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Sex-Specific Health Challenges: A Study of Women with Epilepsy Across the Lifespan

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Abstract

In Canada, it is estimated that 300,000 people are living with epilepsy, half of whom are women (Patel & Grindrod, 2020). A diagnosis of epilepsy brings inherent psychosocial challenges including increased risks of developing mood disorders, interpersonal and institutional stigma, reduced employment rates, increased mortality rates, low socioeconomic status, and reduced quality of life (Thomas & Nair, 2011; Josephson & Jetté, 2017; Josephson et al., 2017). In addition to the inherent challenges of living with epilepsy, women with epilepsy (WWE) face difficulties with fertility and family planning, contraception, teratogenicity, sexual function, management of care during and after pregnancy, safety while caring for children, hormonal influences on seizure frequency, and additional bone health issues (Aylward, 2008; Crawford et al., 1999; Herzog et al., 2016; Noe, 2007; Pack et al., 2009). The purpose of this study was to explore the implementation of the recommended care for WWE for sex-specific health issues from the perspective of the WWE. Using a cross-sectional survey, we investigated the experience of WWE regarding menstruation, family planning, prenatal and perinatal care, hormonal influences and therapies, and bone health. From the perspective of knowledge translation, this study is one measure of the recommended care reaching the patient.

Keywords: Epilepsy, women with epilepsy, knowledge translation

Dedication

I would like to dedicate my thesis to my father, Iraeneus D. Redhead. You are not here with me to celebrate this milestone, but I find comfort in the love and support that you gave me, which is the foundation for all my successes.

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Table of Contents

List of Tables

List of Figures

List of Appendices

Chapter One

Introduction

In Canada, it is estimated that 300,000 people are living with epilepsy, half of whom are women (Patel & Grindrod, 2020). For the purpose of this study a woman is defined as any person who identifies as a woman and/or was assigned the female sex at birth. The diagnosis of epilepsy brings inherent psychosocial challenges including increased risk of developing mood disorders, interpersonal and institutional stigma, reduced employment rates, low socioeconomic status, increased mortality rates, and reduced quality of life (Josephson & Jetté, 2017; Josephson et al., 2017; Thomas & Nair, 2011). In addition to the inherent challenges of living with epilepsy, women with epilepsy (WWE) face sex-specific difficulties, including family planning, contraception, teratogenicity, management of care during and after pregnancy, and hormonal influences on seizure frequency (Aylward, 2008; Crawford et al., 1999; Herzog et al., 2016; Noe, 2007; Pack et al., 2009).

In Ontario, provincial guidelines on how to manage epilepsy in adults and children were published nearly a decade ago (Epilepsy Implementation Task Force, 2015). The various aspects of sex-specific care of WWE were addressed in these guidelines. For instance, recommendations were made about the appropriate use of oral contraceptives, preconception planning, intra-partum care, breastfeeding, and menopause. The provincial guidelines also included an epilepsy education checklist that healthcare providers could use to guide health teaching for people with epilepsy. International guidelines are also available from the International League Against Epilepsy (ILAE). The guidelines from the ILAE provide recommendations on caring for WWE during pregnancy (Tomson et al., 2019), prescribing valproic acid for WWE (Tomson et al., 2015), folic acid use (Harden et al., 2009), and adjustment of anti-seizure medication (ASM)

doses during pregnancy (Harden et al., 2009). There is also a body of literature outlining recommendations for the care of WWE, primarily focusing on contraception, pre- and intrapartum care, and the use of folic acid.

The primary researcher, who is an experienced nurse specializing in epilepsy care, has noted discrepancies in clinical practice where WWE often do not receive care that aligns with established guidelines or is informed by current research. It is possible that some WWE do not receive adequate care because some healthcare providers, particularly those not specialized in epilepsy, may not be aware of the guidelines and research and, thus, are not comfortable discussing epilepsy care with patients. For instance, primary care physicians (PCPs) may face several challenges in addressing epilepsy care with patients. These challenges may include accessing epilepsy education and connecting with epilepsy specialists. For example, ECHO Ontario offers the continuing medical education program, Epilepsy Across the lifespan. These ECHO sessions are conducted virtually and are facilitated by an epilepsy specialist, with support from the multidisciplinary team from a tertiary epilepsy center. The goal of these sessions is to provide epilepsy teaching to PCPs and give them the opportunity to discuss challenging cases with an epilepsy specialist. Unfortunately, these sessions are poorly attended by PCPs, possibly because they occur during standard work hours. In a survey of obstetricians, neurologists, nurses and midwives specialized in epilepsy, and general midwives, Taylor et al. (2022) observed that, collectively, most providers had moderate to high confidence in talking to WWE about their risk for seizures during pregnancy. When the professions were analyzed separately, most neurologists were very confident talking to WWE about their seizure risk during pregnancy and epilepsy specialist nurse and midwives were either moderately or very confident (Taylor et al., 2022). However, most general practice midwives were not confident talking to WWE about their

seizure risk during pregnancy (Taylor et al., 2022). This is indicative of how specialized knowledge improves providers' confidence in providing care and the need for collaboration between specialized and general practice providers.

Despite the existence of guidelines and research emphasizing sex-specific care for WWE, there is a notable discrepancy between these recommendations and the actual quality of care delivered to WWE in practice. This congruence can be investigated at some key points of the knowledge translation process. Researchers like Taylor et al. (2022) aim to fill this gap in research by assessing the knowledge of healthcare providers. In the current study the aim is to contribute to filling this gap at the implementation stage of the knowledge translation process by exploring how effectively the recommended sex-specific healthcare practices for WWE are being applied from the perspective of the women. The knowledge gained from this study can be used to guide research priorities, healthcare provider education, and the development of health teaching tools.

Literature Review

For this study, a narrative literature review was conducted using the following databases: the Cumulative Index of Nursing and Allied Health Literature (CINAHL), PubMed, and Web of Science. The search terms were chosen to reflect the various sex-specific health issues affecting WWE (see Appendix A for a complete list of terms). Article relevance was determined by its correspondence with this study's background, focus, and population of interest. Peer-reviewed articles published in English were included for review. Because of the paucity of existing research, no date limit was placed on the literature review. Unpublished manuscripts such as abstracts, theses, and dissertations were excluded.

The narrative literature review was structured to address two main areas. First, care recommendations for WWE regarding sex-specific health issues was reviewed, including an examination of practice guidelines from the international League Against Epilepsy (ILAE) (Harden et al., 2009; Tomson et al., 2019), as well as recommendations from various epilepsy experts. Following this, the review will explored existing literature on care for WWE from the perspective of WWE themselves. This latter section focused on the experiences and viewpoints of WWE regarding their care, providing insight into the patient's perspective on these important health issues.

Sex-specific Care Recommendations for Women with Epilepsy

Hormonal Influences on Seizure Frequency

Catamenial epilepsy is defined as a two-fold or more increase in seizure frequency that consistently occurs at a specific point of a woman's menstrual cycle or when seizures occur exclusively at a specific point of the menstrual cycle (Bui, 2022; Herzog, 2008; Noe, 2007). Many women report that their menstrual cycle affects the occurrence of seizures, with 30 to 50% reporting the symptoms of catamenial epilepsy (Noe, 2007). WWE experience changes in seizure frequency related to the menstrual cycle because of the cyclical changes of estrogen (a proconvulsant) and progesterone (an anticonvulsant) and due to the effects of these hormones on the neurological system (Herzog, 2008; Noe, 2007; Pennell, 2009).

Three patterns of catamenial epilepsy have been identified: C1, C2 and C3 (Herzog et al., 1997). The catamenial patterns are correlated to the estradiol-to-progesterone ratio in the serum (Herzog et al., 1997). In the C1 or perimenstrual pattern, seizures are triggered by the rapid decrease in progesterone levels (Herzog, 2008; Herzog et al., 1997). In the C2 or periovulatory pattern, seizures are triggered by a rapid increase in estrogen levels without a concurrent increase

in progesterone (Herzog, 2008; Herzog et al., 1997). In the C3 or inadequate luteal pattern, seizures are triggered by lower-than-usual progesterone levels caused by an inadequate luteal phase (Herzog, 2008; Herzog et al., 1997).

Treatment options for catamenial epilepsy include add-on progesterone hormonal therapy, an additional anti-seizure medication (ASM) to be taken at the point of or in anticipation of increased seizure frequency, and a temporary increase in the dose of the existing ASM regimen in anticipation of the increased seizure activity (Bui, 2022; Lukić, 2018). WWE should be screened for catamenial epilepsy, and options to counteract the effects of hormonal changes on seizure frequency should be discussed (Lukić, 2018).

Fertility and Family Planning

Antiseizure medications and the condition of epilepsy can have negative effects on fertility (Crawford et al., 1999). Some studies suggest an increased risk of infertility among WWE which is possibly related to the increased incidence of polycystic ovary syndrome, menstrual disorders, and anovulatory cycles (Crawford et al., 1999; Nappi et al., 1994). Fertility and family planning counselling should start as early as adolescence to educate WWE about the interactions between ASMs and contraceptives, the increased teratogenicity risk posed by ASMs, and to work with the WWE to achieve seizure control before pregnancy (Dupont & Vercueil, 2021).

WWE can experience an alteration in how sexual stimuli are processed, resulting in sexual dysfunction (Rees et al., 2007). This altered processing may be related to ASM use, having a temporal lobe seizure focus, or experiencing depression and/or anxiety related to living with epilepsy (Rees et al., 2007). Sexual dysfunction can negatively affect the quality of life and can possibly affect fertility and conception efforts (Penovich, 2000; Rees et al., 2007). Sexual

dysfunction assessments should be included in the neurological assessment of the WWE, so that sexual dysfunction can be identified and treated and any ASMs that impact sexual function can be changed as appropriate (Rees et al., 2007).

Hormonal Therapies: Contraception, Menopause, and Transgender

In addition to the increased teratogenic risk associated with taking ASMs, WWE have been found to have higher rates of unintended pregnancies than women in the general population (Herzog et al., 2017). For that reason, the use of contraceptives among WWE is highly recommended. However, contraceptive use among WWE is challenging because systemic hormonal birth-control medications can interact with ASMs, resulting in decreased ASM efficacy, decreased contraceptive efficacy, and decreased seizure control (Barnard & French, 2019; Patel & Grindrod, 2020; Reimers, 2020). Enzyme-inducing ASMs, such as carbamazepine and phenytoin, can decrease the effectiveness of hormonal birth-control medications (Guillemette & Yount, 2012; Reimers, 2020). Hormonal birth-control medications can decrease the effectiveness of ASMs, particularly lamotrigine and valproic acid (Guillemette & Yount, 2012; Reimers, 2020). Therefore, intrauterine devices (IUDs), including hormonal IUDs, which do not have systemic effects, are the recommended form of contraception for WWE (Guillemette & Yount, 2012; Patel & Grindrod, 2020). WWE should be counselled on the benefits and disadvantages of various methods of contraception and alternative ASMs (Patel & Grindrod, 2020).

During perimenopause and menopause, WWE may experience increased seizure frequency due to the decrease in progesterone (an anticonvulsant), the variability in estrogen levels (a proconvulsant), and poor sleep hygiene due to frequent arousals caused by nocturnal hot flashes (Harden, 2008; Noe, 2007; Sveinsson & Tomson, 2014). Women who experience severe

menopause symptoms may require hormone replacement therapy (HRT), which includes estrogen (Crawford et al., 1999; Noe, 2007). The estrogen in HRT can interact with enzyme-inducing ASMs, resulting in decreased ASM efficacy, decreased HRT efficacy, and decreased seizure control (Harden, 2008; Noe, 2007; Sveinsson & Tomson, 2014). Counselling about menopause should start in the perimenopause period and should include discussions about HRT/ASM interactions, the effects of HRT on seizure control, and ASM adjustment to maintain seizure control (Crawford et al., 1999; Gooneratne & Wimalaratna, 2016; Noe, 2007; Tüscher & van Elst, 2010).

Transgender persons transitioning from male to female, or transwomen, undergo hormone therapy (HT) that typically entails estrogen (Johnson & Kaplan, 2017). The bidirectional interaction between estrogen and ASMs has been associated with a loss of seizure control (Johnson & Kaplan, 2017). An additional concern for transwomen is that enzyme-inducing ASMs can increase the metabolization of estrogen, resulting in a decrease in the feminizing effects of estrogen (Johnson & Kaplan, 2017). Trans-WWE should be counselled about the ASM-HT interactions and the effects on seizure control and gender transition (Johnson & Kaplan, 2017).

Management of Care During and After Pregnancy

During pregnancy, consideration must be given to both the woman with epilepsy and the unborn child (Tomson et al., 2013). Experiencing seizures and taking ASMs during pregnancy increases the risk of intra- and postpartum complications for both WWE and their children. Maternal complications include pre-eclampsia, gestational diabetes, pre-term delivery, caesarean delivery, prolonged hospital stay, and maternal death (including Sudden Unexpected Death in Epilepsy (SUDEP)) (Knight, 2021; Mueller et al., 2022). Complication for the child include

congenital malformations, fetal death, small for gestational age, low birth weight, admission to the neonatal intensive care unit, impaired cognitive development, and behavioral disorders (Knight, 2021; Laganà et al., 2016; MacDonald et al., 2015; Mueller et al., 2022).

Pregnancy counselling should begin well before the woman with epilepsy plans to get pregnant and should include contraception use to prevent unplanned pregnancies (as discussed above), seizure control, appropriate choice of ASM, and folic acid use. Due to the high rate of unplanned pregnancies among WWE, pre-pregnancy counselling should occur regularly and with all women with child-bearing potential (Dupont & Vercueil, 2021; Tomson et al., 2019). Ideally WWE will attain seizure control at least one year before they get pregnant because the level of seizure control that the woman attains pre-pregnancy is usually maintained during pregnancy (Dupont & Vercueil, 2021; Tomson et al., 2019). The goal should be to achieve seizure control using ASM monotherapy, using the lowest dose possible, and avoiding ASMs with increased teratogenic risk (Dupont & Vercueil, 2021; Borgelt et al., 2016; Tomson et al., 2019).

The intrapartum care plan must also include appropriate ASM dose increases to compensate for the decline in plasma concentration of ASMs during the first and second trimesters of pregnancy (Laganà et al., 2016; Tomson et al., 2013). After birth, however, the drug plasma levels return to pre-pregnancy levels, and if the dosage is not adjusted within the first few weeks of the postpartum period it may lead to maternal toxicity (Crawford et al., 1999). However, after giving birth some WWE are exposed to additional stress and sleep deprivation, which could facilitate a reduction in their seizure threshold (Nucera et al., 2022). In those cases, a dose of ASM higher than the pre-pregnancy dose may be recommended (Nucera et al., 2022).

During pregnancy WWE should be counselled on the safety of breastfeeding, childcare safety, medication compliance, stress management, and good sleep hygiene (Crawford et al., 1999; Laganà et al., 2016; Leach et al., 2017). In general, breastfeeding is encouraged because there are known health benefits to mother and child (Meador et al., 2010; Powell, 2015). However, among WWE there is apprehension surrounding breastfeeding due to concerns that the infant will be exposed to ASMs in the breastmilk (Powell, 2015; Veiby et al., 2013). The effects of exposure to ASMs in breastmilk are worrying because of the possibility that the effects can be similar to the teratogenic effects of ASM exposure in the womb (Veiby et al., 2013). Although more research is needed, existing studies show that ASM exposure through breastmilk has no negative effects on children of WWE (Meador et al., 2010; Powell, 2015; Veiby et al., 2013). This reduced risk regarding breastfeeding is possibly due to the negative effects of ASMs on child development usually being dose-dependent, and the concentration of ASMs in breastmilk is lower than in the uterine blood supply (Meador et al., 2010; Powell, 2015; Veiby et al., 2013). Based on current evidence, WWE should be encouraged to breastfeed, particularly because the benefit of breastfeeding is potentially a protective factor against any possible negative effects of ASM exposure (Meador et al., 2010; Powell, 2015; Veiby et al., 2013).

WWE are more likely to develop postpartum depression (PPD) and postpartum anxiety (PPA) than women without epilepsy, with the symptoms of PPD usually beginning intrapartum (Bjørk et al., 2015; Meador et al., 2022; Tomson et al., 2019; Turner et al., 2006). A diagnosis of anxiety and/or depression before pregnancy, ASM polytherapy, a lack of seizure control, unplanned pregnancy, and low socioeconomic status put WWE at a higher risk of developing PPD and PPA than women without epilepsy (Bjørk et al., 2015; Galanti et al., 2009; Meador et al., 2022). PPD and PPA can impact both mother and child negatively. These negative effects

include low birth weight, ineffective mother-child attachment, impaired cognitive child development, and an increased risk of the child developing behavioral and emotional disorders (Bjørk et al., 2015; Turner et al., 2019). Healthcare professionals should be more vigilant in screening WWE for PPD and PPA, and the screening should begin in the intrapartum period (Bjørk et al., 2015; Meador et al., 2022; Stephen et al., 2019).

