of last residence as captured by the death certificate, and when death certificate residence was not available, the residence on the birth or fetal death certificate was used. Urban classification includes metropolitan division (≥2,500,000) and metropolitan (≥50,000–2,499,999); Rural classification includes micropolitan (10,000–49,999) and rural (<10,000) as captured in MMRIA.

Whether an individual had a previous cesarean section is documented in prenatal care record as 'method of delivery' for previous pregnancies as well as on birth/fetal death certificate parent section as a numeric value of previous cesareans, as well as on the birth certificate in the form of a drop-down menu from a list of risk factors (with prior cesarean being listed as a risk factor). Upon further inspection, it was decided that due to the degree of missingness for this variable, it would not be reported in this manuscript.

The pregnancy-related deaths due to hemorrhage were also characterized using committee determination of preventability, underlying cause of death, contributing factor class,

contributing factor level, recommendation level, discrimination contribution, obesity contribution, mental health contribution, and substance use disorder contribution. These variables were presented as the percentage of the deaths that had the variable value where a determination for the variable was made.

When MMRCs identify a death as pregnancy-related, a preventability determination is made. A death is considered preventable if the committee determines that there was at least some chance of the death being averted by one or more reasonable changes to patient, family, provider, facility, system and/or community factors. A determination of either 'yes', 'no', or 'unable to determine' is made.

The committee also decides whether obesity, mental health, discrimination, and/or substance use disorder contributed to the death. The responses to these variables are "yes", "probably", "no" or "unable to determine." It is important to note that for this variable, data were restricted to include deaths with a committee review date after the discrimination variable was added (May 29th, 2020).

Type of hemorrhage death is an assigned underlying cause of death determined by the review committee. The PMSS codes associated with hemorrhage are summarized below.

10.1	Hemorrhage – Uterine Rupture
10.2	Placental Abruption
10.3	Placenta Previa
10.4	Ruptured Ectopic Pregnancy
10.5	Hemorrhage – Uterine Atony/Postpartum Hemorrhage
10.6	Placenta Accreta/Increta/Percreta
10.7	Hemorrhage due to Retained Placenta
10.9	Other Hemorrhage/NOS
10.10	Hemorrhage – Laceration/Intra-Abdominal Bleeding

Preventable Pregnancy-Related Deaths with an Underlying Cause of Hemorrhage

A sub-analysis of the preventable hemorrhage deaths was performed to summarize the contributing factor classes, contributing factor levels, recommendation levels, and the concordance among the recommendation and contributing factor levels. For deaths deemed preventable, MMRCs identify contributing factors classes from a list of twenty-eight pre-determined factors listed on the MMRC Committee Decisions Form and they are listed in the table below.

Contributing Factor Classes			
1. Access/financial	8. Cultural/religious	15. Law Enforcement	22. Structural racism
2. Adherence	9. Delay	16. Legal	23. Substance use disorder - alcohol, illicit/prescription drugs
3. Assessment	10. Discrimination	17. Mental health conditions	24. Tobacco use
4. Chronic disease	11. Environmental	18. Outreach	25. Trauma
5. Clinical skill/ quality of care	12. Equipment/ technology	19. Policies/procedures	26. Unstable Housing
6. Communication	13. Interpersonal racism	20. Referral	27. Violence
7. Continuity of care/ care coordination	14. Knowledge	21. Social support/ isolation	28. Other

MMRCs also provide a free-text description of each factor and a categorization of the factor at the patient/family, provider, facility, community, or systems level. Contributing factors may be documented at multiple levels. MMRCs also document actionable recommendations that address the identified contributing factors and specify a recommendation level of patient/family, provider, facility, community, or systems. The top five contributing factor classes for each contributing factor level were summarized. Contributing factor and recommendation levels were summarized and compared for concordance where both were non-missing. Recommendation levels were also filtered for those entered after October 9th, 2020, when the recommendation level field was added.

