A life-course theory exploration of opioid-related maternal mortality in the United States

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ABSTRACT

Background and Aims Between 2007 and 2016, pregnancy-associated mortality resulting from overdose more than doubled in the United States. This study explored the circumstances surrounding maternal opioid-related morbidity and mortality, using the life-course theory as a sensitizing framework to examine how each participant’s life-course contributed to her substance use, relapse, recovery or overdose. Design A mixed-methods study using semi-structured, in-depth face-to-face interviews and focus groups were conducted. Setting Texas, United States. Participants Women who had relapsed into opioid use or experienced a ‘near-miss’ overdose and family members of women who had died during the maternal period due to opioid overdose were interviewed (n = 99). Measurements A socio-demographic questionnaire captured participants’ ethnicity, age, marital status, medical and mental health history and employment status. The Stressful Life Events Screening Questionnaire—revised (SLESQ-R) assessed life-time exposure to trauma. Findings Women reported histories of abuse and loss of a loved one through homicide or suicide. Participants indicated that limited social support, interpersonal conflict with their partner and unaddressed mental illness made recovery more challenging. Additionally, losing their children through the child welfare system was described as punitive and placed them at greater risk for relapse and overdose. Conclusions A life-course theory approach to examining maternal opioid-related morbidity and mortality in Texas, United States reveals the complex needs of women at risk for opioid use relapse and overdose and the significant role of previous traumatic experiences.

Keywords Maternal mortality, mixed-methods research, opioid use disorders, opioids, overdose death, substance use.

INTRODUCTION

Pregnancy-associated mortality is defined as a death occurring during pregnancy or the following year [1]. Between 2007 and 2016, pregnancy-associated mortality resulting from overdose more than doubled in the United States [2]. Further, in a 2016 report of the Texas Maternal Mortality and Morbidity Taskforce, overdose was identified as the leading cause of maternal mortality for the state [3]. Case records, including postmortem toxicology and police reports, indicated that most of these deaths (58%) involved prescription or illicit opioids [3]. Similar state-specific trends have been reported in Colorado, Utah, Maryland and Massachusetts [4–7].

Clearly, the current US opioid crisis has had an unanticipated impact on women of childbearing age. While, nationally, overdose death rates have increased for both men and women, women are outpacing men. Accidental poisoning deaths (largely due to prescription opioids) increased 121% between 2005 and 2013 for white, non-Hispanic women aged 15–44 years, compared to an 80% increase in men [8]. As a result, in 2017, there were 47,600 opioid-related overdose deaths in the United States; one-third of these deaths occurred in women [9].

Little is known about the contributing factors to opioid overdose-related maternal mortality. Therefore, the purpose of this study was to provide an understanding of the context surrounding these deaths. Our goal for this research is the early identification of women at risk for overdose, so supportive interventions may be implemented to prevent these deaths.
METHODS

Design

We used a mixed-methods design, incorporating both qualitative and quantitative data, to gain a better understanding of maternal overdose death. For the qualitative component, we used qualitative description to understand the meaning of the women’s lived experiences [10]. The quantitative portion included the collection of socio-demographic data and, based on the literature showing high incidences of repeated exposures to stress and trauma in this population, we used the Stressful Life Events Screening Questionnaire—revised (SLESQ-R).

We applied the life-course theory (LCT) as a sensitizing framework to comprehensively examine the contextual factors surrounding opioid-related maternal mortality. We will touch upon our significant findings as they relate to the core themes of LCT: pathways, risk factors and critical or sensitive experiences [11]. However, a complete review of all our study findings is beyond the limitations of this paper, and will be presented in future publications focused on barriers and facilitators to recovery and stigma, which is pervasive in this population.

Pathways refers to a sequence of exposures and outcomes affecting health during a person’s life-course and can be predicted based upon socio-economic and environmental experiences or exposures [11]. For example, childhood trauma, such as abuse, is positively correlated with prescription opioid misuse [12]. Risk factors are threats (e.g. family, community and social policies) to overall health [11]. Women with opioid use disorder (OUD) often have disrupted social support systems that can make long-term recovery difficult. Additionally, co-occurring mental illness is a common underlying cause of substance use [13]. Critical or sensitive experiences describe how life events can have the greatest impact on individuals during critical or sensitive time-periods [11]. As such, the loss of children to the child welfare system due to parental substance use is a critical experience that can cause trauma for both parents and children.