Teratogenicity

Children of WWE who use ASMs (e.g., phenobarbital, valproic acid, phenytoin, carbamazepine, and topiramate) experience two to four times the occurrence of adverse intrauterine and postnatal outcomes, with valproic acid showing the highest prevalence of adverse outcomes (Bhakta et al., 2015; Mazzone et al., 2023; Tomson & Battino, 2012). The risk of adverse outcomes increases at higher doses of the ASM and with ASM polytherapy, particularly if the combination includes valproic acid (Tomson & Battino, 2012). These adverse outcomes include fetal hydantoin syndrome, cleft lip, cleft palate, neural tube defects, cardiac defects, small for gestational age, impaired cognitive development, and behavioral disorders (Bhakta et al., 2015; Mazzone et al., 2023; Tomson & Battino, 2012).

In preconception planning and during pregnancy, physicians must work with WWE to balance the teratogenic risks posed by ASMs and the need to achieve seizure control (Tomson & Battino, 2012). Also, due to the high rate of unintended pregnancies among WWE, physicians should encourage all WWE with childbearing potential to take folic acid supplements to protect the fetus from the teratogenic effects of ASMs (Bhakta et al., 2015; Sadat-Hossieny et al., 2021). Folic acid has been found to be protective against neural tube defects (Dupont & Vercueil, 2021). Neural tube defects usually occur during the first four weeks of pregnancy, when most women are unaware that they are pregnant (Dupont & Vercueil, 2021). The

recommended dose of folic acid, in general, is 0.4 mg per day (Asadi-Pooya. 2015; Dupont & Vercueil, 2021; Sadat-Hossieny et al., 2021). It is suggested that WWE take a higher dose of folic acid because some ASMs impair the metabolism of folic acid resulting in low serum levels of folate (Asadi-Pooya. 2015). The dose of folic acid used by WWE ranges from 1mg to 5mg (Asadi-Pooya. 2015; Dupont & Vercueil, 2021; Sadat-Hossieny et al., 2021).

Bone Health

Smoking, menopause, and insufficient weight-bearing exercise are common risk factors for the general population for developing osteoporosis (Jackson, 2006). WWE face additional factors that threaten bone health. Several ASMs increase the risk of developing osteoporosis and the occurrence of fractures, particularly phenytoin, carbamazepine, phenobarbital, and divalproex/valproic acid (Brodie et al., 2013; Harden, 2008; Jackson, 2006; Perucca et al., 2013). Moreover, compared to the general population, people living with epilepsy (PWE) are more likely to be smokers (Konda et al., 2009; Torriani et al., 2016) and are less likely to be active and exercise (Hinnell et al., 2010; Pimentel et al., 2015). WWE face an elevated risk for diminished bone mineral density partly because enzyme-inducing ASMs can cause vitamin D deficiency and bone demineralization, with menopause heightening this risk (Carbone et al., 2010; Crawford et al., 1999). Due to the increased risk of developing osteoporosis and the increased risk of bone fractures due to seizure-related falls and the side effects of ASMs (e.g., unsteady gait, dizziness), WWE should be encouraged to take vitamin D and calcium supplements as appropriate, be physically active, and if relevant stop smoking (Carbone et al., 2010; Jackson, 2006; Sveinsson & Tomson, 2014). WWE should also be screened so that those who face a particularly high risk of developing osteoporosis should also be referred for regular bone mineral density scans (Jackson, 2006; Sveinsson & Tomson, 2014).

Studies Exploring the Care of Women with Epilepsy from the Perspective of the Women

As discussed above, the amount of literature published on the assessment of the implementation of the recommended care for WWE is limited. Research that measures this implementation from the perspective of WWE is also limited. Bell et al. (2002) surveyed WWE to assess their recall of health teaching regarding contraception, pre-pregnancy planning, the teratogenic risk of ASMs, vitamin K used during the last month of pregnancy, childcare safety, and breastfeeding. Harris et al. (2020) used surveys and interviews to assess the understanding of risks associated with taking ASMs during pregnancy of WWE using valproic acid and a WWE control group. Johnson et al. (2018) surveyed WWE and women without epilepsy during their post-partum period to analyze primary pregnancy outcomes, contraceptive use, breastfeeding practices, infant outcomes, and the length of time it took for them women to know they were pregnant. Kampman et al. (2005) reviewed case notes and surveyed WWE to analyze the care that WWE received. For the survey portion of the study, Kampman et al. (2005) analyzed the WWE's recall of health teaching on pregnancy planning, ASM-contraceptive interactions, folic acid use, and the effects of ASMs on developing osteoporosis. Pack et al. (2009) used surveys to assess WWE's knowledge of interactions between ASMs and oral contraceptives and the teratogenic effects of ASMs.

Summary of the Literature

The studies that have been published so far that explore care for WWE from the perspective of WWE have been focused on a few aspects of the experience of WWE, namely family planning and the intrapartum and postpartum periods. Even with a focus on the post-partum period, the experience surrounding postpartum mental health has not been explored. Also, there are no studies that explore care related to menstruation, hormone therapy for

transgender women and women experiencing menopause, and bone health from the perspective of WWE.

Significance and Purpose of the Study

Experts in the field of epilepsy have long acknowledged that WWE require dedicated care for sex specific issues (Bui, 2022; Crawford et al., 1999; Jackson, 2006; Stephen et al., 2019). However, as previously stated, there is very little research on the incorporation of the recommended care into clinical practice. For example, on the topic of caring for transgender WWE, only two expert opinion articles have been published. Both Johnson and Kaplan (2017) and Waldman and Benson (2022) discuss the interaction between gender-affirming hormone therapy and enzyme-inducing ASMs. In both articles this interaction is not based on research involving transgender participants but is based on information extrapolated from existing research. There is no research on the implementation of this knowledge.

The main issue that WWE face is the lack of understanding of all the factors associated with health for people living with epilepsy, the variability of opinions, the lack of standardized practice, as well as the range of information relayed to WWE. For these reasons, we are proposing in this study to learn from WWE living in Southwestern Ontario through listening to their experiences and issues associated with women's health. In order to assess the translation of knowledge it is important to assess all stakeholders, including clinicians and the public (Graham et al., 2006). Using the example of transgender WWE, this means that any research that assesses the implementation of transgender epilepsy care should include the perspective of transgender WWE.

The purpose of this study was to explore the implementation of the recommended care for WWE for sex-specific health issues from the perspective of the WWE. Using a cross-

sectional survey, we investigated the experience of WWE regarding menstruation, family planning, prenatal and perinatal care, hormonal influences and therapies, and bone health. From the perspective of knowledge translation, this study is one measure of the recommended care reaching the patient.

Theoretical Framework

In the early 1990s, the term 'evidence-based medicine' was created to support the incorporation of the best available evidence into clinical practice (Mackey & Bassendowski, 2017). Later, the term evidence-based medicine was renamed 'evidence-based practice' to acknowledge its use by other health care professions (Mackey & Bassendowski, 2017). Despite this attempt, it was still found that there was a significant gap between the production of research and its implementation in clinical practice (Olson & Oudshoorn, 2020; Scott et al., 2012). This led to the development of the concept of knowledge translation (Olson & Oudshoorn, 2020). The purpose of the knowledge translation process is to improve care by actively incorporating research knowledge into practice (Canadian Institutes of Health Research, 2016; Olson & Oudshoorn, 2020).

The knowledge translation process comprises several components, including knowledge creation, knowledge synthesis, and presenting the synthesized knowledge to professionals in a way that suits the situational context of their practice (Canadian Institutes of Health Research, 2016; Olson & Oudshoorn, 2020). These components aid healthcare professionals in incorporating knowledge into actionable practice to achieve the intended goal of knowledge translation, which is to improve health outcomes (Olson & Oudshoorn, 2020; Scott et al., 2012). When assessing the effectiveness of knowledge translation, it is important to assess if the recommended care is reaching the patient by evaluating change in public health outcomes,

clinical practice, and patient education (Graham et al., 2006; Olson & Oudshoorn, 2020). In this study knowledge translation is evaluated by surveying WWE. Several articles have been published with recommendations on how to care for WWE for sex-specific health issues. However, there has been relatively little research into the implementation of these recommendations, particularly from the perspective of WWE. In this study, we seek to continue to contribute to filling this knowledge gap by adding to research that explores knowledge translation from the perspective of the care recipients.

Research Objectives

This study is a descriptive exploratory survey with a cross-sectional design, examining the experience of WWE for sex-specific health issues. The researchers set research objectives for the study. The research objectives are to explore:

1. If WWE are being screened for a catamenial pattern in relation to their seizures and if treatment changes were implemented because a catamenial pattern was identified.
2. If WWE are receiving the recommended family planning counselling regarding folic acid use and contraceptive use.
3. If WWE are receiving the recommended intra- and postpartum care regarding medications prescribed, polypharmacy, teratogenic risks associated with ASMs, postpartum mental health, breastfeeding counselling, and child safety counselling.
4. If WWE are receiving the recommended counselling about the interactions between hormone replacement therapy and ASMs for WWE experiencing perimenopause/menopause and interactions between hormonal therapy and ASMs for persons undergoing gender transitions.

5. If WWE are receiving the recommended bone health counselling regarding ways to improve bone health and ASMs that increase osteoporosis risk.

Chapter Two

Methods

Design

In this study, descriptive exploratory survey with a cross-sectional design was used to explore the implementation of the recommended care for WWE for sex-specific health issues from the perspectives of the WWE living in southwestern Ontario. The information presented here from participants in Southwestern Ontario is a sub-analysis of a larger exploratory, international study. In non-experimental research the variables are not manipulated; they are investigated as they naturally occur (LoBiondo-Wood & Haber, 2018; Polit and Beck, 2021). The non-experimental survey method is an appropriate way to obtain data about variables when assessing practices and when working towards improving clinical practice (LoBiondo-Wood & Haber, 2018). A non-experimental survey design was appropriate to this study because the goal is to investigate the care that WWE receive as reported by WWE, that is, the care as it naturally occurred. Ethical approval was received from Western University's Health Sciences Research Ethics Board and Lawson Health Research Institute (Appendix B).

Participant Recruitment

This thesis is part of a larger, ongoing international study. In the international study, the non-probability sampling technique of convenience sampling is being used. In convenience sampling, the most easily accessed participants of the target population are recruited (LoBiondo-Wood & Haber, 2018; Polit and Beck, 2021). In the ongoing international study participants are being recruited from the clinical areas where the researchers practice and where available, with the assistance of the local epilepsy community partner organization. For this thesis, the target population was WWE living in southwestern Ontario. Recruitment focused primarily on

prospective participants who were patients admitted to the Epilepsy Monitoring Unit (EMU) or had appointments at the outpatient epilepsy clinics at University Hospital, London Health Sciences Centre, London, Ontario, Canada, and WWE who engaged with the social media accounts of Epilepsy Southwestern Ontario and the social media accounts of the researchers.

The recruitment strategy included handing the survey (see Appendix C) directly to the patient, placing the recruitment poster (see Appendix D) in strategic areas of the hospital, and sharing the recruitment poster online. The recruitment poster gave a brief explanation of the study and included a quick response code (QR code), which the participant could scan to access the digital version of the survey. Participants were primarily recruited from the EMU and the outpatient epilepsy clinics at University Hospital, London Health Sciences Centre, London, Ontario, Canada.

The EMU is a 10-bed inpatient unit that provides surgical investigations and diagnostic clarification for people diagnosed with epilepsy as well as drug-resistant epilepsy. Drug-resistant epilepsy is defined as failure to achieve seizure control after trialling two tolerated and suitable ASMs (Kwan et al., 2010). The EMU also provides diagnostic clarification for people misdiagnosed with epilepsy or were misdiagnosed with another medical or psychiatric condition, for example, a parasomnia or anxiety, but who have epilepsy. The survey study was included in the admission package. During the admission process, the nurse would identify the patients who met the inclusion criteria and give the patient the survey. If the patient did not meet the inclusion criteria, the survey was removed from the admission package. Patients were approached during their admission to confirm that they received the survey, answer any questions they had, and to direct them on how to hand in the survey if they chose to complete it. Recruitment posters were

also placed at the entrance to the EMU and in the hallway outside the EMU so that patients could scan the QR code and submit the survey electronically if they preferred.

In the epilepsy outpatient clinic, the physicians gave a photocopy of the recruitment poster to patients who met the inclusion criteria. The physician would explain to the potential participant the purpose of the study and that completing the survey is voluntary. The recruitment posters were placed in the neurology outpatient clinic, epilepsy outpatient clinic and electroencephalogram outpatient waiting areas at University Hospital. The patient could scan the QR code on the photocopy of the poster to access the digital version of the survey. For online recruitment, the recruitment poster was shared through the investigators' social media accounts. The community organization Epilepsy Southwestern Ontario was contacted, and they shared the recruitment poster via their social media accounts.

The inclusion criteria for the study were as follows: (1) any adult identifying as a woman and/or was assigned the female sex at birth; (2) aged 18 years or older; (3) able to read English or had a support person who could read English; and (4) a diagnosis of epilepsy and/or psychogenic non-epileptic events (PNEE). While this study did not have specific exclusion criteria, the survey was designed so that individuals could not access and complete the survey unless they met the eligibility criteria.

Sample Size

There was no comparative statistical analysis of the data in this study. Therefore, determining a sample size by performing a power analysis was not possible. The sample sizes of studies that used similar recruitment strategies were used as a guide for the current study. Bell et al. (2002) received 795 responses to their survey. Harris et al. (2019) recruited 100 participants for their study: 50 WWE and 50 women without epilepsy. In the patient questionnaire portion of

the study by Kampman et al. (2005), 112 participants completed the questionnaire. In the study by Pack et al. (2009), 148 WWE completed the survey. Based on the sample sizes in these studies and in an attempt to get an adequate number of responses in each category, the sample size for the larger international study was set to 500 participants. The current study is the sub-analysis of Southwestern Ontario participants, which is part of the larger international study. For this thesis, the survey responses of eighty-nine participants from Southwestern Ontario were analyzed.

Data Collection

The survey was developed by the principal researcher (CR) under the guidance of the co-supervisor (AS). The questions were chosen to cover all aspects of sex-specific health issues that WWE experience, including menstruation (Bui, 2022; Lukić, 2018; Noe, 2007), family planning and contraception (Crawford et al., 1999; Guillemette & Yount, 2012; Reimers, 2020), intra- and post-partum care (Crawford et al., 1999; Dupont & Vercueil, 2021; Laganà et al., 2016 ; Meador et al., 2010; Tomson et al., 2019), hormonal therapies for menopause (Crawford et al., 1999; Harden, 2008; Noe, 2007) and gender transition (Johnson & Kaplan, 2017), and bone health (Carbone et al., 2010; Jackson, 2006; Sveinsson & Tomson, 2014). The questions in each category were chosen to allow for comparison with the existing studies and to explore aspects not yet investigated, such as post-partum mental health and gender transition. Also, because this study is rooted in knowledge translation, questions in the survey reflect the knowledge that is available to healthcare providers.

Research Electronic Data Capture (REDCap) was used to manage all the survey data. When a participant completed the paper copy of a survey, one of the research team members entered the information electronically in REDCap. Participants could access the online version of

the survey by scanning the QR code located on the recruitment posters. The online surveys were produced using REDCap. When a participant completed a survey online, the information would be uploaded directly into the REDCap database for this study. In the EMU, interested participants had the option of using the paper copy or scanning the QR code to access the online survey. As per ethics guidelines, the paper copies are kept in secure storage in the research assistant's office at University Hospital. Participants who visited the epilepsy clinic at University Hospital or interacted with the online posts had to scan the QR code to access the online survey.

Each participant had to give their consent to be included in the study. The question requesting consent was located at the end of the Letter of Information at the beginning of the survey (see Appendix B). In the online version of the survey, the participant could not access the rest of the survey if they did not answer the question or answered "No" to the consent question. If the person did not answer the question or answered "No" to the consent question in the paper survey, the information was not input into the REDCap system.

When the paper survey was given to the patients in the EMU, it was explained to them that two questions were mandatory and that the remaining questions were optional. The questions regarding diagnosis and age were mandatory questions, as these related to the eligibility criteria of the current study. For the remaining questions, the participants recruited from the EMU were asked to only answer the questions that applied to their experience. They were instructed to disregard any questions that were not applicable or they did not feel comfortable answering. For the online version of the survey, participants could not complete the survey unless they gave consent and selected a diagnosis of epilepsy only or epilepsy and psychogenic non-epileptic events (PNEE). After that, the only question that required an answer

was the question pertaining to participant age. Participants accessing the online survey could skip any of the remaining questions.

Data Analysis

Analysis of the data collected in this study was conducted using the Statistical Package for Social Sciences (SPSS), Version 29.0, from International Business Machines Corporation [IBM]. Before analysis, the data was reviewed to ensure congruence of answers with the collected survey responses. For example, if a participant answered that they had never been pregnant and had no children but answered that they were not screened for PPD or PPA, the mental health screening data were removed to make the data congruent. A descriptive statistical analysis comprised measures of mean, central tendency, and frequency distributions was conducted for the total sample and variables of interest.

