

**Heterogeneity of Symptoms, Outcomes, and Characteristics of Patients in Treatment for
Endometriosis**

BY

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THESIS

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KAO

PREFACE

This research focuses on those assigned female at birth (AFAB) though much of the literature uses “women” and “female” when discussing patients. Endometriosis affects all genders and we take efforts to use AFAB whenever possible during this dissertation.

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LIST OF ABBREVIATIONS

AFAB	Assigned Female at Birth
DE	Deep Endometriosis
EFA	Exploratory Factor Analysis
GI	Gastrointestinal
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OC	Oral Contraceptives
OMA	Ovarian Endometrioma
OR	Odds Ratio
RCTs	Randomized Controlled Trials
rAFS	Revised American Fertility Society
SES	Socioeconomic Status
SPE	Superficial Endometriosis
SPiTE	Heterogeneity of Symptoms, outcomes, and characteristics in Patients undergoing Treatment for Endometriosis Study
WERF EPHect	World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project
95% CI	95% CI Confidence Interval

SUMMARY

Endometriosis is a prevalent and chronic disease characterized by the growth of endometrial-like tissue outside the uterine cavity. These lesions can be found in various organs throughout the body, including the pelvic cavity, liver, lungs, and brain. Despite its high prevalence of approximately 10% among individuals assigned female at birth (AFAB) and its significant public health impact, endometriosis remains poorly understood and understudied. The existing classification systems and subtypes have proven inadequate in describing the disease and correlating with symptoms and patient experiences. Patients typically face a diagnostic delay of 7 to 10 years from the onset of symptoms. However, they have demonstrated exceptional knowledge about their condition and exhibit excellent recall when reporting their diagnosis, making them an ideal population for surveys.

The purpose of this dissertation was to leverage the knowledge of this population through an online survey. The survey utilized the validated World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project (WERF ePHect) survey as its foundation and assessed participants' lesion locations, symptoms, surgical history, and additional demographic information. Recruitment efforts involved utilizing social media groups on platforms such as Reddit, Instagram, and Facebook, as well as leveraging ResearchMatch and distributing flyers in the Chicago metropolitan area. In total, 1,156 responses were collected, with a completion rate of nearly 80%.

Based on the collected data, we explored the use of factor analysis as a suitable method for grouping lesion locations and investigated their associations with current endometriosis classifications and with how participants seek medical care, surgical complications, and

SUMMARY (continued)

demographic characteristics. In our first aim, we described the demographics related to each lesion location factor. Our findings revealed that the digestive-urinary factor, our first factor, was associated with more complex cases and a longer diagnostic delay. The reproductive factor, our second factor, was linked to lower obesity rates, lower educational attainment, superficial endometriosis (SPE), and negatively correlated with ovarian endometrioma (OMA). The Douglas-ligaments factor, our third factor, was positively associated with lower socioeconomic status, more surgically complex disease, and negatively associated with diagnostic delay. These findings provide potential avenues for subtyping endometriosis based on lesion location.

Furthermore, we examined the association between these lesion location factors and presenting symptoms. Our analysis revealed a positive association between the reproductive factor and pain presentation, as well as a positive association with experiencing worsened bowel symptoms or pain during intercourse. Regarding infertility presentation, a negative association was found with the reproductive factor and noncyclic pelvic pain, while positive associations were noted with the digestive-urinary factor, diagnostic delay, and number of pregnancies. While these associations diminished when restricted to participants with infertility as the sole presenting issue, this may be due to the limited number of participants reporting infertility only. The negative association between the reproductive factor and infertility presentation, if validated, presents important implications for both diagnosis and treatment plans for those with endometriosis.

Finally, we explored the association between lesion location factors and surgical complications. The digestive-urinary factor exhibited positive associations with all surgical

SUMMARY (continued)

complication analyses, including the occurrence of any complications, gastrointestinal (GI) complications, urinary complications, pain complications, complications categorized as "other," as well as the overall number of complications. In our analysis of urinary complications, we identified an interaction with the Douglas-ligaments factor and diagnostic delay. As for the other factors, the reproductive factor was marginally associated with having gastrointestinal complications, but not the other models and the Douglas-ligaments factor was only associated with urinary complications model only in participants without diagnostic delay. Given that endometriosis patients often require multiple surgeries, making them a high-risk group for surgical complications, our findings underscore the need for enhanced surveillance and surgical expertise, such as interdisciplinary surgical teams, for these patients.

The implications of this research, if fully realized, suggest the potential use of exploratory factor analysis (EFA) in predicting and planning patient treatment. This technique could aid in identifying additional lesion locations during surgery and planning for different sets of skills to prevent and minimize surgical complications. Future investigations should focus on fully characterizing all lesion locations in patients' bodies by closely collaborating with patients and surgical teams during the surgical process. Furthermore, efforts should be made to include diverse participant pools, and researchers should actively engage with the highly involved endometriosis patient community, as evidenced by their vibrant social media groups.

I INTRODUCTION AND SPECIFIC AIMS

Endometriosis is a prevalent and poorly understood chronic gynecological condition that affects approximately 10% of individuals assigned female at birth (AFAB). It is characterized by the presence of endometrial-like tissue outside the uterine cavity and is associated with debilitating symptoms, including chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria, dyschezia, and chronic fatigue. Moreover, endometriosis is a leading cause of infertility (Zondervan, Becker, and Missmer 2020), affecting 30 to 50% of individuals with the condition. The psychological, economic (Della Corte et al. 2020; Sperschneider et al. 2019; Federica Facchin et al. 2019; Armour et al. 2019), and long-term health impacts of endometriosis are significant (Kvaskoff et al. 2015; 2020). Even a modest improvement in symptoms can greatly enhance the quality of life for those affected (Armour et al. 2019; Gerlinger et al. 2010).

Currently, the etiology of endometriosis remains unclear, and effective treatment options are limited (Bulun 2009; Giudice and Kao 2004). The complexity of studying endometriosis stems from its high heterogeneity and methodological challenges. Research often focuses on individuals with surgically confirmed disease, introducing selection biases related to healthcare access. Endometrial lesions can manifest in various locations, including reproductive organs, peritoneum, and intestines, and it is hypothesized that the site of the lesion may influence disease progression and response to therapy (Porpora et al. 1999). Additionally, the prolonged time to diagnosis (8 to 10 years) hampers the use of medical records for participant identification, as vital information about symptom onset and disease course may be lost due to record retention policies (Bontempo and Mikesell 2020). These factors further complicate the study of this intricate disease.

The overarching objective of my research is to enhance our understanding of the associations among lesion location, demographics, symptoms, and treatment in order to gain insights into the heterogeneity of endometriosis. To achieve this, I have modified the validated WERF EPHeCT survey, which assesses endometriosis symptoms, severity, treatment, as well as demographic and lifestyle factors. The modified survey instrument was distributed through established social media groups of endometriosis patients, allowing for the collection of self-reported data. The primary hypothesis of this dissertation is that endometriosis subtypes, distinguished by lesion location, exhibit distinct disease courses, associations, and complications. The specific aims of my research are as follows:

1. To describe associations of personal characteristics by endometriosis lesion location.
 - a. Hypothesis: Individual characteristics differ by endometriosis lesion location including demographics, hormonal characteristics, and lifestyle factors.
 - b. Hypothesis: Current subtyping schemes and surgical staging do not align with factor scores.
2. To determine if presenting symptoms for endometriosis differ by lesion location.
 - a. Hypothesis: Presenting symptoms of infertility and pelvic pain differ by endometriosis lesion location.
3. To determine whether endometriosis occurring in different anatomical locations have different surgical outcomes.
 - a. Hypothesis: Surgical complications related to the urinary and gastrointestinal tract, infertility, and pelvic pain differ by endometriosis lesion location.

This dissertation addresses a crucial knowledge gap pertaining to the heterogeneity of endometriosis and its implications for symptoms, treatment, and outcomes. The research conducted sheds some light on the diverse nature of the disease process, thereby offering valuable insights that can potentially enhance the precision of diagnosis, treatment approaches, and comprehension of associated complications. Knowledge gained from this study has the potential to alleviate the significant morbidity and pain experienced by individuals affected by endometriosis. Moreover, the outcomes of this research may have the capacity to facilitate earlier detection, leading to a reduction in morbidity and pain. A heightened understanding of the specific lesion locations associated with endometriosis may contribute to improved treatment strategies and enhanced detection methods for this condition.

II BACKGROUND AND LITERATURE REVIEW

A. Overview

Despite its estimated prevalence of 10% among individuals assigned female at birth (AFAB), endometriosis remains an enigmatic condition with limited treatment options and a lengthy average time to diagnosis of 8 to 10 years (Bulun 2009; Giudice and Kao 2004; Ahn, Singh, and Tayade 2017). The underlying causes of this disease are still poorly understood (Koninckx et al. 2021). While surgical visualization with histological confirmation of excised lesions remains the gold standard for diagnosis, this criterion presents challenges in estimating the true prevalence of endometriosis due to the overlapping symptomatology with other gynecological conditions, unequal access to surgical diagnosis, and the exclusion of asymptomatic cases (P. Vercellini et al. 2009; K. D. Ballard et al. 2008; Shafrir et al. 2021; Fuldeore and Soliman 2017; Zhang et al. 2021; Zondervan, Cardon, and Kennedy 2002; Chapron et al. 2019). Individuals with endometriosis endure various symptoms, including pelvic pain, infertility, and significant psychological and social impacts (Bulun 2009). The range of symptoms can encompass dysmenorrhea, dyspareunia, dysuria, dyschezia, and chronic fatigue, while endometriosis has also been linked to several other diseases (Kvaskoff et al. 2015). Notably, Simoens et al. estimated that the economic burden of endometriosis amounted to \$22 billion in 2002, encompassing both direct costs and productivity losses (Simoens, Hummelshoj, and D'Hooghe 2007).

B. Sex and Gender

Existing research has predominantly overlooked or neglected to collect data on the gender identity of participants, often relying on broad categorizations such as "female" or

"women" without explicit collection of additional data on gender identity. Consequently, determining the gender identity of participants in most studies has become a challenging task. Given this ambiguity, this dissertation will primarily utilize the designation "assigned female at birth" or AFAB. Notably, a study involving 35 transmasculine adolescents with dysmenorrhea revealed that all seven individuals who underwent laparoscopy were diagnosed with endometriosis (Shim, Laufer, and Grimstad 2020). Similarly, another study involving 67 transmasculine individuals undergoing hysterectomy for gender affirmation indicated that 50.7% of participants reported pelvic pain, with 26.9% receiving an endometriosis diagnosis (Ferrando, Chapman, and Pollard 2021). Research on endometriosis in transmasculine individuals remains scarce. Furthermore, rare case reports (approximately 20 documented cases) have documented instances of endometriosis in individuals assigned male at birth (Jabr and Mani 2014; Martin and Hauck 1985; Al-Obaidy and Idrees 2019).

C. Risk Factors

The etiology of endometriosis remains inadequately understood, with several established risk factors identified thus far. Reproductive factors, such as early age at menarche and short menstrual cycle length, as well as lean body size, have been recognized as potential risk factors (P. Viganò et al. 2004; Shafir et al. 2018; Missmer et al. 2004; Matalliotakis et al. 2008; Sangi-Haghpeykar and Poindexter 1995). Additionally, other factors including physical activity, parity, oral contraception use, moderate alcohol intake, dioxin exposure, and family history have been suggested as potential contributors to endometriosis risk. However, findings related to irregular menstrual cycles, smoking, and lactation have been inconsistent across

studies, and potentially confounded by access to care or other biases (Shafrir et al. 2018; Sangi-Haghpeykar and Poindexter 1995; Parazzini et al. 1995).

Moreover, there exists a notable research gap concerning the exploration of circulating hormonal levels during crucial periods such as the prenatal phase, adolescence, and adulthood, including investigations into in utero exposures encompassing nutrition and environmental factors. These areas of research remain poorly understood and warrant further investigation to elucidate their potential associations with endometriosis (Shafrir et al. 2018; Vannuccini et al. 2016; Wolff et al. 2013; Benagiano and Brosens 2014).

Furthermore, endometriosis has been inconsistently linked to various other diseases, including cardiovascular disease; ovarian, breast, and thyroid cancer; allergies; and various autoimmune conditions (Kvaskoff et al. 2020; 2015). Additionally, endometriosis has been associated with various mental health diagnoses, such as anxiety and depression. However, unraveling the complexity of this relationship is challenging, as these conditions may arise as consequences of endometriosis, pain, inflammation, experiences with the medical community, or other factors. It is plausible that a feedback loop involving multiple factors contributes to this intricate association (K. Ballard, Lowton, and Wright 2006; Pope et al. 2015; Vitale et al. 2016; Cavaggioni et al. 2014).

Historically, endometriosis was often associated with stereotypes and biases that portrayed it as a condition primarily affecting "career women" with a drive for success, emphasizing their appearance and figure (Buttram 1979). This perspective suggested that the disease predominantly impacted those who delayed marriage and childbirth, particularly white women in higher income brackets, as stated by a gynecologist in 1956 (Olga Bougie, Healey,

and Singh 2019; Carpan 2003; Darrow et al. 1994; Meigs 1941; Hayden 1956). Such beliefs, coupled with the inherent challenges of studying a surgically diagnosed disease, have resulted in a scarcity of research on endometriosis among individuals of color. Notably, in 1976, Chatman highlighted the potential negative consequences of accepting such disparities as common knowledge, suggesting that this could lead to Black individuals receiving inadequate care and enduring unnecessary, prolonged, and unrelieved discomfort. Chatman advocated for a more inclusive approach, recommending the liberal use of diagnostic laparoscopy to rule out endometriosis, regardless of race (Chatman 1976). A systematic review conducted by Bougie et al. in 2019, encompassing 18 studies, found significant racial and ethnic influences on endometriosis diagnosis. The review revealed that Black individuals had a reduced odds ratio (OR) of diagnosis (0.49) compared to their white counterparts. Conversely, Asian individuals exhibited a higher likelihood of diagnosis when examining (OR 1.63, 95% CI 1.03-2.58), although the body of high-quality research on this specific topic is limited (O. Bougie et al. 2019). While several studies have indicated a potential disparity in endometriosis prevalence among Black individuals AFAB within the broader endometriosis literature, evidence suggests that no significant difference exists among those presenting with infertility (O. Bougie et al. 2019).

D. Comorbidities

The association between endometriosis and comorbidities has yielded conflicting results across studies, contributing to the complexity of understanding the disease. Among the comorbidities, the strongest evidence supports the link between endometriosis and ovarian cancer, infertility, and various gynecological conditions (Kvaskoff et al. 2020; 2015). However, the evidence remains inconclusive and inconsistent for autoimmune diseases, malignancies,

and mental health conditions. Studies examining the relationship between endometriosis and comorbidities often encounter methodological challenges, such as limited information on the specific type and extent of endometriosis or sub-classifications of the comorbid conditions. Endometriosis has been associated with a range of other diseases, including cardiovascular disease, ovarian, breast, and thyroid cancers, allergies, irritable bowel syndrome, migraines, and various autoimmune conditions (Kvaskoff et al. 2020; 2015). However, the evidence for associations with endometrial cancer and cutaneous melanoma remains conflicting and uncertain (Kvaskoff et al. 2020). It is important to note that many of these associations may be influenced by shared risk factors or exposures (Kvaskoff et al. 2015; Teng et al. 2016). While there is a possibility of spurious associations, it is also plausible that the heightened inflammatory responses observed in both endometriosis and certain diseases may contribute to these associations (Kvaskoff et al. 2015). However, it is crucial to acknowledge that research on these comorbid conditions in relation to endometriosis is still in its preliminary stages and requires further exploration and investigation.

E. Lesion Locations

Endometriosis poses significant challenges in terms of diagnosis and research due to its intricate and diverse nature, with varied presentations of lesions throughout the body leading to a wide range of symptoms and varying levels of severity. Previous studies have often categorized different presentations of the disease under a broad umbrella, overlooking the potential heterogeneity in risk factors and manifestations across sub-populations. Currently, there is no universally accepted classification system, and ongoing research is dedicated to addressing this issue, particularly considering the limited correlation between existing

classification scales and patient symptoms (Lee, Koo, and Lee 2020). Furthermore, there is often a lack of correlation between the extent of the disease and the symptoms experienced by individuals. Some may exhibit extensive disease based on surgical findings but report minimal or no symptoms, while others may display severe symptoms despite the presence of early-stage or mild disease (Zondervan, Becker, and Missmer 2020). The delayed time to diagnosis further complicates the study of endometriosis, as important information regarding the onset of symptoms and the disease's progression may be lost due to medical record retention requirements being exceeded (Bontempo and Mikesell 2020).

F. Classification Systems

Endometriosis lesions exhibit a wide distribution throughout the body, with the pelvic region being the most common site of occurrence. However, due to the reliance on surgical diagnosis, determining the prevalence of lesions at each location remains challenging. Within the pelvic region, the ovaries, uterine ligaments, pouch of Douglas, and fallopian tubes are frequently affected (Alimi et al. n.d.; Klemmt and Starzinski-Powitz 2018; Macer and Taylor 2012). Lesions can also be found in extrapelvic locations, including the gastrointestinal tract, lungs, abdomen, and pericardium (Alimi et al. n.d.; Machairiotis et al. 2013). A comprehensive analysis of lesion location is crucial for addressing the current gap in disease subtyping.

Presently, endometriosis classification relies on various criteria, such as lesion location, pelvic vs. extrapelvic presentation, surgical stages (I-IV), and subtypes like superficial peritoneal endometriosis (SPE), endometrioma (OMA), or deep endometriosis (DE). Different groups and professional organizations have proposed their own classification schemes, with some suggesting that SPE, OMA, and DE represent distinct diseases rather than a progressive

continuum (Nisolle and Donnez 1997; Koninckx et al. 2011). While these classifications partially consider lesion location and severity, with SPE generally regarded as the least severe and DE as the most severe form, significant gaps remain regarding disease progression and identification. Furthermore, the current classification system does not account for the coexistence of multiple subtypes (Piriyev, Schiermeier, and Römer 2021).

Surgical staging is another approach to subtype endometriosis, ranging from stage I (minimal) to stage IV (severe) based on the number of implants and the extent of infiltration, including the color and depth of lesions. The revised American Society for Reproductive Medicine (rASRM) classification, originally proposed in 1985 and revised in 1996, is widely used due to its simplicity in explaining disease extent to patients. However, there are challenges with discrepancies between visual staging and histological findings, as well as poor reproducibility of rASRM scoring. Studies have demonstrated disagreements in staging using rASRM checklist algorithms compared to empirical assessment, and the rASRM classification fails to adequately consider DE in all potential locations (Lee, Koo, and Lee 2020; Paolo Vercellini et al. 2006).

To complement rASRM, the ENZIAN classification system was developed in 2005, providing a means to classify disease extent observed during surgery. However, its usage remains limited primarily to German-speaking countries, and patient comprehension can be a challenge (Lee, Koo, and Lee 2020). Other proposed scales include the Endometriosis Fertility Index predicts pregnancy rates in surgically diagnosed patients but has limited applicability outside of infertility cases. The American Association of Gynecological Laparoscopists has also introduced a classification system assigning scores (0-10) based on lesion site importance and

outcomes related to pain, infertility, and surgical procedure difficulty. Although promising, this system requires further validation (Lee, Koo, and Lee 2020).

G. Lesion Location and Pain

Numerous studies have investigated the association between lesion location and pain symptoms in endometriosis, yielding mixed results. For instance, a study by Hsu et al. explored the relationship between pelvic pain location and endometriosis lesion location, revealing an association between bladder peritoneal lesions and dysuria, but no significant correlation with other areas of pelvic pain (Hsu et al. 2011). Another study focusing on DE lesion locations and pelvic pain symptoms found an association between the characteristics of pelvic pain and the location of DE lesions (Fauconnier et al. 2002). Additionally, a cross-sectional study discovered that DE lesions were linked to the use of oral contraceptives (OCs) (Moawad and Caplin 2013). Although this association is unlikely to be causal, long-term oral contraceptives (OC) use and the relief they provide may serve as markers for DE in endometriosis patients. Moreover, OC use may be associated with a reduced need for bowel resection (Moawad and Caplin 2013; Chapron et al. 2011).

Chronic pain can lead to the sensitization of the central nervous system, potentially resulting in generalized hypersensitivity in individuals with endometriosis. The persistence or recurrence of pain in affected areas following lesion removal raises questions about the mechanisms through which these lesions generate pain, including speculation on the growth of nerve fibers into implants (Berkley, Rapkin, and Papka 2005). However, some studies indicate at least partial symptom relief following lesion excision (Hsu et al. 2011).

In terms of specific symptoms associated with lesion location, a study examining 1,054 patients found a significant association between lesions in the posterior cul-de-sac and painful intercourse (P. Vercellini et al. 2007). However, this study excluded patients who had undergone medical treatment for endometriosis, with limited exceptions within the six months preceding the study, which may limit the generalizability of the results. Furthermore, it did not consider symptoms other than pelvic pain or the social context of the patients (P. Vercellini et al. 2007). Similar limitations regarding scope and lack of social context have been observed in other studies focusing on pelvic pain and various subtypes, potentially leading to mixed findings (Porpora et al. 1999; P. Vercellini et al. 2007; Schliep et al. 2015). Another prospective cohort study of 116 patients found that those with rectal lesions were more likely to experience gastrointestinal issues such as constipation, painful defecation, and appetite disorders (Roman et al. 2012).

To explore the impact of endometriosis subtypes on disease outcomes, some studies have examined recurrence rates and surgical outcomes. However, the available randomized controlled trials (RCTs) on this topic primarily investigated surgical outcomes and were hindered by small sample sizes, short follow-up periods, and limited subtyping or detailed disease descriptions (P. Vercellini et al. 2009). Nirgianakis et al. demonstrated that individuals with SPR or OMA who experienced recurrence were more likely to present with the same subtype initially but often progressed to the more severe form of the disease, DE (Nirgianakis et al. 2020). The visualization of OMA lesions through noninvasive imaging methods, such as MRI, has been replicated in other studies (Buck Louis et al. 2011; Eskenazi et al. 2001). Disease

relapse rates varied widely across different stages, ranging from 3% to 23% among 537 infertile patients (Paolo Vercellini et al. 2006).

The effectiveness of surgical intervention in endometriosis has been examined in several studies. Abbott et al. compared the outcomes of full excision surgery versus diagnostic procedures with a repeat laparoscopy after six months, and found symptom improvement and a lack of disease progression in the excision group. However, this study only explored the Revised American Fertility Society (rAFS) staging of disease and did not consider further subtyping (Abbott et al. 2004). Evidence suggests that the benefits of surgery may diminish over time, with re-operation rates as high as 50% (P. Vercellini et al. 2009). Studies specifically focusing on rectovaginal endometriosis have shown a 70% improvement in symptoms following surgery, but approximately 50% of patients required analgesics or hormonal treatment after one year (Moawad and Caplin 2013). Postoperative complications can include bleeding, fistulas, strictures, and chronic constipation (Moawad and Caplin 2013). A retrospective surgical cohort study by Clark et al. in 2020 reported a major perioperative complication rate of 4.5% within 60 days of surgery, particularly among patients with advanced-stage disease and rectovaginal involvement (Clark et al. 2020). To date, no study has comprehensively examined the role of lesion location in endometriosis symptoms, including pain, leaving significant gaps in knowledge.