Participants

Institutional Review Board (IRB) approval was obtained prior to the onset of data collection. We partnered with community-based, gender-specific addiction treatment providers throughout Texas for assistance with recruitment of participants. Contact information of treatment providers was obtained from our state health department. We also recruited locally using a ‘street outreach’ approach distributing study flyers outside methadone clinics, where we had permission to recruit. The study was also advertised in a local newspaper. For our state-wide outreach, treatment providers assisted with the organization of focus groups and/or individual interviews. We traveled to six geographically different regions of the state, ensuring that we collected data from both rural and urban communities, as well as border and coastal towns.

Eligibility for study participation included: English-speaking and at least 18 years of age. Women who had experienced a ‘near-miss’ overdose or relapse into opioid use during the maternal period were invited to participate in the study. We included these women as relapse is often a precursor to overdose due to decreased opioid tolerance following periods of abstinence or reduction in use. Finally, we recruited family members and significant others of women who had relapsed or died from overdose during the maternal period.

We reviewed an information sheet about the study with participants prior to the onset of data collection. Time was allowed for questions and answers and verbal consent to participate was obtained. We reassured participants that discontinuation in the study was possible at any time without negative consequences.

Measures

Individual interview participants were asked to complete a socio-demographic questionnaire. Items included questions about ethnicity, age, marital status, medical and mental health history and employment status. These participants also completed the SLESQ-R [14], which is a 13-item self-report measure that assesses life-time exposure to trauma such as life-threatening accidents, physical and sexual abuse, or witnessing a person being killed or assaulted. Respondents were asked to indicate if the event occurred and specific items related to the event, such as its frequency, duration and description. The SLESQ-R has demonstrated good reliability (Cronbach’s $\alpha = 0.86$) and validity and has been used with diverse populations [15]. Significant others/family members participating in individual interviews were asked to complete a socio-demographic survey about their loved one who relapsed or overdosed. Items included substance use history and treatment, age at the time of the incident and prior medical history, including mental health. Women participating in focus groups were asked to fill out a brief demographic questionnaire for ethnicity, age, relationship status, number of children, education and income.

Data collection

Using the process described by Morgan & Krueger (1998) [16], two to four members of our experienced qualitative research team conducted focus groups. We also collected data through individual interviews for participants who preferred to be interviewed alone or when there were too few participants to form a focus group. Focus groups and
interviews were semi-structured, consisting of open-ended questions designed to ensure rich, descriptive data (see Table 1). One member of our research team facilitated the conversation while the others took notes and recorded non-verbal observations. Digital recorders were used to capture the data and these recordings were later transcribed verbatim by a professional transcription service. Data were collected in semi-private meeting rooms or private office spaces located in the treatment centers. Debriefing of participants took place immediately following interviews or focus groups, and all participants were compensated $20 for their time.

Analyses

We used the Statistical Package for the Social Sciences (SPSS) version 26 software for our quantitative data analysis. Descriptive statistics including frequencies, percentages and measures of central tendency were analyzed to present the data from the SLESQ-R and socio-demographic questionnaires. Directed content analysis was used to analyze our qualitative data. This type of analysis is used when ‘existing theory or prior research exists that would benefit from further description’ [10]. The process began with a line-by-line analysis of the transcribed interviews. All four researchers familiarized themselves with the data by reading and re-reading the interview transcripts and field notes, followed by systematically coding the data according to the LCT categories. Definitions and descriptions of each LCT component were used as a guide as each segment of data was analyzed. Table 2 displays representative quotes including definitions and descriptions of each LCT component used.

To address research bias, trustworthiness was achieved through criticality, credibility and authenticity [17]. Criticality was ensured through audit trails documenting each aspect of the study and analyses. Authenticity was achieved through repeated data immersion. Credibility was accomplished as the authors analyzed and reviewed all data for confirmation of the interpretation. The writing of this report was the final step in the data analysis process and consisted of a collaborative process among the researchers. Our research question and analysis plan were not pre-registered on a publicly available platform; therefore, the following results should be considered exploratory.

RESULTS

Sample

During a 2-year period, participants (N = 99) took part in focus groups (n = 13) or individual interviews (n = 25). Focus groups consisted of three to 14 participants. Ten focus groups (n = 47) included women who had experienced a relapse into opioid use or a near-miss overdose during the maternal period and three focus groups (n = 27) consisted of family members who had lost a woman to overdose during this time. Of the 25 in-depth individual interviews, 23 consisted of women who had relapsed and/or overdosed during the maternal period. All the women who participated were actively involved in OUD treatment. Recruitment and data collection continued until data saturation was achieved, at which time no new data were being discovered and the data became redundant [18].