Results

Demographics

Eighty-nine individuals responded to the survey. The age range is 18 to 66, with a mean age of 36.14 (SD ±13.12) (see Table 1). On the survey, participants were able to choose multiple racial/ethnic backgrounds. The most selected racial/ethnic background was White (see Figure 1). Approximately 73% (n=52) lived in an urban location and 26.8% (n=19) lived in a rural location (see Table 2). Seventy-one participants answered the question on education level. Approximately 27% (n=19) of completed high school, 36.6% (n=26) completed a college or vocational degree, and 33.8% (n=24) completed a university degree (see Table 2). Participants were more likely to be employed or receiving government-issued financial aid, with 34.7% (n=25) being employed full time, 12.5% (n=9) being employed part-time, and 20.8% (n=15) receiving government-

issued financial assistance (see table 2). For full demographics see Tables 1 and 2 and Figures 1 and 2.

Table 1

Current Age and Age at Epilepsy Diagnosis

	Minimum	Maximum	Mean	n	SD
Current age	18	66	36.14	74	13.12
Age at diagnosis	1	62	22.84	67	13.58

Table 2

Demographics

	Frequency	Percent (%)
Location (n=71)		
Rural	19	26.8
Urban	52	73.2
Education level (n=71)		
Grade school	1	1.4
High school	19	26.8
College or vocational degree	26	36.6
University degree	24	33.8
Not applicable	0	0
Other	1	1.4
Prefer not to say	0	0
Employment status (n=72)		
Full-time	25	34.7
Part-time	9	12.5
Unemployed	6	8.3
Retired	1	1.4
Government issued financial support	15	21
Student	8	11.1

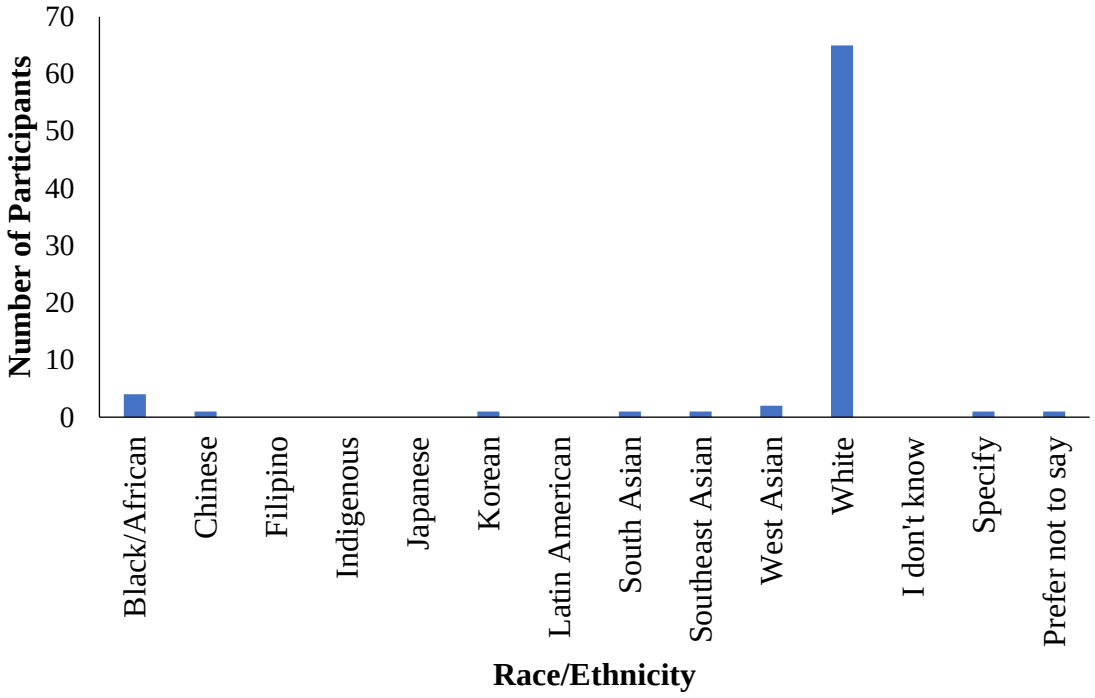
	Frequency	Percent (%)
Other	8	11.1
Prefer not to say	0	0
Annual Income (n=72)		
$0-$25,000	29	40.3
$25,001-$50,000	14	19.4
$50,001-$99,000	15	20.8
$99,001-$152,000	4	5.6
$152,001-$217,000	1	1.4
$217,001+	1	1.4
Prefer not to say	8	11.1
Marital Status (n=71)		
Single	34	47.9
Married	20	28.2
Common-law	9	12.7
Divorced	3	4.2
Separated	0	0
Widowed	2	2.8
Other	3	4.2
Prefer not to say	0	0

Diagnosis, Seizure Types and Medications

Ninety-one percent (n=81) of responders were diagnosed with epilepsy only and 9% (n=9) were diagnosed with epilepsy and psychogenic non-epileptic events (PNEE). On the survey, participants were able to select all the seizure types with which they have been diagnosed and all the ASMs that they were using when they completed the survey. The most common seizure types diagnosed were focal seizures and generalized tonic-clonic seizures (see Figure 2). The most prescribed ASMs, in descending order, were lamotrigine, clobazam, lacosamide, and lorazepam (see Table 3 and Figure 3).

Figure 1

Racial/Ethnic Background



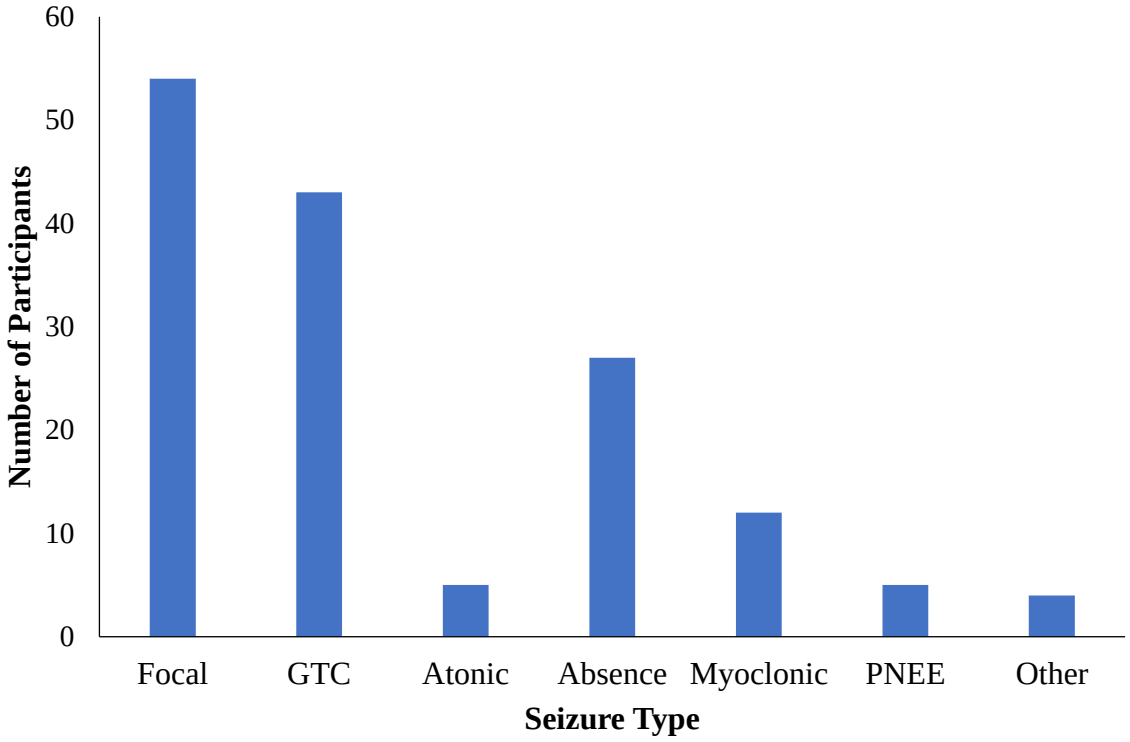
Note. Based on responses from 72 participants.

Menstruation

Approximately 58% (n=50) of participants menstruated. Reasons for not menstruating included experiencing perimenopause/menopause, use of birth control, hysterectomy, and oophorectomy (see Table 4). Approximately 48% (n=24) reported that their menses affect the frequency of their seizures. For the question on treatment changes due to having a catamenial seizure pattern, participants were able to select all the answers that applied to them. Twenty of the participants who reported that their menses affect their seizure frequency answered the treatment change question. There were no treatment changes for most of the participants who reported having a catamenial seizure pattern (see Figure 4).

Figure 2

Epilepsy Diagnosis by Seizure Types



Note. GTC=generalized tonic-clonic. PNEE=psychogenic non-epileptic event. Based on responses from 72 participants.

Table 3

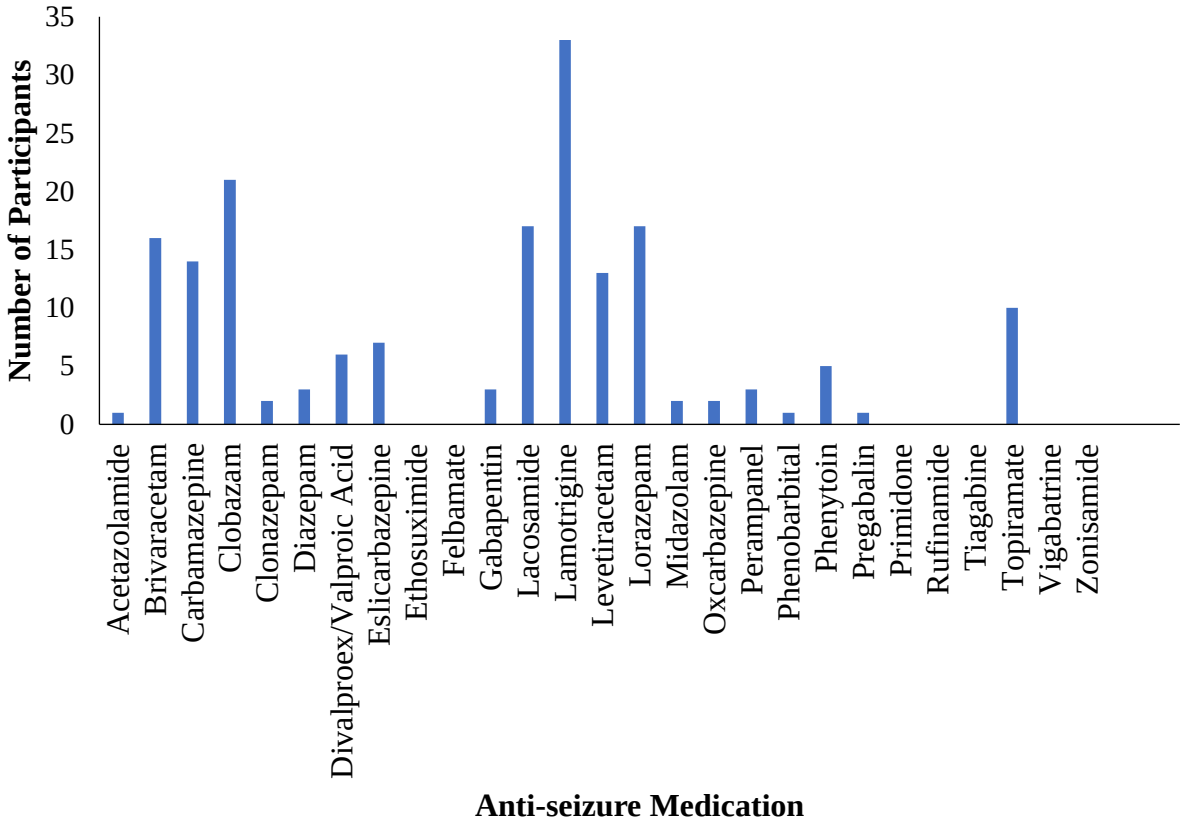
Epilepsy Diagnosis and Currently Taking Anti-seizure Medications

	Frequency	Percent (%)
Epilepsy diagnosis (n=89)		
Epilepsy Only	89	91
Epilepsy and PNEE	9	9
Taking anti-seizure medication (n=72)		
Yes	69	95.8
No	3	4.2

Note. PNEE=psychogenic non-epileptic events

Figure 3

Current Anti-seizure Medications



Note. Based on responses from 69 participants.

Table 4

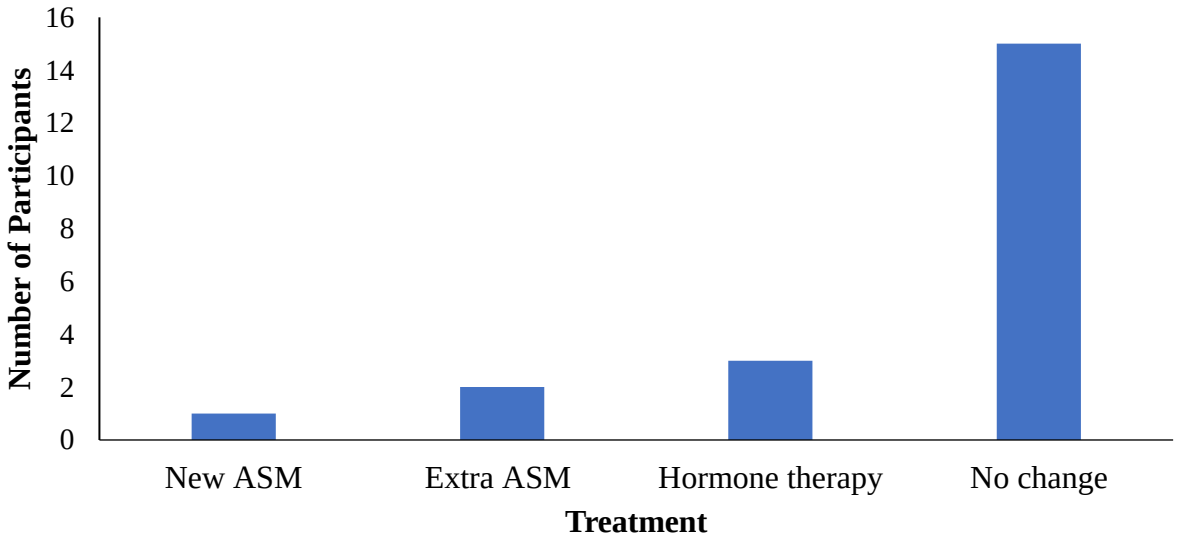
Menstruation Status and Catamenial Epilepsy Tendency and Treatment

	Frequency	Percent (%)
Menstruation status (n=86)		
Menstruates	50	58.1
Does not menstruate - pre-menopause or menopause	14	16.2
Does not menstruate - using birth control	11	12.8
Does not menstruate – oophorectomy	1	1.2
Does not menstruate – hysterectomy	9	10.5

	Frequency	Percent (%)
Does not menstruate – other reason	1	1.2
Menses affect seizure frequency (n=49)		
Yes	24	49
No	25	51
Discussed catamenial pattern with a physician? (n=24)		
Yes	20	83.3
No	4	16.7

Figure 4

Treatment Changes due to Catamenial Seizure Pattern



Note. ASM=Antiseizure medication. Based on responses from 20 participants.

Family Planning

Eighty-one participants answered the question on family planning intention. Approximately 6% (n=5) reported that had previously tried to get pregnant, 1.2% (n=1) were trying to get pregnant, 26% (n=21) planned to get pregnant in the future, 33.3% (n=27) had no plans to get pregnant, and 33.3% (n=27) did not fit into any of these categories (see Table 5).

Seventy-eight participants answered the question on contraceptive use and type. Approximately 61% (n=48) of responders did not use contraceptives. IUD was the most common contraceptive used (see Figure 5). Further analysis of the 48 participants who do not use contraceptives showed that one was trying to get pregnant, 17 did not plan on getting pregnant, 10 planned to get pregnant in the future, three tried to get pregnant in the past, 15 were experiencing perimenopause or menopause, and two had other reasons not listed (see Table 5). Of the six responders using hormonal pills as their contraception method, four discussed the interaction between the hormonal pills and their ASMs with a physician and two did not discuss the interaction with a physician (see Table 5).

For the question regarding folic acid use, participants were able to select when they were counselled to use folic acid and the recommended dose. Fifteen participants reported that they were advised to take folic acid during pregnancy only, 22 reported that they were advised to take folic acid before and during pregnancy, and 28 were not advised to use folic acid. Two participants were advised to use 0.5mg of folic acid, 15 were advised to take 1mg, two were advised to take 4 mg, and 12 were advised to take 5mg (see Figure 6). For the questions about barriers to using folic acid, participants were able to select all the barriers that applied to them. Forgetting to take folic acid was the most common barrier (see Figure 8). On the survey, participants were able to make multiple selections from the list of diagnoses that impact fertility. Thirty-seven participants answered this question. An irregular period pattern was the most common diagnosis that impacted fertility (see Figure 9).