H. Symptoms

The manifestations of endometriosis extend beyond pelvic pain, painful intercourse, and infertility, encompassing a range of symptoms that can significantly impact patients' well-being. Fatigue, anxiety, depression, low back pain, and urinary and gastrointestinal symptoms are

commonly reported among individuals with endometriosis (Ramin-Wright et al. 2018; Laganà et al. 2017). The mental health symptoms experienced by these patients may contribute to the perception of pain, as heightened levels of anxiety and depression have been linked to increased pain severity (Laganà et al. 2017). In rare cases, affected individuals may also encounter symptoms such as chest pain, headaches, or seizures (Ichida et al. 1993; Huang et al. 2013). It is worth noting that patients presenting with pain tend to experience a longer delay in diagnosis compared to those presenting with infertility (K. Ballard, Lowton, and Wright 2006). A case-control study involving 5,540 individuals with endometriosis and 21,239 controls without the condition revealed that cases sought medical consultation more frequently and were more likely to report abdominopelvic pain, dysmenorrhea, subfertility, and a diagnosis of irritable bowel syndrome (K. D. Ballard et al. 2008). The relationship between lesion location and endometriosis symptoms has been investigated in various studies, which has been discussed further in the section dedicated to lesion location.

Infertility is a significant consequence of endometriosis, as it is a prominent factor contributing to reproductive challenges (Bulun 2009; Macer and Taylor 2012; Bulletti et al. 2010). A case-control study analyzing commercial claims data from 26,961 endometriosis cases and 107,844 controls identified associations between endometriosis and infertility/subfertility, ovarian cysts, uterine fibroids, pelvic inflammatory disorder, interstitial cystitis, ovarian cancer, and irritable bowel syndrome (Surrey et al. 2018). These associations have also been observed in other studies examining various gynecological conditions and their correlation with endometriosis (K. D. Ballard et al. 2008; P. Viganò et al. 2004; Teng et al. 2016; Uimari, Järvelä, and Ryyänänen 2011; Tai et al. 2018; Paulson and Delgado 2007; D. Viganò, Zara, and Usai 2018).

While some of these associations may be influenced by misdiagnosis (Bontempo and Mikesell 2020; Issa et al. 2016; Leone Roberti Maggiore et al. 2016), there are plausible shared biological mechanisms, including increased inflammation and genetic factors, that may contribute to these relationships (Kvaskoff et al. 2015). Ovarian cancer is often mentioned as having a strong association with endometriosis. Although the absolute risk of developing ovarian cancer remains low even in the presence of endometriosis (2.5%), the potential malignancy remains an important concern for individuals with endometriosis (Kvaskoff et al. 2020; 2015; Kok et al. 2015). Notably, significant knowledge gaps persist in the study of endometriosis lesion location and its correlation with symptoms.

I. Treatment

Treatment outcomes for endometriosis often fall short of patient expectations, necessitating subsequent surgeries or additional interventions to manage symptoms after the initial diagnosis. Surgery remains a critical therapeutic approach, given that many medical treatments, such as contraceptive or hormone therapy, can interfere with a patient's fertility aspirations, if desired, and have unacceptable side effects (P. Vercellini et al. 2009). Laparoscopy with excision surgery, involving the skilled removal of implants by a surgeon, is considered the gold standard. Laparoscopy with ablation, where lesions are burned or removed at a superficial level, carries an elevated risk of recurrence and incomplete symptom control. Hysterectomy, with or without oophorectomy, also presents the risk of disease relapse and is not suitable for individuals seeking to conceive or those unsuitable for hormone replacement therapy due to comorbidities, side effects, or contraindications (Abbott et al. 2004; Clark et al. 2020; Yeung, Shwayder, and Pasic 2009; Pundir et al. 2017). Neither ablation treatment nor

hysterectomy is considered curative. Long-term oral contraceptives are commonly employed as a primary therapy; however, they frequently fail to provide relief and are inappropriate for individuals planning to conceive or those unable to tolerate oral contraceptives. Other therapies, such as gonadotropin agonists, pelvic floor physical therapy, and analgesics, offer limited therapeutic value (“Practice Bulletin No. 114: Management of Endometriosis” 2010; Dmowski et al. 1989). Many individuals report incomplete symptom control and may require further treatment, including surgeries, even after receiving gold standard care (Zondervan, Becker, and Missmer 2020; P. Vercellini et al. 2009).

Patients often encounter challenges in accessing appropriate care. A qualitative study conducted in 2006 to examine the diagnostic delay in endometriosis identified factors such as pain symptoms being normalized by family doctors, intermittent symptom suppression through oral contraceptives, and non-specific diagnostic procedures as potential reasons for medical delays (K. Ballard, Lowton, and Wright 2006). Moreover, treatment decisions can be complicated by findings observed during surgical confirmation that may not directly correlate with the disease process but instead be influenced by the lack of adequate care or prior treatments. Additionally, the extent of the disease can impact the choice of surgical treatment (K. Ballard, Lowton, and Wright 2006). Finally, accessing a qualified surgeon can pose challenges, particularly within restricted insurance networks prevalent in the United States. To date, studies have not sufficiently explored the relationship between treatment modalities and the location of endometriosis lesions.

J. Significance

In a qualitative study conducted published in 2023, the perspectives of 1,000 participants from the ComPaRe-Endometriosis program were sought regarding improvements in their healthcare. The participants provided 2,487 ideas, which were categorized into five main themes: (1) enhancing healthcare providers' knowledge about the disease, (2) improving management of daily pain and pain attacks, (3) recognizing and addressing patient-reported symptoms, (4) standardizing diagnostic processes for early detection, and (5) fostering better communication and listening from healthcare providers (Solène Gouesbet et al. 2023; S Gouesbet et al. 2021). The present investigation aligns with the overarching goals of group 1 (knowledge acquisition about the disease), group 3 (serious consideration of patient-reported symptoms), and group 5 (improved patient-provider communication), while also touching upon group 4 (enhanced early detection).

Endometriosis is a prevalent condition associated with a considerable delay in diagnosis, often accompanied by instances of misdiagnosis and psychological distress (Della Corte et al. 2020; K. Ballard, Lowton, and Wright 2006; F. Facchin et al. 2017; Bontempo and Mikesell 2020). The prolonged delay complicates retrospective studies that rely on chart reviews, as the onset of symptoms and other relevant information related to the disease course may be lost due to medical record retention limitations (Bontempo and Mikesell 2020). Endometriosis affects approximately 6-16% of individuals AFAB in the US and up to 50% of those experiencing infertility (Bulletti et al. 2010; Fuldeore and Soliman 2017). It is recognized as a significant contributor to infertility, pelvic pain, and decreased productivity (Fuldeore and Soliman 2017; Macer and Taylor 2012; Porpora et al. 1999; Sperschneider et al. 2019; Federica Facchin et al.

2019; Armour et al. 2019). Endometrial lesions can manifest on reproductive organs, peritoneum, intestines, and other sites, and it is hypothesized that the location of lesions may influence disease progression and response to treatment (Porpora et al. 1999). Consequently, endometriosis not only poses a threat to the health of individuals but also has broader societal implications, with implications for equity and inclusion. Notably, previous endometriosis research in the US has predominantly involved white participants (Bontempo and Mikesell 2020; Olga Bougie, Healey, and Singh 2019; O. Bougie et al. 2019; HOUSTON et al. 1987). To address this disparity, the current study employed a diverse recruitment approach, including engagement with social media support groups, advocacy organizations, and flyer dissemination across UIC's West Campus.

Unlike many other chronic pain conditions where a reduction of over 30% in symptoms is considered necessary for substantial relief, evidence suggests that even a modest reduction of over 10% in pain would significantly enhance the quality of life for individuals with endometriosis (Armour et al. 2019). Therefore, even incremental improvements can be of great benefit to many patients. A better understanding of the location of endometriosis lesions has the potential to enhance diagnosis, treatment, and outcomes for those affected, leading to non-invasive diagnostic tools and more targeted therapies that shorten the time to diagnosis and appropriate treatment. Moreover, this understanding can help address the frustration reported by many patients, as there are notable disparities between patient experiences and clinical descriptions of endometriosis symptoms (Fauconnier et al. 2013). Furthermore, comprehending endometriosis subtypes and phenotypes has been identified as a high priority by the World Endometriosis Society (Johnson et al. 2017). Presently, research has not

adequately explored the connection between demographic and lifestyle factors, lesion location, treatment, and outcomes of endometriosis. A closer examination of these relationships will contribute to a more comprehensive characterization of individuals with endometriosis and foster a better understanding of the impact of each lesion location.

K. Data Source: SPiTE Survey

The study employed a primary data collection approach within the United States, focusing on analyzing the associations among lesion location, demographics, symptoms, and surgical complications, while minimizing the number of lesion locations examined. To recruit participants, a survey specifically designed for this study was launched on social media platforms and shared in various endometriosis-related groups and through collaboration with influential figures in the field. Additionally, ResearchMatch was utilized as a distribution channel for the survey.

Passive recruitment methods were employed, targeting social media groups, communities dedicated to endometriosis, and advocacy groups focused on endometriosis. Standardized and Institutional Review Board approved language was used to request permission to post or distribute the recruitment tools within these groups. Eligible participants, aged 18 years or older, residing in the US, and having a surgical diagnosis of endometriosis with knowledge of the anatomical location of their lesions, were directed to a RedCap screening instrument. Those who met the eligibility criteria and provided consent were then directed to the RedCap survey, consisting of nine sections that collected data on demographics, menstrual characteristics, infertility and pregnancy history, experiences with pain and other symptoms related to endometriosis, as well as past treatments, complications, and comorbidities. The

estimated completion time for the survey ranged from 20 to 40 minutes. The survey was available from June 2022 to December 2022. This instrument was adapted from the validated WERF EPHeC (World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonisation Project) survey, customized to focus on the areas relevant to this dissertation by removing certain questions (e.g., phenotype-related questions) or condensing others (e.g., collapsing response age ranges in detailed questions about menstrual history over the lifespan) to reduce participant burden.

Participants were not required to provide any identifying information, except for their email address if they wished to participate in a raffle for compensation or if they expressed interest in being re-contacted for future research. Participants were given the option to indicate their willingness to be contacted for follow-up in case additional research opportunities arose. The collected data were analyzed to address the three objectives of this project, utilizing logistic regression and factor analysis with covariates including age, race, hormonal history, health and care history, physical characteristics, and lifestyle factors. Data were captured in RedCap, and de-identified data were securely stored in designated locations. Subsequently, the data underwent thorough cleaning and preparation for analysis.

III FACTOR ANALYSIS IN THE CATEGORIZATION OF ENDOMETRIOSIS LESION LOCATION: THE SPITE STUDY

A. Rationale

Endometriosis is a prevalent, chronic gynecological condition characterized by the presence of endometrial-like tissue outside the uterine cavity. It affects approximately 10% of individuals assigned female at birth and is associated with a range of distressing symptoms, including chronic pelvic pain, dysmenorrhea, dyspareunia, dysuria, dyschezia, and chronic fatigue. Furthermore, endometriosis is a leading cause of infertility, with 30 to 50% of affected individuals experiencing difficulties conceiving (Zondervan, Becker, and Missmer 2020). While endometriosis lesions can be found in various parts of the body, they are most commonly observed within the reproductive organs, peritoneum, and digestive tract. However, awareness of extrapelvic manifestations of the disease is growing (Della Corte et al. 2020; Sperschneider et al. 2019). Endometriosis has significant psychological, economic, and potential long-term health consequences, such as an increased risk of cancer, cardiovascular diseases, and autoimmune disorders (Federica Facchin et al. 2019; Armour et al. 2019; Kvaskoff et al. 2020; 2015; Gerlinger et al. 2010; Bulun 2009). Despite the substantial burden it poses, even a slight improvement in the frequency and severity of symptoms can have a meaningful impact on the quality of life of individuals with endometriosis (Kvaskoff et al. 2020; Giudice and Kao 2004).

The etiology of endometriosis remains poorly understood. Established risk factors include early age at menarche, short menstrual cycle length, and lean body size (Porpora et al. 1999; Bontempo and Mikesell 2020; Ahn, Singh, and Tayade 2017; Koninckx et al. 2021; P. Vercellini et al. 2009). Other potential risk factors under investigation include physical activity,

parity, oral contraception use, moderate alcohol intake, exposure to dioxins, and family history. However, findings regarding irregular menstrual cycles, smoking, and lactation have been inconsistent across studies and may be influenced by access to healthcare and other biases (Bontempo and Mikesell 2020; P. Vercellini et al. 2009; K. D. Ballard et al. 2008). The role of hormonal levels during prenatal, adolescent, and adult stages, as well as in utero exposures such as nutrition and environmental factors, represents an area of endometriosis research that requires further investigation (Bontempo and Mikesell 2020; Shafrir et al. 2021; Fuldeore and Soliman 2017; Zhang et al. 2021).

The current categorization of endometriosis lacks comprehensiveness. The commonly used surgical staging system, rAFS, suffers from poor correlation with symptoms, lack of consensus among surgeons, and inadequate consideration of all potential lesion locations (Lee, Koo, and Lee 2020; Paolo Vercellini et al. 2006). Other less widespread classification systems, such as EIZAIN and the Endometriosis Fertility Index, have their own limitations and are not universally applicable (Lee, Koo, and Lee 2020; Paolo Vercellini et al. 2006). The absence of a clear and consistent categorization scheme hampers our understanding of factors influencing the presentation of endometriosis lesion locations.

To date, comprehensive exploration of endometriosis demographics and the relationship between demographics and lesion location remains largely unexplored. Research has yet to investigate the association between various demographic factors and commonly co-occurring endometriosis lesion locations. Further investigation into such groupings and alternative categorizations of the disease holds promise for improving diagnostics and treatment. This is particularly crucial given the current lengthy lag time to diagnosis and the

need for a deeper understanding of this complex disease (Zondervan, Cardon, and Kennedy 2002).

B. Methods

1. Study Population and Covariates

Participants were recruited through various endometriosis social media outlets, research focused recruitment tools such as ResearchMatch, and flyers posted in the Chicago-area with a focus on the area around the University of Illinois Chicago. Recruitment remained open from June of 2022 to December of 2022. Participants were eligible if they were 18 years of age or older, live in the US, have surgically-confirmed diagnosis of endometriosis and knew where the endometriosis was found in the body. Participants completed the survey via RedCap based on the WERF ePHect clinical questionnaire. The purpose of this questionnaire is to enable robust epidemiological research using standardized, detailed clinical and phenotypic data in a way that is comparable across studies. The questionnaire was modified to add detailed questions on gender identity, race, ethnicity, and sexuality and some questions concerning menstrual characteristics were truncated or removed. As part of the data cleaning process, bots and other malicious data entry was defined using an assessment of extremely quick data entry from form to form, duplicate entries, and nonsensical or impossible responses such as nonsensical combinations of pregnancies, sex assigned at birth, and open text responses.

2. Description of Factor Analysis and Covariates

Exploratory factor analysis is a method used often in psychology and other fields to reduce a large number of variables into a more manageable set for analysis which can then be used to explain underlying or unobserved commonalities among those variables, called factors.

Factor analysis, unlike the related method principal component analysis, assumes that the measure variables are correlated due to some underlying construct (Watkins 2018; Henson and Roberts 2006). The purpose of this study was to find latent factors and describe them, we have used factor analysis for our study. These factors may influence more than one observed variable or measure and the correlations found between them (Watkins 2018; Reio and Shuck 2015; Henson and Roberts 2006).

Once factors are obtained using the selected variables, in the case of this study the lesion locations, we selected the number of factors to retain. This was accomplished by exploring the scree plot visually looking for the bend in the scree plot and confirmed using parallel analysis (Watkins 2018). Lastly, a rotation was selected. Rotations help to simplify and make the factors more conceptually meaningful by rotating the axes in space to bring them closer to the variables selected (Watkins 2018; Reio and Shuck 2015). While many different rotations exist, we selected the varimax rotation as after rotation each factor tends to have a small number of large loadings which simplifies interpretation and is best for uncorrelated data which we observed when examining the correlation table (Abdi 2003; Reio and Shuck 2015). All analyses were performed in SAS 9.4 with visuals created using the EFashiny R package.

Based on prior literature, race, ethnicity, gender identity, sexual orientation, age, age at diagnosis, diagnostic delay, education, income, employment, smoking status, alcohol usage, history of living in a rural area, age of menarche, number of pregnancies, breastfeeding history, comorbidities (includes mental health conditions, cancer, diabetes, other gynecological conditions such as fibroids, and autoimmune diseases such as Hashimoto's, among others), a

diagnosis of superficial (SPE), ovarian endometrioma (OMA), or deep endometriosis (DE) and surgical stage were selected to be potential covariates.

In total, 1189 participants initially consented to the study. Of these, 258 did not provide a lesion location within the survey and were excluded. Of the 931 who reported lesion locations, 33 additional records were identified as malicious bots leaving a total of 898 possible records. Lastly, all observations missing any of the variables selected were removed for a complete case analysis with 652 observations. Variables with the most missingness included diagnostic delay ($n = 121$), early menarche ($n = 36$), and number of pregnancies ($n = 32$). A table which describes the missingness can be found in appendix xx. We examined distributions of lesion factors and key demographic covariates by missingness status using Student's t-tests and Chi-square tests to examine potential selection bias in the complete case analysis.

3. Statistical Analysis

a. Subtypes and Lesion Location

To investigate how the factor scores related to surgically-defined endometriosis subtype and surgical stage, we used ANOVA to model each factor against prevalence of individual endometriosis subtypes (OMA, SPE, DE and, multiple subtypes) and surgical stage, with post hoc Tukey's adjustment for multiple comparisons and additional control for age, race, BMI, and income. The sample was restricted to those who had a defined subtype and surgical stage by excluding individuals with unspecified or unknown data. In the subtype ANOVA the sample size was 434 while in the surgical stage model the sample size was 302. All analyses were performed in SAS 9.4.

b. Individual Characteristics and Lesion Location

To identify demographic predictors of the factor scores, participant characteristics were modeled in ordinal logistic regression with the factor score divided into quartiles as the outcome to obtain odds ratios (OR) and 95% confidence intervals (95% CI). Based on the literature, race, BMI, diagnostic delay, early menarche, and number of pregnancies were selected as *a priori* variables to remain in the model. Backwards selection was performed, and the full model was reduced until a final model could be obtained using a p-value of 0.05. All analyses were performed in SAS 9.4.

C. Results

Three lesion location factors met criteria for inclusion into our models. Factor one had high loadings of locations on the digestive tract (0.5), bladder (0.5), and ureters (0.5) and will be referred to as the digestive-urinary factor. Factor two had high loadings on the fallopian tubes (0.6) and ovaries (0.6) and will be referred to as the reproductive factor. Factor three had high loadings on the uterosacral ligaments (0.7), pouch of Douglas (0.6), and round ligaments (0.5) and will be referred to as the Douglas-ligaments factor. Factor loadings and the scree plot are shown in Figure 1 and 2 and the table of eigenvalues are in Table II. A table of the analytic sample is found in Table I. Distribution of covariates by quartiles of each factor are shown in Table III.

TABLE I ANALYTIC SAMPLE (N = 652)

Variable	N (%)
Number of Locations	
1	191 (29.3)
2	137 (21.0)
3+	324 (49.7)
Right Ovary	
Selected	234 (35.9)
Not Selected	418 (64.1)
Left Ovary	
Selected	244 (37.4)
Not Selected	408 (62.6)
Unknown Ovary	
Selected	102 (15.6)
Not Selected	550 (84.4)
Right Fallopian Tube	
Selected	130 (19.9)
Not Selected	522 (80.1)
Left Fallopian Tube	
Selected	125 (19.2)
Not Selected	527 (80.8)
Unknown Fallopian Tube	
Selected	67 (10.3)
Not Selected	585 (89.7)
Uterus	
Selected	359 (55.1)
Not Selected	293 (44.9)
Vagina	
Selected	65 (10.0)
Not Selected	587 (90.0)
Pouch of Douglas	
Selected	138 (21.2)
Not Selected	514 (78.8)
Digestive Tract	
Selected	208 (31.9)
Not Selected	444 (68.1)

TABLE I ANALYTIC SAMPLE (N =652) (continued)

Variable	N (%)
Abdominal Wall	
Selected	213 (32.7)
Not Selected	439 (67.3)
Bladder	
Selected	160 (24.5)
Not Selected	492 (75.5)
Ureters	
Selected	72 (11.0)
Not Selected	580 (89.0)
Kidney	
Selected	16 (2.5)
Not Selected	636 (97.6)
Uterosacral Ligaments	
Selected	108 (16.6)
Not Selected	544 (83.4)
Round Ligaments	
Selected	52 (8.0)
Not Selected	600 (92.0)
Diaphragm	
Selected	29 (4.5)
Not Selected	623 (95.6)
Other Location	
Selected	53 (8.1)
Not Selected	599 (91.9)
Have Surgical Reports	
Yes	367 (56.3)
No	285 (43.7)
Race	
White	527 (80.8)
Other Race	36 (5.5)
Black	24 (3.7)
AAPI	65 (10.0)
BMI	
< 18.5	30 (4.6)

TABLE I ANALYTIC SAMPLE (N =652) (continued)

Variable	N (%)
18.5 - 24.9	240 (36.8)
25-29.9	184 (28.2)
>=30	198 (30.4)
Diagnostic Delay	
Incidental or < 1 Year	95 (14.6)
1-5 Years	166 (25.5)
6-10 Years	137 (21.0)
11-15 Years	100 (15.3)
> 15 years	154 (23.6)
Early Menarche	
Before Age 12	153 (23.5)
Age 12 or Later	499 (76.5)
Number of Pregnancies	
0	351 (53.8)
1	67 (10.3)
2+	234 (35.9)
Gender	
Cis woman	628 (96.3)
Other	24 (3.7)
Sexuality	
Heterosexual/Straight	485 (74.4)
Other	167 (25.6)
Age Diagnosed	
Less than 18	35 (5.4)
18 - 35	497 (76.2)
36-45	97 (14.9)
46 and up	23 (3.5)
Income Levels	
60k +	414 (63.5)
30k to 59K	140 (21.5)
Less than 30k	98 (15.0)
Employment	
Employed Full Time	371 (56.90)
Employed Part Time	97 (14.9)

TABLE I ANALYTIC SAMPLE (N =652) (continued)

Variable	N (%)
Unemployed, Student, Retired, or Homemaker	142 (21.8)
Disabled	42 (6.4)
Education	
Bachelor's Degree or Higher	462 (70.9)
Some College	154 (23.6)
High School Degree and Less	36 (5.5)
Smoking Status	
Never Smoker	464 (71.2)
Started at 18 or older	78 (12.0)
Started Before 18	110 (16.9)
Alcohol Use	
Non-Drinker	278 (42.6)
Light Drinker	289 (44.3)
Moderate/Heavy Drinker	85 (13.0)
Lived in Rural Area > 1 Year	
Never	426 (65.3)
18 or Older	70 (10.7)
Before 18	156 (23.9)
Ever Breast/Chest Fed	
No	96 (14.7)
Yes	205 (31.4)
Never Pregnant	351 (53.8)
Number of Comorbidities	
0	70 (10.7)
1	72 (11.0)
2	91 (14.0)
3	100 (15.3)
4 or More	319 (48.9)
Family History	
Any Family History	355 (54.5)
No Known Family History	297 (45.6)
Subtypes/Related Disease	
SPE	52 (8.0)
OMA	124 (19.0)