Quantitative data

Demographic data were collected from a total of 61 participants of focus groups (n = 36) and individual interviews (n = 25). Women were aged 20–50 years (mean age = 33) and most identified as Hispanic (57%). Many women (39%) were single and had an average of three children. More than half (65%) had a high school diploma/general education diploma (GED) or less, third grade being the lowest grade completed and a bachelor’s degree being the highest. Almost all women were unemployed (79%) and most (70%) had a yearly household income of $9999 or less. The average age at time of relapse or overdose was 28.8 years. Most of the women had a diagnosis of mental illness prior to the perinatal period and more than half (54%) received treatment for substance use during pregnancy. The SLESQ-R indicated high rates of exposure to multiple stressful and traumatic life events beginning early and extending into adulthood. Of the 13 events, women had experienced an average of 6.1 [standard deviation (SD) = 1.98] stressful/traumatic events, with most reporting at least four or more (91.3%). Table 3 presents findings from the socio-demographic and SLESQ-R survey.
Table 2  Life-course theory components, definitions and representative quotes.

| Life-course theory codes and definitions                                      | Code examples                                                                 | Representative quotes                                                                 |
|------------------------------------------------------------------------------|-------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| Pathways—a sequence of exposures and outcomes that affect health and can be  | Trauma such as loss of a loved one history of physical, sexual and emotional   | ...My dad being abusive and being and living in a home like that. My mother was great  |
| predicted based upon socio-economic and environmental experiences or exposures| abuse                                                                          | but my dad was very abusive... Physical, mental... And he was abused by his father   |
| Risk factors—contributing factors (i.e. family, community and social policies)| Limited social support: lack of support and/or resources to manage day-to-day  | I do not have support from my family. Like I said earlier, there’s people that need  |
| that diminish health                                                          | tasks                                                                          | that—I don’t have my mom. I don’t have my dad. I don’t have my cousin. Nobody       |
|                                                                              | Interpersonal conflict: relationship issues with significant other             | My husband and I was separated, um, and he caused a lot of problems, like, he would  |
|                                                                              | Unaddressed mental illness                                                    | try to get a hold of me however he could and terrorize me. And so that’s the root   |
| Critical and sensitive experiences—the acknowledgement that events and       | Uncertainty and fear of losing their infant to the child welfare system        | of it and I didn’t know that... So, now that I’m getting the mental health care... I  |
| exposures can impact individuals the greatest during sensitive periods        |                                                                               | have not had anything in my body except for psych meds                               |

Qualitative data

Pathways reflected the women’s life experiences and exposures that influenced their overall health. Traumatic experiences during childhood were common among the women as they recalled witnessing their parents’ death from suicide, homicide or an accident. They also described an awareness that these events may have led to their initiation of substance use as a coping mechanism. One woman explained: ‘I lost my parents at a very young age. I was 12 years old when my parents passed away. So that’s why I turned to drugs. That was my way of coping.’ Incidences of domestic violence or abuse were also pervasive, as women identified trusted individuals or family members as perpetrators of these events. They explained how the enduring effects impacted their future social interactions and relationships with others: ‘I was raised by my aunt and uncle. I was touched in the wrong way. When I think about it, it takes me back. I don’t feel comfortable with men. I’m more comfortable with women.’

Women described growing up in an environment where drug use was prevalent. They recalled using drugs with friends and observing family members use or sell drugs. They also explained their struggle for sobriety, especially when deeply embedded in an environment where their significant other and peers continued to use drugs. ‘My biggest problem with using is just easy access. If somebody around me offers it to me, I’ll do it’. Another participant explained how she used substances to maintain her relationships:

My relapse was always because of a partner. Like the father of my son, when I first got with him, he said, ‘Any female I get with is gonna use’. So, in order to keep him, I used with him.