Table 5

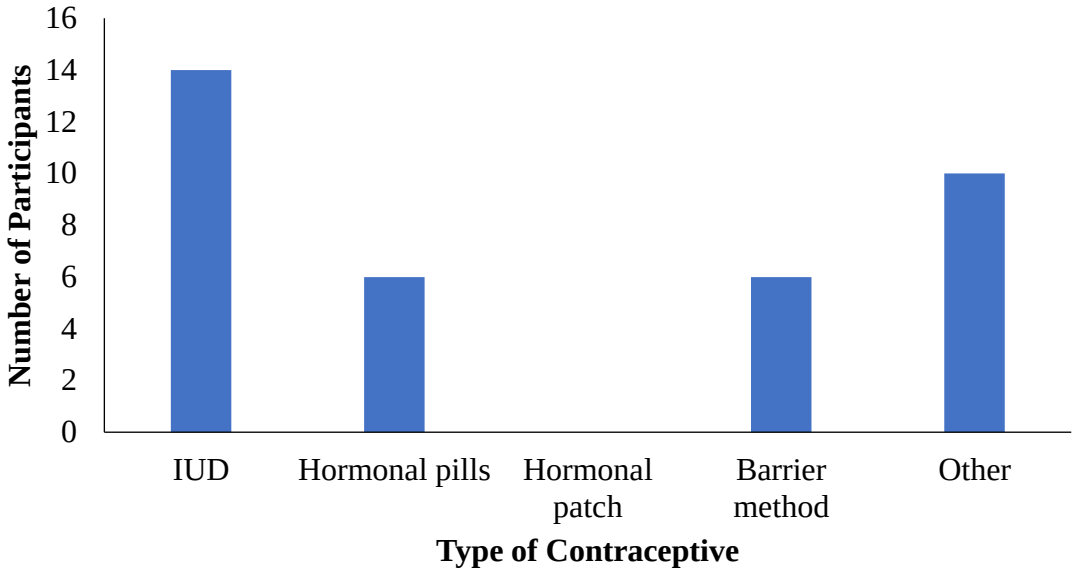
Family Planning Intention and Contraception Counselling

	Frequency	Percent (%)
Family planning intention (n=81)		
Tried to get pregnant	5	6.2
Trying to get pregnant	1	1.2
Plan on getting pregnant in the future	21	26
Do not plan on getting pregnant	27	33.3
None of these apply	27	33.3
Contraceptive use (n=78)		
No	48	61.5
Yes	30	38.5
Discussed interaction between hormonal contraceptive and ASM? (n=6)		
Yes	4	66.7
No	2	33.3
I do not remember	0	0
Reason for not using contraception (n=48)		
Trying to get pregnant	1	2.1
Do not plan on getting pregnant	17	35.4
Planning to get pregnant	10	20.8
Tried to get pregnant	3	6.3
Perimenopause/menopause	15	31.2
Other	2	4.2

Note. ASM=Anti-seizure medication. IUD=Intrauterine device.

Figure 5

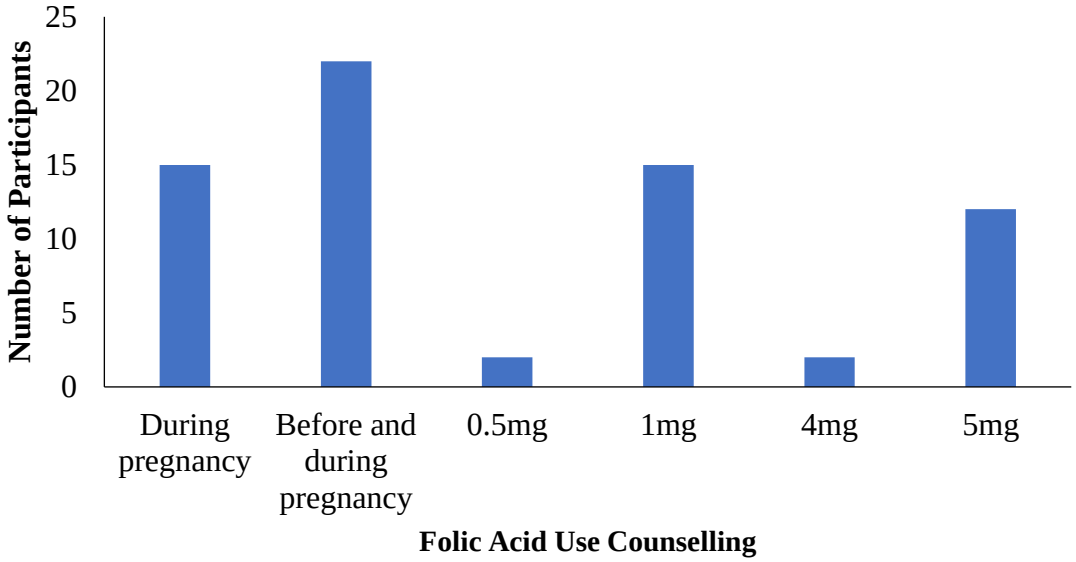
Types of Contraceptives Used



Note. IUD=intrauterine device. Based on responses from 30 participants.

Figure 6

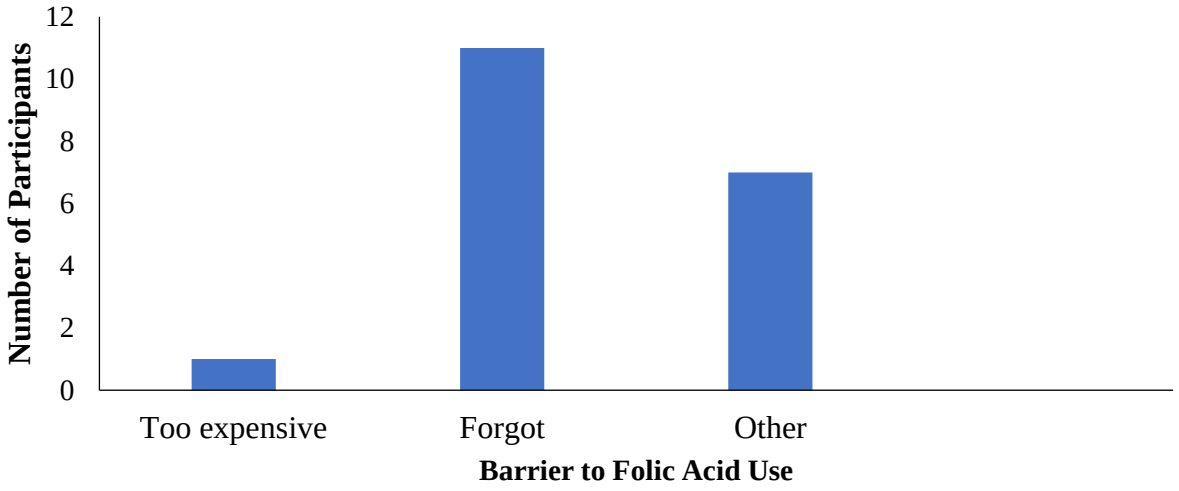
Folic Acid Counselling Received and Dose Recommended



Note. Based on responses from 50 participants.

Figure 7

Barriers to Folic Acid Use



Note. Based on responses from 17 participants.

Table 6

Folic Acid Use

	Frequency	Percent (%)
Advised to use folic acid (n=78)		
Yes	50	64.1
No	28	35.9

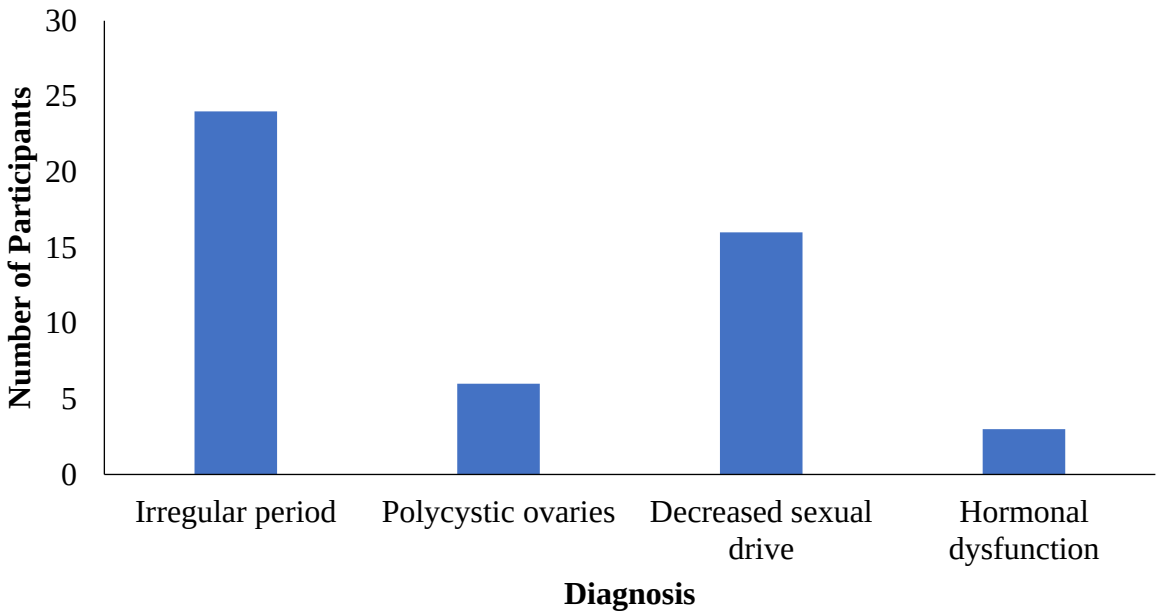
Pregnancy

Of the 73 responders who completed the pregnancy section, 52.1% (n=38) had been pregnant. The number of children that responders had ranged from 0 to 4, with a mean of 1.29 children (SD ±1.01). Approximately 32% (n=12) responders planned their pregnancies, 51.4% (n=19) did not plan their pregnancies, 13.5% (n=5) had both planned and unplanned pregnancies, and 2.7% (n=1) preferred not to answer. For most planned pregnancies changes were made to the ASMs that the participant was taking and for most unplanned pregnancies no changes were made

to the ASMs. Participants were as likely to be on ASM monotherapy as ASM polytherapy during pregnancy. Forty-five percent of participants (n=9) were taking one ASM and 55% (n=11) of participants were taking two or more ASMs. Participants were more likely to discuss the effects of ASMs on child development, with 27.3% (n=6) discussing ASM effect on thinking and learning, 9.1% (n=2) discussing ASM effect on thinking only, and 9.1% (n=2) discussing ASM effect on learning only. Of the three participants who took divalproex/valproic acid during pregnancy, one was counselled on how it affects thinking only, one was counselled on how it affects learning only, and one was not counselled. In the survey, participants were able to select all the complications they experienced during pregnancy. Fourteen participants experienced seizures during pregnancy and 10 participants gave birth prematurely (see Figure 10). See Table 7 for full results and Figure 9 for ASMs used during pregnancy.

Figure 8

Diagnoses that Affect Fertility



Note. Based on responses from 37 participants.

Table 7

Planned and Unplanned Pregnancies and ASM Use and Counselling

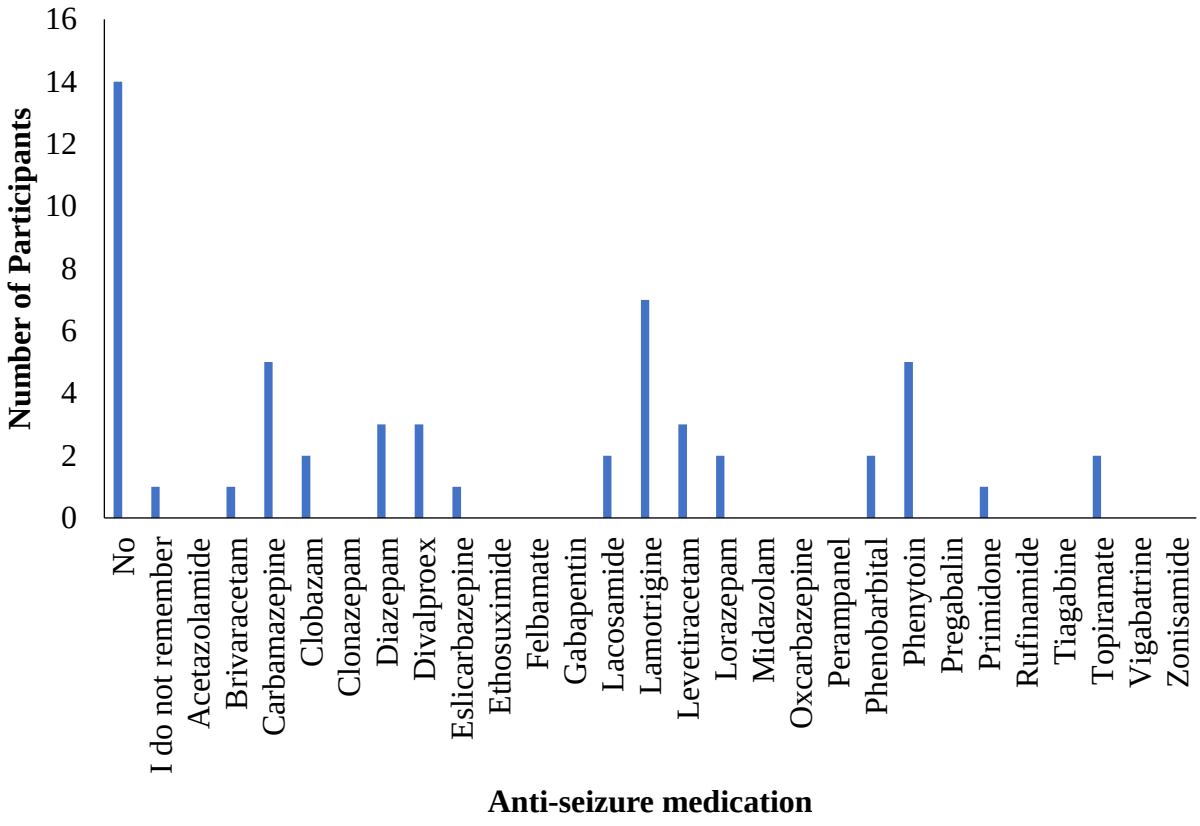
	Frequency	Percent (%)
Planned pregnancies (n=37)		
Yes	12	32.4
No	19	51.4
Some pregnancies were planned, and some were not	5	13.5
I prefer not to answer	1	2.7
ASM changes because of a planned pregnancy (n=13)		
I do not remember	2	15.4
No changes were made	5	38.4
Medications were increased	0	0
Medications were decreased	2	15.4
I was prescribed a new medication	4	30.8
ASM changes because of an unplanned pregnancy (n=23)		
I do not remember	2	8.7
No changes were made	14	60.9
Medications were increase	0	0
Medications were decreased	4	17.4
I was prescribed a new medication	3	13
Took ASMs during pregnancy (n=35)		
Yes	20	57.1
No	14	40
I do not remember	1	2.9
Number of ASMs used during pregnancy (n=20)		
1	9	45
2	7	35
3	3	15
4	0	0
5 or more	1	5

	Frequency	Percent (%)
Discussed effects of ASMs on child development (n=22)		
No	9	40.9
I do not remember	3	13.6
Yes, effects on thinking	2	9.1
Yes, effect on learning was discussed	2	9.1
Yes, effect on thinking and learning was discussed	6	27.3

Note. ASM=Anti-seizure medication.