TABLE I ANALYTIC SAMPLE (N =652) (continued)

Variable	N (%)
DE	44 (6.8)
Adenomyosis	45 (6.9)
Not Specified	173 (26.5)
Multiple Subtypes	214 (32.8)
Surgical Stage	
Not Mentioned	189 (29.0)
Stage I	53 (8.1)
Stage II	96 (14.7)
Stage III	63 (9.7)
Stage IV	90 (13.8)
Unknown	161 (24.7)
Age	
Average	39.5 (SD 12.8)
Year of Diagnosis	
Average	2011 (SD 10.8)

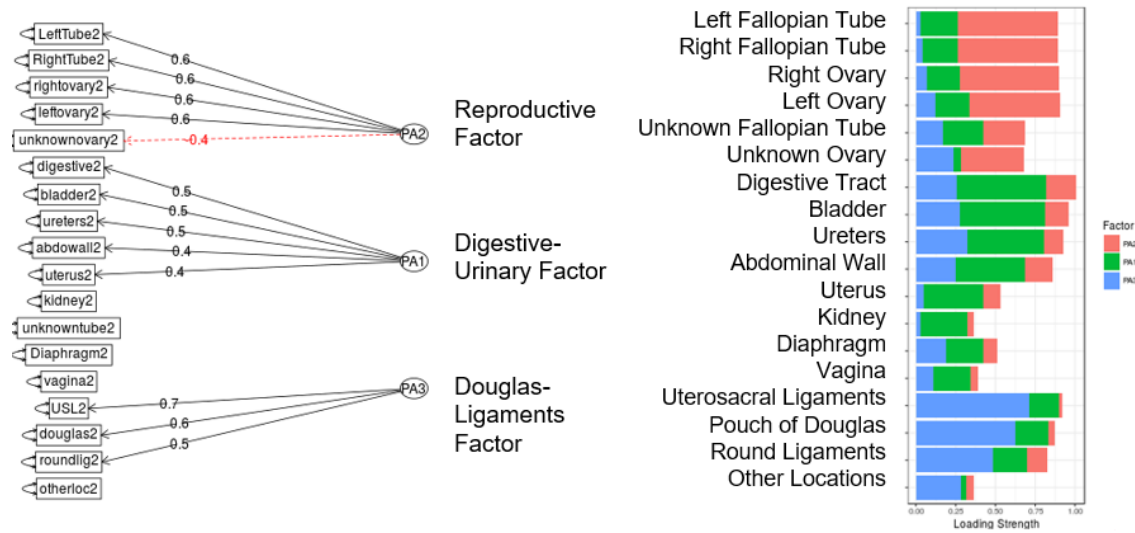


Figure 1. Factor loadings

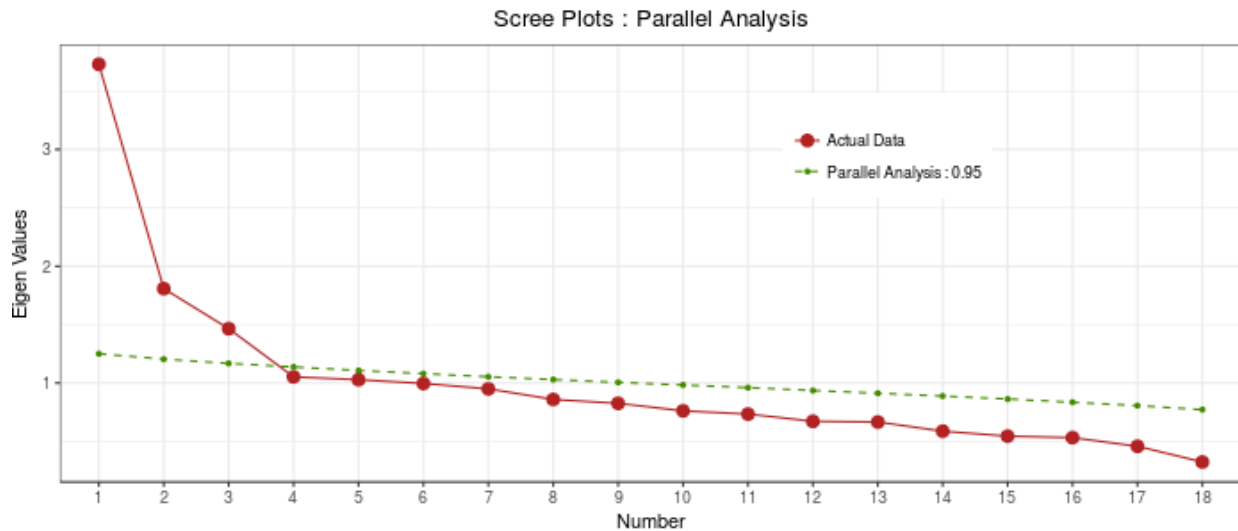


Figure 2. Scree plot for lesion location factors

TABLE II EIGENVALUES FOR LESION LOCATIONS FACTOR ANALYSIS

Factor	Eigenvalue	Proportion
Digestive-Urinary	3.07	0.62
Reproductive	1.20	0.49
Douglas-Ligaments	0.70	0.14

TABLE III DEMOGRAPHICS OF FACTOR SCORES BY QUARTILE (continued)

Variable	Demographics for Quartiles of Digestive-Urinary Factor Score (n = 652)				Demographics for Quartiles of Reproductive Factor Score (n = 652)				Demographics for Quartiles of Douglas-Ligaments Factor Score (n = 652)			
	(Lowest) Quartile 1 N = 154	Quartile 2 N = 154	Quartile 3 N = 159	(Highest) Quartile 4 N = 185	(Lowest) Quartile 1 N = 166	Quartile 2 N = 158	Quartile 3 N = 159	(Highest) Quartile 4 N = 170	(Lowest) Quartile 1 N = 157	Quartile 2 N = 160	Quartile 3 N = 178	(Highest) Quartile 4 N = 157
Heterosexual/ Straight	111 (72.1)	121 (78.6)	122 (76.7)	131 (70.8)	128 (77.1)	124 (78.5)	112 (70.4)	121 (71.2)	123 (78.3)	122 (76.3)	130 (73.0)	110 (70.1)
Other	43 (27.9)	33 (21.4)	37 (23.3)	54 (29.2)	38 (22.9)	34 (21.5)	47 (29.6)	49 (28.8)	34 (78.3)	38 (23.8)	48 (27.0)	47 (29.9)
Age												
Continuous	41.6 (SD 14.9)	38.2 (SD 12.1)	38.2 (SD 11.5)	39.9 (SD 12.5)	41.9 (SD 13.3)	39.9 (SD 13.5)	39.2 (SD 13.6)	36.9 (SD 10.4)	37.2 (SD 10.7)	38.1 (SD 12.1)	40.8 (SD 14.6)	41.7 (SD 13.1)
Age Diagnosed												
Less than 18	10 (6.5)	8(5.2)	9 (5.7)	8 (4.3)	10 (6.0)	5 (3.2)	10 (6.3)	10 (5.9)	3 (1.9)	10 (6.3)	12 (6.7)	10 (6.4)
18 - 35	109 (70.8)	124 (80.5)	121 (76.1)	143 (77.3)	128 (77.1)	122 (77.2)	116 (73.0)	132 (77.7)	134 (85.4)	121 (75.6)	129 (72.5)	113 (72.0)
36-45	26 (16.9)	18 (11.7)	23 (14.5)	30 (16.2)	22 (13.3)	22 (13.9)	31 (19.5)	22 (12.9)	16 (10.2)	26 (16.3)	27 (15.2)	28 (17.8)
46 and up	9 (5.8)	4 (2.6)	6 (3.7)	4 (2.2)	6 (3.6)	9 (5.7)	2 (1.3)	6 (3.5)	4 (2.6)	3 (1.9)	10 (5.6)	6 (3.8)
Income Levels												
60k +	77 (50.0)	99 (64.3)	110 (69.2)	128 (69.2)	102 (61.5)	96 (60.8)	95 (59.8)	122 (71.8)	110 (70.1)	105 (65.6)	105 (59.0)	94 (59.9)
30k to 59K	44 (28.6)	34 (22.1)	25 (15.7)	37 (20.0)	35 (21.1)	39 (24.7)	39 (24.5)	27 (15.9)	30 (19.1)	37 (23.1)	38 (21.4)	35 (22.3)
Less than 30k	33 (21.4)	21 (13.6)	24 (15.1)	20 (10.8)	29 (17.5)	23 (14.6)	25 (15.7)	21 (12.4)	17 (10.8)	18 (11.3)	35 (19.7)	28 (17.8)
Employment												
Employed Full Time	76 (49.4)	95 (61.7)	91 (57.2)	109 (58.9)	92 (55.4)	95 (60.1)	85 (53.5)	99 (58.2)	96 (61.2)	96 (60.0)	97 (54.5)	82 (52.2)

TABLE III DEMOGRAPHICS OF FACTOR SCORES BY QUARTILE (continued)

Variable	Demographics for Quartiles of Digestive-Urinary Factor Score (n = 652)				Demographics for Quartiles of Reproductive Factor Score (n = 652)				Demographics for Quartiles of Douglas-Ligaments Factor Score (n = 652)			
	(Lowest) Quartile 1 N = 154	Quartile 2 N = 154	Quartile 3 N = 159	(Highest) Quartile 4 N = 185	(Lowest) Quartile 1 N = 166	Quartile 2 N = 158	Quartile 3 N = 159	(Highest) Quartile 4 N = 170	(Lowest) Quartile 1 N = 157	Quartile 2 N = 160	Quartile 3 N = 178	(Highest) Quartile 4 N = 157
Employed Part Time	26 (176.9)	20 (13.0)	26 (16.4)	25 (13.5)	28 (16.9)	20 (12.7)	35 (22.0)	14 (8.2)	18 (11.5)	27 (16.9)	28 (15.7)	24 (15.3)
Unemployed, Student, Retired, or Homemaker	41 (26.6)	31 (20.1)	32 (20.1)	38 (20.5)	34 (20.5)	31 (19.6)	32 (20.1)	46 (27.1)	33 (21.0)	28 (17.5)	43 (24.2)	38 (24.2)
Disabled	11 (7.1)	8 (5.2)	10 (6.3)	13 (7.0)	12 (7.2)	12 (7.6)	7 (4.4)	11 (6.5)	10 (6.4)	9 (5.6)	10 (5.6)	13 (8.3)
Education												
Bachelor's Degree or Higher	91 (59.1)	110 (71.4)	118 (74.2)	143 (77.3)	111 (66.9)	112 (70.9)	97 (61.0)	143 (84.1)	126 (80.3)	108 (67.5)	121 (68.0)	107 (68.2)
Some College	51 (33.3)	36 (23.4)	31 (19.5)	36 (19.5)	45 (27.1)	41 (26.0)	48 (30.2)	20 (11.8)	23 (14.7)	42 (26.3)	47 (26.4)	42 (26.8)
High School Degree and Less	12 (7.8)	8 (5.2)	10 (6.3)	6 (3.2)	10 (6.0)	5 (3.2)	14 (8.8)	7 (4.1)	8 (5.1)	10 (6.3)	10 (5.6)	8 (5.1)
Smoking Status												
Never Smoker	101 (65.6)	114 (74.0)	120 (75.5)	129 (69.7)	113 (68.1)	109 (69.0)	112 (70.4)	130 (76.5)	119 (75.8)	114 (71.3)	128 (71.9)	103 (65.6)
Started at 18 or older	25 (16.2)	14 (9.1)	17 (10.7)	22 (11.9)	22 (13.3)	16 (10.1)	24 (15.1)	17 (10.0)	14 (8.9)	15 (9.4)	22 (12.4)	27 (17.2)
Started Before 18	28 (18.2)	26 (16.9)	22 (13.8)	34 (18.4)	31 (18.7)	33 (20.9)	23 (14.5)	23 (13.5)	24 (15.3)	31 (19.4)	28 (15.7)	27 (17.2)
Alcohol Use												
Non-Drinker	68 (44.2)	69 (44.8)	74 (46.5)	67 (36.2)	79 (47.6)	56 (35.4)	70 (44.0)	73 (42.9)	66 (42.0)	77 (48.1)	72 (40.5)	63 (40.1)
Light Drinker	57 (37.0)	63 (40.9)	67 (42.1)	102 (55.1)	69 (41.6)	77 (48.7)	64 (40.3)	80 (47.1)	74 (47.1)	62 (38.8)	80 (44.9)	73 (46.5)

TABLE III DEMOGRAPHICS OF FACTOR SCORES BY QUARTILE (continued)

Variable	Demographics for Quartiles of Digestive-Urinary Factor Score (n = 652)				Demographics for Quartiles of Reproductive Factor Score (n = 652)				Demographics for Quartiles of Douglas-Ligaments Factor Score (n = 652)			
	(Lowest) Quartile 1 N = 154	Quartile 2 N = 154	Quartile 3 N = 159	(Highest) Quartile 4 N = 185	(Lowest) Quartile 1 N = 166	Quartile 2 N = 158	Quartile 3 N = 159	(Highest) Quartile 4 N = 170	(Lowest) Quartile 1 N = 157	Quartile 2 N = 160	Quartile 3 N = 178	(Highest) Quartile 4 N = 157
Moderate/Heavy Drinker	29 (18.8)	22 (14.3)	18 (11.3)	16 (8.7)	18 (10.8)	25 (15.8)	25 (15.7)	17 (10.0)	17 (10.8)	21 (13.1)	26 (14.6)	21 (13.4)
Lived in Rural Area > 1 Year												
Never	109 (70.8)	107 (69.5)	104 (65.4)	106 (57.3)	104 (62.7)	100 (63.3)	111 (69.8)	111 (65.3)	107 (68.2)	96 (60.0)	118 (66.3)	105 (66.9)
18 or Older	9 (5.8)	8 (5.2)	20 (12.6)	33 (17.8)	21 (12.7)	14 (8.9)	13 (8.2)	22 (12.9)	19 (12.1)	17 (10.6)	18 (10.1)	16 (10.2)
Before 18	36 (23.4)	39 (25.3)	35 (22.0)	46 (24.9)	41 (24.7)	43 (27.2)	35 (22.0)	37 (21.8)	31 (19.8)	47 (29.4)	42 (23.6)	36 (22.9)
Ever Breast/Chest Fed												
No	20 (13.0)	19 (12.3)	28 (17.6)	29 (15.7)	79 (47.6)	88 (55.7)	88 (55.4)	96 (56.5)	30 (19.1)	17 (10.6)	30 (16.9)	19 (12.1)
Yes	47 (30.5)	50 (32.5)	52 (32.7)	56 (30.3)	64 (38.6)	45 (28.5)	48 (30.2)	49 (28.8)	45 (28.7)	51 (31.9)	54 (30.3)	55 (35.0)
Never Pregnant	87 (56.5)	85 (55.2)	79 (49.7)	100 (54.1)	23 (13.9)	25 (15.8)	23 (14.5)	25 (14.7)	82 (52.2)	92 (57.5)	94 (52.8)	83 (52.9)
Number of Comorbidities												
0	23 (14.9)	17 (11.4)	15 (9.4)	15 (8.1)	14 (8.4)	18 (11.4)	22 (13.8)	16 (9.4)	19 (12.1)	12 (7.5)	25 (14.0)	14 (8.9)
1	26 (16.9)	30 (19.5)	9 (5.7)	7 (3.8)	14 (8.4)	25 (15.8)	24 (15.1)	10 (5.9)	21 (13.4)	20 (12.5)	19 (10.7)	12 (7.6)
2	24 (15.6)	19 (12.3)	27 (17.0)	21 (11.4)	27 (16.3)	24 (15.2)	20 (12.6)	20 (11.8)	19 (12.1)	23 (14.4)	24 (12.5)	25 (15.9)

TABLE III DEMOGRAPHICS OF FACTOR SCORES BY QUARTILE (continued)

	Demographics for Quartiles of Digestive-Urinary Factor Score (n = 652)				Demographics for Quartiles of Reproductive Factor Score (n = 652)				Demographics for Quartiles of Douglas-Ligaments Factor Score (n = 652)			
Variable	(Lowest) Quartile 1 N = 154	Quartile 2 N = 154	Quartile 3 N = 159	(Highest) Quartile 4 N = 185	(Lowest) Quartile 1 N = 166	Quartile 2 N = 158	Quartile 3 N = 159	(Highest) Quartile 4 N = 170	(Lowest) Quartile 1 N = 157	Quartile 2 N = 160	Quartile 3 N = 178	(Highest) Quartile 4 N = 157
3	21 (13.6)	23 (14.9)	35 (22.0)	21 (11.4)	26 (15.7)	18 (11.4)	26 (16.4)	30 (17.7)	29 (18.5)	24 (15.0)	25 (14.0)	22 (14.0)
4 or More	60 (39.0)	65 (42.2)	73 (45.9)	121 (65.4)	85 (51.2)	73 (46.2)	67 (42.1)	94 (55.3)	69 (44.0)	81 (50.6)	85 (47.8)	84 (53.5)
Family History												
Any Family History	71 (46.1)	85 (55.2)	92 (57.9)	107 (57.8)	97 (58.4)	87 (55.1)	79 (49.7)	93 (54.7)	91 (58.0)	91 (56.9)	92 (51.7)	81 (51.6)
No Family History	32 (20.8)	26 (16.4)	26 (16.4)	38 (20.5)	36 (21.7)	29 (18.4)	26 (16.4)	31 (18.2)	31 (19.8)	35 (21.9)	30 (16.9)	26 (16.6)
I Don't Know	51 (33.1)	43 (27.9)	41 (25.8)	40 (21.6)	33 (19.9)	42 (26.7)	54 (34.0)	46 (27.1)	35 (22.3)	34 (21.3)	56 (31.5)	50 (31.9)
Subtypes/Related Disease												
SPE	16 (10.4)	13 (8.4)	19 (12.0)	4 (2.2)	6 (3.6)	12 (7.6)	13 (8.2)	21 (12.4)	12 (13.4)	13 (8.1)	12 (6.7)	6 (3.8)
OMA	41 (26.6)	45 (29.2)	24 (15.1)	14 (7.6)	42 (25.3)	43 (27.4)	32 (20.1)	7 (4.1)	33 (21.0)	31 (19.4)	32 (18.0)	28 (17.8)
DE	8 (5.2)	12 (7.8)	9 (2.7)	15 (8.1)	16 (9.6)	9 (5.7)	10 (6.3)	9 (5.3)	7 (4.5)	11 (6.9)	10 (5.6)	16 (10.2)
Adenomyosis	21 (13.6)	9 (5.8)	8 (5.0)	7 (3.8)	7 (4.2)	15 (9.6)	11 (6.9)	12 (7.1)	11 (7.0)	4 (2.5)	18 (10.1)	12 (7.6)
Not Specified	58 (37.7)	53 (34.4)	40 (25.2)	22 (11.9)	30 (18.1)	44 (28.0)	52 (32.7)	47 (27.7)	34 (21.7)	44 (27.5)	55 (30.9)	40 (25.5)
Multiple Subtypes	10 (6.5)	22 (14.3)	59 (37.1)	123 (66.5)	65 (39.2)	34 (21.7)	41 (25.8)	74 (43.5)	51 (32.5)	57 (35.6)	51 (28.7)	55 (35.0)

TABLE III DEMOGRAPHICS OF FACTOR SCORES BY QUARTILE (continued)

	Demographics for Quartiles of Digestive-Urinary Factor Score (n = 652)				Demographics for Quartiles of Reproductive Factor Score (n = 652)				Demographics for Quartiles of Douglas-Ligaments Factor Score (n = 652)			
Variable	(Lowest) Quartile 1 N = 154	Quartile 2 N = 154	Quartile 3 N = 159	(Highest) Quartile 4 N = 185	(Lowest) Quartile 1 N = 166	Quartile 2 N = 158	Quartile 3 N = 159	(Highest) Quartile 4 N = 170	(Lowest) Quartile 1 N = 157	Quartile 2 N = 160	Quartile 3 N = 178	(Highest) Quartile 4 N = 157
Surgical Stage												
Not Mentioned	46 (29.9)	49 (31.8)	44 (27.7)	50 (27.0)	45 (27.1)	51 (32.5)	45 (28.3)	48 (28.2)	60 (38.2)	49 (30.6)	51 (28.7)	29 (18.5)
Stage I	19 (12.3)	20 (13.0)	14 (8.8)	0	11 (6.6)	14 (8.9)	19 (12.0)	9 (5.3)	12 (7.6)	14 (8.8)	17 (9.6)	10 (6.4)
Stage II	22 (14.3)	32 (20.8)	27 (17.0)	15 (8.1)	15 (9.0)	28 (17.8)	23 (14.5)	30 (17.7)	37 (23.6)	22 (13.8)	16 (9.0)	21 (13.4)
Stage III	6 (3.9)	13 (8.4)	13 (8.2)	31 (16.8)	21 (12.7)	11 (7.0)	12 (7.6)	19 (11.2)	10 (6.4)	16 (10.0)	17 (9.6)	20 (12.7)
Stage IV	3 (2.0)	7 (4.6)	18 (11.3)	62 (33.5)	32 (19.3)	12 (7.6)	11 (6.9)	35 (20.6)	21 (13.4)	27 (16.9)	17 (9.6)	25 (15.9)
Unknown	58 (37.7)	33 (21.4)	43 (27.0)	27 (14.6)	42 (25.3)	41 (26.1)	49 (30.8)	29 (17.1)	17 (10.8)	32 (20.0)	60 (33.7)	52 (33.1)

1. Subtypes and Lesion Location

When examining the associations of the lesion location factors with endometriosis subtypes, a significant association was identified for the digestive-urinary factor (p-value <0.0001), and a significant difference was found between multiple subtypes and DE, SPE, and OMA as well as between DE and OMA in post hoc pairwise comparisons, with strongest positive association with multiple subtypes, followed by DE subtype. These associations persisted after adjusting for age, race, BMI, and income.

In the surgical stage model a significant association was also found in the initial ANOVA and Kruskal-Wallis nonparametric models (p-value <0.0001). In the Tukey's multiple comparison model an association between stage IV and III, II, and I as well as between stage III and II and I in the unadjusted model. The association with surgical stage persisted after adjustment. In the Tukey's adjustment in the adjusted model a significant difference was found between stage I and stage III and IV, between stage II and stage III and IV, and between stage III and stage IV.

In the reproductive subtype ANOVA model, the initial model showed a significant association (<0.0001) indicating the need for a multiple comparison model. Significant differences were seen between SPE and DE as well as OMA and multiple subtypes and OMA. The association in the adjusted model persisted. No association was seen with the surgical staging ANOVA adjusted for age, race, BMI, and income.