Qualitative Analysis of Contributing Factors Descriptions and Recommendations for Preventable, Ectopic Ruptures

A hybrid deductive and inductive thematic analysis was performed on the contributing factor description and recommendation free-text fields for preventable, pregnancy-related deaths where hemorrhage due to ruptured ectopic pregnancy is listed as the underlying cause of death where contributing factors and/or recommendations were non-missing (n=20). The qualitative analysis was done to better understand how MMRCs characterize the contributing factors for and recommendations to prevent pregnancy-related deaths with an underlying cause of ectopic rupture. Data preparation included filtering cases by underlying cause of death of ectopic rupture or PMSS code 10.4. Data from contributing factor descriptions and recommendations free-text fields were combined into a single document for each case, cleaned, and imported to MAXQDA qualitative software. An initial codebook was created from key terms and concepts derived from a review of the literature, and the contributing factor and recommendation fields in MMRIA. The codebook contains a definition of each term/concept, inclusion criteria, exclusion criteria, and an example (where necessary). The two coders individually applied initial codes to four (4) randomly selected cases and review together for agreement. Any discrepancies were reconciled, and additional codes and definitions were added or edited as necessary. Next, a random selection (20%) of the coded excerpts were reviewed by a third, independent coder for validation. Any discrepancies were addressed and reviewed by all coders for agreement. Upon consensus, the remaining cases (16) were divided equally among the two main coders, who applied initial codes, exchanged, and reviewed coded excerpts for agreement, and reconciled any differences. The coded excerpts were then equally divided among the main coders and grouped into categories that were defined and reviewed for agreement and consensus. 20% of the coded and categorized excerpts were randomly selected for validation by the third, independent reviewer

and any discrepancies addressed were reviewed by all coders for agreement and consensus. The contributing factor and recommendation fields were analyzed for concepts related to the research question and literature including as delay, quality of care, policies and procedures, and knowledge. However, new codes were added to the codebook as they emerged from the text. After two rounds of coding, common themes found in the contributing factors and recommendations were summarized and sample quotes were selected that exemplify the corresponding themes.

Results

Quantitative Results

Among all deaths reviewed by MMRCs in 36 states from 2017-2019, 29 states had hemorrhage deaths. Within the 29 states, there were 133 total pregnancy-related with an underlying cause of death of hemorrhage. Race, ethnicity, and age were available for 99.2% of these cases. 39.4% of pregnancy-related deaths with an underlying cause of hemorrhage were among non-Hispanic white women and 34.1% of the deaths were among those aged 30-34. Educational attainment was available for 97.7% of deaths and 40% were high school graduates or completed their GED. Urbanicity was missing for 15.8% of deaths, and most of the deaths were among those with an urban place of residence (83.9%). Timing of death in relation to the end of pregnancy was available for 99.2% of deaths and day of delivery was the most common timing of death at 39.4% of cases.

Ruptured ectopic pregnancy was the most common specific etiology of the pregnancy-related deaths due to hemorrhage with 21.1% of cases having this determination. The highest etiology overall was the “other hemorrhage/not otherwise specified” determination at 22.6% of cases. A preventability determination was made for 99.2% of the pregnancy related deaths due to

hemorrhage and it was found that 90.1% were determined to be preventable. Discrimination, obesity, mental health conditions, and substance use disorder were noted in fewer than 10% of hemorrhage deaths.

When examining the contributing factor and recommendation levels assigned to the preventable pregnancy-related deaths due to hemorrhage, the most common contributing factor level was the provider level (36.3% of contributing factors had this designation). The most common recommendation level however was the facility level at 31.2% of cases. The most common contributing factor classes among the patient/family and provider levels was knowledge and delay while the most common contributing factor class among the facility, systems, and community levels was clinical skills/quality of care. Additionally, it is also of importance to note that where both contributing factor level and recommendation level were both non-missing, they were assigned the same level 46% of the time and assigned different levels 54% of the time.

Thematic Analysis of Contributing Factors and Recommendations

Barriers to Care

MMRCs described in the contributing factors several types of health care barriers experienced by individuals with ectopic rupture. The most common barriers described include interpersonal barriers such as domestic violence and discrimination/bias. Discrimination was found to be a barrier in relation to obesity, race, and autism. For example, "*Patient pain level dismissed although she was in moderate distress, tearful and not contributive to history. Care not responsive to patient's neurocognitive needs (autism).*" Patient-provider communication was also noted as a major barrier and can be exemplified by the quote: "*Difficulty in communication with patient and her family*." These barriers led to delays in care (assessment, screening, treatment). Recommendations were provided to address these barriers and the resultant delays in

care. These recommendations to address these barriers included providing better domestic violence screening and community support services, interpretation and autism support services, and provider bias training. One recommendation outlined concrete steps addressing domestic violence as a barrier to care, "*Hospitals should work with obstetric providers who provide prenatal and postpartum care to ensure that IPV screening is incorporated into prenatal and postpartum care and that systems are in place for women who screen positive to receive appropriate referral, resources and follow up*."