Figure 9

Medications Taken During Pregnancy

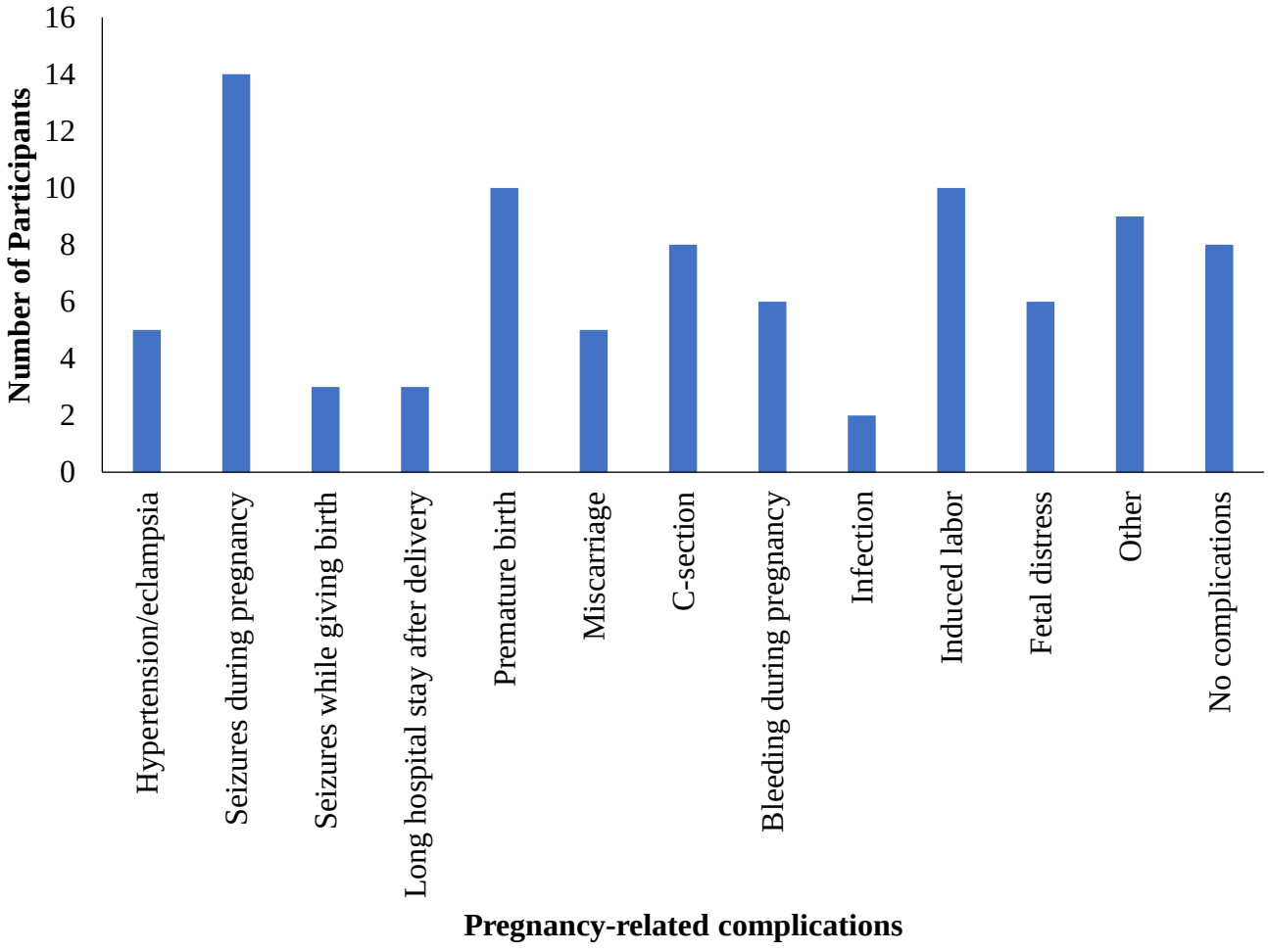


Note. Based on responses from 35 participants.

Approximately 65% (n=22) of participants did not have a mental health diagnosis before they were pregnant (see Table 8). In the survey, participants were able to select all the mental health diagnoses that applied to them. Depression, anxiety, and epilepsy/seizure-related psychosis were the most common mental health diagnoses before pregnancy. Regardless of their mental health status before pregnancy, most participants were not screened for post-partum depression or anxiety (see Figure 11).

Figure 10

Pregnancy-related Complications



Note. Based on responses from 34 participants.

Table 8

Postpartum Mental Health Care

	Frequency	Percent (%)
Diagnosed with a mental health disorder before pregnancy (n=34)		
No	22	64.7
Yes	12	35.3
I do not remember	0	
Pre-pregnancy mental health diagnosis (n=12)		
Anxiety	5	
Depression	7	
Bipolar disorder	1	
Personality disorder	3	
Schizophrenia	1	
Epilepsy or seizure related psychosis	5	
Screened for PPD/PPA (n=35)		
Yes	11	31.4
No	22	62.9
I do not remember	2	5.7
Received a post-partum mental health diagnosis (n=32)		
No	24	75
Yes	8	25
Post-partum diagnosis and treatment (n=8)		
Diagnosed with PPD	4	
Diagnosed with PPA	2	
Received counselling	2	
Prescribed medications	2	
Diagnosed but no treatment	3	

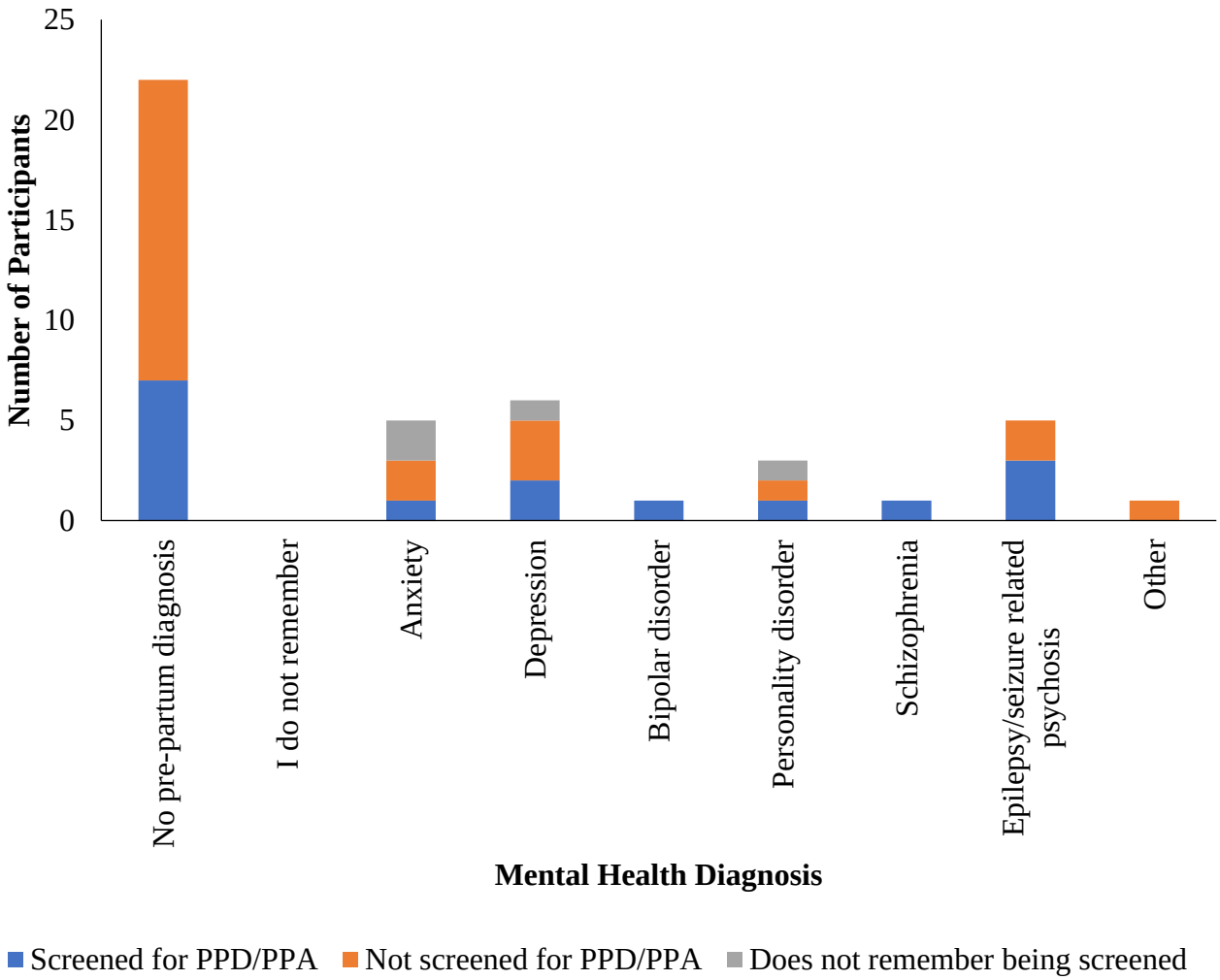
Note. PPA=post-partum anxiety. PPD=post-partum depression

Approximately 83% (n=28) of participants did not discuss child safety with a physician. Most participants, 52.9% (n=18), breast fed their children. Participants were more likely to not

discuss the safety of breastfeeding while using ASMs. Approximately 55% (n=17) of participants did not discuss the safety of breastfeeding while using ASMs with a physician, 32.3% (n=10) discussed breastfeeding safety with a physician, and 12.9% (n=4) of participants do not remember if they had this discussion. See Table 9 for more details.

Figure 11

Prepartum Mental Health Diagnosis and Postpartum Depression/Post-partum Anxiety (PPD/PPA) Screening



Note. Based on responses from 34 participants.

Table 9

Child Care Safety Counselling and Breastfeeding Choice and Counselling

	Frequency	Percent (%)
Discussed childcare safety (n=34)		
Yes	6	17.6
No	28	82.4
Breastfed children (n=34)		
Yes	18	52.9
No, concerns about ASM use	3	8.8
No, not recommended	2	5.9
No, other reason given	11	32.4
Discussed breastfeeding safety (n=31)		
Yes	10	32.3
No	17	54.8
I do not remember	4	12.9

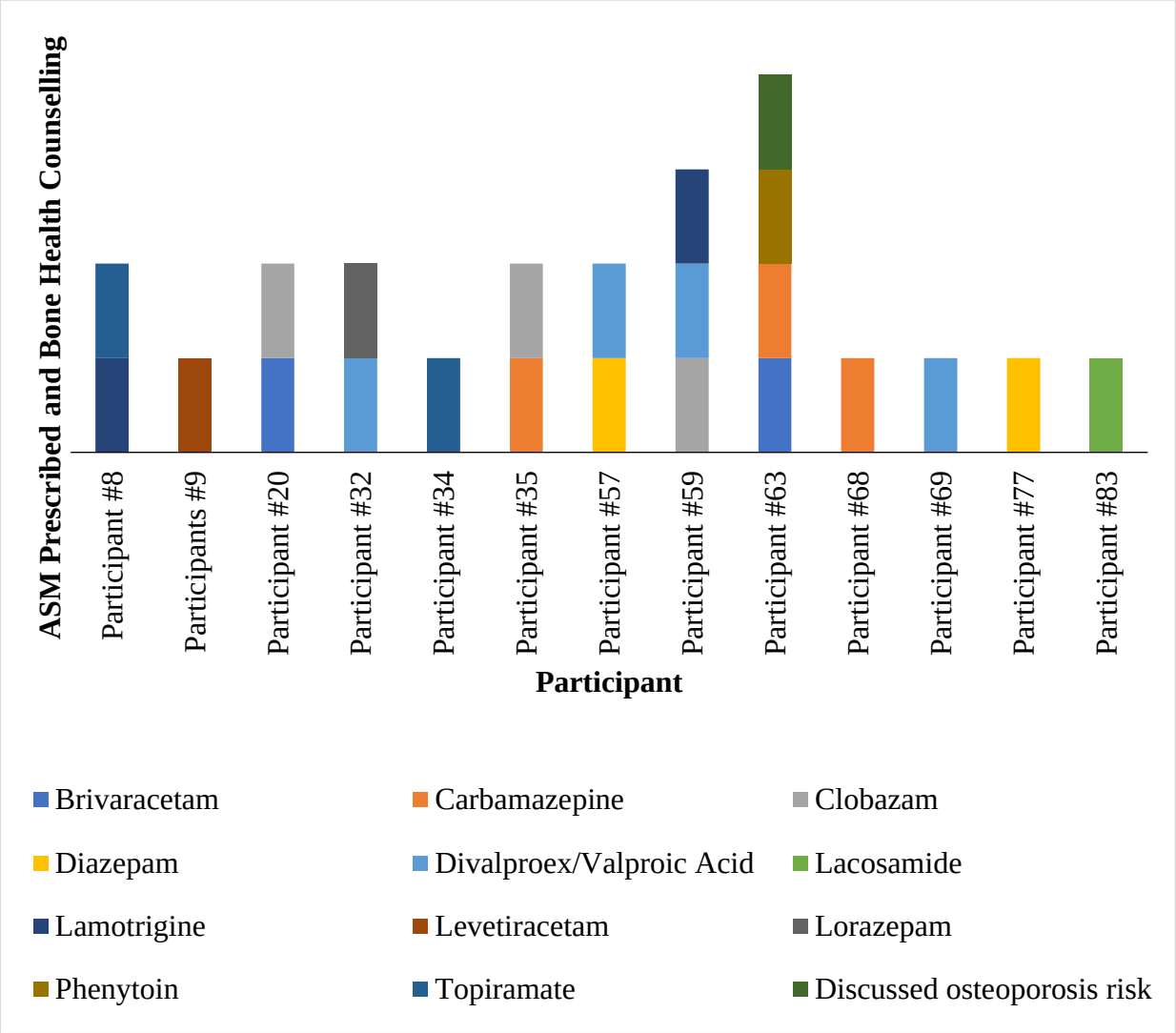
Note. ASM=Anti-seizure medication.

Hormonal Therapies: Menopause and Transgender

Thirteen participants reported experiencing perimenopause or menopause. Of these thirteen participants, one participant was using hormone replacement therapy (HRT). This participant was taking carbamazepine and clobazam and did not respond to the question regarding discussing the HRT-ASM interaction with a physician. Of the 13 participants experiencing perimenopause or menopause, 12 answered the question about discussing osteoporosis risk due to ASM use. Approximately 92% (n=11) did not discuss osteoporosis risk with a physician and 8.3% (n=1) discussed osteoporosis risk with a physician. Three of the thirteen participants experiencing perimenopause or menopause were prescribed carbamazepine, three were prescribed divalproex/valproic acid, and one was prescribed phenytoin (see Figure 12). One participant was undergoing gender transition, taking levetiracetam, and did not discuss the interaction between hormonal therapy and ASMs.

Figure 12

Medications Used by Participants Experiencing Perimenopause/Menopause and Bone Health Counselling



Bone Health

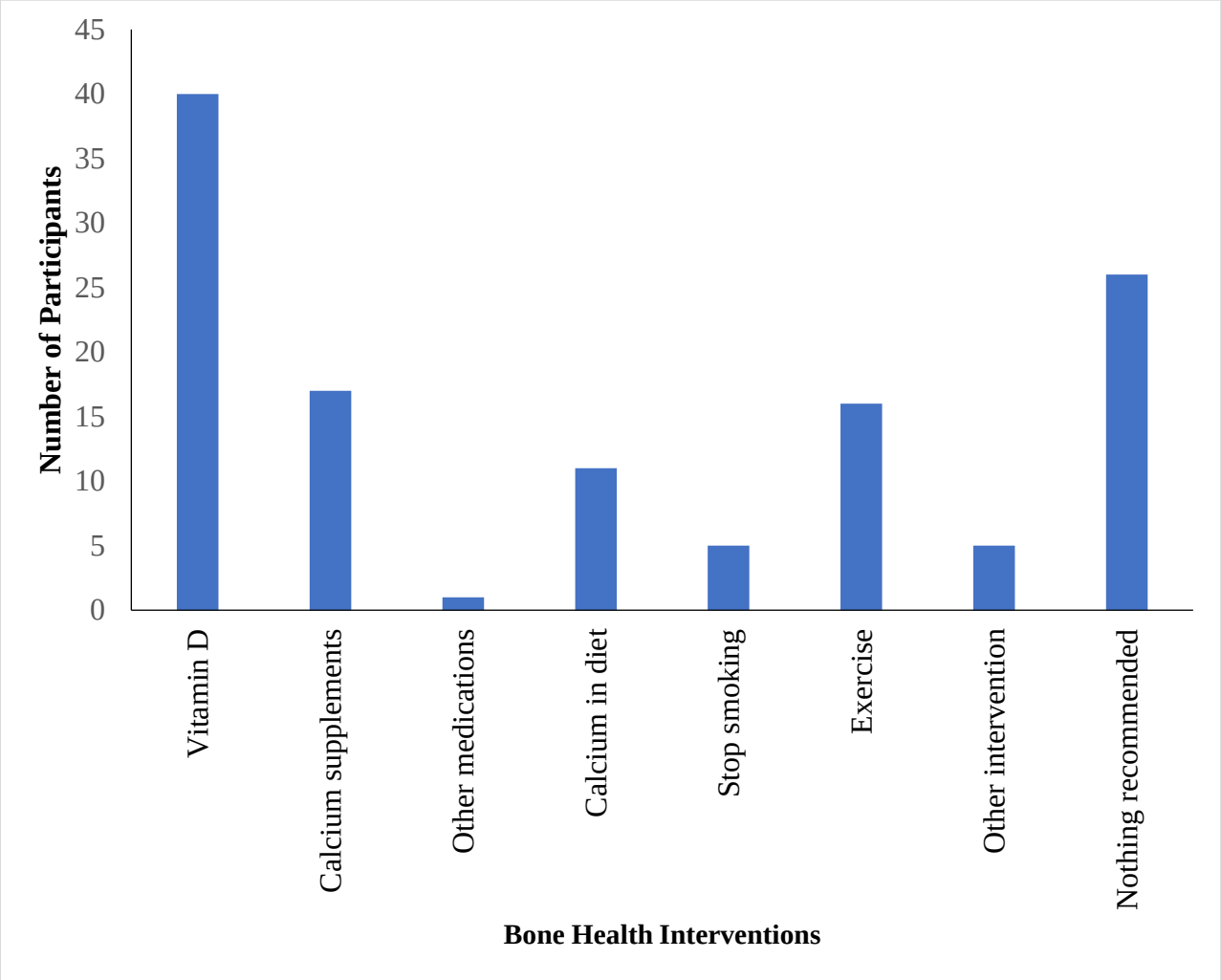
Ninety percent (n=63) of participants who completed this section were not diagnosed with a bone condition, 2.9% (n=2) were diagnosed with osteoporosis, 2.9% (n=2) were diagnosed with osteopenia, and 4.3% (n=3) were diagnosed with fragile bones (see Table 10). Twenty-six participants were not advised by a physician of interventions to increase their bone

health. The most recommended bone health interventions were taking vitamin D supplements and calcium supplements (see Figure 13).