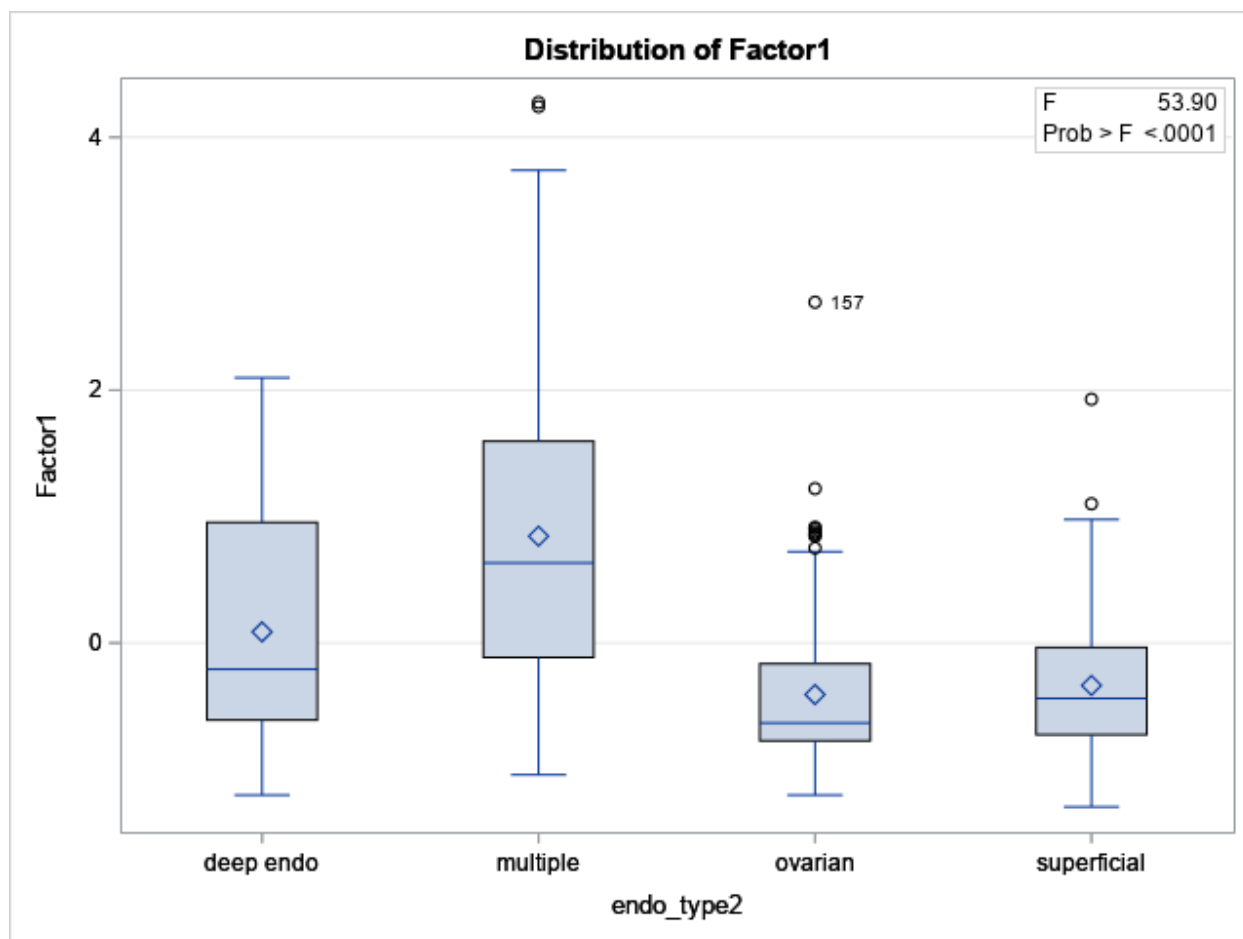


Figure 3. Digestive-urinary and subtype (unadjusted)

TABLE IV SUBTYPES AND DIGESTIVE-URINARY FACTOR LEAST SQUARES MEANS ADJUSTMENT FOR MULTIPLE COMPARISONS AND COVARIATES

Subtype	Estimate (95% CI)	P-Value
DE	0.14 (-0.13, 0.42)	0.30
OMA	-0.37 (-0.54, -0.21)	<.0001
SPE	-0.34 (-0.60, -0.08)	0.01
Multiple Subtype	0.8147 (0.69, 94)	<.0001

TABLE V DEMOGRAPHICS BY SURGICAL STAGING (N = 302)

Variable	Stage I N = 53	Stage II N = 96	Stage III N = 63	Stage IV N = 90
	N (%)	N (%)	N (%)	N (%)
Number of Locations				
1	28 (52.8)	35 (36.5)	8 (12.7)	2 (2.2)
2	14 (26.4)	22 (22.9)	9 (14.3)	12 (13.3)
3+	11 (20.8)	39 (40.6)	46 (73.0)	76 (84.4)
Right Ovary				
Selected	10 (18.9)	19 (19.8)	35 (55.6)	64 (71.1)
Not Selected	43 (81.1)	77 (80.2)	28 (44.4)	26 (28.9)
Left Ovary				
Selected	10 (18.9)	24 (25.0)	33 (52.4)	66 (73.3)
Not Selected	43 (81.1)	72 (75.0)	30 (47.6)	24 (26.7)
Unknown Ovary				
Selected	6 (11.3)	21 (21.9)	9 (14.3)	7 (7.8)
Not Selected	47 (88.7)	75 (78.1)	54 (85.7)	83 (92.2)
Right Fallopian Tube				
Selected	3 (5.7)	12 (12.5)	15 (23.8)	34 (37.8)
Not Selected	50 (94.3)	84 (87.5)	48 (76.2)	56 (62.2)
Left Fallopian Tube				
Selected	3 (5.7)	10 (10.4)	18 (28.6)	29 (32.2)
Not Selected	50 (94.3)	86 (89.6)	45 (71.4)	61 (67.8)
Unknown Fallopian Tube				
Selected	7 (13.2)	8 (8.3)	7 (11.1)	10 (11.1)
Not Selected	46 (86.8)	88 (91.7)	56 (88.9)	80 (88.9)
Uterus				
Selected	22 (41.5)	35 (36.5)	47 (74.6)	61 (67.8)
Not Selected	31 (58.5)	61 (63.5)	16 (25.4)	29 (32.2)
Vagina				
Selected	10 (18.9)	12 (12.5)	8 (12.7)	17 (18.9)
Not Selected	43 (81.1)	84 (87.5)	55 (87.3)	73 (81.1)
Pouch of Douglas				
Selected	6 (11.3)	23 (24.0)	22 (34.9)	40 (44.4)
Not Selected	47 (88.7)	73 (76.0)	41 (65.1)	50 (55.6)
Digestive Tract				
Selected	6 (11.3)	23 (24.0)	26 (41.3)	59 (65.6)
Not Selected	47 (88.7)	73 (76.0)	37 (58.7)	31 (34.4)

TABLE V DEMOGRAPHICS BY SURGICAL STAGING (N = 302) (continued)

Variable	Stage I N = 53	Stage II N = 96	Stage III N = 63	Stage IV N = 90
	N (%)	N (%)	N (%)	N (%)
Abdominal Wall				
Selected	4 (7.6)	21 (21.9)	27 (42.9)	56 (62.2)
Not Selected	49 (92.5)	75 (78.1)	36 (57.1)	34 (37.8)
Bladder				
Selected	5 (9.4)	19 (19.8)	25 (39.7)	48 (53.3)
Not Selected	48 (90.6)	77 (80.2)	38 (60.3)	42 (46.7)
Ureters				
Selected	1 (1.9)	3 (3.1)	12 (19.1)	33 (36.7)
Not Selected	52 (98.1)	93 (96.9)	51 (81.0)	57 (63.3)
Kidney				
Selected	0 (0.0)	0 (0.0)	2 (3.2)	7 (7.8)
Not Selected	53 (100.0)	96 (100.0)	61 (96.8)	83 (92.2)
Uterosacral Ligaments				
Selected	4 (7.6)	18 (18.8)	13 (20.6)	33 (36.7)
Not Selected	49 (92.5)	78 (81.3)	50 (79.4)	57 (63.3)
Round Ligaments				
Selected	0 (0.00)	7 (7.3)	8 (12.7)	15 (16.7)
Not Selected	53 (100.0)	89 (92.7)	55 (87.3)	75 (83.3)
Diaphragm				
Selected	0 (0.0)	3 (3.1)	4 (6.4)	15 (16.7)
Not Selected	53 (100.0)	93 (96.9)	59 (93.7)	75 (83.3)
Other Location				
Selected	0	3 (3.1)	5 (7.9)	17 (18.9)
Not Selected	53 (100.0)	93 (96.9)	58 (92.1)	73 (81.1)
Have Surgical Reports				
Yes	39 (73.6)	56 (58.3)	49 (77.8)	61 (67.8)
No	14 (26.4)	40 (41.7)	14 (22.2)	29 (32.2)
Race				
White	34 (64.2)	75 (78.1)	48 (76.2)	79 (87.8)
Other Race	2 (3.8)	1 (1.0)	2 (3.2)	5 (5.6)
Black	4 (7.6)	4 (4.2)	4 (6.4)	2 (2.2)
AAPI	13 (24.5)	16 (16.7)	9 (14.3)	4 (4.4)
BMI				
< 18.5	2 (3.8)	2 (3.8)	8 (12.7)	1 (1.1)
18.5 - 24.9	24 (45.3)	24 (45.3)	23 (36.5)	41 (45.6)

TABLE V DEMOGRAPHICS BY SURGICAL STAGING (N = 302) (continued)

Variable	Stage I N = 53	Stage II N = 96	Stage III N = 63	Stage IV N = 90
	N (%)	N (%)	N (%)	N (%)
25-29.9	15 (28.3)	15 (28.3)	18 (28.6)	22 (24.4)
>=30	12 (22.6)	12 (22.6)	14 (22.2)	26 (28.9)
Diagnostic Delay				
Incidental or < 1 Year	19 (35.9)	21 (21.9)	8 (12.7)	7 (7.8)
1-5 Years	14 (26.4)	33 (34.4)	18 (28.6)	14 (15.6)
6-10 Years	8 (15.1)	15 (15.6)	13 (20.6)	17 (18.9)
11-15 Years	3 (5.7)	7 (7.3)	11 (17.5)	20 (22.2)
> 15 years	9 (17.0)	20 (20.8)	13 (20.6)	32 (35.6)
Early Menarche				
Before Age 12	12 (22.6)	11 (11.5)	16 (25.4)	24 (26.7)
Age 12 or Later	41 (77.4)	85 (88.5)	47 (74.6)	66 (73.3)
Number of Pregnancies				
0	35 (66.0)	63 (65.6)	36 (57.1)	53 (58.9)
1	5 (9.4)	10 (10.4)	9 (14.3)	10 (11.1)
2+	13 (24.5)	23 (24.0)	18 (28.6)	27 (30.0)
Gender				
Cis woman	52 (98.1)	94 (97.9)	56 (88.9)	90 (100.0)
Other	1 (1.9)	2 (1.1)	7 (11.1)	0 (0.0)
Sexuality				
Heterosexual/Straight	38 (71.7)	75 (78.1)	38 (60.3)	73 (81.1)
Other	15 (28.3)	21 (21.9)	25 (39.7)	17 (18.9)
Age Diagnosed				
Less than 18	8 (15.1)	2 (2.1)	4 (6.4)	5 (5.6)
18 - 35	41 (77.4)	81 (84.4)	55 (87.3)	62 (68.9)
36-45	3 (5.7)	12 (12.5)	4 (6.4)	22 (24.4)
46 and up	1 (1.9)	1 (1.0)	0 (0.0)	1 (1.1)
Income Levels				
60k +	29 (54.7)	50 (52.1)	41 (65.1)	71 (78.9)
30k to 59K	19 (35.9)	26 (27.1)	13 (20.6)	13 (14.4)
Less than 30k	5 (9.4)	20 (20.8)	9 (14.3)	6 (6.7)
Employment				
Employed Full Time	32 (60.4)	70 (72.9)	37 (58.7)	59 (65.6)
Employed Part Time	7 (13.2)	15 (15.6)	8 (12.7)	9 (10.0)
Unemployed, Student, Retired, or Homemaker	13 (24.5)	11 (11.5)	15 (23.8)	19 (21.1)
Disabled	1 (1.9)	0 (0.0)	3 (4.8)	3 (3.3)

TABLE V DEMOGRAPHICS BY SURGICAL STAGING (N = 302) (continued)

Variable	Stage I N = 53	Stage II N = 96	Stage III N = 63	Stage IV N = 90
	N (%)	N (%)	N (%)	N (%)
Education				
Bachelor's Degree or Higher	32 (60.4)	57 (59.4)	50 (79.4)	73 (81.1)
Some College	18 (34.0)	34 (35.4)	10 (15.9)	15 (16.7)
High School Degree and Less	3 (5.7)	5 (5.2)	3 (4.8)	2 (2.2)
Smoking Status				
Never Smoker	38 (71.7)	69 (71.9)	49 (77.8)	68 (75.6)
Started at 18 or older	6 (11.3)	16 (16.7)	9 (14.3)	10 (11.1)
Started Before 18	9 (17.0)	11 (11.5)	5 (7.9)	12 (13.3)
Alcohol Use				
Non-Drinker	34 (64.2)	43 (44.8)	33 (52.4)	31 (34.4)
Light Drinker	11 (20.8)	32 (33.3)	21 (33.3)	53 (58.9)
Moderate/Heavy Drinker	8 (15.1)	21 (21.9)	9 (14.3)	6 (6.7)
Lived in Rural Area > 1 Year				
Never	40 (75.5)	70 (72.9)	40 (63.5)	58 (64.4)
18 or Older	5 (9.4)	10 (10.4)	9 (14.3)	10 (11.1)
Before 18	8 (15.1)	16 (16.7)	14 (22.2)	22 (24.4)
Ever Breast/Chest Fed				
No	7 (13.2)	15 (15.6)	11 (17.5)	11 (12.2)
Yes	11 (20.8)	18 (18.8)	16 (25.4)	26 (28.9)
Never Pregnant	35 (66.0)	63 (65.6)	36 (57.1)	53 (58.9)
Number of Comorbidities				
0	7 (13.2)	17 (17.7)	11 (17.5)	11 (12.2)
1	12 (22.6)	21 (21.9)	5 (7.9)	7 (7.8)
2	8 (15.1)	13 (13.5)	10 (15.9)	11 (12.2)
3	8 (15.1)	18 (18.8)	8 (12.7)	8 (8.9)
4 or More	18 (34.0)	27 (28.1)	29 (46.0)	53 (58.9)
Family History				
Any Family History	31 (58.5)	54 (56.3)	37 (58.7)	51 (56.7)
No Known Family History	22 (41.5)	42 (43.8)	26 (41.3)	39 (43.3)
Subtypes/Related Disease				
SPE	12 (22.6)	13 (13.5)	2 (3.2)	0 (0.0)
OMA	16 (30.2)	29 (30.2)	7 (11.1)	16 (17.8)
DE	5 (9.4)	11 (11.5)	9 (14.3)	5 (5.6)
Adenomyosis	4 (7.6)	6 (6.3)	2 (3.2)	3 (3.3)
Not Specified	6 (11.3)	10 (10.4)	8 (12.7)	6 (6.7)
Multiple Subtypes	10 (18.9)	27 (28.1)	35 (55.6)	60 (66.7)

TABLE V DEMOGRAPHICS BY SURGICAL STAGING (N = 302) (continued)

Variable	Stage I N = 53	Stage II N = 96	Stage III N = 63	Stage IV N = 90
	N (%)	N (%)	N (%)	N (%)
Age				
Mean	30.4 (SD 6.6)	34.4 (SD 9.0)	34.1 (SD 9.4)	39.8 (SD 11.5)
Year of Diagnosis				
Mean	2017 (SD 4.6)	2016 (SD 6.7)	2014 (SD 8.3)	2012 (SD 10.0)

TABLE VI DEMOGRAPHICS BY SUBTYPE (N = 434)

Variable	SPE (N = 52) N(%)	OMA (N = 124) N(%)	DE (N = 44) N(%)	Multiple (N = 214) N(%)
Number of Locations				
1	21 (40.4)	57 (46.0)	17 (38.6)	13 (6.1)
2	15 (28.9)	32 (25.8)	4 (9.1)	27 (12.6)
3+	16 (30.8)	35 (28.2)	23 (52.3)	174 (81.3)
Right Ovary				
Selected	4 (7.7)	47 (37.9)	12 (27.3)	127 (59.4)
Not Selected	48 (92.3)	77 (62.1)	32 (72.7)	87 (40.7)
Left Ovary				
Selected	7 (13.5)	49 (39.5)	13 (29.6)	131 (61.2)
Not Selected	45 (86.5)	75 (60.5)	31 (70.5)	83 (38.8)
Unknown Ovary				
Selected	6 (11.5)	34 (27.4)	7 (15.9)	14 (6.5)
Not Selected	46 (88.5)	90 (72.6)	37 (84.1)	200 (93.5)
Right Fallopian Tube				
Selected	4 (7.7)	25 (20.2)	16 (36.4)	60 (28.0)
Not Selected	48 (92.3)	99 (79.8)	28 (62.6)	154 (72.0)
Left Fallopian Tube				
Selected	4 (7.7)	22 (17.7)	13 (29.6)	61 (28.5)
Not Selected	48 (92.3)	102 (82.3)	31 (70.5)	153 (71.5)
Unknown Fallopian Tube				
Selected	5 (9.6)	10 (8.1)	6 (13.6)	20 (9.4)
Not Selected	47 (90.4)	114 (91.9)	38 (86.4)	194 (90.7)
Uterus				
Selected	17 (32.7)	52 (41.9)	22 (50.0)	142 (66.4)
Not Selected	35 (67.3)	72 (58.1)	22 (50.0)	72 (33.6)
Vagina				
Selected	4 (7.7)	9 (7.3)	2 (4.6)	41 (19.2)
Not Selected	48 (92.3)	115 (92.7)	42 (95.5)	173 (80.8)
Pouch of Douglas				
Selected	17 (32.7)	5 (4.0)	7 (15.9)	82 (38.3)
Not Selected	35 (67.3)	119 (96.0)	37 (84.1)	132 (61.7)
Digestive Tract				
Selected	7 (13.5)	12 (9.7)	20 (45.5)	116 (54.2)
Not Selected	45 (86.5)	112 (90.3)	24 (54.6)	98 (45.8)

TABLE VI DEMOGRAPHICS BY SUBTYPE (N = 434) (continued)

Variable	(SPE N = 52)	(OMA N = 124)	(DE N = 44)	(Multiple N = 214)
	N(%)	N(%)	N(%)	N(%)
Abdominal Wall				
Selected	17 (32.7)	16 (12.9)	10 (22.7)	117 (54.7)
Not Selected	35 (67.3)	108 (87.1)	34 (77.3)	97 (45.3)
Bladder				
Selected	9 (17.3)	11 (8.9)	18 (40.9)	93 (43.5)
Not Selected	43 (82.7)	113 (91.1)	26 (59.1)	121 (56.5)
Ureters				
Selected	2 (3.9)	4 (3.2)	4 (9.1)	54 (25.2)
Not Selected	50 (96.2)	120 (96.8)	40 (90.9)	160 (74.8)
Kidney				
Selected	0 (0.0)	1 (0.8)	2 (4.6)	8 (3.7)
Not Selected	52 (100.0)	123 (99.2)	42 (95.5)	206 (96.3)
Uterosacral Ligaments				
Selected	9 (17.3)	1 (0.8)	4 (9.1)	71 (33.2)
Not Selected	43 (82.7)	123 (99.2)	40 (90.9)	143 (66.8)
Round Ligaments				
Selected	3 (5.8)	0 (0.0)	1 (2.3)	39 (18.2)
Not Selected	49 (94.2)	124 (100.0)	43 (97.7)	175 (81.8)
Diaphragm				
Selected	0 (0.0)	3 (2.4)	1 (2.3)	21 (9.8)
Not Selected	52 (100.0)	121 (97.6)	43 (97.7)	193 (90.2)
Other Location				
Selected	5 (9.6)	1 (0.8)	5 (11.4)	26 (12.2)
Not Selected	47 (90.4)	123 (99.2)	39 (88.6)	188 (87.9)
Have Surgical Reports				
Yes	37 (71.2)	58 (46.8)	25 (56.8)	158 (73.8)
No	15 (28.9)	66 (53.2)	19 (43.2)	56 (26.2)
Race				
White	45 (86.5)	91 (73.4)	33 (75.0)	174 (81.3)
Other Race	2 (3.9)	4 (3.2)	1 (2.3)	17 (7.9)
Black	1 (1.9)	7 (5.7)	4 (9.1)	8 (3.7)
AAPI	4 (7.7)	22 (17.7)	6 (13.6)	15 (7.0)
BMI				
< 18.5	4 (7.7)	5 (4.0)	3 (6.8)	12 (5.6)
18.5 - 24.9	18 (34.6)	47 (37.9)	13 (29.6)	95 (44.4)
25-29.9	15 (28.9)	46 (37.1)	19 (43.2)	50 (23.4)

TABLE VI DEMOGRAPHICS BY SUBTYPE (N = 434) (continued)

Variable	SPE N = 52	OMA N = 124	DE N = 44	Multiple N = 214
	N(%)	N(%)	N(%)	N(%)
>=30	15 (28.9)	26 (21.0)	9 (20.5)	57 (26.6)
Diagnostic Delay				
Incidental or < 1 Year	10 (19.2)	23 (18.6)	11 (25.0)	22 (10.3)
1-5 Years	15 (28.9)	45 (36.3)	13 (29.6)	35 (16.4)
6-10 Years	10 (19.2)	22 (17.7)	11 (25.0)	44 (20.6)
11-15 Years	8 (15.4)	12 (9.7)	6 (13.6)	38 (17.8)
> 15 years	9 (17.3)	22 (17.7)	3 (6.8)	75 (35.1)
Early Menarche				
Before Age 12	11 (21.2)	28 (22.6)	9 (20.5)	59 (27.6)
Age 12 or Later	41 (78.9)	96 (77.4)	35 (79.6)	155 (72.4)
Number of Pregnancies				
0	32 (61.5)	66 (53.2)	25 (56.8)	127 (59.4)
1	8 (15.4)	13 (10.5)	3 (6.8)	25 (11.7)
2+	12 (23.1)	45 (36.3)	16 (36.4)	62 (29.0)
Gender				
Cis woman	48 (92.3)	123 (99.2)	44 (100.0)	209 (97.7)
Other	4 (7.7)	1 (0.8)	0 (0.0)	5 (2.3)
Sexuality				
Heterosexual/Straight	36 (69.2)	95 (76.6)	33 (75.0)	156 (72.9)
Other	16 (30.8)	29 (23.4)	11 (25.0)	58 (27.1)
Age Diagnosed				
Less than 18	6 (11.5)	7 (5.7)	4 (9.1)	11 (5.1)
18 - 35	42 (80.8)	90 (72.6)	38 (86.4)	165 (77.1)
36-45	2 (3.9)	20 (16.1)	2 (4.6)	34 (15.9)
46 and up	2 (3.9)	7 (5.7)	0 (0)	4 (1.9)
Income Levels				
60k +	35 (67.3)	67 (54.0)	25 (56.8)	152 (71.0)
30k to 59K	11 (21.2)	34 (27.4)	15 (34.1)	36 (16.8)
Less than 30k	6 (11.5)	23 (18.6)	4 (9.1)	26 (12.2)
Employment				
Employed Full Time	32 (61.5)	75 (60.5)	31 (70.5)	124 (57.9)
Employed Part Time	6 (11.5)	25 (20.2)	4 (9.1)	31 (14.5)
Unemployed, Student, Retired, or Homemaker	11 (21.2)	17 (13.7)	8 (18.2)	45 (21.0)
Disabled	3 (5.8)	7 (5.7)	1 (2.3)	14 (6.5)