Delay in Identification, Treatment, and Transfer of Care

MMRCs identified delays in treatment, identification, and transfer of care as contributing factors to preventable deaths due to ectopic rupture. These delays were related to identification of pregnancy and ectopic pregnancy via ultrasound, delays in evaluation, delays in getting patient to the operating room, and delays in transferring decedent to a higher level of care when necessary. Delay in identification can be exemplified with the quotes, "*Provider failed to notice ectopic pregnancy in first scans from radiology.*" and "*Pt was sent home following a U/S where they did not rule out an ectopic".* Delay in treatment was also found in the following excerpts, 1) "*Delays in getting her to OR"* 2) "*OB was called twice but took 2 hours to contact*." There were no clear themes among the recommendations related to solutions in preventing these delays.

Clinical Skill & Quality of Care

Assessment. MMRCs also described the lack of proper assessment of individuals with ectopic pregnancies as contributing factors. Committees cited lack of expertise and resources and a lack of diagnostic tests administered as common contributing factors related to assessment. For example, "*missed diagnosis of ectopic pregnancy, unclear whether appropriate personnel were available and who did the ultrasound*," and put more simply, "*Patient was not adequately*

assessed." To address these issues in assessment, committees recommended that all hospital emergency departments have point of care ultrasounds available and that providers in emergency departments should be educated on how to read ultrasound results and identify signs of ectopic pregnancy. An example of a recommendation related to expertise and resources of hospital staff includes, 1) "*Provider should have ordered additional tests/imaging given the amount of pain patient was in, rapid heartbeat, etc.*" and 2) "*When obesity makes U/S difficult or unusable, there should be an elevation of expertise on who administers ultrasound, or an alternative method should be used to confirm location of the pregnancy."*

Continuity of Care & Care Coordination. MMRCs identified lack of continuity of care and care coordination as critical contributing factors. Lack of close follow-up, appropriate transition of care, and warm handoffs were all cited in the free-text fields. The contributing factor descriptions of "*EMS brought her to a level 0 (non-birthing hospital)"* and "*Delay in care the second ED visit; may have been due to patient's poor understanding of need to return"* exemplify the theme of a lack of care coordination and continuity of care. In order to address these issues, MMRCs recommended that providers and care team members provide ongoing support to patients, especially those who struggle with substance abuse. Committees also suggested that patients with an ectopic pregnancy or rupture need to be followed closely throughout the entire course of care and when transfer of care or specialty is needed a more direct and collaborative approach should be taken by the providers. For example, 1) "*medical management of ectopic pregnancy requires close follow-up,*" 2) "*postpartum visit provider should have facilitated warm hand-off to provider for tubal ligation rather than just giving number to call,"* and 3) *"The EMS system and perinatal center of the region should develop a medical control agreement to enable EMS consult with the perinatal center (via telemedicine) to*

guide care and transport decisions for pregnant and postpartum women" exemplify strong recommendations related to care coordination and continuity of care.

Policies and Procedures. In response to some of the contributing factors related to clinical skill/quality of care and delay, MMRCs identified recommendations for the development of a standard of care for the assessment and treatment of ectopic pregnancy and rupture. For example, "*All EDs should have a plan and process in place for the accurate diagnosis and treatment of ectopic pregnancy, including ruptured ectopic pregnancy*" and "*Facilities, especially smaller facilities that see fewer pregnant patients, should have mechanisms and processes in place to effectively screen for ectopic pregnancy*" were cited as recommendations related to establishing a standard of care at the facility level. Recommendations related to transfer of care were also common, for example, "*Facilities and healthcare systems should have processes in place for transferring patients to higher levels of care. (Address issues with EMTALA violations).*"