Approximately 22% (n=15) of participants discussed the potential risk for osteoporosis posed by their ASM, and approximately 78% (n=53) did not have this discussion. Further analysis of these data showed that of the participants taking ASMs that pose the highest risk for developing osteoporosis were not advised of this risk (see Figure 14).

Figure 13

Recommended Bone Health Interventions



Note. Based on responses from 43 participants.

Table 10

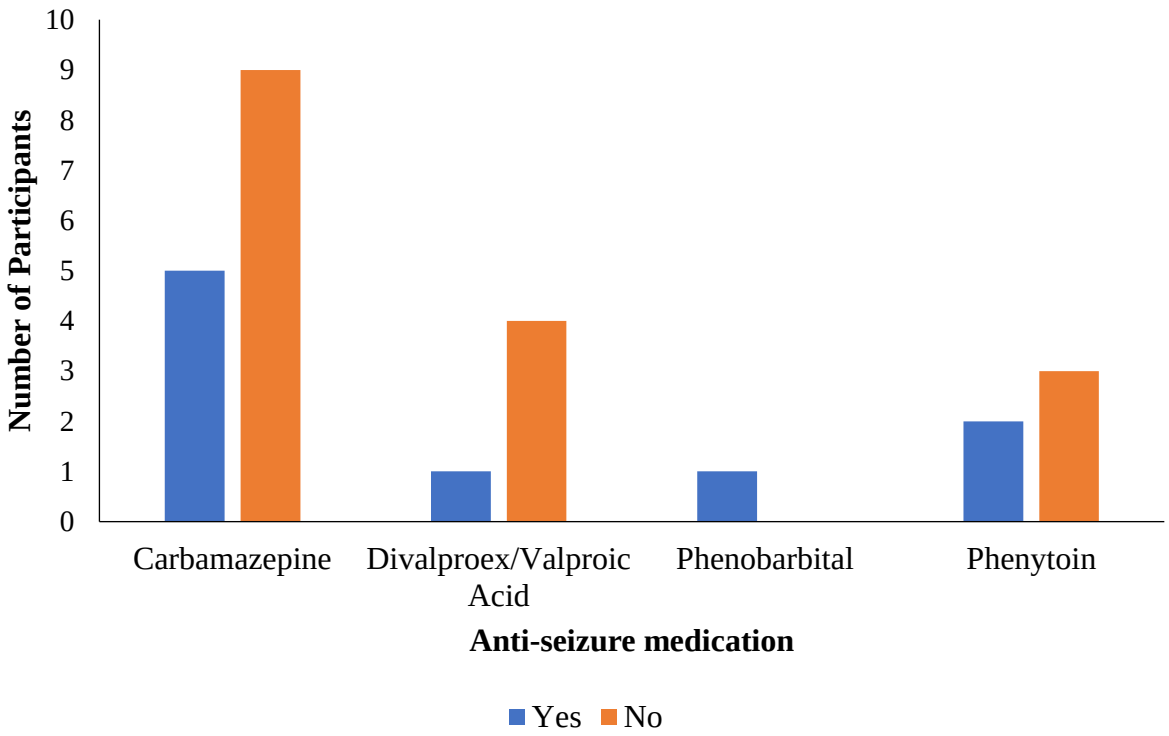
Bone Health Diagnosis

	Frequency	Percent (%)
Bone health diagnosis (n=70)		
Osteoporosis	2	2.9
Osteopenia	2	2.9
Fragile bones	3	4.2
No bone health diagnosis	63	90
Discussed osteoporosis risk due to ASM use (n=68)		
Yes	15	22.1
No	53	77.9

Note. ASM=Anti-seizure medication.

Figure 14

Advised of the Increased Risk for Developing Osteoporosis Based on Specific Anti-Seizure Medications



Chapter Three

Discussion

The purpose of this study was to explore the implementation of the recommended care for WWE for sex-specific health issues from the perspective of the WWE. Using a cross-sectional survey, we investigated the experience of WWE regarding menstruation, family planning, prenatal and perinatal care, hormonal influences and therapies, and bone health. Ideally all WWE would receive the recommended care and counselling for sex-specific health issues.

From the perspective of knowledge translation, this study is one indicator of whether the recommended counselling and care is reaching the patient. From the care and counselling that participants reported, there are some aspects of care of WWE that were adequately addressed and others requiring significant improvement. The areas of care that require significant improvement may be indicative of areas that the antecedents of knowledge translation are not present. The antecedents of knowledge translation include knowledge, receptive healthcare professionals, and a practice environment that facilitates learning and the incorporation of practice changes (Olson & Oudshoorn, 2020). For aspects such as caring for WWE undergoing a gender transition or child safety, knowledge is very limited. Therefore, it is challenging to evaluate effectiveness of knowledge translation for these elements of WWE care.

Menstruation

This incidence of catamenial epilepsy observed in this study is consistent with the rates of catamenial epilepsy seen in previous studies. In the study by Kumar et al. (2020), catamenial epilepsy was observed in 37.9% of patients. Herzog et al. (1997) found that when they defined catamenial epilepsy as a twofold increase in seizures at a specific point of the menstrual cycle,

34.7% of women met the criteria for catamenial epilepsy. Kim et al. reported that 46.8% of the patients in their study experienced a catamenial pattern to their seizures. In this study, for the sake of simplicity in the survey, the participants were asked if their menstrual cycle affected their seizure frequency. Of the 50 WWE who menstruate, 49% reported that their seizure frequency is affected by their menstrual cycle.

A significant portion of the WWE who reported that their seizures are affected by their menstrual cycle, 83.3% (n=24), discussed this possible catamenial seizure pattern with a physician. Previous research has not investigated the counselling that WWE received on catamenial epilepsy, making it difficult to compare these finding. However, 83.3% is a good sign that the WWE in this study received the recommended care in this aspect of care. Although 75% (n=24) of these participants did not have any changes made to their treatment, this is not indicative of a care deficit. As discussed previously, potential treatments for catamenial epilepsy include add-on progesterone hormonal therapy, an additional ASM to be taken at the point of or in anticipation of increased seizure frequency, and a temporary increase in the dose of the existing ASM regimen in anticipation of the increased seizure activity (Bui, 2022; Lukić, 2018). However, a standardized, approved treatment for catamenial epilepsy is not currently available (Bui, 2022). This is because of the heterogeneity of WWE and the lack of research on the potential treatments (Lukić, 2018; Bui, 2022). Also, for the ASM regimen to be effective, the woman with epilepsy needs to have a predictable cycle, but WWE have a greater incidence of irregular periods than women without epilepsy (Bui, 2022; Lukić, 2018; Noe, 2007). In this survey, the participants were not asked about the characteristics that could indicate that a treatment change would be appropriate or if a physician discussed treatments with them.

Therefore, a conclusion on how this reflects on the quality of care that the participants received cannot be made at this juncture.

Fertility and Family Planning

Contraception counselling for WWE is important because of the rate of unplanned pregnancies and the teratogenic effects of ASMs (Crawford et al. 1999; Barnard & French, 2019; Bui, 2022). In this study, 61.5% (n=78) of participants did not use contraception. Further analysis of the participants who were not using contraception showed that 35.4% (n=48) did not plan on getting pregnant. This 35.4% did not include the participants experiencing pre-menopause or menopause. Considering that for WWE roughly 50% of pregnancies are unplanned (Bui, 2022), the number of participants not using contraception and having no intention of getting pregnant is a cause for concern.

It is promising, however, that of the participants using contraception, the most used contraceptive method is the IUD (i.e., 14 of 30 participants). The responses from the patient questionnaire in the study by Kampman et al. (2005) showed that of the women who needed contraception, 25 of 70 used hormonal contraceptives and 20 of 70 women used IUDs. Herzog et al. (2016) analyzed information from 796 WWE in the Epilepsy Birth Control Registry and found that 46.6% used systemic hormonal contraception and 17% used IUDs. Considering that Kampman et al. (2005) and Herzog et al. (2016) analyzed data for a significantly larger number of participants than in this study, it is still possible that the results in this study indicate that over time there has been a shift in the type of contraception recommended to WWE.

Of the six participants who use hormonal pills, 66.7% discussed the interaction between the hormonal pills and their ASMs. In the study by Kampman et al. (2005), 71% of the 56 women who used enzyme-inducing ASMs were aware of the interaction between the enzyme-

inducing ASMs and oral contraceptives. Kampman et al. (2005) also found that three of the seven women using both an enzyme-inducing ASM and an oral contraceptive were not aware of the interaction between the two medication types. Of the six participants in this study who use hormonal pills, 5 answered the question about the ASMs they currently take and from whom 60% also take enzyme-inducing ASMs. It is also worrying that of those five participants, 80% take lamotrigine. The appropriateness of these medications cannot be assessed because the participants were not asked about their medication history. It is possible that these are the medications that help the participants achieve the best seizure control possible, especially since four out of the five participants were on ASM polytherapy.

Folic acid use by all WWE of childbearing potential, regardless of family planning choices, is very important because of an increased risk for birth defects posed by taking ASMs and the rate of unplanned pregnancies among WWE (Bhakta et al., 2015; Bui, 2022; Sadat-Hossieny et al., 2021). In this study, 35.9% (n=78) of participants were not advised to take folic acid. Participants who received folic acid counselling were more likely to be advised to take folic acid before and during pregnancy, with 22 of 50 participants being advised to take folic acid before and during pregnancy and 15 of the 50 advised to take folic acid during pregnancy only. In the study by Johnson et al. (2018), 43.6% of women reported that they used prenatal vitamins or folic acid. It is difficult to compare the results in this study to those published by Johnson et al. (2018) because Johnson et al. (2018) did not inquire if the women received counselling but faced barriers to taking prenatal vitamins or folic acid. In this study 17 of the 50 participants who received folic acid counselling reported barriers to use, including forgetting and folic acid being too expensive. From this information it can be extrapolated that 66% of the participants used folic acid. Responses to the questionnaire used by Bell et al. (2002) showed that 38% of women

were advised to take folic acid before pregnancy and early in pregnancy. Because Bell et al. (2002) did not separate the women who received advice to use folic acid before pregnancy from those advised to use folic acid during pregnancy, it is difficult to compare the results of the two studies. In their study Kampman et al. (2005) found that 77% of women knew that all women with childbearing potential should take folic acid every day.

There is no agreed upon dose of folic acid that physicians to recommend that patients take (Asadi-Pooya, 2015; Bui, 2022). Traditionally 0.4 mg a day is the recommended dose for all women (Asadi-Pooya, 2015; Bui, 2022). However, for WWE there is an increased risk of birth defects posed by ASM use, a risk of decreased serum folate level related to taking ASMs, and pregnancy complications due to low serum folate levels (Asadi-Pooya, 2015; Bui, 2022). However, WWE could be advised to take up to 5 mg of folic acid a day (Asadi-Pooya, 2015). But there have been concerns about the safety of high doses of folic acid. Most recently a study by Vergim et al. (2022) found the potential association between the risk of developing childhood cancer associated and high doses folic acid. In this study the most recommended doses of folic acid were 1 mg and 5 mg. These results may indicate that physicians still have the opinion that the standard 0.4 mg of folic acid is not sufficient to mitigate the risks that WWE face and that among physicians, there is a lack of consensus for the optimal dose of folic acid for WWE.

Pregnancy

The percentage of participants in this study who reported having unplanned pregnancies, 51.4% (n=38), is consistent with the rate of unplanned pregnancies observed among WWE in previous studies. Divalproex/valproic acid was taken by 3 of the 22 of the participants during pregnancy. Being prescribed divalproex during pregnancy may not be a sign of inappropriate care. For some WWE this medication is necessary to achieve seizure control. Harris et al. (2019)

found that women taking valproic acid had trialed more ASMs than women not taking valproic acid. They also found that the reason women taking valproic acid failed previously used ASMs was a lack of seizure control, whereas the reason women not taking valproic acid failed previously used ASMs was due to side effects (Harris et al., 2020). The participants in this study were asked about ASM changes in relation to their pregnancies, but they were not asked about the specific medication. Therefore, it is difficult to compare the results in both studies. Of the three participants in this study who took divalproex/valproic acid during their pregnancies, one discussed the potential effects of medication on a child's thinking ability only, one participant discussed the potential effects on a child's learning ability only, and one participant received no counselling. In their study, Harris et al. (2020) observed that 64% of women were able to state a specific risk that valproic acid posed to children. Although only three participants in this study used divalproex/valproic acid during pregnancy, the statistics are comparable. Two of three participants recalled being told about the risks to learning and thinking ability, which equals 66.7%.

Twenty-five percent (n=32) of the participants who had been pregnant were diagnosed with PPD or PPA. This is somewhat similar to the incidence of PPD and PPA observed in previous studies. Bjørk et al. (2015) observed that 26.7% and 22.4% of the women in their study were diagnosed with PPD and PPA respectively. The challenge in comparing the Bjørk et al. (2015) study to the present one is the significantly larger sample size and the separation of the PPD and PPA diagnoses. In this study participants were able to select both diagnoses if appropriate. Galanti et al. (2009) had a smaller sample size, 56 women, and assessed for PPD only. They found that 25% of women had a Beck Depression Inventory score that was indicative of PPD (Galanti et al., 2009). Turner et al. (2019) also had a smaller sample size of 35 WWE and

also assessed for PPD only. They found that 29% of WWE received a score indicative of PPD when screened (Turner et al., 2019).

In the study by Turner et al. (2019) none of the WWE had a previous diagnosis of depression. Galanti et al. (2009) showed that in both the WWE group and the control group, a prior diagnosis of major depressive disorder increased the likelihood of a PDD diagnosis. Similarly, Bjørk et al. (2015) observed that a previous diagnosis of depression or anxiety elevated the risk of a PPD or PPA diagnosis among WWE. It is, therefore, worrying that in the present study, a previous mental health disorder did not increase the likelihood that respondents recalled being screened for PPD and PPA. A low screening rate naturally leads to a low rate of diagnosis and assessment of treatment needs. Although the incidence of PPD and PPA in this study seems on par with previous studies, because of the lack of screening, the validity of incidence must be questioned. This also brings into question the post-partum care provided to WWE.

Only 17.6% (n=34) of participants who had been pregnant received child safety counselling. Parents must have child safety measures in place during the postpartum period because seizures during this period can result in the child being seriously harmed (Crawford et al., 1999). Even if the woman with epilepsy has seizure control before and during pregnancy, seizures can occur during the post-partum period (Crawford et al., 1999). In a pilot study Fox and Betts (1999) found that WWE who were counselled on child safety were less likely to experience an accident that resulted in significant harm to their child. Fox and Betts (1999) observed that all the accidents in their study were avoidable. In this study, the participants were not asked about the incidence of accidents while caring for their children or about the measures

they took to ensure child safety. However, because of the importance of child safety, the fact that only 17.6% (n=34) of participants received counselling is grounds for concern.

Similar to women without epilepsy, breastfeeding is beneficial for both WWE and their children (Bui, 2022). Historically both healthcare providers and WWE have been cautious about breastfeeding due to concerns that the infant will be harmed by exposure to ASMs in the breastmilk (Powell, 2015; Veiby et al., 2013). As more research is emerging, breastfeeding is now encouraged as it is thought that the benefits of breastfeeding outweigh the possible harms (Bui, 2022). In this study 32.3% (n=34) of participants discussed the safety of breastfeeding with a physician. It is encouraging that despite this statistic, 52.9% (n=31) of participants were able to breastfeed their children. It is also reassuring that only 5.9% (n=34) of participants were advised to not breastfeed their child/children. Bell et al. (2002) reported that 23.6% of women recalled being counselled on breastfeeding. Bell et al. (2002) stated that they were unable to fully interpret their results because they did not ask the women about their pregnancy history. For that reason, this study is only partly comparable to the study by Bell et al. (2002). Johnson et al. (2018) found that 69.1% of WWE breastfed their child/children. Johnson et al. (2018) analyzed data from a postpartum monitoring system, so it can be surmised that all their participants had given birth. Johnson et al. (2018) did not have data on the counselling that the women received on breastfeeding. But, as with this study, it is encouraging to observe that most WWE breastfed their children.