TABLE VI DEMOGRAPHICS BY SUBTYPE (N = 434) (continued)

Variable	SPE N = 52	OMA N = 124	DE N = 44	Multiple N = 214
	N(%)	N(%)	N(%)	N(%)
Education				
Bachelor's Degree or Higher	41 (78.9)	74 (59.7)	24 (54.6)	166 (77.6)
Some College	9 (17.3)	42 (33.9)	18 (40.9)	40 (18.7)
High School Degree and Less	2 (3.9)	8 (6.5)	2 (4.6)	8 (3.7)
Smoking Status				
Never Smoker	42 (80.8)	82 (66.1)	26 (59.1)	163 (76.2)
Started at 18 or older	6 (11.5)	18 (14.5)	9 (20.5)	20 (9.4)
Started Before 18	4 (7.7)	24 (19.4)	9 (20.5)	31 (14.5)
Alcohol Use				
Non-Drinker	19 (36.5)	54 (43.6)	23 (52.3)	91 (42.5)
Light Drinker	22 (42.3)	48 (38.7)	13 (29.6)	107 (50.0)
Moderate/Heavy Drinker	11 (21.2)	22 (17.7)	8 (18.2)	16 (7.5)
Lived in Rural Area > 1 Year				
Never	35 (67.3)	89 (71.8)	32 (72.7)	133 (62.2)
18 or Older	4 (7.7)	7 (5.7)	5 (11.4)	32 (15.0)
Before 18	13 (25.0)	28 (22.6)	7 (15.9)	49 (22.9)
Ever Breast/Chest Fed				
No	12 (23.1)	18 (14.5)	6 (13.6)	28 (13.1)
Yes	8 (15.4)	40 (32.3)	13 (29.6)	59 (27.6)
Never Pregnant	32 (61.5)	66 (53.2)	25 (56.8)	127 (59.4)
Number of Comorbidities				
0	5 (9.6)	18 (14.5)	3 (6.8)	20 (9.4)
1	6 (11.5)	27 (21.8)	14 (31.8)	11 (5.1)
2	7 (13.5)	16 (12.9)	8 (18.2)	26 (12.2)
3	11 (21.2)	18 (14.5)	2 (4.6)	35 (16.4)
4 or More	23 (44.2)	45 (36.3)	17 (38.6)	122 (57.0)
Family History				
Any Family History	34 (65.4)	60 (48.4)	19 (43.2)	136 (63.6)
No Known Family History	18 (34.6)	64 (51.6)	25 (56.8)	78 (36.5)
Surgical Stage				
Not Mentioned	16 (30.8)	28 (22.6)	5 (11.4)	50 (23.4)
Stage I	12 (23.1)	16 (12.9)	5 (11.4)	10 (4.8)
Stage II	13 (25.0)	29 (23.4)	11 (25.0)	27 (12.6)
Stage III	2 (3.9)	7 (5.7)	9 (20.5)	35 (16.4)
Stage IV	0 (0.0)	16 (12.9)	5 (11.4)	60 (28.0)
Unknown	9 (17.3)	28 (22.6)	9 (20.5)	32 (15.0)

TABLE VI DEMOGRAPHICS BY SUBTYPE (N = 434) (continued)

Variable	SPE N = 52	OMA N = 124	DE N = 44	Multiple N = 214
	N(%)	N(%)	N(%)	N(%)
Age				
Mean	32.4 (SD 10.0)	39.2 (SD 12.4)	34.4 (SD 11.4)	37.8 (SD 10.3)
Year of Diagnosis				
Mean	2016 (SD 6.9)	2012 (SD 9.1)	2013 (SD 10.1)	2013 (SD 10.0)

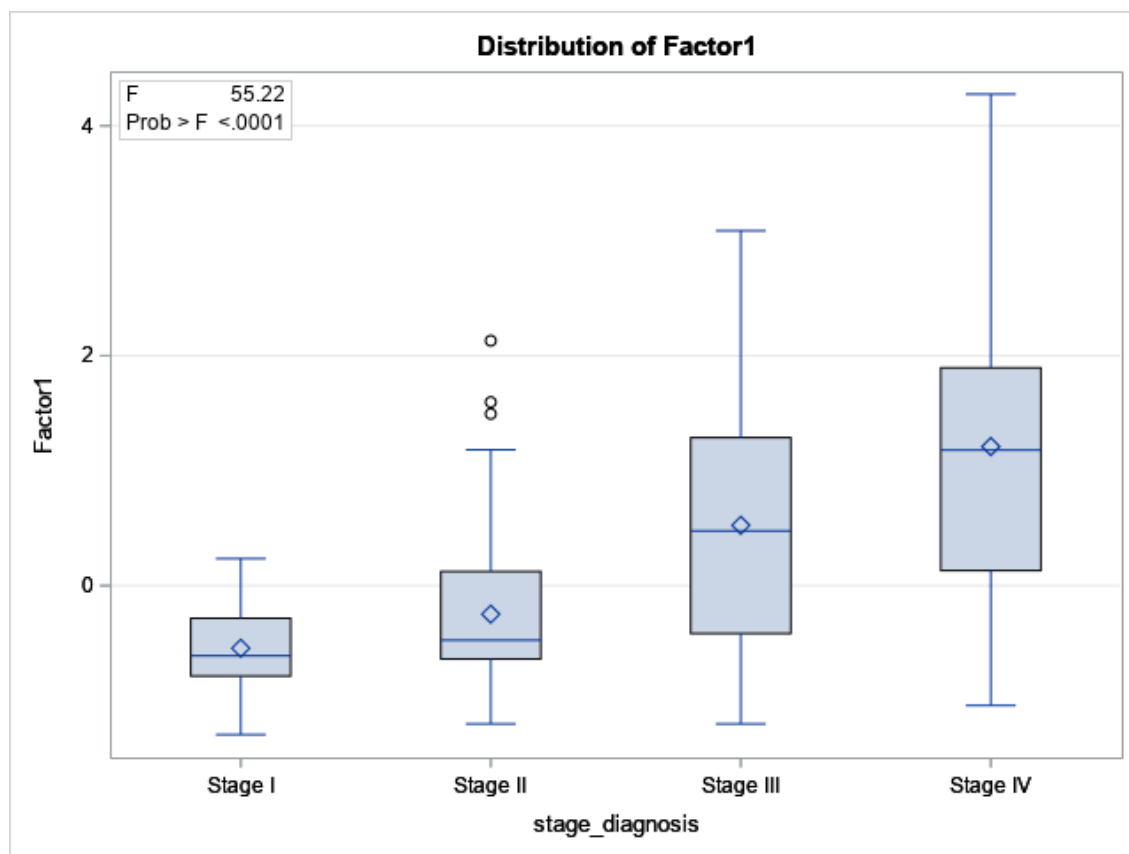


Figure 4. Digestive-urinary and surgical stage (unadjusted)

**TABLE VII SURGICAL STAGE AND DIGESTIVE-URINARY FACTOR LEAST SQUARES MEANS
ADJUSTMENT FOR MULTIPLE COMPARISONS AND COVARIATES**

Subtype	Estimate (95% CI)	P-Value
Stage I	-0.47 (-0.72, -0.21)	0.0004
Stage II	-0.23 (-0.41, -0.04)	0.02
Stage III	0.54 (0.31, 0.77)	<.0001
Stage IV	1.13 (0.92, 1.33)	<.0001

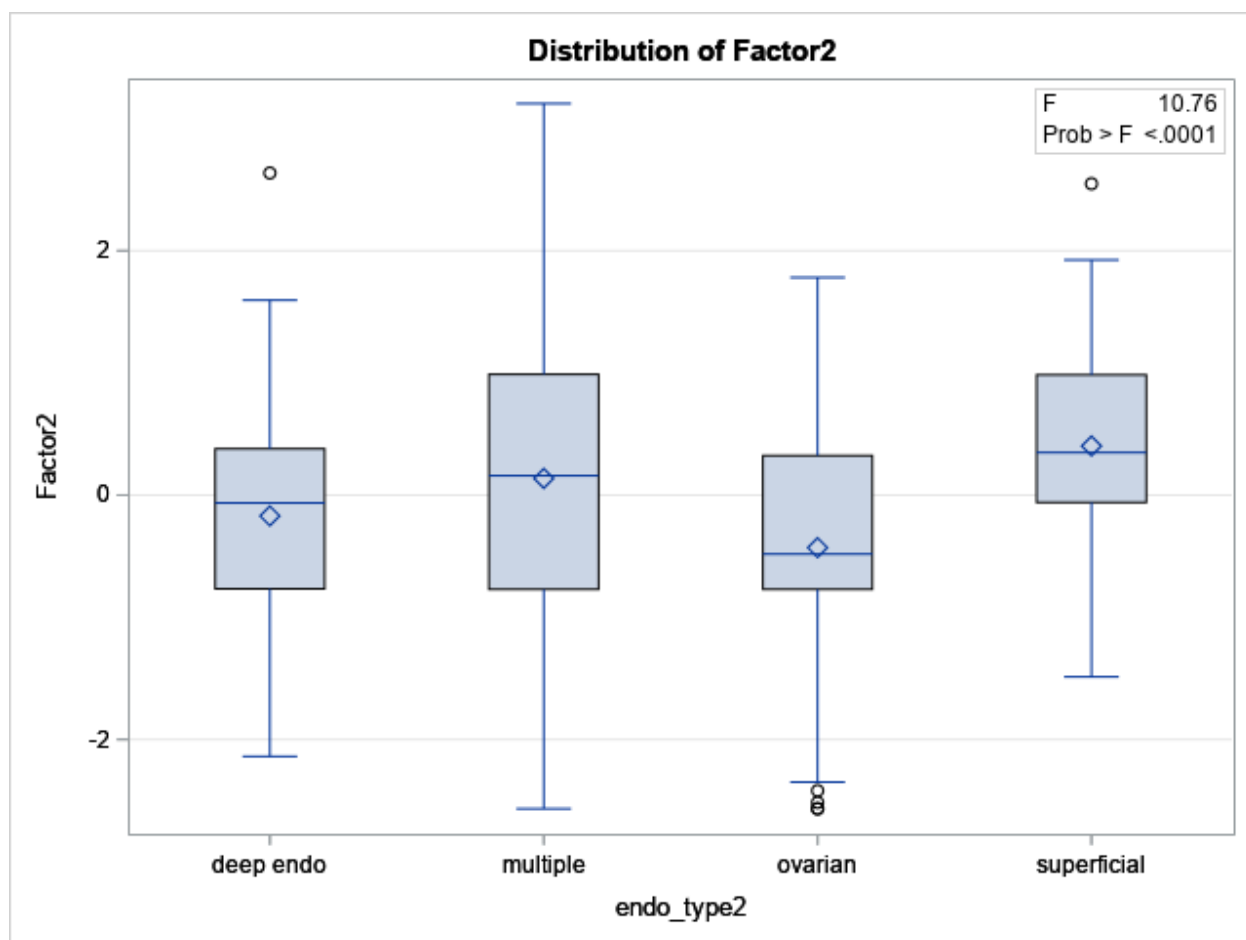


Figure 5. Reproductive and subtype (unadjusted)

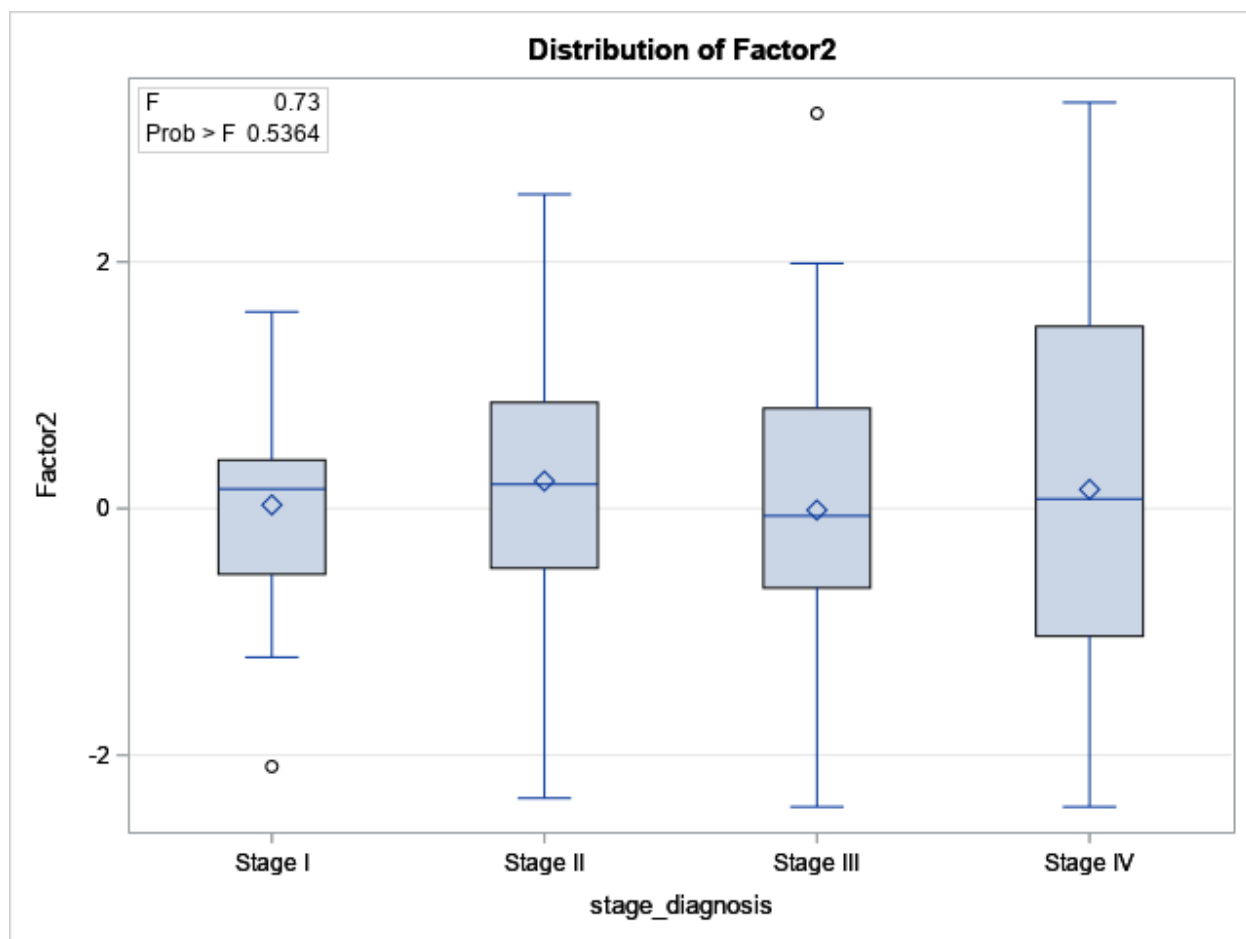


Figure 6. Reproductive and surgical stage (unadjusted)

**TABLE VIII SUBTYPES AND REPRODUCTIVE FACTOR LEAST SQUARES MEANS ADJUSTMENT
FOR MULTIPLE COMPARISONS AND COVARIATES**

Subtype	Estimate (95% CI)	P-Value
DE	-0.18 (-0.49, 0.13)	0.25
OMA	-0.37 (-0.56, -0.18)	0.08
SPE	0.32 (0.03, 0.61)	0.0001
Multiple Subtype	0.12 (-0.02, 0.26)	0.03

**TABLE IX SURGICAL STAGE AND REPRODUCTIVE FACTOR LEAST SQUARES MEANS
ADJUSTMENT FOR COVARIATES**

Stage	Estimate (95% CI)	P-Value
Stage I	-0.02 (-0.32, 0.28)	0.28
Stage II	0.25 (0.03, 0.47)	0.47
Stage III	-0.03 (-0.30, 0.24)	0.24
Stage IV	0.16 (-0.07, 0.40)	0.40

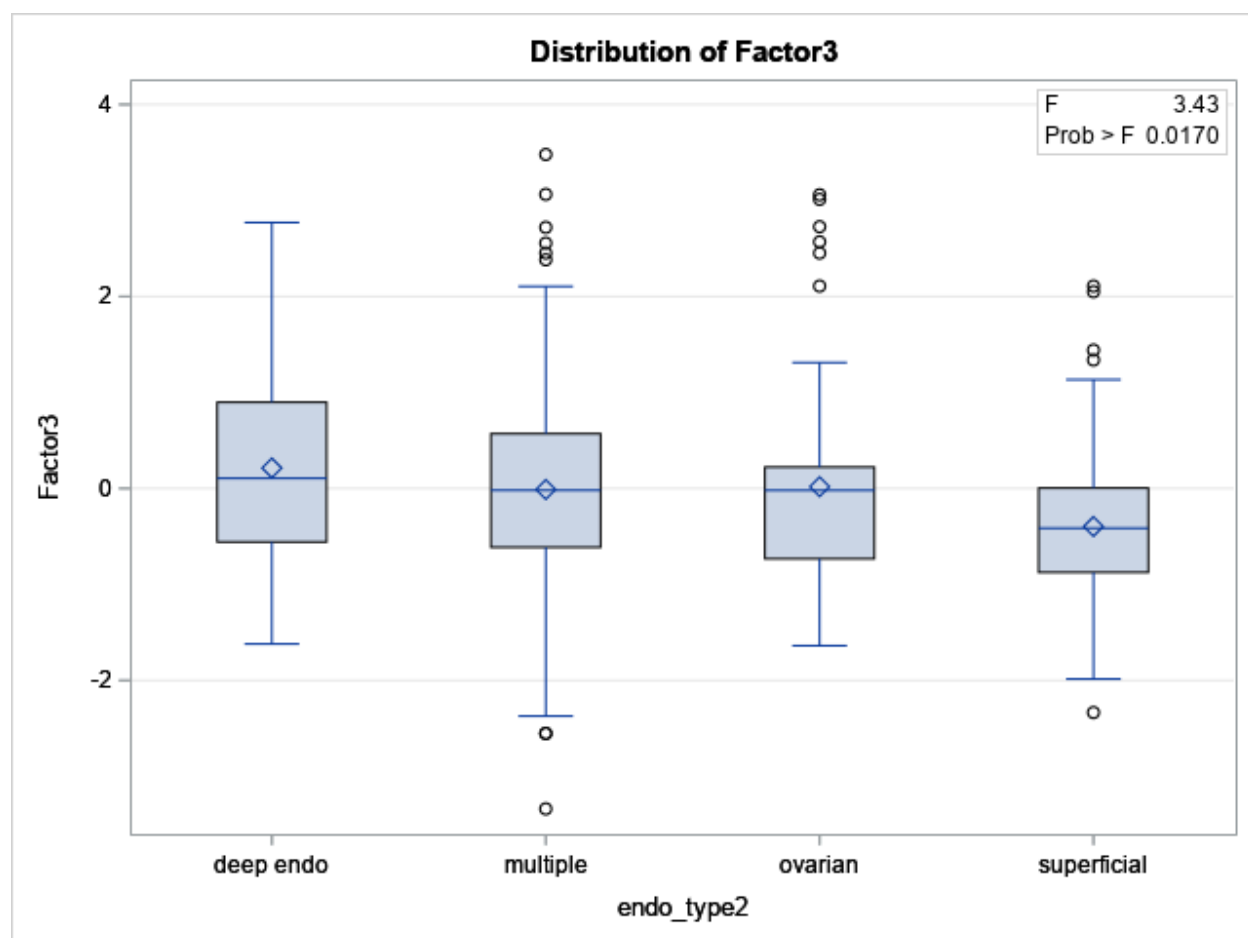


Figure 7. Douglas-ligaments and subtype (unadjusted)

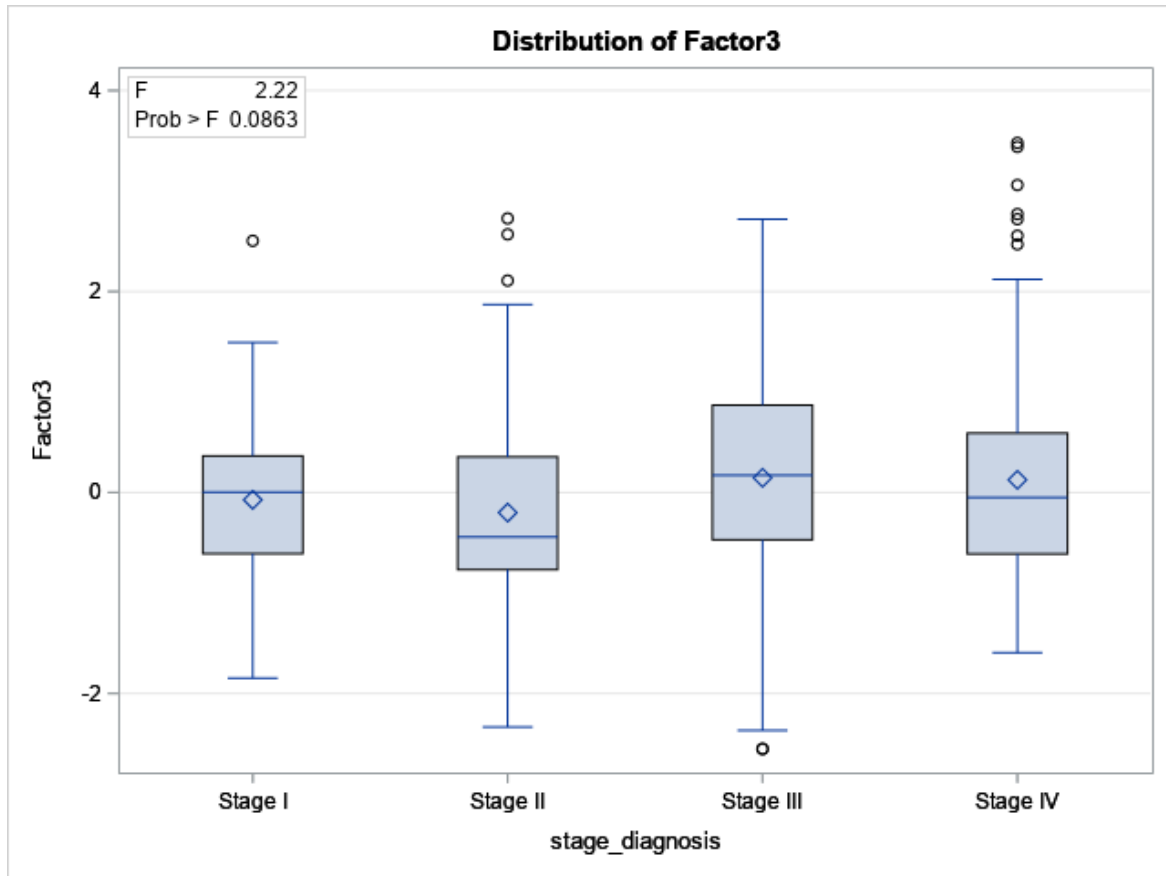


Figure 8. Douglas-ligaments and surgical stage (unadjusted)

**TABLE X SUBTYPES AND DOUGLAS-LIGAMENTS FACTOR LEAST SQUARES MEANS
ADJUSTMENT FOR MULTIPLE COMPARISONS AND COVARIATES**

Subtype	Estimate (95% CI)	P-Value
DE	0.23 (-0.06, 0.52)	0.1183
OMA	-0.02 (-0.20, 0.16)	0.8232
SPE	-0.34 (-0.61, -0.07)	0.0131
Multiple Subtype	-0.01 (-0.14, 0.13)	0.921

**TABLE XI SURGICAL STAGE AND DOUGLAS-LIGAMENTS FACTOR LEAST SQUARES MEANS
ADJUSTMENT FOR COVARIATES**

Stage	Estimate (95% CI)	P-Value
Stage I	-0.02 (-0.30, 0.26)	0.91
Stage II	-0.20 (-0.41, 0.001)	0.05
Stage III	0.16 (-0.09, 0.41)	0.21
Stage IV	0.08 (-0.14, 0.30)	0.45

Finally, in the Douglas-ligaments ANOVA subtype model, a significant p-value was found in the initial ANOVA model (0.02). In the Tukey's adjusted model, an association was found between DE and SPE. Then the model was adjusted for all covariates described previously and the association persisted (p-value 0.01) and an association was seen between DE and SPE again. In the surgical stage ANOVA model, no association was found in the initial model (p-value 0.10) so no Tukey's adjustment was performed on the unadjusted model. In the adjusted model, an association was found in the initial adjusted model (p-value 0.01), but this was not significant for surgical stage or any of the pairwise comparisons.