Awareness, Knowledge, & Education

MMRCs acknowledged the lack of awareness (knowledge) as a major contributing factor and related to this lack of awareness is delay in seeking care. Examples of contributing factor descriptions related to awareness or recognition of symptoms include "*Patient and family were seemingly unaware of the warning signs of an ectopic pregnancy"* and *"Lack of knowledge about warning signs of ectopic pregnancy."* Recommendations addressed this lack of awareness/knowledge by recommending the development of public health campaigns to educate community members about the signs and symptoms of ectopic pregnancy. For example. "*Providers should ensure patients are counseled regarding signs and symptoms of ectopic pregnancy and other life-threatening conditions and when to return for follow-up"* and *"Education is needed on signs/symptoms of ectopic pregnancy, what is normal early pregnancy*

pain and what is to be considered pain/symptoms that would require a visit to the ER or clinic" both exemplify recommendations related to increasing education on signs and symptoms. Recommendations also advocated for the physician's role in educating patients about ectopic pregnancy and rupture and how organizations such as the American College of Obstetricians and Gynecologists (ACOG) have a role in educating physicians about standards of care and patient education. For example, the recommendation, *"ACOG/other key convening bodies should train providers who treat people with substance use disorder to ask about reproductive health needs and to evaluate and refer patients to preconception care."* stresses the importance of the providers role in educating patients.

Reproductive Health Services

MMRCs provided recommendations related to increasing funding for community reproductive health and family planning services, reducing barriers to accessing reproductive healthcare, and educating patients on contraception and the importance of prenatal care. Recommendations included action items such as 1) "*Providers should educate women during routine visits on preventive health care, contraception, early signs of pregnancy* including ectopic pregnancy," 2) "*Continue to support funding for comprehensive health care for reproductive age women,*" and 3) *"Providers should conduct and document comprehensive contraceptive counseling during prenatal care, at the delivery hospitalization and during postpartum visits."* An interesting theme that emerged tied together prenatal care and substance use disorder (SUD) and how special care should be taken to educate and provide resources to pregnant people with SUD. For example, *"ACOG/other key convening bodies should train providers who treat people with substance use disorder to ask about reproductive health needs and to evaluate and refer patients to preconception care"* and *"Community-based organizations*

should educate women on the importance of getting prenatal care and substance use treatment early in pregnancy, as way to increase chances of a healthy pregnancy and of being able to parent baby" are both recommendations that exemplify this theme.