Risk factors

Participants described multiple risk factors such as stress, lack of social support, interpersonal conflict and mental illness that contributed to their relapse and for some, an overdose. Several women reported feeling judged, chastised and rejected by their families when family support may have had the greatest impact on their recovery. Parenting women described feeling isolated as they navigated parenthood alone. One participant recalled the relentless criticism of her family after childbirth. The demands of infant care became so overwhelming it eventually resulted in her relapse and subsequent overdose:

I had to move back home with family, and the pressure... it was just overwhelming and caused me to use continuously. I was running on no sleep. My grandmother is a very hard lady. She was breathing down my neck all the time... criticizing me and I was trying to stay sober. She said, ‘You’re a horrible mother’. She was driving me nuts, so I went out and used that day and that’s when I overdosed. I still had some heroin, so I did the rest and overdosed.

Another participant described how she believed interpersonal conflict led to the overdose death of her family member:
She used heroin, but she wasn’t hooked. That one time she just… I don’t know how much she drew up, but she injected it all. She didn’t wake up. Left two kids behind. It was all the arguing and stuff she was going through. She was just fed up with the world.

Additionally, the conflict between women and their partners often caused psychological distress and was a trigger for relapse. ‘Stress overload… that’s gonna push us to go get high. It’s our environment. If I’m pregnant and my boyfriend is beating me, I’m gonna go get high.’

Women expressed the toll stress had on their mental health. However, some were unaware they were experiencing mental illness as they were preoccupied with substance use recovery, parenthood and day-to-day challenges. Many did not discuss their mental health concerns, and the result of internalizing these negative emotions contributed to relapse:

I suffered from postpartum [depression] very badly. I didn’t even know what that was. I didn’t know that until I had my first child. My doctor finally said, ‘You have postpartum depression, and it’s getting worse’. I didn’t even know that’s what was going on. I was just, coping with drugs to make me feel a different way than I felt so, it was dangerous territory.

Women reported histories of post-traumatic stress, depression, anxiety and bipolar disorder. Some conveyed that unaddressed mental health concerns persisted during the course of their life which led to the use of licit and illicit substances for relief:

Had I known that was my problem my whole life, I would have not automatically gone to drugs to make me feel good, to make me feel normal. I started popping a lot of pills— Xanax, Percocets—everything, just to make me feel normal.

Additionally, dying was an option some participants had considered as a means for escaping their perceived powerlessness. One woman described her loss of hope:

You just don’t think that you’re ever gonna get help. You don’t think that you’re ever gonna be who you were before. I can say for myself, I went through the time-period where hopefully, this amount that I’m gonna take right now—I just won’t wake up. That’s when you’re in the hardest of it. You don’t see the hope. You don’t see the light anymore.

The timing of critical and sensitive experiences can impact health across the life-span. Participants expressed their
motivation to initiate and continue treatment and achieve recovery. Keeping the family intact became their primary goal, and having a child provided a sense of purpose. However, this purpose was threatened by separation. Women described their constant fear of child welfare involvement and child removal and their view of this being punitive and counterproductive to recovery. Losing their children caused some women to spiral into depression and grief thus threatening recovery. One mother explained:

[Women] get depressed. They feel like they have nothing to look forward to. They feel hopeless. There’s no kids. ‘What do I got to wake up for? What do I got to start my day for? I don’t have nothing.’

The cousin of a woman who died in 2009, at age 30 years, from overdose following the removal of her children by child welfare stated:

She finally gave up. She didn’t want nothing to do with life anymore; her children were gone, and I think she [overdosed] on purpose. [Our family] doesn’t believe she was trying to kill herself, but I do.

In addition to their recovery classes, many women were also required to attend parenting and probation classes and counseling. While these were intended to facilitate treatment, the women felt overwhelmed as they juggled their time to attend classes while fulfilling their roles as wives, care providers and mothers. These unrealistic expectations became challenging to manage, as one woman described her frustration with the system as setting her up to fail:

I was doing counseling and parenting classes... and still being a mom and being a wife and everything just got to me. I cracked underneath all the pressure they put on me. The things that they overwhelm you with, for a minute I was like man, I should have just stayed in jail. They want you to do all these classes, but they want you to work too. I had like 15 classes and five case workers and... [Narcotics Anonymous], parenting, family violence, and all this other stuff. But our bosses want us at work when they want us at work. [The system] wants you to fail. You can’t do everything. So, they set you up for failure.