2. Individual Characteristics and Lesion Location

In the ordinal logistic model for the digestive-urinary factor, an inverse effect was found for those who identified as Asian-American or Pacific Islander (OR 0.47 95% CI 0.28, 0.80) vs those who identified as white, having a BMI between 25-29.9 (OR 0.65 95% CI 0.45, 0.93) vs a BMI between 18.5-24.9, and having an income of less than 30k (OR 0.59 95% CI 0.39, 0.90) vs having an income of 60k or more. An increasing association was seen with diagnostic delay vs

**TABLE XII ORDINAL LOGISTIC REGRESSION FOR QUARTILES OF THE DIGESTIVE-URINARY
FACTOR SCORE (N = 652)**

Variable	OR (95% CI)	P Value
Race		0.03
White	Ref	Ref
Other Race	0.69 (0.37, 1.30)	
Black	0.76 (0.34, 1.67)	
AAPI	0.47 (0.28, 0.80)	
BMI		0.08
< 18.5	1.21 (0.60, 2.47)	
18.5 - 24.9	Ref	Ref
25-29.9	0.65 (0.45, 0.93)	
>=30	0.91 (0.63, 1.30)	
Diagnostic Delay		0.0002
Incidental or < 1 Year	Ref	Ref
1-5 Years	1.38 (0.85, 2.26)	
6-10 Years	2.14 (1.27, 3.59)	
11-15 Years	2.79 (1.60, 4.88)	
> 15 years	2.96 (1.71, 5.12)	
Early Menarche		0.1
Before Age 12	1.33 (0.94, 1.88)	
Age 12 or Later	Ref	Ref
Number of Pregnancies		0.88
0	Ref	Ref
1	1.06 (0.65, 1.74)	
2+	1.09 (0.78, 1.53)	
Year of Diagnosis		0.26
Continuous	0.99 (0.96, 1.01)	
Age		0.003
Continuous	0.97 (0.95, 0.99)	
Income Levels		0.02
60k +	Ref	Ref
30k to 59K	0.71 (0.49, 1.03)	
Less than 30k	0.59 (0.39, 0.90)	
Lived in Rural Area > 1 Year		0.001
Never	Ref	Ref
18 or Older	2.48 (1.51, 4.06)	
Before 18	1.06 (0.75, 1.50)	

**TABLE XII ORDINAL LOGISTIC REGRESSION FOR QUARTILES OF THE DIGESTIVE-URINARY
FACTOR SCORE (N = 652) (continued)**

Variable	OR (95% CI)	P Value
Number of Comorbidities		0.002
0	Ref	Ref
1	0.73 (0.39, 1.37)	
2	1.18 (0.66, 2.12)	
3	1.27 (0.72, 2.26)	
4 or More	1.87 (1.13, 3.07)	

TABLE XIII ORDINAL LOGISTIC REGRESSION FOR QUARTILES OF REPRODUCTIVE FACTOR SCORE (N = 652)

Variable	OR (95% CI)	P Value
Race		0.26
White	Ref	Ref
Other Race	0.93 (0.5, 1.73)	
Black	0.64 (0.3, 1.4)	
AAPI	0.63 (0.38, 1.04)	
BMI		0.05
< 18.5	0.99 (0.49, 1.98)	
18.5 - 24.9	Ref	Ref
25-29.9	0.97 (0.68, 1.38)	
>=30	0.63 (0.44, 0.9)	
Diagnostic Delay		0.22
Incidental or < 1 Year	Ref	Ref
1-5 Years	1.38 (0.86, 2.23)	
6-10 Years	1.4 (0.84, 2.32)	
11-15 Years	1.35 (0.78, 2.32)	
> 15 years	1.9 (1.12, 3.22)	
Early Menarche		0.28
Before Age 12	0.83 (0.59, 1.16)	
Age 12 or Later	Ref	Ref
Number of Pregnancies		0.28
0	Ref	Ref
1	1.32 (0.81, 2.15)	
2+	0.87 (0.63, 1.22)	
Year of Diagnosis		0.72
Continuous	1 (0.98, 1.03)	
Age		0.03
Continuous	0.98 (0.96, 1)	
Employment		0.04
Employed Full Time	Ref	Ref
Employed Part Time	0.74 (0.49, 1.11)	
Unemployed, Student, Retired, or Homemaker	1.45 (1.01, 2.09)	
Disabled	0.67 (0.3, 1.51)	
Family History		0.03
Any Family History	0.73 (0.54, 0.97)	
No Family History	Ref	Ref

an incidental finding, living in a rural area at 18 or older (OR 2.50 95% CI 1.50, 4.10) vs never having lived in a rural area, and having 4 more comorbidities (OR 1.99 9% CI 1.24, 9.86). No association was found with gender, sexuality, age diagnosed, employment, education, smoking status, alcohol use, breast or chest feeding, or family history.

In the ordinal logistic model for the reproductive factor, an inverse effect was found with having any family history (OR 0.73 95% CI 0.54, 0.97) vs having no family history. An increasing association was found with being unemployed, student, retired, or a homemaker (OR 1.45 95% CI 1.01, 2.09) vs being employed full time and having a BMI of greater than or equal to 30 (OR 0.63 95% CI 0.44, 0.90). No association was found with race, diagnostic delay, early menarche, number of pregnancies, year of diagnosis, gender, sexuality, age of diagnosis, income level, education, smoking status, alcohol use, living in a rural area, ever breast or chest fed, or number of comorbidities.

In the ordinal logistic model for the Douglas-ligaments factor, an increasing association was found with identifying as a sexuality other than heterosexuality (OR 1.45 95% CI 1.04, 2.02) vs identifying as heterosexual, being diagnosed between 36 and 45 (OR 2.01 95% CI 1.33, 3.06) vs being diagnosed between 18 and 35. No association was found with race, BMI, diagnostic delay, early menarche, number of pregnancies, early menarche, gender, age, employment, education, smoking, alcohol use, living in a rural area, ever breast or chest fed, number of comorbidities, or family history.

**TABLE XIV ORDINAL LOGISTIC REGRESSION FOR QUARTILES OF DOUGLAS-LIGAMENTS SCORE
(N = 652)**

Variable	Final Model	
	OR (95% CI)	P Value
Race		0.95
White	Ref	Ref
Other Race	1.07 (0.57, 1.98)	
Black	1.25 (0.57, 2.73)	
AAPI	0.99 (0.6, 1.63)	
BMI		0.26
< 18.5	0.72 (0.36, 1.46)	
18.5 - 24.9	Ref	Ref
25-29.9	1.32 (0.93, 1.89)	
>=30	1.15 (0.8, 1.63)	
Diagnostic Delay		0.001
Incidental or < 1 Year	Ref	Ref
1-5 Years	0.77 (0.48, 1.23)	
6-10 Years	1.51 (0.91, 2.51)	
11-15 Years	1.05 (0.61, 1.81)	
> 15 years	0.62 (0.37, 1.05)	
Early Menarche		0.8
Before Age 12	1.05 (0.75, 1.46)	
Age 12 or Later	Ref	Ref
Number of Pregnancies		0.56
0	Ref	Ref
1	0.79 (0.49, 1.28)	
2+	0.88 (0.64, 1.23)	
Year of Diagnosis		0.001
Continuous	0.97 (0.96, 0.99)	
Sexuality		0.03
Heterosexual/Straight	Ref	Ref
Other	1.45 (1.04, 2.02)	
Age Diagnosed		0.003
Less than 18	1.69 (0.88, 3.23)	
18 - 35	Ref	Ref
36-45	2.01 (1.33, 3.06)	
46 and up	0.67 (0.3, 1.51)	

D. Discussion

Endometriosis, despite its prevalence, continues to pose challenges for research due to various factors such as limited funding, methodological complexities in studying a surgically diagnosed disease, and institutional biases. For example, the literature suggests that existing categorization systems fail to adequately capture the true impact of the disease or its diverse presentations and symptoms within the body. This study identified three distinct factors that offer partial categorization of specific subtypes of the disease: digestive-urinary, reproductive, and Douglas-ligament factors.

The first factor, digestive-urinary, explained the largest proportion of total variance in lesion location (62%). Participants with multiple endometriosis lesion subtypes, followed by the deep endo (DE) subtype had significantly higher digestive-urinary factor levels, than those with SPE and OMA, regardless of adjustment for age, race, BMI, and income. Higher surgical stage was associated with higher digestive-urinary factor in a dose-dependent manner. Significant predictors of the digestive-urinary factor included longer diagnostic delay, living in a rural area as an adult, increasing number of comorbidities, higher income, white race, and younger age. This paints a potential profile of those who have may be linked to a highly monitored population, as discussed by Kvaskoff et al. and other studies, as well as having more economic privilege to pursue diagnosis (Kvaskoff et al. 2015; Kok et al. 2015; Surrey et al. 2018). Patients living a rural area may lack access to care due to lack of endometriosis specialists or surgical care which may increase diagnostic delay and exacerbate symptoms (As-Sanie et al. 2019). Patients who score highly in the digestive-urinary factor may have more severe disease based on both subtype and surgical stage, and so may require more specialized care during treatment.

If verified, understanding that patients fitting this profile may have a higher likelihood of having more complex disease has the potential to improve diagnosis and surgical planning.

The reproductive factor explained 49% of the variation in lesion locations and was highest in participants with superficial endometriosis (SPE). This factor did not have an association with the OMA subtype, which is unexpected as the factor has high loadings on the ovaries. However, the positive association with SPE indicates some additional factors may be involved, which the current subtyping system is not taking into consideration, or that clinicians may not be appropriately recognizing and categorizing endometriosis subtypes. It may also be that OMA lesions tend to be more superficial. No association was found between the reproductive factor with any level of surgical staging in the adjusted model. The factor also explained substantially less of the variance than the digestive-urinary factor and so may not explain sufficient variance accurately capture these lesion locations. Participants with higher levels of the reproductive factor were characterized by less stable employment, longer diagnostic delay, less obesity, and with no known family history of endometriosis. These individuals may be less privileged and have more difficulty accessing care or may be less knowledgeable about the disease from lack of exposure through family. Given the lengthy lag time to diagnosis and the under researched nature of endometriosis, patients often need to advocate strongly for care, which may influence associations with certain variables like family history. They may also differ in other important socioeconomic ways which this study did not have sufficient sample sizes to fully explore.

The Douglas-ligaments factor levels were highest in DE and lowest in SPE, suggesting an association with deeper disease. However, no association was found with any surgical stage

and the Douglas-ligaments factor. DE may be diagnosed based on lesions in the Pouch of Douglas as well as the uterosacral ligaments, which overlaps with this factor, and so the lack of association with DE is unexpected and would warrant further exploration in future research. This factor also explained a relatively small amount of the variance observed and so this factor may also not represent as promising of a factor when considering potential for guiding care. Higher Douglas-ligaments factor was associated with identifying as a sexuality other than heterosexual as well as being diagnosed during the reproductive years. This may indicate a difference by which those with high Douglas-ligaments score interact with the healthcare system, as those who are not heterosexual may seek care in ways that are distinct from those who identify as heterosexual, especially during the reproductive years. People throughout the LGBTQIA+ community may have different care seeking behaviors but this study did not have sufficient sample size to explore this further.

1. Strengths and Limitations

This study has limitations, including limiting to surgically diagnosed individuals, the possibility of unreported lesion locations due to limited exploration or patient recall, and the reliance on self-reported data for lesion locations and demographic factors, which may be susceptible to recall bias. Selection bias may also result from the use of complete case analysis as those who were missing on the covariates may differ from those who completed all relevant questions. We note that the mean digestive-urinary factor was significantly higher in complete cases compared with those excluded due to missing covariates, but differences were not found for the other two factors. This supports further evaluation of these hypotheses using other statistical methodology to address missingness, such as multiple imputation methods.

Furthermore, the targeted social media groups used for recruitment may differ from the broader endometriosis patient population, potentially introducing selection bias. Additionally, those who frequent social media groups may differ from all those who present with endometriosis and those in social media groups may be younger, more likely to live in areas with better internet access, or work in different professional areas than all people with endometriosis.

The study's strengths lie in its use of a validated endometriosis survey as the foundation, a larger and more diverse sample of participants compared to prior research predominantly focused on white individuals, inclusion of novel demographic factors (e.g., sexuality and gender), and detailed information on smoking initiation and rural residency.

Future studies should consider incorporating factor analysis and similar methodologies to explore latent characteristics of endometriosis lesions, facilitating the development of improved classification schemes. These findings underscore the deficiencies in current classification systems and suggest the potential for leveraging demographic factors in surgical planning, an avenue that warrants further investigation. Enhanced understanding of the association between demographic factors and endometriosis lesion location may lead to improved diagnostic and surgical planning tools. Additionally, future studies should investigate the interaction between endometriosis patients and the healthcare system and how symptoms and outcomes are influenced by this experience, as well as validate and ensure better understanding of surgical stage and subtypes within surgical records.

2. Conclusions

This is the first study to use factor analysis to group endometriosis lesion locations and subsequently explore the associations of the factors with participant characteristics in a large cross-sectional survey of endometriosis patients. Most importantly, we found both overlap with existing methods of endometriosis classifications as well as differences not previously seen before, offering an important glimpse into the gaps in our current systems of classification. This study highlights an important opportunity for healthcare providers where patients presenting with suspected endometriosis could be examined based on their history and demographics and have their surgeries targeted for these lesion location factors. This may include by having interdisciplinary teams brought in for suspected lesions on the digestive or urinary tracts based on demographics or planning to focus on specific areas of the body for more thorough examination for lesions based on the patient profile. Additional research should examine methods of ensuring that all lesion locations are identified and documented as well as further build upon this method of factor analysis in different populations.

IV IMPACT OF ENDOMETRIOSIS LESION LOCATION FACTOR ON PRESENTING SYMPTOMS

A. Rationale

Endometriosis, a prevalent and debilitating gynecological condition characterized by the growth of endometrial-like tissue outside the uterine cavity, remains poorly understood, leading to limited treatment options and significant delays in diagnosis (Zondervan, Becker, and Missmer 2020; Della Corte et al. 2020; Sperschneider et al. 2019). It affects approximately 10% of individuals AFAB and has an average diagnostic delay of 8 to 10 years (Federica Facchin et al. 2019; Armour et al. 2019; Kvaskoff et al. 2015). The underlying causes of the disease are still not well-established (Zondervan, Becker, and Missmer 2020; Bulun 2009). Certain risk factors, such as early age at menarche, short menstrual cycles, dioxin exposure, family history, and moderate alcohol intake, have been identified, but a comprehensive understanding of the etiology is lacking (Gerlinger et al. 2010; Bulun 2009; Giudice and Kao 2004; Porpora et al. 1999).

The symptoms of endometriosis are diverse and include dysmenorrhea, dyspareunia, dysuria, dyschezia, and chronic fatigue. The disease is also associated with various other conditions, including cardiovascular disease; ovarian, breast, and thyroid cancer; atopy; and autoimmune disorders (Bontempo and Mikesell 2020; Ahn, Singh, and Tayade 2017; Kvaskoff et al. 2015). Moreover, endometriosis significantly contributes to infertility (Koninckx et al. 2011; P. Vercellini et al. 2009; K. D. Ballard et al. 2008). Patients typically seek medical attention due to pain, infertility, or may incidentally be diagnosed during unrelated surgical procedures. Patients presenting with infertility tend to experience shorter diagnostic delays compared to those presenting with pain (Kvaskoff et al. 2015).

Endometriosis is a complex and heterogeneous disease that poses challenges in both diagnosis and research. Lesions have been found in numerous anatomical locations, including the pelvic cavity and even the brain (Zondervan, Becker, and Missmer 2020; Shafrir et al. 2021; Fuldeore and Soliman 2017; Zhang et al. 2021; Zondervan, Cardon, and Kennedy 2002). However, it remains uncertain whether the pelvic cavity is genuinely the most common location or if inadequate diagnostic techniques have influenced this observation (Fuldeore and Soliman 2017; Chapron et al. 2011; Simoens, Hummelshoj, and D'Hooghe 2007). Existing research and classification systems have attempted to categorize endometriosis lesions based on factors such as color, shape, depth, and location, but these approaches have proven insufficient due to the limited correlation between symptoms and disease extent (Shim, Laufer, and Grimstad 2020). This lack of clarity hinders the identification of distinct subpopulations within the disease (Shafrir et al. 2021; Zondervan, Cardon, and Kennedy 2002; Shim, Laufer, and Grimstad 2020; Ferrando, Chapman, and Pollard 2021; Jabr and Mani 2014; O. Bougie et al. 2019). Recognizing the importance of understanding endometriosis subtypes and phenotypes, the World Endometriosis Society has prioritized research in this area (Johnson et al. 2017).

One study involving 1,054 patients explored the association between lesion type, disease stage, and symptoms of endometriosis, identifying a correlation between lesions in the posterior cul-de-sac and painful intercourse. However, the study excluded patients who had received medical treatment for endometriosis, other than non-steroidal anti-inflammatory drugs (NSAIDs), in the six months preceding the study, limiting the generalizability of the findings. Furthermore, the study did not consider symptoms beyond pelvic pain or the social context in which patients lived (P. Vercellini et al. 2007). Similar limitations, such as restricted

scope and lack of social context, have been observed in other studies focusing mainly on pelvic pain and various endometriosis subtypes, yielding mixed results (P. Vercellini et al. 2007; Al-Obaidy and Idrees 2019; P. Viganò et al. 2004; Schliep et al. 2015). Additionally, a small prospective cohort study involving 116 patients found that those with rectal lesions were more likely to experience gastrointestinal issues, including constipation, pain during defecation, and appetite disorders (Roman et al. 2012).

B. Methods

1. Study Population

Participants were recruited through various endometriosis social media outlets, various research focused recruitment tools such as ResearchMatch, and flyers posted in the Chicago-area with a focus on the area around the University of Illinois Chicago to the heterogeneity of Symptoms, outcomes, and characteristics in Patients undergoing Treatment for Endometriosis Study (SpiTE). The recruitment window extended between June of 2022 and December of 2022. Participants were eligible if they were 18 years of age or older, live in the US, have surgically-confirmed diagnosis of endometriosis and knew where the endometriosis was found in the body. Participants completed the survey via RedCap based on the WERF ePHect clinical questionnaire. The purpose of this questionnaire is to enable robust epidemiological research using standardized, detailed clinical and phenotypic data in a way that is comparable across studies. The questionnaire was modified to add detailed questions on gender identity, race, ethnicity, and sexuality and some questions concerning menstrual characteristics were truncated or removed.

2. Symptom Classification and Lesion Factor Description

Participants were asked for the symptom which prompted them to seek diagnosis: infertility or pain (pelvic or otherwise). These symptoms at presentation were not mutually exclusive, with 571/616 presenting with pain and 124/616 presenting with infertility.

Lesion locations were grouped using exploratory factor analysis to reduce the dimensionality of the data. The exploratory factor analysis has been described in Chapter III of this dissertation. In summary, the three factors can be described as follows: digestive-urinary factor, associated with participants who are more likely to be more complex cases and have longer diagnostic delay; reproductive factor, associated with participants who are less educated individuals with less significant disease and the Douglas-ligaments factor, associated with participants who had lower socioeconomic status (SES), a younger age at diagnosis, and more severe disease. The urinary-digestive factor had high loadings of locations on the digestive tract (0.5), bladder (0.5), and ureters (0.5). The reproductive factor had high loadings on the fallopian tubes (0.6) and ovaries (0.6). The Douglas-ligaments factor had high loadings on the uterosacral ligaments (0.7), pouch of Douglas (0.6), and round ligaments (0.5). Lesion locations were not mutually exclusive as many participants reported multiple lesion locations.

3. Statistical Methods

Logistic regression was used to model the associations of the three lesion factors simultaneously with pain vs. no pain at presentation and with infertility vs. no infertility at presentation. In addition, age, age at first symptoms, any BMI, bowel movement symptoms, cyclic pelvic pain, diagnostic delay, age of menarche, gastrointestinal (GI) symptoms, noncyclic pelvic pain, pain with intercourse, number of pregnancies, pregnancy complications, race and

ethnicity, and year of diagnosis were considered as covariates based on their potential relationship with both the outcome (presenting symptom) and exposure (factor score). Based on prior literature, race and ethnicity, BMI, diagnostic delay, menstrual history, year of diagnosis and parity were selected as *a priori* variables. History of infertility was included in the pain presenting model but was not included in the infertility presenting model due to lack of information on timing of infertility. Interactions were explored with each factor and age at time of survey, race, and diagnostic delay in years using cross product variables for the factor and potential modifier. These interactions were selected based on their potential to affect how a participant may seek care. Potential interactions were removed if the p-value was less than 0.01 and potential confounders were removed using a 10% change rule after exploring interactions. All analyses were done in SAS 9.4.

C. Results

In this sample, 92.7% (n = 571) of participants presented with pain and only 7.3% (n = 45) presented with some other symptom. Additionally, 402 participants (65.3%) presented with pain only and not any other symptoms. Participants varied on certain characteristic including: average age, age at first symptoms, having any infertility, having worse bowel symptoms, having cyclic pain, gastrointestinal symptoms, non-cyclic pain, intercourse pain, having pregnancy complications.

The model exploring pain as a presenting symptom found that a higher reproductive factor score was associated with a higher odds of presenting with pain (OR 1.50, 95% CI 1.05, 2.15) controlling for all other factors, race, BMI, diagnostic delay, age, and age of menarche.