Figure 1. Exclusion cascade diagram

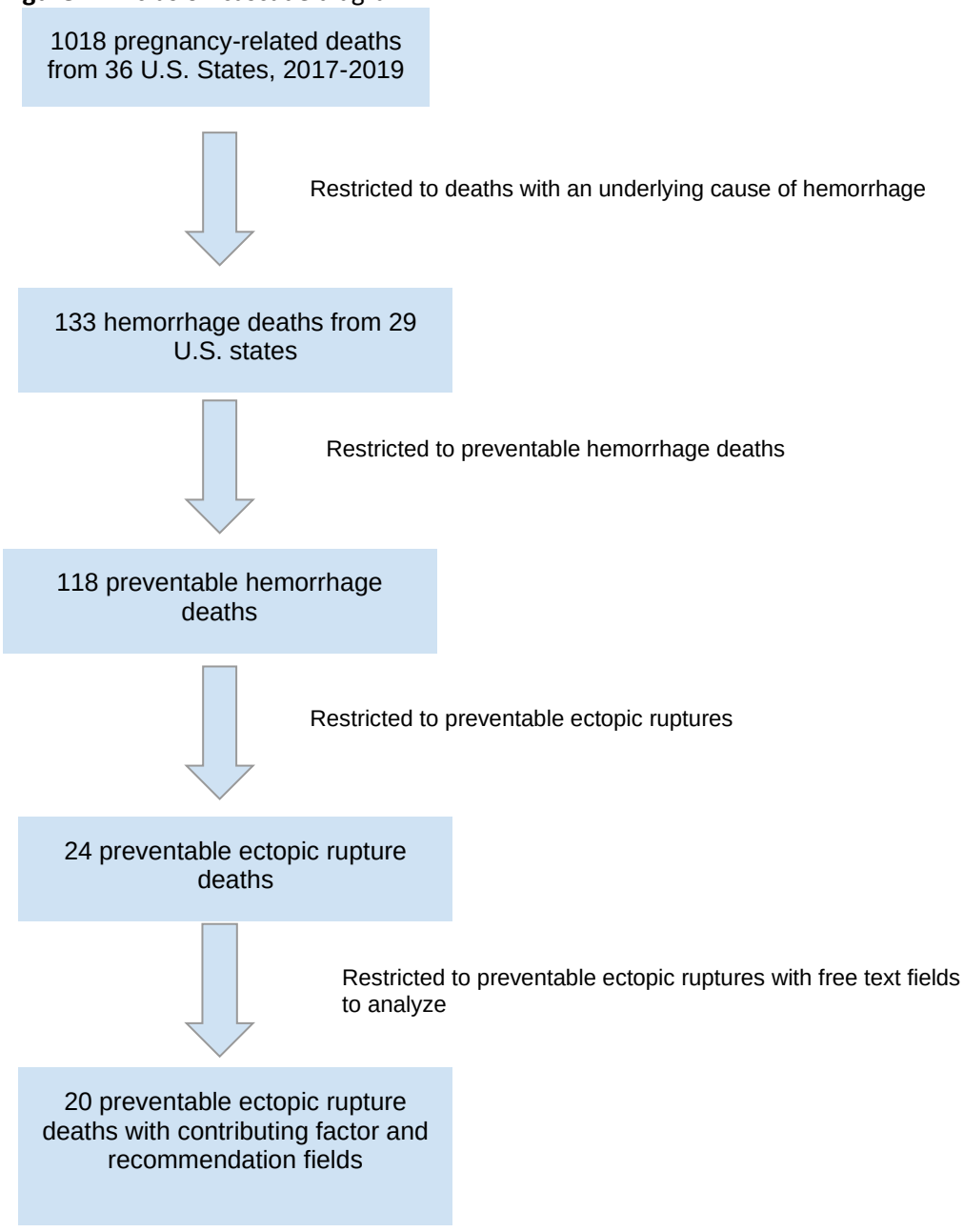

Table 1. Characteristics of pregnancy-related deaths due to hemorrhage among residents of 29 US States, 2017-2019

	Total (N= 133)	
	n	**%**
Race/ethnicity		
Hispanic	29	22.0
non-Hispanic AIAN	2	1.5
non-Hispanic Asian	10	7.8
non-Hispanic Black	33	25.0
non-Hispanic NHOPI	1	0.8
non-Hispanic White	52	39.4
non-Hispanic all other/multiple races	5	3.8
Missing	1	-
Age (years)		
15-19	1	0.8
20-24	12	9.0
25-29	22	16.5
30-34	45	33.8
35-39	36	27.1
40-44	16	12.0
45+	1	0.8
Educational Attainment		
12th grade or less; no diploma	18	13.8
High school grad or GED	52	40.0
Some college credit; no degree	22	16.9
Associate or bachelor's degree	29	22.3
Advanced degree	9	6.9
Missing	3	-
Urbanicity of place of last residence		
Urban	94	83.9
Rural	18	16.1
Missing	21	-
Timing of Death		
Pregnant at time of death	37	28.0
Day of delivery	52	39.4
1-6 days after end of pregnancy	26	19.7
7-42 days after end of pregnancy	13	9.9
43 days-1 year after end of pregnancy	4	3.0

Missing	1	-

Table 2. Committee determinations on circumstances of pregnancy-related deaths due to hemorrhage among residents of 29 US States, 2017-2019

	Total (N= 133)	
	n	**%**
Was the death preventable?		
Yes	118	90.1
No	13	9.9
Unable to determine	1	-
Missing	1	-
Did discrimination contribute to the death?*		
Yes	4	7.7
Probably	8	15.4
No	40	76.9
Unknown	26	-
Missing	4	-
Did obesity contribute to the death?		
Yes	8	6.5
Probably	14	11.4
No	101	82.1
Unknown	9	-
Missing	1	-
Did mental health conditions contribute to the death?		
Yes	1	0.9
Probably	5	4.3
No	111	94.9
Unknown	16	-
Did substance use disorder contribute to the death?		
Yes	9	7.5
Probably	2	1.7
No	109	90.8
Unknown	13	-

* This field was added to the MMRIA Committee Decisions Form in May 2020, so we only report on the **82 deaths** that occurred between 2017-2019 and were reviewed after May 29, 2020

Table 3. Specific etiology of pregnancy-related deaths due to hemorrhage among residents of 29 US States, 2017-2019.