**DISCUSSION**

Despite the ongoing efforts to address the current US opioid crisis, our results indicate that pregnant and parenting women have been uniquely impacted by its detrimental effects. The LCT can be used to provide insight into an individual’s life history and the impact it has on health, disease progression and substance use [19]. Through this lens, we gained a better understanding of how women’s life experiences and substance use are shaped by the social context of their environment [11]. Our study also helps to fill the gaps in knowledge about maternal overdose death. We will focus our discussion on the insightful ways our participants explained the contextual factors leading to their relapse or overdose event.

**Pathways**

Our participants revealed traumatic life experiences that resulted in substance use, relapse and, in several cases, overdose. Loss, such as the death of a loved one, impacted their coping processes and contributed to their use of substances. Further, participants described the pervasiveness of drug use in their social environments. They felt they were predisposed to substance use disorders (SUDs), and repeated triggers made it difficult to maintain their recovery during the already stressful maternal period. Our findings from the SLEQS-R indicated that participants had experienced significant individual stressful/traumatic life-course events. This is consistent with the literature, which shows that 50–90% of individuals who seek substance use treatment have experienced one or more previous traumatic event [20]. Further, early childhood trauma is positively associated with substance use in women, and the severity of that trauma predicts relapse [21] and a more difficult recovery [22].

As such, health-care providers and others who serve this population must be equipped to understand and manage the complex needs of women at risk for opioid use relapse and overdose, taking into consideration their life-course and previous traumatic experiences. Trauma-informed care (TIC) should be used to address the needs of individuals who have experienced trauma [23]. A primary goal is to prevent re-traumatization [23]. Incorporating TIC into practice requires trauma-specific interventions, such as modified assessment and treatment modalities and the integration of organization-level TIC principles. Further, the use of peer support may be an important strategy for decreasing rates of relapse and overdose. Peers with similar lived experiences may more readily establish trust and foster a collaborative healing partnership [23].

**Risk factors**

Similar to previous research, our study revealed that issues of infidelity or interpersonal violence [24] often strained women’s intimate relationships. Additionally, while family
members may be great supporters, they also could be critical, establishing unrealistic expectations that jeopardized recovery. Moreover, our participants reported that conflict with their intimate partners and a lack of familial support added stress to their lives.

Co-occurring mental illness such as depression, post-traumatic stress disorder (PTSD) and anxiety can be as high as 70% among pregnant women who use substances [25–28]. Several participants in our study reported that post-traumatic stress had a major negative impact on their mental health, and further jeopardized their quality of life. These are important findings, as strained familial relationships [24] and mental illness [29] contribute to the premature discontinuation of SUD treatment, thereby increasing risk for relapse and overdose.

A unique finding of our study is the role substances played in ‘escaping’ adverse conditions and emotions. The women described unmanaged depression and anxiety and explained how they used substances to feel ‘normal’. Further, their inability to recognize mental illness symptoms reinforces the importance of mental health awareness among women, so symptoms can be recognized early and addressed. We also discovered a sense of isolation and powerlessness. As many women were single parents experiencing unstable relationships, this is understandable. Therefore, empowering women with the skills necessary to build nurturing and supportive relationships may be key to achieving long-term substance use recovery.

Finally, we found an overall sense of hopelessness that may contribute to overdose. This was particularly noteworthy for women who took opioids hoping to ‘just [not] wake up’. We discovered similar experiences among participants who denied planning their suicide but instead described no longer wanting to live.

**Critical and sensitive experiences**

Women may be more motivated to engage in treatment services during pregnancy and postpartum out of fear of child welfare involvement [24]. Our participants confirmed that the prenatal and postpartum periods were a time of uncertainty and fear due to child welfare. Previous research [30] shows that women view their experiences with child welfare as creating insurmountable barriers to their recovery. Further, an overwhelming sense of maternal shame and guilt for having exposed their children to substances *in utero* has been identified, and this is a common contributing barrier to accessing needed services [30].

In our study, we discovered that the demands placed on parenting women were unrealistic, leaving them to believe they were intentionally set up for failure. Thus, better coordination of demands made by the legal and child welfare systems is needed. For example, colocating required probation and parenting classes and/or consolidating curricula to eliminate redundancy may improve the success of families attempting recovery. Further, pregnancy and becoming a mother is a sentinel event for most women that may be leveraged as a strength and motivation for recovery. Therefore, this time-period may be a golden yet often missed opportunity with the potential to impact the life-course of future generations.