TABLE XV DEMOGRAPHICS BY PRESENTING SYMPTOM (N = 616)

Variable	Pain at Presenting (N = 571)	No Pain at Presenting (N = 45)	Infertility at Presenting (N = 492)	No Infertility at Presenting (N = 124)
Factor 1 Quartiles				
Q1	134 (23.5)	11 (24.4)	128 (26.0)	17 (13.7)
Q2	133 (23.3)	13 (28.9)	125 (25.4)	21 (16.9)
Q3	136 (23.8)	9 (20.0)	106 (21.5)	39 (31.5)
Q4	168 (29.4)	12 (26.7)	133 (27.0)	47 (37.9)
Factor 2 Quartiles				
Q1	144 (25.2)	16 (35.6)	112 (22.8)	48 (38.7)
Q2	141 (24.7)	12 (26.7)	131 (26.6)	22 (17.7)
Q3	137 (24.0)	11 (24.4)	129 (26.2)	19 (15.3)
Q4	149 (26.1)	6 (13.3)	120 (24.4)	35 (28.2)
Factor 3 Quartiles				
Q1	140 (24.5)	10 (22.2)	117 (23.8)	33 (26.6)
Q2	130 (22.8)	13 (28.9)	114 (23.2)	29 (23.4)
Q3	148 (25.9)	15 (33.3)	134 (27.2)	29 (23.4)
Q4	153 (26.8)	7 (15.6)	127 (25.8)	33 (26.6)
Race				
White	490 (85.8)	38 (84.4)	416 (84.6)	112 (90.3)
Other Race	81 (14.2)	7 (15.6)	76 (15.5)	12 (9.7)
BMI				
Continuous	27.5 (7.4)	26.0 (5.8)	27.4 (7.4)	27.3 (7.1)
Diagnostic Delay				
Continuous	10.1 (8.8)	9.5 (10.3)	9.6 (1.8)	11.9 (8.4)
Age of Menarche				
Continuous	12.6 (1.7)	13.0 (1.8)	12.6 (1.8)	12.6 (1.6)
Number of Pregnancies				
Continuous	1.2 (1.7)	1.1 (1.3)	1.1 (1.6)	1.7 (1.8)
Year of Diagnosis				
Continuous	2011 (10.8)	2009 (13.6)	2011 (10.7)	2009 (12.1)
Age				
Continuous	39.7 (12.8)	45.0 (16.2)	39.5 (13.2)	42.6 (12.4)
Age Symptoms Starts				
19 or Older	195 (34.2)	16 (35.6)	172 (35.0)	39 (31.5)
18 or Younger	331 (58.0)	17 (37.8)	269 (54.7)	79 (63.7)
Never Had Symptoms	45 (7.9)	12 (26.7)	51 (10.4)	6 (4.8)

TABLE XV DEMOGRAPHICS BY PRESENTING SYMPTOM (N = 616) (continued)

Variable	Pain at Presenting (N = 571)	No Pain at Presenting (N = 45)	Infertility at Presenting (N = 492)	No Infertility at Presenting (N = 124)
Any Infertility				
Yes	198 (34.7)	20 (44.4)	-	-
No	373 (65.3)	25 (55.6)	-	-
Any Worse Bowel Symptoms				
Yes	486 (85.1)	27 (60.0)	409 (83.1)	104 (83.9)
No	85 (14.9)	18 (40.0)	83 (16.9)	20 (16.1)
Any Cyclic Pain				
Yes	59 (90.9)	32 (71.1)	441 (89.6)	110 (88.7)
No	52 (9.1)	13 (28.9)	51 (10.4)	14 (11.3)
Any GI Symptoms				
Yes	135 (23.6)	6 (13.3)	114 (23.2)	27 (21.8)
No	436 (76.4)	39 (86.7)	378 (76.8)	97 (78.2)
Any Non-Cyclic Pain				
Yes	425 (74.4)	21 (46.7)	364 (74.0)	82 (66.1)
No	146 (25.6)	24 (53.3)	128 (26.0)	42 (33.9)
Any Intercourse Pain				
Yes	439 (76.9)	17 (37.8)	370 (75.2)	86 (69.4)
No	132 (23.1)	28 (62.2)	122 (24.8)	38 (30.7)
Pregnancy Complications				
No Complications	123 (21.5)	7 (15.6)	97 (19.7)	33 (26.6)
Any Pregnancy Complications	147 (25.7)	14 (31.1)	118 (24.0)	43 (34.7)
Never Pregnant	301 (52.7)	24 (53.3)	277 (56.3)	48 (38.7)

**TABLE XVI LOGISTIC REGRESSION FOR PAIN PRESENTING USING CONTINUOUS FACTORS
SCORE (N = 616)**

Variable	OR (95% CI)	P Value
Digestive-Urinary Factor		0.99
Continuous	1 (0.67, 1.51)	
Reproductive Factor		0.03
Continuous	1.5 (1.05, 2.15)	
Douglas-Ligaments		0.57
Continuous	1.12 (0.76, 1.65)	
Race		0.32
White	Ref	Ref
Other Race	0.6 (0.22, 1.63)	
BMI		0.1
Continuous	1.05 (0.99, 1.11)	
Diagnostic Delay		0.85
Continuous	1 (0.96, 1.03)	
Age of Menarche		0.74
Continuous	0.97 (0.78, 1.19)	
Number of Pregnancies		0.67
Continuous	1.05 (0.84, 1.32)	
Year of Diagnosis		0.2
Continuous	0.97 (0.93, 1.02)	
Age		0.02
Continuous	0.96 (0.92, 0.99)	
Worse Bowel Symptoms		0.01
Yes	2.8 (1.26, 6.22)	
No	Ref	Ref
Intercourse Pain		0.0002
Yes	3.95 (1.91, 8.15)	
No	Ref	Ref

The urinary-digestive factor (OR 1.00, 95% CI 0.67, 1.51) and the Douglas-ligaments factor (OR 1.12, 95% CI 0.76, 1.65) did not have an association with presenting pain in the final model. In addition, an association was found for presenting with pain and with having any worse bowel symptoms (OR 2.81, 95% CI 1.26, 6.22), and experiencing any intercourse pain (OR 3.95, 95% CI 1.91, 8.15). No interactions were found in this model.

Overall, 79.9% (n = 492) of participants presented with infertility and 20.1% (n = 124) presented with some other symptom. Only 21 participants (3.4%) presented with infertility only. The model exploring infertility as a presenting symptom found that a higher urinary-digestive factor score was associated with a higher odds of presenting with infertility (OR 1.23, (95% CI 1.01, 1.49) and a reproductive factor was associated with a reduced odds of presenting with infertility (OR 0.82, 95% CI 0.67, 1.00) in the final model controlling for the Douglas-ligaments factor, race, BMI, diagnostic delay, age, age of menarche, number of pregnancies, year of diagnosis, worse bowel symptoms, and non-cyclic pain. The Douglas-ligaments factor did not show a relationship with presentation for infertility. In addition, an association was found for presentation for infertility with diagnostic delay (OR 1.04, 95% CI 1.01, 1.07), number of pregnancies (OR 1.21, 95% CI 1.07, 1.37), and non-cyclic pain (OR 0.53, 95% CI 0.32, 0.86). No significant interactions were found in the infertility model.

D. Discussion

The findings of this study suggest a potential association between factor scores based on endometriosis lesion location and presenting with pain or with infertility. In the case of pain presentation, a higher reproductive lesion factor score was modestly linked to increased odds of presenting with pain. Previous research in this population indicated that individuals with a

TABLE XVII LOGISTIC REGRESSION FOR INFERTILITY PRESENTING USING CONTINUOUS FACTORS SCORE (N = 616)

Variable	OR (95% CI)	P Value
Digestive-Urinary Factor		0.04
Continuous	1.23 (1.01, 1.40)	
Reproductive Factor		0.049
Continuous	0.82 (0.67, 1)	
Douglas-Ligaments Factor		0.34
Continuous	0.9 (0.72, 1.12)	
Race		0.39
White	Ref	Ref
Other Race	1.37 (0.67, 2.8)	
BMI		0.45
Continuous	0.99 (0.96, 1.02)	
Diagnostic Delay		0.01
Continuous	1.04 (1.01, 1.07)	
Age of Menarche		0.5
Continuous	1.05 (0.92, 1.19)	
Number of Pregnancies		0.003
Continuous	1.21 (1.07, 1.37)	
Year of Diagnosis		0.09
Continuous	0.97 (0.94, 1.01)	
Age		0.32
Continuous	0.99 (0.96, 1.02)	
Non-Cyclic Pain		0.01
Yes	0.53 (0.32, 0.86)	
No	Ref	Ref

higher reproductive factor score had less significant disease and limited access to endometriosis specialists. It is plausible that these individuals may possess less knowledge or resources related to endometriosis, leading them to seek treatment for new or worsening pain. In addition, presenting with pain was associated with the presence of more severe bowel symptoms and pain during intercourse. These non-menstrual pain symptoms may be more influential in motivating individuals to seek treatment compared to cyclic pain associated with menstruation.

Regarding infertility presentation, a higher score in the digestive-urinary lesion factor and a lower score in the reproductive factor were associated with presenting with infertility rather than other symptoms. Individuals with a high digestive-urinary factor score are more likely to have complex cases and experience longer diagnostic delays. These individuals closely resemble the typical endometriosis patients described in the literature. This contrasts with individuals with a higher reproductive factor score, who may have limited access to specialized care. It is possible that individuals with higher digestive-urinary factor scores have greater access to infertility treatments that may not be available to others. However, it is important to note that both these associations are weak and may not be statistically significant due to their proximity to the null hypothesis.

Several limitations should be acknowledged in this study. The reliance on self-reported data for endometriosis lesion location and other covariates, the inclusion of only surgically diagnosed individuals in the US through an online cross-sectional survey, and incomplete information on socioeconomic status and privilege all restrict the generalizability of the results and the ability to thoroughly explore and describe these associations. We were also unable to

conduct analyses using only pain or only infertility presenting individuals due to small numbers of individuals who presented with only one symptom. Additionally, those who frequent social media groups may differ from all those who present with endometriosis and may overrepresent those who present with pain as those in social media groups may be younger, more likely to live in areas with better internet access, or work in different professional areas than all people with endometriosis and may be less likely to know if they are experiencing infertility if they have yet to attempt pregnancy. Conversely, strengths of this study include a diverse population, surgical information on lesion location, and details about the onset of symptoms and various types of pain. Future studies should aim to collect more comprehensive data on presenting symptoms and further investigate the latent factors underlying endometriosis lesion locations to gain deeper insights into the relationship between healthcare access and diagnostic pathways.

E. Conclusions

This study expands upon the previous research in this dissertation by extending the examination of lesion location to presenting symptom. Presenting symptom is a patient's first contact with the medical system and can change the diagnostic pathways. In this study, lesion location factors have an association with presenting symptom, particularly infertility presentation. Most interesting, the reproductive factor, with high loadings on the ovaries and fallopian tubes, was negatively associated with presenting with infertility though this may be a result of a bias due to the recruitment methods of this study as those who use social media may differ in important ways from other endometriosis patients. Future studies should more extensively characterize participant infertility and pain and assess temporal relationships by longitudinally examining the initiation of any potential endometriosis-associated symptom and

the time elapsed between initial symptoms and the onset of the symptom leading to seeking care. Future studies should also consider how these factors can influence healthcare provider's protocols and policy concerning presenting symptom and suspected lesion locations based on the factors described here. It may be possible for surgeries to be targeted for these lesion location factors.

V IMPACT OF ENDOMETRIOSIS LESION LOCATION FACTOR ON SURGICAL COMPLICATIONS

A. Rational

Endometriosis, a prevalent gynecological condition characterized by the growth of endometrial-like tissue outside the uterus, remains poorly understood (Zondervan, Becker, and Missmer 2020; Della Corte et al. 2020). It manifests through a range of symptoms including pelvic pain, both cyclic and non-cyclic, infertility, urinary and gastrointestinal symptoms, fatigue, and mental health issues (Della Corte et al. 2020; Sperschneider et al. 2019; Federica Facchin et al. 2019). These symptoms have significant social and economic implications, as chronic pain can adversely affect relationships and employment opportunities (Armour et al. 2019; Kvaskoff et al. 2015). Surgical laparoscopy remains the gold standard for diagnosis, although there is growing interest in exploring less invasive diagnostic methods such as imaging, symptomatology, or biomarkers (Kvaskoff et al. 2020; Gerlinger et al. 2010; Bulun 2009; Giudice and Kao 2004). Given the varied factors involved, including lesion locations, treatment techniques, and surgeon expertise, endometriosis patients are at risk of surgical complications (Porpora et al. 1999; Bontempo and Mikesell 2020; Ahn, Singh, and Tayade 2017; Koninckx et al. 2021).

Treatment options heavily rely on surgical interventions, particularly when first-line approaches like hormonal contraception and pain relievers prove ineffective. Surgical procedures involve either lesion ablation or excision by a skilled surgeon, although reoperation rates remain high (P. Vercellini et al. 2009; K. D. Ballard et al. 2008; Shafrir et al. 2021). Treatment outcomes often fall short of patients' expectations, leading to subsequent surgeries

or additional therapies to manage symptoms. Surgery holds particular importance since many medical treatments, such as hormonal or contraceptive therapies, can hinder a patient's fertility desires, thus necessitating a focus on surgical interventions for research purposes (Bontempo and Mikesell 2020; Fuldeore and Soliman 2017; Zhang et al. 2021; Zondervan, Cardon, and Kennedy 2002; Chapron et al. 2019). Many individuals report inadequate symptom control and require further treatments, including surgeries, even after receiving gold standard care (P. Vercellini et al. 2009; Della Corte et al. 2020).

Furthermore, limited research has explored the relationship between lesion location in endometriosis and surgical complications, with the primary focus on locations near the digestive tract, such as rectovaginal endometriosis or deep infiltrating disease (P. Vercellini et al. 2009; Simoens, Hummelshoj, and D’Hooghe 2007; Shim, Laufer, and Grimstad 2020; Ferrando, Chapman, and Pollard 2021). This limited focus may stem from the heightened sensitivity of these affected areas and the potential for adhesions, which can involve the bowel, bladder, or other extrapelvic regions (Brady, Missmer, and Laufer 2017; Moawad and Caplin 2013; Nisolle and Donnez 1997; Moawad and Caplin 2013). To date, no comprehensive studies have examined how lesion location relates to surgical complications, nor do we have a complete understanding of potential variations in complications across different populations.

B. Methods

1. Study Population

This study utilizes the SPiTE dataset. In SPiTE, participants were recruited through various endometriosis social media outlets, and various research focused recruitment tools such as ResearchMatch, and flyers posted in the Chicago-area with a focus on the area around

the University of Illinois Chicago. The recruitment window extended between June of 2022 and December of 2022. Participants were eligible if they were 18 years of age or older, live in the US, have surgically-confirmed diagnosis of endometriosis and knew where the endometriosis was found in the body. Participants completed the survey via RedCap based on the WERF ePHect clinical questionnaire. The purpose of this questionnaire is to enable robust epidemiological research using standardized, detailed clinical and phenotypic data in a way that is comparable across studies. The questionnaire was modified to add detailed questions on gender identity, race, ethnicity, and sexuality and some questions concerning menstrual characteristics were truncated or removed.

2. Factor Description

The factors have been described previously, but in summary factor one, digestive-urinary factor, are those who are more likely to be more complex cases and have longer diagnostic delay; factor two, the reproductive factor, are those who are less educated and with less significant disease, and factor three, Douglas-ligaments factor, are those who had lower SES, with a younger age at diagnosis and more severe disease. Factor one, the digestive-urinary factor, had high loadings of locations on the digestive tract (0.5), bladder (0.5), and ureters (0.5). Factor two, the reproductive factor, had high loadings on the fallopian tubes (0.6) and ovaries (0.6). Factor three, the Douglas-ligaments factor had high loadings on the uterosacral ligaments (0.7), pouch of Douglas (0.6), and round ligaments (0.5). Lesion locations were not mutually exclusive as many participants reported multiple lesion locations.

3. Statistical Analysis

Participants were asked about the number and type of complications they experienced. Information was also collected on race, BMI, diagnostic delay, age of menarche, number of pregnancies, year of diagnosis, number of comorbidities, number and type of endometriosis-related surgeries, alcohol use, smoking, experience with infertility, hormone use, and if their endometriosis lesions were removed during any of their surgeries. Of these covariates, alcohol use, BMI, diagnostic delay, age of menarche, race, number of pregnancies, smoking, and year of diagnosis were selected as *a priori* variables to remain in the model based on the literature. Potential interaction was also explored with each factor and diagnostic delay, number of endometriosis related surgeries, and race. These were selected as potential effect modifiers based on the potential for surgical complications. All analyses were done in SAS 9.4.

The outcome of the logistic regression was having any complications vs having no complications and the central exposures were the digestive-urinary factor, reproductive factor, and Douglas-ligaments factor as continuous scores, adjusting for the covariates described previously. Additionally, separate logistic regressions were constructed with individual complications as the outcomes: urinary, gastrointestinal, pain, and any other complications. The same set of covariates were used in each model. Finally, a negative binomial model was constructed with the number of complications as the outcome and using the same set of covariates. All potential interactions were assessed using a <0.01 cut off and a 10% change rule was used to assess potential confounding.

C. Results

Participants were more likely to have never had any complications related to their endometriosis surgeries (N = 502) than to have any complications (N = 146). Those with surgical complications were more likely to be white than those without surgical complications (93.8% vs 84.5%) and less likely to be never smokers (65.8% vs 72.9%). Most participants had more than one surgery type (71.2% in the surgical complication group and 50% in the no surgical complication group). Having any surgical complications was positively associated with the digestive-urinary factor (OR 1.46, 95% CI 1.20, 1.79) in the final model when controlling for the other two factor scores, race, BMI, diagnostic delay, age of menarche, number of pregnancies, year of diagnosis, alcohol use, number of comorbidities, and number of endometriosis-related surgeries. Surgical complications were also positively associated with year of diagnosis, number of comorbidities, number of endometriosis-related surgeries, and having started smoking before 18 and negatively associated with BMI (OR, 0.96 95% CI 0.93, 0.99). No significant associations were seen with the other factors or covariates.

Next, associations of individual complications with lesion factors were explored. In the urinary complications model, an association was found with the digestive-urinary factor (OR 1.68, 95% CI 1.33, 2.13) and an interaction was found with the Douglas-ligaments factor and diagnostic delay (Beta 0.05, p-value 0.002). A positive association was also seen with starting smoking at a young age and an inverse effect for being a moderate or heavy drinker. No other associations were found in this model.

TABLE XVIII DEMOGRAPHICS BY ANY SURGICAL COMPLICATIONS (N = 647)

Variable	Any Complications (N = 145)	No Complications (N = 502)
Digestive-Urinary Factor Quartiles		
Q1	18 (12.4)	122 (24.3)
Q2	18 (12.4)	129 (25.7)
Q3	39 (26.9)	126 (25.1)
Q4	70 (48.3)	125 (24.9)
Reproductive Factor Quartiles		
Q1	41 (28.3)	131 (26.1)
Q2	30 (20.7)	127 (25.3)
Q3	23 (15.8)	130 (25.9)
Q4	51 (35.2)	114 (22.7)
Douglas-Ligaments Factor Quartiles		
Q1	36 (24.8)	128 (25.5)
Q2	42 (29.0)	110 (21.9)
Q3	26 (17.9)	147 (29.3)
Q4	41 (28.3)	117 (23.3)
Race		
White	136 (93.8)	424 (84.5)
All Other	9 (6.2)	78 (15.5)
BMI		
Continuous	26.8 (7.8)	27.7 (7.2)
Diagnostic Delay		
Continuous	11.1 (8.6)	9.4 (8.7)
Age of Menarche		
Continuous	12.5 (1.6)	12.6 (1.8)
Number of Pregnancies		
Continuous	1.4 (1.8)	1.1 (1.6)
Year of Diagnosis		
Continuous	2011 (10.4)	2011 (10.9)
Number of Comorbidities		
Continuous	5.2 (3.0)	3.8 (2.9)
Number of Endometriosis Surgeries		
Continuous	2.6 (2.0)	1.8 (1.4)

TABLE XVIII DEMOGRAPHICS BY ANY SURGICAL COMPLICATIONS (N = 647) (continued)

Variable	Any Complications (N = 145)	No Complications (N = 502)
Alcohol Use		
Non-Drinker	63 (43.5)	210 (41.8)
Light Drinker	73 (50.3)	218 (43.4)
Moderate/Heavy Drinker	9 (6.2)	74 (14.7)
Smoking		
Never Smoker	95 (65.5)	366 (72.9)
Started Smoking at 18 or later	12 (8.3)	68 (13.6)
Started Smoking Before 18	38 (26.2)	68 (13.6)
Infertility		
Yes	43 (29.7)	174 (34.7)
No	102 (70.3)	328 (65.3)
Surgery Type		
Diagnostic Lap	32 (22.1)	114 (22.7)
Excision	3 (2.1)	40 (8.0)
Hysterectomy	3 (2.1)	34 (6.8)
Other Surgeries	3 (2.1)	63 (12.6)
Multiple Surgeries	104 (71.2)	251 (50.0)
Hormone Use		
Yes	134 (92.4)	394 (78.5)
No	11 (7.6)	108 (21.5)
Endometriosis Lesions Removed		
Yes	127 (87.6)	365 (72.7)
No	10 (6.9)	90 (17.9)
Unsure	8 (5.5)	47 (9.4)

TABLE XIX DEMOGRAPHICS BY SURGICAL COMPLICATIONS BY TYPE (N = 647)

Variable	Any Urinary Complications (N = 94)	No Urinary Complications (N = 553)	Any GI Complications (N = 83)	No GI Complications (N = 564)	Any Pain Complications (N = 110)	No Pain Complications (N = 537)	Any Other Complications (N = 45)	No Other Complications (N = 602)
Digestive-Urinary Factor Quartiles								
Q1	7 (7.5)	133 (24.1)	11 (13.3)	129 (22.9)	12 (10.9)	128 (23.8)	3 (6.7)	137 (22.8)
Q2	13 (13.8)	134 (24.2)	11 (13.3)	136 (24.1)	16 (14.6)	131 (24.4)	7 (15.6)	140 (23.3)
Q3	26 (27.7)	139 (25.1)	20 (24.1)	145 (25.7)	27 (24.6)	138 (25.7)	11 (24.4)	154 (25.6)
Q4	48 (51.1)	147 (26.6)	41 (49.4)	154 (27.3)	55 (50.0)	140 (26.1)	24 (53.3)	171 (28.4)
Reproductive Factor Quartiles								
Q1	27 (28.7)	145 (26.2)	18 (21.7)	154 (27.3)	28 (25.5)	144 (26.8)	16 (35.6)	156 (25.9)
Q2	19 (20.2)	138 (25.0)	21 (25.3)	136 (24.1)	26 (23.6)	131 (24.4)	9 (20.0)	148 (25.6)
Q3	11 (11.7)	142 (25.7)	14 (16.9)	139 (24.7)	16 (14.6)	137 (25.5)	6 (13.3)	147 (24.4)
Q4	37 (39.4)	128 (23.2)	30 (36.1)	135 (23.9)	40 (36.4)	125 (23.3)	14 (31.1)	151 (25.1)
Douglas-Ligaments Factor Quartiles								
Q1	27 (28.7)	137 (24.8)	19 (22.9)	145 (25.7)	28 (25.5)	136 (25.3)	9 (20.0)	155 (25.8)
Q2	19 (20.2)	123 (22.2)	21 (25.3)	131 (23.2)	30 (27.3)	122 (22.7)	16 (35.6)	136 (22.6)
Q3	11 (11.7)	156 (28.2)	14 (16.9)	159 (28.2)	20 (18.2)	153 (28.5)	5 (11.1)	168 (27.9)
Q4	37 (39.4)	137 (24.8)	29 (34.9)	129 (22.9)	32 (29.1)	126 (23.5)	15 (33.3)	143 (23.8)