Hormonal Therapies: Menopause and Transgender

In this study, 8% (n=13) of respondents, specifically women experiencing perimenopause or menopause were using HRT and 91% were not. It is challenging to determine if this is within the range of what is normally observed for women in Canada as data is limited. In a cross-

sectional analysis of data from a Canadian longitudinal study on aging in women, Costanian et al. (2018) observed that 9.5% of women were current users of HRT, 21.9% were past users, and 68.6% had never used HRT. Comparison of the results of the current study to those of Costanian et al. (2018) is difficult because the women were enrolled into Costanian's study between 2010 to 2013, coinciding with a rapid decline in HRT prescriptions (Costanian et al., 2018). The participant using HRT did not answer the question about discussing HRT-ASM interactions with a physician, therefore, it cannot be analyzed whether this participant received the recommended care.

For all women, menopause brings an increased risk of developing osteoporosis. At the same time, WWE have an additional likelihood of developing osteoporosis related to ASM use. For this reason, WWE experiencing perimenopause or menopause be counselled on ASM use and osteoporosis risk and be advised to adjust their lifestyle to improve bone health. It is therefore worrying that in this study, of the 12 participants experiencing perimenopause/menopause who answered the bone health questions, only one received bone health advice. That participant was the only perimenopausal/menopausal participant taking phenytoin and one of three perimenopausal/menopausal participants taking carbamazepine. None of the three perimenopausal/menopausal participants taking divalproex/valproic acid received bone health advice. There are no published studies with which to compare these results.

One participant was using hormonal therapy (HT) for the purpose of a gender transition, but they did not receive counselling about HT-ASM interactions. As this participant was taking levetiracetam, an ASM that does not interact with HT, this may not demonstrate inadequate care. There is no published research to which this result can be compared.

Bone Health

It is a reassuring result that although 10% of participants were diagnosed with a bone health condition, 62.3% received at least one recommendation to improve their bone health. In their study Kampman et al. (2005) reviewed the patient charts for documentation of patients being advised to use vitamin D and calcium and asked WWE about vitamin D and calcium use in the patient questionnaire. Fewer than 5% of charts had documentation that WWE received vitamin D and calcium counselling and the statistics from the patient questionnaire were not included in their study (Kampman et al., 2005). It has been almost twenty years since the article by Kampman et al. (2005) was published. Comparing Kampman's study to the present study, there has been significant improvement in the bone health interventions advice that WWE receive.

Although most participants received advice on how to improve their bone health, counselling about the increased risk of developing osteoporosis posed by ASMs was lacking. Approximately 22% (n=68) of participants were counselled on the added risk of developing osteoporosis due to taking ASMs. Another matter of concern for the present study is that of the participants taking carbamazepine, divalproex/valproic acid, phenobarbital, and phenytoin, the ASMs with the highest risk of developing osteoporosis, most were not advised of this risk. Kampman et al. (2005) observed similar results. Kampman et al. (2005) asked participants if they were aware that certain ASMs could put WWE at higher risk for osteoporosis, and 12% of 112 WWE responded that they were aware.

Limitations

One of the main limitations of this study is that participants were asked about the counselling they received from physicians. Although the type of physician was not specified to prevent limiting the source of information, a large portion of healthcare providers was excluded

by specifying physicians. Advice and counselling can be provided by all categories of nurses and allied health professionals. It is possible that some information was not captured because of this. For instance, the survey results indicate that most participants engaged in breastfeeding their children, even though most did not receive targeted breastfeeding counselling. It is possible that the participants were counselled by a healthcare professional other than a physician, and that is why they chose to breastfeed.

Another limitation is that participants were not asked about their seizure control status and history and their ASM trial history. Not having this information meant that some data could not be more wholly interpreted. For example, when interpreting the results on hormonal contraception and ASM use, there was no way to decipher if lamotrigine was an appropriate ASM choice without knowing the participant's seizure control and ASM trial history. The inconsistent answering of questions within sections also limits the making of more definitive conclusions about the results of this study. For example, 34 participants answered the question on breastfeeding, but 31 responded to the question on breastfeeding advice. Only two questions were mandatory in the survey, the questions on diagnosis and age. The purpose of this was to respect the right of participants to disclose the information that they are comfortable sharing.

There is also the limitation that this study is based on memory recall, particularly because the method of data collection was a self-reporting survey. There is no way to confirm that the participants in this study recalled their health teaching accurately. Memory recall is particularly important among people with epilepsy (PWE) as memory impairment is a prime complaint for PWE (Butler and Zeeman, 2008). There is a growing body of research to objectively support that PWE experience impaired memory consolidation and memory recall (Cassel et al., 2016; Rayner et al., 2020; Steimel et al, 2023). In future research, one possible option to test for

accurate memory recall is to use a method similar to Kampman et al. (2005), where participants are surveyed, and their health records are reviewed. But, as Kampman et al. (2005) state, this approach is constrained by the information that the healthcare professional documents. However, the approach should be tried as it gives a more holistic image of patient care and provides the opportunity to simultaneously assess efficacy of knowledge translation for the healthcare professionals and the patient.

The use of convenience sampling may impede the ability to generalize the results of this study to the broader population of WWE. Furthermore, convenience sampling from the EMU means that many of the participants in this study were diagnosed with drug-resistant epilepsy (DRE). Approximately 33% of the population of people with epilepsy are diagnosed with DRE (Couper et al. 2024). Thus, this study sample may be skewed towards individuals with more severe or treatment-resistant epilepsy, which may not accurately represent the experiences of WWE with well-controlled epilepsy. This limitation emphasizes the need for caution when interpreting and applying the study's findings to the broader population of WWE, as the results may be more applicable to those with DRE or those requiring specialized care in an EMU setting.

Implications for Knowledge Translation

When investigating the effectiveness of knowledge translation, assessing the knowledge of healthcare practitioners is only part of the investigation. The care that reaches the patient from the perspective of the patient must also be assessed. Knowledge translation research must assess both to be holistic and complete. In this study, the folic acid results showed that counselling from the healthcare provider is not enough. Care will not reach WWE if they face barriers to enacting the advice. For this reason, future progression should incorporate the concept of shared decision-

making. Shared decision-making supports self-management among people with epilepsy by encouraging the healthcare provider, the person with epilepsy, and their support persons to explore the person's barriers to and strengths for self-management (Pickrell et al., 2015; Shafer, 2015). Knowledge translation theory development that incorporates shared decision making will inherently focus on both WWE and the healthcare professional that guide their care.

Implications for Education

The findings in this study can be used to identify gaps in knowledge of healthcare professionals and WWE. The results from this study and others show that while the knowledge of some issues is being translated into practice relatively well, there is still room for improvement, for both healthcare professionals, students in healthcare programs, and WWE. Healthcare professional education needs to focus on the implementation of the knowledge that is available. The education also needs to focus on shared decision making between the healthcare professional and the WWE. In this way the woman with epilepsy will be better educated on their individual health and risk factors and more likely to enact the agreed upon care plan.

Implications for Practice

The results from this study illustrate the gaps in care provided to WWE. There are aspects of WWE care that need improvement and aspects that are insufficient. To change practice, healthcare professionals must be made aware of the results through knowledge dissemination. The researchers in this study have already begun disseminating preliminary results through poster presentations at national and international epilepsy conferences. Epilepsy conferences are usually attended by healthcare professionals and epilepsy advocates. Advocates are uniquely positioned to disseminate information to the receivers of care and the people who support them. As the information from this study will be disseminated to professionals and WWE, the hope is

that professionals will be motivated to educate themselves more about care for WWE and WWE will be empowered to discuss their health needs with their care providers.

Epilepsy care is most effective when provided using a multidisciplinary approach. Nurses can improve the care of WWE by advocating for the development of pathways that direct the care of WWE. For example, a nurse who works in an antenatal clinic can advocate for a care pathway that starts with the nurse screening for PPD and PPA. WWE who display the signs of PPA and PPD would then be directed to a psychologist for further assessment and a social worker for community support. Nurses can also advocate for care pathways to include nurse-led health teaching for WWE. For example, in an epilepsy clinic, nurses can provide health teaching on contraception and folic acid to WWE with child-bearing potential. The expanded scope of practice of advanced practice nurses also provides the opportunity for nurses to improve the care of WWE. For example, an advanced practice nurse can assess WWE for increased risk of compromised bone health and then order bone density scans for WWE identified to be at increased risk.

Implications for Further Research

The results from this study reveal the areas of WWE care that lack research and dissemination of existing expert advice. For example, the WWE who were experiencing perimenopause/menopause did not receive bone health advice despite some of them taking ASMs with known osteoporosis risks, which represents a gap in care. This is a reflection that the amount of research available on menopause and bone health in WWE is minimal. It is also a sign that the existing expert opinions are not being disseminated to healthcare professionals. Future research should focus in-depth focus on the health issues related to each stage of WWE's lifespan. As the knowledge is produced, researchers should then begin to focus on investigating

the effectiveness of the knowledge translation. Evaluation of the effectiveness of knowledge translation must include evaluating the knowledge and barriers to enacting knowledge for both WWE and healthcare professionals.

Future research should be conducted with a health equity lens. The diagnosis of epilepsy brings inherent psychosocial challenges related to the social determinants of health, such as including reduced employment rates, low socioeconomic status, decreased income, and lower level of education achieved (Szaflarski, 2014; Josephson & Jetté, 2017; Josephson et al., 2017; Thomas & Nair, 2011). As with other stigmatized health conditions, a person with epilepsy can experience the compounding of health disparities leading to further barriers to accessing care and decreasing the person's motivation to enact health teaching (Szaflarski, 2014). Developing research projects with the goal of analyzing health disparities is one way to obtain a realistic picture of healthcare delivery (Szaflarski, 2014). Analyzing the demographic results from this study for health disparities is beyond the scope of this thesis, however, they were collected for the purpose of completing this analysis in the future.

Conclusion

The results of this study show the gaps in care for WWE for sex-specific health issues. In some areas, the gaps in care observed reflect the gaps in knowledge translation. In some instances, the knowledge is available but seemingly not translated into practice, such as use of contraceptives regardless of family planning intention and folic acid use. In other areas, knowledge is not translated into practice because there is very little or no knowledge available, such as post-partum mental health screening, counselling on childcare safety, and bone health counselling during perimenopause and menopause. Future efforts should focus on both knowledge generation and knowledge translation. Knowledge translation initiatives should

target healthcare professionals, healthcare professional students, and WWE and their families and caregivers. When the effectiveness of knowledge translation is being investigated, memory recall impairment and health disparities should be incorporated into the investigation to guide the development of more successful knowledge translation strategies.

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Appendix A

Literature Review Search Strategy

In order to gain a greater understanding of the concepts and variables presented in this present study, a search of the literature was conducted in the following databases: the Cumulative Index of Nursing and Allied Health Literature (CINAHL), PubMed, and Web of Science.

The following key words and terms were used as search terms in various combinations: “epilepsy”, “seizure”, “women”, “menstruate”, “antiseizure medication”, “medication”, “menses”, “catamenial”, “antiseizure”, “treatment”, “hormone”, “hormonal”, “hormone therapy”, “progesterone”, “estrogen”, “folic acid”, “folate”, “contraception”, “contraceptive”, “fertility”. “infertility”, “family planning”, “intrauterine device”, “birth control”, “barrier method”, “pregnant”, “pregnancy”, “child development”, “maternal complications”, “fetal complications”, “mental health”, “postpartum”, “depression”, “anxiety”, “child safety”, “breastfeed”, “breastfeeding”, “menopause”, “perimenopause”, “hormone replacement therapy”, “transgender”, “gender transition”, “bone health”, “osteoporosis”, osteopenia”, “fragile bones”, “Vitamin D”, “calcium”, “smoking”, “exercise”, and “physical activity”.

Boolean operators such as “AND” and truncation symbols such as an asterisk “*” were also used in conjunction with the search terms (Polit & Beck, 2021).

The articles from the search results that were relevant to this study were reviewed to identify references and cited articles that were also relevant. Additionally, an ancestry approach was utilized. This involved tracing the citations from the relevant articles to discover earlier

references that informed the current study and subsequent articles that cited these sources to ensure a comprehensive understanding of the topic.

Appendix B

Ethical Approval

Western Research

Date: 26 October 2022

To: Assistant Professor Ana Suller Marti

Project ID: 121511

Review Reference: 2022-121511-72436

Study Title: Women with Epilepsy Across the Lifespan

Application Type: HSREB Initial Application

Review Type: Delegated

Full Board Reporting Date: 08/Nov/2022

Date Approval Issued: 26/Oct/2022 12:01

REB Approval Expiry Date: 26/Oct/2024

Dear Assistant Professor Ana Suller Marti

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above mentioned study as described in the WREM application form, as of the HSREB Initial Approval Date noted above. This research study is to be conducted by the investigator noted above. **All other required institutional approvals and mandated training must also be obtained prior to the conduct of the study**.

Documents Approved:

Document Name	Document Type	Document Date
WomenWithEpilepsyAcrosstheLifespan_Poster	Recruitment Materials	24/Aug/2022
Final Ethics Protocol 2	Protocol	05/Oct/2022
WWE Email Script	Recruitment Materials	11/Oct/2022
WWE LOI print out	Written Consent/Assent	26/Oct/2022
Menstruation_WomenWithEpilepsy-2	Paper Survey	25/Aug/2022
FertilityAndFamilyPlanning_Wom	Paper Survey	25/Aug/2022
Pregnancy_WomenWithEpilepsyAcr-2	Paper Survey	25/Aug/2022
HormonesAndMenopause_WomenWith-2	Paper Survey	25/Aug/2022
BoneHealth_WomenWithEpilepsyAc	Paper Survey	25/Aug/2022
DemographicsAndMedications_Wom-2	Paper Survey	01/Oct/2022
ConfirmationOfDiagnosis_WomenW-2	Paper Survey	05/Oct/2022
Menstruation_WomenWithEpilepsy	Online Survey	07/Aug/2022
FertilityAndFamilyPlanning_Wom-2	Online Survey	26/Oct/2022
Pregnancy_WomenWithEpilepsyAcr	Online Survey	07/Aug/2022
HormonesAndMenopause_WomenWith	Online Survey	07/Aug/2022
DemographicsAndMedications_Wom-3	Online Survey	05/Oct/2022
ConfirmationOfDiagnosis_WomenW-3	Online Survey	26/Oct/2022

No deviations from, or changes to, the protocol or WREM application should be initiated without prior written approval of an appropriate amendment from Western HSREB , except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Electronically signed by:

Karen Gopaul , Ethics Officer on behalf of Dr. Emma Duerden, HSREB Vice-Chair, 26/Oct/2022 12:01

Reason: I am approving this document

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations, See Electronic System Compliance Review)

ReDA ID: 12705 Notification: Lawson Approval Awarded

LAWSON APPROVAL

LAWSON APPROVAL NUMBER: R-22-514

PROJECT TITLE: Women with Epilepsy Across the Lifespan

PRINCIPAL INVESTIGATOR: Ana SullerMarti

LAWSON APPROVAL DATE: Wednesday, 26 October 2022

ReDA ID: 12705

Overall Study Status: Active

Please be advised the above project was reviewed by Lawson Administration and the project was approved. Your official approval document can be found in the documents section of your study in ReDA.

Appendix C

Women with Epilepsy Across the Lifespan Survey

Women with Epilepsy LOI

Please complete the survey below.

Thank you!

[Attachment: "WWE LOI print out.pdf"]

LAWSON
HEALTH RESEARCH INSTITUTE

LETTER OF INFORMATION & CONSENT

Research Project Title: Women with Epilepsy Across the Lifespan

Principal Investigator: Dr. Ana Suller Marti

In this study description, "you" always refers to the study participant. If you are someone other than the study participant, and you are helping the participant complete this survey, please remember that "you" refers to the study participant.

Introduction

You are being invited to participate in a research study and this letter of information includes detailed information about the study. Please read this description carefully so that you can decide if you want to take part in the study. Please call the study doctor about any questions that you may have about this study.

What is this survey for?

In Canada, an estimated 300,000 persons live with epilepsy, half of whom are women. In addition to the challenges of living with epilepsy, women with epilepsy (WWE) also face difficulties with fertility and family planning, contraception, teratogenicity (birth defects that result from a person taking a specific medication while pregnant), sexual function, management of care during and after pregnancy, safety while caring for children, hormonal influences on seizure frequency, and bone health. From our experience of working in the Epilepsy Monitoring Unit of the Western Epilepsy Program at University Hospital (London Health Sciences Centre) in London, Ontario, these gender-specific issues not only pose health teaching and treatment challenges, but they also affect the psychosocial functioning and the quality of life of WWE. Medical professionals and researchers have suggested particular ways of how to care for WWE. It is important to know if WWE are receiving the care that is recommended. This survey seeks to explore the experiences of WWE when accessing healthcare for gender-specific health issues.

Who should take part in this survey?

This survey is open to any person who identifies as a woman or was assigned to the female sex at birth and has been diagnosed with epilepsy and/or psychogenic non-epileptic seizures/events/attacks (PNES/E/A). The person must also be 18 years of age or older. The person must be able to read and write in English, or have a family member, friend, or caregiver who can read and write in English and assist with completion of the survey. We are looking to receive at least 500 responses.

What do I need to do?

We are asking you to fill the questionnaire. It should be pretty self-explanatory, but there are some instructions (example: “Select Yes or No”). You will be able to submit your online answers electronically. If you are filling out a paper survey, please note that you do not have to write your name or any other identifying information. When you are finished, please give the survey to a member of your healthcare team.