Unfortunately, the current US opioid crisis has also resulted in a national child welfare crisis. Between 2012 and 2016, a 10% increase in children entering foster care occurred after more than a decade of sustained decline. Additionally, in the six states most impacted by the opioid crisis (Alaska, Georgia, Minnesota, Indiana, Montana and New Hampshire), there was a 50% increase during this same 4-year period [31]. Clearly, new ideas and approaches are needed to preserve families and prevent the multi-generational trauma caused by parent–child separation that may not be fully appreciated for decades.

One recommendation is to require any individual working with this population to complete specialized training on parental SUDs and the family. Key individuals to receive this training should include: (a) child welfare supervisors and investigators, (b) state health department program officers and directors, (c) health-care providers including physicians and nurses and (d) substance use treatment personnel such as counselors and peer recovery coaches. Quality curricula already exist and would, therefore, only need to be implemented. For example, the Substance Abuse and Mental Health Services Administration (SAMHSA) offers webinars and other materials such as: (a) parenting in recovery: challenges and opportunities [32], (b) recovery-oriented practice: person/family-centered recovery planning [33] and (c) recovery supports for children and families [34]. Further, state-based programs such as MOMS Ohio [35] and the Texas Mommies Program [36] offer fully developed toolkits with resources for best practices in the care of pregnant and parenting women with SUDs. Organizations can capitalize upon these materials to provide training of their personnel to better meet the needs of families impacted by SUDs.

Finally, our hope is that the findings of this research will be utilized to advocate for local and federal policy change accompanied by funding allocation to support the needs of pregnant and parenting women with SUDs. Currently, in 23 states and the District of Columbia, substance use during pregnancy constitutes child abuse under civil child welfare statutes [37]. An additional three states have the ability to impose civil commitment of pregnant substance using women as a means for deterring drug use [37]. However, none of these states require an assessment of parenting willingness and capacity prior to filing a child welfare report [38]. Further, case workers, probation officers and judges have been known to order women to discontinue prescribed medication assisted treatment for an OUD—
the only Food and Drug Administration-approved treatment for OUD [39,40]. These practices unnecessarily place women at risk for relapse and overdose death [38]. They also lack an evidence base and must be discontinued if women’s lives are to be saved and families preserved.

Strengths and limitations

A strength of our study is the use of a mixed-methods design, which is ideal for the exploration of broad and multi-faceted research questions [39]. Further, this approach has the potential to harness the strengths and counterbalance the weaknesses of using quantitative or qualitative methods alone [40] and can be especially powerful when addressing complex health conditions such as addiction [41]. An additional strength of our study is the large sample size \( n = 99 \) from a variety of locations throughout Texas and the inclusion of women as well as their family members.

With that said, one limitation of our study is not having asked our participants if they had experienced a termination of parental rights. Certainly, a traumatic experience such as this could have influenced their overall perceptions. Further, our data collection was conducted in one state and only in English. Our next steps include the use of our findings to develop a brief screening instrument to help identify women at risk for maternal overdose. We are currently piloting this instrument in Texas and then will do so on a national level to help address issues of limited generalizability.

In summary, we applied the LCT to this mixed-methods study that explored the contextual factors surrounding maternal opioid-related morbidity and mortality. A better understanding of these phenomena will support more targeted interventions and lead to better outcomes. Applying LCT allowed us to examine how participant’s life-course contributed to their substance use, relapse, recovery or overdose. Further, a mixed-methods approach ensured rich descriptive data. Our plans for instrument development may help to identify women at risk for maternal overdose so that life-saving interventions can be made. Prevention of maternal opioid-related morbidity and mortality offers the potential to positively impact the life-course of future generations.

Declaration of interests

The authors declare that there are no conflicts of interest regarding the publication of this paper. All authors have contributed to the preparation of the manuscript and have read and approved the submitted manuscript. All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors and are in agreement with the manuscript. All relevant ethical safeguards have been met in relation to patient or subject protection or animal experimentation, including, in the case of all clinical and experimental studies, review by an appropriate ethical review committee and written informed patient consent. The research complies with the World Medical Association. The work is original and not under consideration by any other journal.

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Author Contributions

Lisa Cleveland: Conceptualization; formal analysis; funding acquisition; investigation; methodology; supervision; validation. Kelly McGlothen-Bell: Data curation; formal analysis; investigation; methodology; validation. Leticia Scott: Data curation; formal analysis; investigation; methodology; validation. Pamela Recto: Data curation; formal analysis; investigation; methodology; validation.

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