	Total (N= 133)	
Condition	**n**	**%**
Uterine Rupture 10.1	21	15.8
Placental Abruption 10.2	11	8.3
Placenta Previa 10.3	2	1.5
Ruptured Ectopic 10.4	28	21.1
Uterine Atony/Postpartum Hemorrhage 10.5	20	15.0
Placenta Accreta/Increta/Percreta 10.6	17	12.8
Laceration/Intra-Abdominal Bleeding 10.10	4	3.0
Other Hemorrhage/NOS 10.9	30	22.6

Table/Figure 4 (bar graph). Contributing factor and recommendation levels among preventable pregnancy-related deaths due to hemorrhage among residents of 29 US states (n=882)

	Contributing Factor (n=586)		Recommendation*(n=266)	
Level	**n**	**%**	**n**	**%**
Patient/Family	105	17.9	5	1.9
Provider	213	36.3	79	29.7
Facility	159	27.1	83	31.2
System	83	14.2	81	30.5
Community	26	4.4	18	6.8
Missing	21	-	95	-

*Review date after 10/09/20

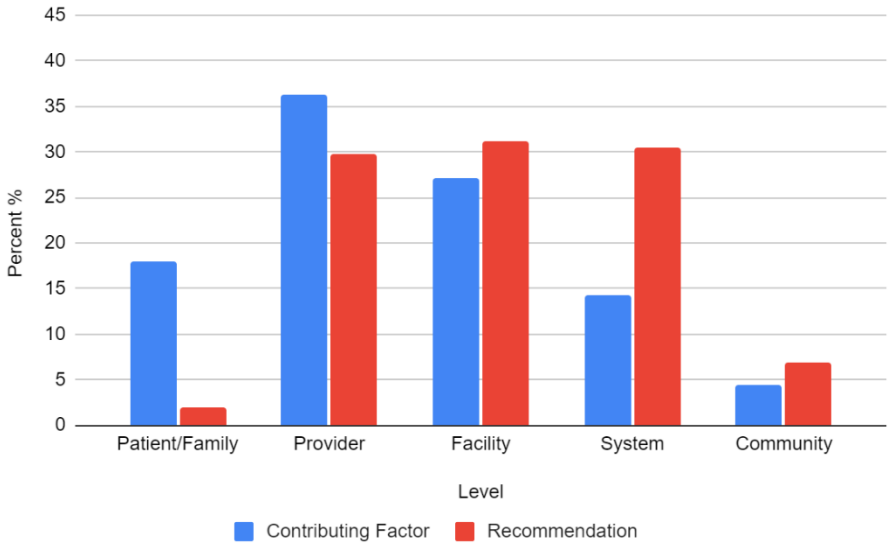

Table 5. Five most frequent contributing factor classes among preventable pregnancy-related deaths due to hemorrhage by level, 29 US States, 2017-2019.

Contributing Factor Classes	n	%
1. Patient/Family Level (n=100)*		
1. Knowledge	29	29.0
2. Delay	20	20.0
3. Adherence	8	8.0
3. Substance Use Disorder	8	8.0
4. Access/Financial	6	6.0
4. Cultural/Religious	6	6.0
4. Chronic Disease	6	6.0
2. Community Level (n=24)**		
1. Knowledge	11	45.8
2. Delay	2	8.3
2. Chronic Disease	2	8.3
3. Access/Financial	2	8.3
3. Provider Level (n=205)		
1. Clinical skill/quality of care	59	28.8
2. Assessment	31	15.1
3. Delay	30	14.6
4. Knowledge	26	12.7
5. Discrimination	16	7.8
4. Facility Level (n=151)		
1. Clinical skill/quality of care	56	37.1
2. Policies/Procedures	36	23.8
3. Delay	13	8.6
4. Continuity of Care/Care Coordination	12	7.9
5. Assessment	10	6.6
5. Systems Level (n=78)		
1. Clinical skill/quality of care	14	17.9
2. Access/financial	12	15.4
3. Continuity of Care/Care Coordination	11	14.1
4. Policies/procedures	10	12.8
5. Communication	8	10.3

*3 contributing factor classes were tied for 4th most frequent, so only the top 3 are shown