Voluntary Participation

Your participation in this study is voluntary and a response to each question is not mandatory. You may decide not to be in this study, or not to complete the full survey.

If you decide to complete the full survey, whether online or on paper, your responses cannot be withdrawn due to the anonymous nature of the survey. If you decide that you do not want to complete the survey, you can close the online survey at any time or choose not to hand in the paper survey. If you decide not to complete the full online survey, the information that was collected before you leave will still be used to help answer the research question.

If you are an LHSC patient, leaving the study at any time will not affect your care. You may give what you have finished to a member of your healthcare team.

What are the possible risks of participating in this study?

There are very little risks to taking part in this study. You may get a little tired reading through all the questions, so you may wish to take a break. Another potential risk would be related to a privacy breach; however, the risk is very minimal as we use a password protected hospital drive. We will always stride to keep your information confidential.

What are the possible benefits of participating in the study?

There are no known direct benefits to you associated with your participation in this research study. However, your help is valuable for better understanding the experience of women with epilepsy when they access healthcare for gender-specific health issues.

What happens next?

Once we have enough responses, we are going to analyze the data and see if there are any interesting trends that can help doctors understand the experience of women with epilepsy when accessing healthcare for gender-specific health issues. The results from the study will be published as articles in various scientific journals. As well, the results, in the form of articles published in scientific journals, may be shared on Dr. Suller Marti's lab website: https://sullermartilab.ca. We are not collecting any identifying information from you (i.e., your name, date of birth, etc.), therefore, no identifying information will be shared.

Will my answers be kept confidential?

Yes, absolutely! We are not asking for your name or other identifying details, so your responses cannot be traced to you. All electronic study data collected form REDCap (a secure electronic data collection program) will be kept on a secure, password protected server as London Health Sciences Centre. In addition, we are keeping any paper responses in our locked study office. Access to electronic and paper documentation will be restricted to research group members.

Representatives of Western University’ Health Sciences Research Ethics Board may require access to the study-related records to monitor the conduct of the research. Representatives from Lawson’s Quality Assurance and Education Program may also have access to study-related information in order to ensure the study is following the proper laws and regulations. By agreeing to participate, you permit such access to study data. Study data will be kept for 15 years as per Lawson Research Institute Policy.

I confirm that I understand the requirements of participating in this study as stated in this form and consent to participate in this survey. All questions have been answered to my satisfaction. By selecting "yes", I consent to participate in the research study. (select either "yes" or "no" to indicate your answer).	◯ Yes ◯ No

Consent Information for Participant

Who can I contact for more information?

If you would like more information about the study, you can contact:

Dr. Ana Suller Marti

[redacted]

Telephone: [redacted]

If you have any questions about your rights as a research participant or the conduct of this study, you may contact the Patient Relations Office at LHSC at [redacted].

If you are in emotional distress and need someone to talk to, please contact the Canada Suicide Prevention Service: toll- free [redacted] French and English, available 24/7 or find a local crisis support here.

Please keep the above text for your records. You will need to indicate your consent by answering the following question for the Project Team's records and for your responses to be counted.

Confirmation of Diagnosis

Please complete the survey below.

Thank you!

What is your diagnosis?

- ◯ Epilepsy only
- ◯ Epilepsy AND Psychogenic non-epileptic seizures/events/attacks
- ◯ Psychogenic non-epileptic seizures/events/attacks only
- ◯ I do not have epilepsy or Psychogenic non-epileptic seizures/events/attacks

Menstruation

Please complete the survey below.

Thank you!

Do you menstruate/have menses/have your period? If no, please explain why you do not menstruate/see your period/have menses	◯ Yes ◯ No, my ovaries were removed (Oophorectomy) ◯ No, my uterus was removed (Hysterectomy) ◯ No, I am using birth control ◯ No, I am experiencing pre-menopause or menopause ◯ No, Other medical condition (please specify)
Please specify other medical condition	_____
If yes, does your period/menses affect your seizure frequency?	◯ Yes ◯ No
Have you discussed the relationship between your period/menses/menstrual cycle and how often you have seizures with any of your doctors?	◯ Yes ◯ No
If yes, did the doctor change your treatment because of this?	☐ A new medication was added ☐ I take extra medication at the time of my period/menses/menstruation ☐ I use hormone therapy ☐ No changes were made (select all that apply)

Fertility and Family Planning

Please complete the survey below.

Thank you!

Do any of the following apply to you?	◯ I tried to get pregnant ◯ I am trying to get pregnant ◯ I plan on getting pregnant in the future ◯ I do not plan on getting pregnant ◯ None of the above apply to me
Did any of your doctors advise you to take folic acid? If yes, please select the dose that was recommended. (please select all that apply)	☐ Yes, during pregnancy ☐ Yes, before and during pregnancy ☐ 0.5 mg ☐ 1 mg ☐ 4 mg ☐ 5 mg ☐ No, I was not advised to take folic acid (select all that apply)
If your doctor recommended that you take folic acid, but you were unable to do so, please explain why.	☐ Price (too expensive) ☐ Forgetting ☐ Other reason (please specify) (select all that apply)
Please specify other reason	_____
Are you presently using any contraceptives? If yes, which ones? (please select all that apply)	☐ No, I am not presently using any contraceptives ☐ Yes, IUD (intrauterine device) ☐ Yes, hormonal therapy, pills ☐ Yes, hormonal therapy, a patch ☐ Yes, barrier methods (e.g. condoms, diaphragm) ☐ Other (please specify) (select all that apply)
Please specify other contraceptive	_____
If you are using hormonal contraception, did your doctor discuss with you the possible interactions between the hormonal contraception and your seizure medication(s)?	◯ Yes ◯ No ◯ I do not remember
Have you been diagnosed with the any of the following conditions? (please select all that apply)	☐ Irregular periods/menstrual cycle ☐ Polycystic ovary syndrome (PCOS) ☐ Decreased sexual drive/low interest in sex ☐ Hormone dysfunction (select all that apply)

Pregnancy

Please complete the survey below.

Thank you!

Have you ever been pregnant?	◯ Yes ◯ No
How many children do you have?	_____
Was your pregnancy/were your pregnancies planned?	◯ Yes ◯ No ◯ Some pregnancies were planned and some were not planned ◯ I do not want to respond/I am not sure
Did any of your doctors change your seizure medications because you planned to get pregnant? (select one)	◯ Yes, increase ◯ Yes, decrease ◯ Yes, started a new medication ◯ No changes were made ◯ I do not remember
For your unplanned pregnancy/pregnancies, did any of your doctors change your seizure medications after you told them you were pregnant (select one)	◯ Yes, increase ◯ Yes, decrease ◯ Yes, started a new medication ◯ No changes were made ◯ I do not remember

Were you diagnosed with any mental health conditions before you were pregnant? If yes, please select all that apply.	☐ I was not diagnosed with any mental health conditions before I was pregnant ☐ I do not remember ☐ Anxiety ☐ Depression ☐ Bipolar disorder ☐ Personality disorder ☐ Schizophrenia ☐ Epilepsy or seizure related psychosis ☐ Other (select all that apply)
Please specify other mental health condition	_____
Were you screened/asked questions about postpartum depression or postpartum anxiety?	◯ Yes ◯ No ◯ I do not remember
Were you diagnosed with postpartum depression (PPD) or postpartum anxiety (PPA)? If yes, did you receive any counselling or medication? (please select all that apply)	☐ No I was not diagnosed with PPD or PPA ☐ Yes I was diagnosed with PPD ☐ Yes I was diagnosed with PPA ☐ I received counselling ☐ I was prescribed medication ☐ I was diagnosed but did not receive counselling or medication (select all that apply)
Did any of you doctors discuss child safety with you? [how to keep your child safe in case you have a seizure while caring for them (e.g. feeding or bathing)]	◯ Yes ◯ No
Did you breastfeed you child/any of your children? If no, why weren't you able to breastfeed?	◯ Yes, I was able to breastfeed my child/children ◯ No, I was concerned about my seizure medication coming out in my breastmilk ◯ No, Breastfeeding was not recommended ◯ No, It was not possible for me to breastfeed (please specify why)
Please specify why you were not able to breastfeed	_____
Did any of your doctors discuss with you the safety of using seizure medications while breastfeeding?	◯ Yes ◯ No ◯ I do not remember

Were you taking seizure medications during your pregnancy/pregnancies? If yes, please select all that apply.	☐ I did not take seizure medication during my pregnancy/pregnancies ☐ I do not remember ☐ I took seizure medication during my pregnancy/pregnancies (select from the list below all that apply) ☐ Acetazolamide/Diamox ☐ Brivaracetam/Brivlera ☐ Carbamazepine/Tegretol ☐ Clobazam/Frisium ☐ Clonazepam/Klonopin/Rivotril ☐ Diazepam/Valium/Diastat ☐ Divalproex/Depakote/Epival/Valproic Acid ☐ Eslicarbazepine/Aptiom ☐ Ethosuximide/Zarontin ☐ Felbamate/Felbatol ☐ Gabapentin/Neurontin ☐ Lacosamide/Vimpat ☐ Lamotrigine/Lamictal ☐ Levetiracetam/Keppra ☐ Lorazepam/Ativan ☐ Midazolam/Versed ☐ Oxcarbazepine/Trileptal ☐ Perampanel/Fycompa ☐ Phenobarbital ☐ Phenytoin/Dilantin ☐ Pregabalin/Lyrica ☐ Primidone/Mysoline/Sertan ☐ Rufinamide/Benzal ☐ Tiagabine/Gabitril ☐ Topiramate/Topamax ☐ Vigabatrin/Sabril ☐ Zonisamide/Zonegran (select all that apply)
Did any of your doctors discuss the effect that your seizure medications could have on your child's/children's development during pregnancy or on their ability to learn or think during their early years of life? If yes, please select all that apply.	☐ This information was not discussed with me ☐ I do not remember ☐ Yes - only thinking ability was discussed ☐ Yes - only learning ability was discussed ☐ Yes- thinking and learning abilities were discussed (select all that apply)
For your pregnancy/pregnancies, did you experience any complications during pregnancy or while giving birth? If yes, please select all that apply.	☐ High blood pressure or pre-eclampsia or eclampsia ☐ Seizures during pregnancy ☐ Seizures while giving birth ☐ Long hospital stay after delivery ☐ Early/premature birth ☐ Stillbirth or miscarriage ☐ Cesarean section (C-section) ☐ Bleeding during pregnancy ☐ Infection ☐ Induced labour ☐ Baby/fetal distress ☐ Other (please specify) ☐ I did not experience any complications during pregnancy or while giving birth (select all that apply)
Please specify other pregnancy complications	_____

Hormones and Menopause

Please complete the survey below.

Thank you!

Are you going through or have you gone through menopause? If yes, are you using or did you use hormone replacement therapy (HRT)?	◯ No ◯ Yes, but I did not use HRT ◯ Yes, and I am using/I did use HRT
Did the average number of seizures change because of menopause?	◯ No ◯ Yes, increase in seizures ◯ Yes, decrease in seizures
Are you going through or have you gone through a gender transition that used hormone therapy?	◯ Yes ◯ No
Did any of your doctors discuss the interaction between hormone replacement or hormone therapy therapy and your seizure medication? If yes, did any of your doctors change (increase, decrease, or start a new medication) your seizure medications because of the hormone replacement therapy (select one)	◯ Nothing was discussed ◯ It was discussed, but no changes were made ◯ Yes and my medication(s) were increased ◯ Yes and my medication(s) were decreased ◯ Yes and I started a new medication

Bone Health

Please complete the survey below.

Thank you!

Have you been diagnosed with any of the following?	◯ Osteoporosis ◯ Osteopenia ◯ Fragile bones ◯ No, I have not been diagnosed with any of these
Did any of your doctors ever suggest that you do any of the following to keep your bones healthy? (select all that apply)	☐ Take vitamin D supplements ☐ Take calcium supplements ☐ Take other medications (please specify) ☐ Increase my calcium intake through my diet (for example drink more milk) ☐ Stop smoking ☐ Start exercising or be more physically active ☐ Other (please specify) ☐ Nothing was suggested (select all that apply)
Please specify other medications and/or actions for bone health	_____
Did any of your doctors discuss with you the risk of developing osteoporosis because of the seizure medications that you take?	◯ Yes ◯ No

Demographics and Medications

Please complete the survey below.

Thank you!

How old are you?	_____
What type of seizures do you have? (select all that apply)	☐ Focal seizures/simple partial/complex partial ☐ Generalized tonic-clonic/Grand mal ☐ Atonic/drop attacks ☐ Absence/petit mal ☐ Myoclonic jerks ☐ Psychogenic non-epileptic seizures/events/attacks ☐ Other (please specify) (select all that apply)
Please specify other seizure type	_____
How old were you when you were diagnosed with epilepsy?	_____
Do you take anti-seizure drugs or medications	◯ Yes ◯ No
If yes, which medications do you take? (select all that apply)	☐ Acetazolamide/Diamox ☐ Brivaracetam/Brivlera ☐ Carbamazepine/Tegretol ☐ Clobazam/Frisium ☐ Clonazepam/Klonopin/Rivotril ☐ Diazepam/Valium/Diastat ☐ Divalproex/Depakote/Epival/Valproic Acid ☐ Eslicarbazepine/Aptiom ☐ Ethosuximide/Zarontin ☐ Felbamate/Felbatol ☐ Gabapentin/Neurontin ☐ Lacosamide/Vimpat ☐ Lamotrigine/Lamictal ☐ Levetiracetam/Keppra ☐ Lorazepam/Ativan ☐ Midazolam/Versed ☐ Oxcarbazepine/Trileptal ☐ Perampanel/Fycompa ☐ Phenobarbital ☐ Phenytoin/Dilantin ☐ Pregabalin/Lyrica ☐ Primidone/Mysoline/Sertan ☐ Rufinamide/Benzal ☐ Tiagabine/Gabitril ☐ Topiramate/Topamax ☐ Vigabatrin/Sabril ☐ Zonisamide/Zonegran (select all that apply)

What is your racial/ethnic background? (Please select all that apply)	☐ Black/African ☐ Chinese ☐ Filipino ☐ Indigenous ☐ Japanese ☐ Korean ☐ Latin American ☐ South Asian ☐ Southeast Asian ☐ West Asian (e.g. Iranian, Afghan, etc.) ☐ White ☐ I don't know ☐ Please specify ☐ I prefer not to say (select all that apply)
Please specify	_____
Where do you live?	◯ Urban ◯ Rural ◯ I prefer not to say
What level of education have you completed?	◯ Grade school ◯ High school ◯ College or vocational degree ◯ University degree ◯ Not applicable ◯ Other (please specify) ◯ I prefer not to say
Please specify education level	_____
Are you	◯ Working full-time ◯ Working part-time ◯ Unemployed ◯ Retired ◯ ODSP or any other government issued financial support ◯ In school ◯ Other (please specify) ◯ I prefer not to say
Please specify other employment	_____
What is your annual income?	◯ $0 to $25,000 ◯ $25,001 to $50,000 ◯ $50,001 to $99,000 ◯ $99,001 to $152,000 ◯ $152,001 to $217,000 ◯ $217,001+ ◯ I prefer not to say

What is your marital status?	◯ Single ◯ Married ◯ Common-law marriage ◯ Divorced ◯ Separated ◯ Widowed ◯ Other (please specify) ◯ I prefer not to say
Please specify other marital status	_____

Appendix D

Recruitment Poster

Curriculum Vitae

Education

- Master of Science Nursing, Western University, London, Ontario (2019-Currently enrolled)
- Bachelor of Science Nursing, Western University, London, Ontario (2011-2013)
- Bachelor of Science Nursing, University of Windsor, Windsor, Ontario (2010-2011) (Transferred to Western University)
- Bachelor of Science (Honours) With Thesis, University of Windsor, Windsor, Ontario (2005-2010)

Employment

- Clinical Navigator, Mental Health Inpatient Unit, Victoria Hospital, London Health Sciences Centre, London, Ontario (2023-2024)
- Staff Nurse, Epilepsy Monitoring Unit, University Hospital, London Health Sciences Centre, London, Ontario (2014-2024)
- Staff Nurse, Complex Continuing Care, Rehabilitation Unit, and Assess and Restore Unit, Timmins and District Hospital (2013-2014)

Publications

- Esmonde-White, C., Mclachlan, R. S., Burneo, J., Arts, J., Redhead, C., & Suller Marti, A. (2023). Nationwide study of postlegalization marijuana use among patients with epilepsy in Canada. Neurology. *Clinical practice, 13*(4), e200174–e200174. Https://doi.org/10.1212/cpj.0000000000200174
- Patel, C. R., Redhead, C., Cervi, A. L., & Zhang, H. (2012). Neural sensitivity to novel sounds in the rat's dorsal cortex of the inferior colliculus as revealed by evoked local field potentials. *Hearing research, 286*(1-2), 41-54. Doi: 10.1016/j.heares.2012.02.007