**All other counts were below 1 for this level

Discussion

The results of this analysis can be used to inform a variety of clinical, social, and epidemiological programs and research activities. While descriptive in nature, these results and trends can be used to inform future association studies such as case-control and cohort studies. With most cases being aged 30-39, it is important to think about how interventions and education can be targeted toward this age group. Additionally, with 90.1% of hemorrhage deaths being deemed preventable, it is important to understand how these deaths could have been prevented. By looking at the distribution of contributing factors alone, over one-third were assigned a provider level, and a little more than one-fourth were at the facility level. As for the recommendations, the distribution of levels is a little more evenly distributed between provider, facility, and system, suggesting that all three levels have a responsibility for preventing future hemorrhage deaths. When examining the contributing factor classes by level, knowledge ranks first for both the community and patient/family level, and clinical skill/quality of care is the first for provider, facility, and systems level, which is later reiterated in the qualitative analysis of preventable ectopic ruptures in the emergent themes. For example, there is consistent emphasis on patient awareness and knowledge about the warning signs of ectopic rupture, and recommendations related to community wide and individual level education about the signs and symptoms and when to seek help. There are also strong themes related to clinical skill and quality of care in both the contributing factors and recommendations. While ectopic ruptures do not represent all hemorrhage deaths, it is interesting to see the parallels that can be drawn from the sub analysis to the larger cohort.

Barriers to care, delay in identification, treatment, and transfer of care, clinical skill and quality of care (including assessment, continuity of care/care coordination, and

policies/procedures), awareness, knowledge, and education, as well as reproductive health were identified as common themes across the contributing factors and recommendations for those who died of preventable ectopic rupture. These findings can help guide prevention and clinical interventions geared toward pregnancy-related deaths due to ectopic rupture. The theme of awareness, knowledge, and education can also be important for the continual development of public health campaigns such as HEAR HER which was created to prevent pregnancy-related deaths by sharing potentially life-saving messages about urgent warning signs.[26] Incorporating the recommendations related to ectopic rupture into these campaigns and increasing the dissemination of this type of messaging can help mitigate risk and delay in seeking care. Review of these recommendations by healthcare professionals and hospital management can also propel innovation and the development of improved standards of care for those with ectopic pregnancies and ectopic ruptures. Furthermore, developing structured bias training for providers, ensuring availability of accommodations for those with disabilities and language impairments, and implementing enhanced screening and referral protocols for domestic violence can help reduce the barriers that stand in the way of receiving care. Finally, ensuring that all women and pregnant people have access to prenatal care, substance use treatment, contraception, and counseling is another key step in mitigating risk.

This mixed methods analysis of pregnancy-related deaths due to hemorrhage, with mostly descriptive quantitative summarization can help advance the understanding of the epidemiology of pregnancy-related mortality. While most of the prior research on the characteristics of pregnancy-related death due to hemorrhage has been clinical in nature, this analysis takes an approach more consistent with social determinants of health which can be used to further future research. Examination of contributing factor and recommendation levels, as well as the

distribution of contributing factor classes allows for insight into the socioecological determinants of pregnancy related mortality due to hemorrhage and why current interventions may not be hitting the mark. Another contribution of this analysis is the systematic examination of a relatively novel and critical population-based surveillance system. While other surveillance systems tend to focus on discrete variables and numeric attribution, MMRIA supplements basic surveillance data with free-text fields such as the contributing factors, recommendations, and case narratives, which provide rich qualitative data that provides not only context but also actionable items to inform clinical and public health work. The continual collection of this type of robust data will help propel progress in reduction of mortality due to hemorrhage.

While this analysis has many strengths, it also comes with some limitations due to the nature of the data. For example, the data is limited by the timely and comprehensive review and reporting of pregnancy related deaths. The thematic analysis of the preventable ectopic ruptures is also limited by the small sample size of n=20. However, even with only 20 deaths, there was an abundance of rich data within the free-text fields analyzed. Additionally, future analyses should also explore the case narratives, which provide dense sociodemographic and clinical context surrounding the decedent's life and terminal event. Future research should also examine the contributing factors and recommendations of all hemorrhage deaths, not just the preventable ectopic ruptures, as hemorrhage has remained a leading cause of maternal mortality overall. It is also important to note that while ectopic rupture was the most common specific cause of hemorrhage, the 'other hemorrhage/NOS' category as the largest category may be an indicator as to why progress in reducing maternal mortality due to hemorrhage has reached a standstill. If the etiology is unknown or unable to be placed into a more widely accepted category, interventions may be difficult to tailor. This of course is simply conjecture and should be further evaluated by

a content analysis of contributing factors, recommendations, and case narratives to understand more about the etiologies of this category.

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