TABLE XIX DEMOGRAPHICS BY SURGICAL COMPLICATIONS BY TYPE (N = 647) (continued)

Variable	Any Urinary Complications (N = 94)	No Urinary Complications (N = 553)	Any GI Complications (N = 83)	No GI Complications (N = 564)	Any Pain Complications (N = 110)	No Pain Complications (N = 537)	Any Other Complications (N = 45)	No Other Complications (N = 602)
Race								
White	86 (91.5)	474 (85.7)	77 (92.8)	483 (85.6)	103 (93.6)	457 (85.1)	43 (95.6)	517 (85.9)
All Other	8 (8.5)	79 (14.3)	6 (7.2)	81 (14.4)	7 (6.4)	80 (14.9)	2 (4.4)	85 (14.1)
BMI								
Continuous	26.6 (8.2)	27.7 (7.2)	27.2 (8.6)	27.6 (7.2)	27.1 (8.0)	27.6 (7.2)	27.9 (9.2)	27.5 (7.2)
Diagnostic Delay								
Continuous	11.4 (8.1)	9.5 (8.8)	11.3 (9.1)	9.6 (8.6)	11.9 (8.3)	9.4 (8.7)	11.6 (8.0)	9.7 (8.7)
Age of Menarche								
Continuous	12.6 (1.8)	12.6 (1.7)	12.6 (1.8)	12.6 (1.7)	12.4 (1.6)	12.6 (1.8)	12.3 (1.3)	12.6 (1.8)
Number of Pregnancies								
Continuous	1.4 (1.7)	1.2 (1.6)	1.5 (1.9)	1.2 (1.6)	1.4 (1.8)	1.2 (1.6)	1.9 (2.1)	1.1 (1.6)
Year of Diagnosis								
Continuous	2012 (10.7)	2011 (10.9)	2010 (11.3)	2011 (10.8)	2012 (9.8)	2011 (11.0)	2009 (11.0)	2011 (10.8)
Number of Comorbidities								
Continuous	5.1 (3.0)	4.0 (3.0)	5.9 (3.0)	3.9 (2.9)	5.5 (2.9)	3.9 (3.0)	5.4 (3.0)	4.1 (3.0)
Number of Endometriosis Surgeries								

TABLE XIX DEMOGRAPHICS BY SURGICAL COMPLICATIONS BY TYPE (N = 647) (continued)

Variable	Any Urinary Complications (N = 94)	No Urinary Complications (N = 553)	Any GI Complications (N = 83)	No GI Complications (N = 564)	Any Pain Complications (N = 110)	No Pain Complications (N = 537)	Any Other Complications (N = 45)	No Other Complications (N = 602)
Continuous	2.6 (2.1)	1.9 (1.5)	2.7 (2.0)	1.9 (1.5)	2.6 (1.9)	1.9 (1.5)	3.0 (2.3)	1.9 (1.5)
Alcohol Use								
Non-Drinker	47 (50.0)	226 (40.9)	38 (45.8)	235 (41.7)	51 (46.4)	222 (41.3)	19 (42.2)	254 (42.2)
Light Drinker	42 (44.7)	249 (45.0)	40 (48.2)	251 (44.5)	54 (49.1)	237 (44.1)	25 (55.6)	266 (44.2)
Moderate/ Heavy Drinker	5 (5.3)	78 (14.1)	5 (6.0)	78 (13.8)	5 (4.6)	78 (14.5)	1 (2.2)	82 (13.6)
Smoking								
Never Smoker	58 (61.7)	403 (72.9)	52 (62.7)	409 (72.5)	75 (68.2)	386 (71.9)	26 (57.8)	435 (72.3)
Started Smoking at 18 or later	10 (10.6)	70 (12.7)	7 (8.4)	73 (12.9)	8 (7.3)	72 (13.4)	3 (6.7)	77 (12.8)
Started Smoking Before 18	26 (27.7)	80 (14.5)	24 (28.9)	82 (14.5)	27 (24.6)	79 (14.7)	16 (35.6)	90 (15.0)
Infertility								
Yes	32 (34.0)	185 (33.5)	29 (34.9)	188 (33.3)	32 (29.1)	185 (34.5)	15 (33.3)	202 (33.6)
No	62 (66.0)	368 (66.6)	54 (65.1)	376 (66.7)	78 (70.9)	352 (65.6)	30 (66.7)	400 (66.5)
Surgery Type								
Diagnostic Lap	18 (19.2)	128 (23.2)	16 (19.3)	130 (23.1)	22 (20.0)	124 (23.1)	8 (17.8)	138 (22.9)
Excision	2 (2.1)	64 (11.6)	2 (2.4)	64 (11.4)	2 (1.8)	54 (11.9)	3 (6.7)	63 (10.5)
Hysterectomy	3 (3.2)	40 (7.2)	2 (2.4)	41 (7.3)	2 (1.8)	41 (7.6)	0 (0.0)	43 (7.1)

TABLE XIX DEMOGRAPHICS BY SURGICAL COMPLICATIONS BY TYPE (N = 647) (continued)

Variable	Any Urinary Complications (N = 94)	No Urinary Complications (N = 553)	Any GI Complications (N = 83)	No GI Complications (N = 564)	Any Pain Complications (N = 110)	No Pain Complications (N = 537)	Any Other Complications (N = 45)	No Other Complications (N = 602)
Other Surgeries	1 (1.1)	36 (6.5)	2 (2.4)	35 (6.2)	2 (1.8)	35 (6.5)	2 (4.4)	35 (5.8)
Multiple Surgeries	70 (74.5)	285 (51.5)	61 (73.5)	294 (52.1)	82 (74.6)	273 (50.8)	32 (71.1)	323 (53.7)
Hormone Use								
Yes	85 (90.4)	443 (80.1)	75 (90.4)	453 (80.3)	103 (93.6)	425 (79.1)	42 (93.3)	486 (80.7)
No	9 (9.6)	110 (19.9)	8 (9.4)	111 (19.7)	7 (6.4)	112 (20.9)	3 (6.7)	116 (19.3)
Endometriosis Lesions Removed								
Yes	81 (86.2)	411 (74.3)	74 (89.2)	418 (74.1)	95 (86.4)	397 (73.9)	38 (84.4)	454 (75.4)
No	9 (9.6)	91 (16.5)	5 (6.0)	95 (16.8)	9 (8.2)	91 (17.0)	6 (13.3)	94 (15.6)
Unsure	4 (4.3)	51 (9.2)	4 (4.8)	51 (9.0)	6 (5.5)	49 (9.1)	1 (2.2)	54 (9.0)

**TABLE XX LOGISTIC REGRESSION FOR HAVING ANY SURGICAL COMPLICATIONS USING
CONTINUOUS OF FACTORS SCORE (N = 647)**

Variable	OR (95% CI)	P Value
Urinary-Digestive Factor		0.0002
Continuous	1.46 (1.20, 1.79)	
Reproductive Factor		0.28
Continuous	1.11 (0.92, 1.34)	
Douglas-Ligaments Factor		0.87
Continuous	1.02 (0.83, 1.24)	
Race		0.12
White	Ref	Ref
Other Selections	0.54 (0.25, 1.18)	
BMI		0.02
Continuous	0.96 (0.93, 0.99)	
Diagnostic Delay		0.77
Continuous	1.00 (0.97, 1.02)	
Age of Menarche		0.61
Continuous	0.97 (0.85, 1.10)	
Number of Pregnancies		0.31
Continuous	1.07 (0.94, 1.23)	
Year of Diagnosis		0.02
Continuous	1.03 (1.01, 1.06)	
Number of Comorbidities		0.0002
Continuous	1.15 (1.07, 1.24)	
Number of Endometriosis Surgeries		0.002
Continuous	1.24 (1.08, 1.42)	
Alcohol Use		0.18
Non-Drinker	Ref	Ref
Light Drinker	1.11 (0.72, 1.71)	
Moderate/Heavy Drinker	0.52 (0.23, 1.17)	
Smoking		0.002
Never Smoker	Ref	Ref
Started Smoking at 18 or later	0.65 (0.31, 1.37)	
Started Smoking Before 18	2.26 (1.31, 3.92)	

In the gastrointestinal symptoms model, an association was found with the digestive-urinary factor (OR 1.56, 95% CI 1.26, 1.93) and a marginal association with the reproductive factor (OR 1.26, 95% CI 1.57) as well as an association with starting smoking before 18 (OR 2.56, 95% CI 1.36, 4.83). No interactions were found in this model.

In the pain complication model, an association was found with the digestive-urinary factor (OR 1.47, 95% CI 1.18, 1.82) as well as number of comorbidities (1.18, 95% CI 1.09, 1.28) and number of endometriosis-related surgeries (OR 1.28, 95% CI 1.10, 1.49). No other associations were found with the other covariates and no interactions were found.

Finally, in the other complications model, an association was found with the digestive-urinary factor (OR 1.67, 95% CI 1.28, 2.18) and starting smoking before 18 (OR 2.71, 95% CI 1.27, 5.78).

Lastly, the association was examined in terms of count of complications. As most participants had no complications, a negative binomial model was used. A positive association was seen with the digestive-urinary factor (Beta= 0.29, 95% CI 0.09, 0.50), number of comorbidities (Beta= 0.12, 95% CI 0.04, 0.20), and smoking before 18 (Beta = 0.93, 95% CI 0.33, 1.51). A negative association was found with having another surgery such as laparotomy cystectomy, appendectomy, or other surgery types vs diagnostic laparotomy (Beta= -1.50, 95% CI -2.51, -0.48). No other associations or interactions were found.

**TABLE XXI LOGISTIC REGRESSION FOR HAVING ANY SURGICAL COMPLICATIONS USING
CONTINUOUS OF FACTORS SCORE (N = 647)**

Variable	Urinary Model		GI Model		Pain Model		Other Complication Model	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Urinary-Digestive Factor		<.0001		<.0001		0.001		0.0002
Continuous	1.68 (1.33, 2.13)		1.56 (1.26, 1.93)		1.47 (1.18, 1.82)		1.67 (1.28, 2.18)	
Reproductive Factor		0.18		0.05		0.26		0.85
Continuous	1.18 (0.93, 1.49)		1.26 (1, 1.57)		1.13 (0.92, 1.38)		1.03 (0.78, 1.36)	
Douglas-Ligaments Factor		0.01		0.06		0.67		0.82
Continuous	Interaction		1.23 (0.99, 1.54)		1.05 (0.85, 1.3)		1.04 (0.77, 1.39)	
Race		0.73		0.57		0.27		0.38
White	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Other Selections	0.86 (0.36, 2.05)		0.76 (0.3, 1.94)		0.61 (0.25, 1.46)		0.51 (0.11, 2.28)	
BMI		0.12		0.75		0.06		0.87
Continuous	0.97 (0.93, 1.01)		0.99 (0.96, 1.03)		0.97 (0.93, 1)		1 (0.96, 1.05)	
Diagnostic Delay		0.75		0.72		0.86		0.91
Continuous	Interaction		1.01 (0.98, 1.04)		1 (0.97, 1.03)		1 (0.96, 1.04)	
Age of Menarche		0.66		0.6		0.42		0.53
Continuous	1.03 (0.89, 1.20)		1.04 (0.9, 1.21)		0.94 (0.82, 1.09)		0.94 (0.77, 1.15)	
Number of Pregnancies		0.47		0.7		0.22		0.06
Continuous	1.06 (0.90, 1.25)		1.03 (0.88, 1.21)		1.1 (0.95, 1.28)		1.2 (0.99, 1.46)	
Year of Diagnosis		0.17		0.89		0.002		0.78
Continuous	1.02 (0.99, 1.05)		1 (0.97, 1.02)		1.05 (1.02, 1.08)		1.01 (0.97, 1.04)	
Number of Comorbidities						<.0001		
Continuous					1.18 (1.09, 1.28)			

**TABLE XXI LOGISTIC REGRESSION FOR HAVING ANY SURGICAL COMPLICATIONS USING
CONTINUOUS OF FACTORS SCORE (N = 647) (continued)**

Variable	Urinary Model		GI Model		Pain Model		Other Complication Model	
	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value	OR (95% CI)	P Value
Number of Endometriosis Surgeries						0.001		
Continuous					1.28 (1.1, 1.49)			
Alcohol Use		0.04		0.35		0.19		0.2
Non-Drinker	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Light Drinker	0.70 (0.42, 1.16)		0.87 (0.52, 1.46)		1.01 (0.62, 1.63)		1.24 (0.63, 2.42)	
Moderate/Heavy Drinker	0.28 (0.10, 0.80)		0.47 (0.17, 1.31)		0.4 (0.14, 1.11)		0.2 (0.03, 1.61)	
Smoking		0.0003		0.01		0.04		0.02
Never Smoker	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Started Smoking at 18 or later	1.24 (0.55, 2.77)		0.91 (0.38, 2.2)		0.53 (0.22, 1.29)		0.71 (0.2, 2.6)	
Started Smoking Before 18	3.96 (2.01, 7.80)		2.56 (1.36, 4.83)		1.75 (0.95, 3.22)		2.71 (1.27, 5.78)	
Surgery Type		0.03						
Diagnostic Lap	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Excision	0.56 (0.14, 2.18)							
Hysterectomy	0.12 (0.01, 1.37)							
Other Surgeries	0.25 (0.05, 1.16)							
Multiple Surgeries	1.37 (0.72, 2.59)							
Interaction								
Diagnostic Delay*Douglas- Ligaments Beta Estimate	0.05							

**TABLE XXII NEGATIVE BINOMIAL MODEL FOR COUNT SURGICAL COMPLICATIONS USING
CONTINUOUS OF FACTORS SCORE (N = 647)**

Variable	Final Model	
	OR (95% CI)	P Value
Urinary-Digestive Factor		0.004
Continuous	0.29 (0.09, 0.50)	
Reproductive Factor		0.23
Continuous	0.13 (-0.08, 0.33)	
Douglas-Ligaments Factor		0.76
Continuous	0.03 (-0.17, 0.24)	
Race		0.96
White	Ref	Ref
Other Selections	-0.02 (-0.71, 0.67)	
BMI		0.14
Continuous	-0.02 (-0.05, 0.01)	
Diagnostic Delay		0.52
Continuous	-0.01 (-0.04, 0.02)	
Age of Menarche		0.39
Continuous	-0.05 (-0.18, 0.07)	
Number of Pregnancies		0.18
Continuous	0.09 (-0.04, 0.22)	
Year of Diagnosis		0.09
Continuous	0.02 (-0.003, 0.05)	
Number of Comorbidities		0.003
Continuous	0.12 (0.04, 0.20)	
Alcohol Use		0.29
Non-Drinker	Ref	Ref
Light Drinker	-0.001 (-0.45, 0.45)	
Moderate/Heavy Drinker	-0.59 (-1.36, 0.17)	
Smoking		0.005
Never Smoker	Ref	Ref
Started Smoking at 18 or later	-0.06 (-0.74, 0.62)	
Started Smoking Before 18	0.92 (0.33, 1.51)	
Surgery Type		0.002
Diagnostic Lap	Ref	Ref
Excision	-0.12 (-1.18, 0.94)	
Hysterectomy	-0.80 (-1.94, 0.34)	
Other Surgeries	-1.50 (-2.51, -0.48)	
Multiple Surgeries	0.30 (-0.21, 0.81)	

D. Discussion

Surgical interventions always carry a risk of complications, and endometriosis patients, in particular, face a high rate of reoperation, with estimates as high as 50% (Guo 2009; Falcone and Flyckt 2018). Consequently, this population is at a heightened risk of surgical complications. Moreover, the understanding of endometriosis lesion locations and classification systems with respect to surgical complications remains unclear. The findings of this study highlight a potential association between factor scores based on endometriosis lesion location and the occurrence of surgical complications. Across all analyses, the digestive-urinary factor showed a significant positive association with experiencing any type of complication as well as the number of complications. On the other hand, the reproductive factor displayed only marginal association with gastrointestinal symptoms, while the Douglas-ligaments factor was associated with urinary complications only in cases without diagnostic delay. Additionally, smoking has been identified as a risk factor for surgical complications, which consistently emerged in the models.

The digestive-urinary factor, previously associated with more complex cases and longer diagnostic delay, may be linked to intricate surgeries with a higher likelihood of complications. Individuals with higher scores in the digestive-urinary factor, characterized by high loadings on the digestive tract, bladder, and ureters, may be more vulnerable to complications due to greater diagnostic delay and having a greater number of comorbidities, as detailed in prior chapters.

This factor also explained most of the variance observed in the exploratory factor analysis (EFA). As seen in Chapter III, patients who score highly in the digestive-urinary factor

may have more severe disease based on both subtype and surgical stage, which may also be related to this association with surgical complication. Patients with high digestive-urinary factor scores may require greater surgical expertise or interdisciplinary approaches, which may not be universally accessible to all individuals with endometriosis.

Several limitations should be acknowledged in this study. These include the reliance on self-reported data for endometriosis lesion location and other covariates, the lack of information on the types and number of surgeries, smoking status at the time of surgery, details on lesion removal methods and locations, as well as factors affecting healthcare access, such as insurance status. Fewer individuals who have had any surgical complications had excision surgery, considered to be the gold standard of endometriosis care, ($n = 3$, 2.1%), hysterectomy ($n = 3$, 2.1%), or other surgeries ($n = 3$, 2.1%) compared with those without complications, where participants had excision ($n = 40$, 8.0%), hysterectomy ($n = 34$, 6.8%), or other surgeries ($n = 63$, 12.6%). These small cell sizes mean results should be interpreted with care. Additionally, those who frequent social media groups may differ from all those who present with endometriosis and may overrepresent those who have had surgery and potentially surgical complications as those in social media groups may be younger, more likely to live in areas with better internet access, or work in different professional areas than all people with endometriosis which give them additional privilege and higher socioeconomic status. These limitations restrict the generalizability of the results and prevent a comprehensive exploration and description of these associations. Nevertheless, the study's strengths lie in its diverse population, availability of information on lesion location, and details on the types of surgeries and complications experienced by participants. Future research should strive to collect more

comprehensive healthcare data and continue investigating the latent factors underlying endometriosis lesion locations to enhance the descriptive understanding of endometriosis.

It is worth noting that excision, the gold-standard treatment for endometriosis involving the surgical removal of lesions by skilled endometriosis experts, was infrequent in this sample, with only 43 participants (6.6%) reporting this treatment. Further research should explore complication rates among those who have undergone excision surgery compared to those who have not, taking into account lesion location. Additionally, future studies should investigate the role of lesion location factors in relation to the duration of complications and the likelihood of additional surgeries.

E. Conclusions

This final study assesses the association between lesion factor scores and surgical complications and is the first study to pair factor analysis with surgical complications in this way. Lesion location can greatly change a surgical approach and complexity. Importantly, our digestive-urinary factor was associated with all complications considered in this study. Building upon this research could potentially lead to considering lesion location to guide surgical planning. This study also represents an opportunity to potentially reduce the number of surgical complications by considering lesion location factors when planning surgery. This may include having interdisciplinary teams brought in for suspected lesions on the digestive or urinary tracts based on demographics which may help reduce the number of complications by way of additional expertise.

VI CONCLUSIONS

A. Summary and Contribution

In prior chapters of this dissertation, a novel strategy for addressing endometriosis classification was outlined and then subsequently applied to better understand the impact of lesion location on symptom presentation and surgical complications. These are extremely relevant areas of concern for a surgically diagnosed disease with a long lag time to diagnosis. Endometriosis is estimated to affect 10% of those assigned female at birth and prior methods of classifying this disease have proven to be inadequate. This method using EFA places importance on lesion location in a way that has not been explored previously in other categorization schemes like subtyping or rAFS. Our findings suggest that lesion location grouping, identified via EFA, both partially align with prior classification systems and provide an extension of those systems as well as the potential for impact on how patients present for clinical care and an association with potentially surgical complications.

In chapter III we described the use data from the SPiTE study, an online survey based on the WERF ePHect survey tool that recruited through social media, to identify factor scores based on lesion location. This represents potential latent factors affecting where lesions are present in the body. We found three distinct factors based on self-reported lesion location in this survey including the digestive-urinary factor, which had high loadings on the digestive system, bladder, and ureters, the reproductive factor, which had high loadings on the fallopian tubes and ovaries, and the Douglas-ligaments factor, which has high loadings on the uterosacral ligaments, pouch of Douglas, and round ligaments.

We explored associations between the lesion location factors and current classification and staging as well as with various demographic characteristics. We found that the digestive-urinary factor associated with more complex cases with longer diagnostic delay. This factor also showed difference in endometriosis subtype and surgical staging with higher levels in those with deep endometriosis, multiple subtypes, and higher stage disease. This factor explained most of the variance observed in the EFA. Patients who score highly in the digestive-urinary factor may have more severe disease requiring greater levels of care, as seen with the surgical complications. The reproductive factor was described as less obese, less securely employed individuals with less known family history of endometriosis and some diagnostic delay. We found that the reproductive factor was highest in persons with SPE, but not OMA nor with surgical stage. This factor explained the second largest amount of variation in lesion locations. Higher levels of the Douglas-ligaments factor was identified in individuals who are not heterosexual and were diagnosed in the later reproductive years. These individuals may interact with the healthcare system differentially than those who are heterosexual. Levels of the Douglas-ligament factor were highest in those with DE and lowest in those with DPE; no associations were found with surgical stage. This factor explained the least amount of variation in our model and had an eigenvalue score of 0.70 which makes this factor the weakest of all the retained factors. It may not explain sufficient variation to be a reliable factor and requires further examination.

In chapter VI, we applied the SPiTE data to investigate the association between lesion location factors described previously and the presenting symptom that drove the participant to seek care. The reproductive factor was marginally associated with pain as the presenting

symptom as well as having worse bowel symptoms and pain with sexual intercourse. No association was found with the digestive-urinary factor or Douglas-ligaments factor for pain presentation. A high digestive-urinary factor and a lower reproductive factor score were associated with infertility presentation. This was especially interesting as the reproductive factor involves high loadings on the ovaries and fallopian tubes.

In chapter V explored these lesion location factors and the presence of surgical complications using the SPITE data. The digestive-urinary factor showed a positive association with surgical complications across all analyses. This suggests a relationship between more complex surgeries, which are more likely to involve the digestive or urinary systems, and a greater probability of complications. This is consistent with results presented in Chapter III as this factor was also associated with more subtypes and higher surgical staging indicating this may be a more complex presentation of endometriosis. The reproductive factor was marginally associated only with having gastrointestinal complications and the Douglas-ligaments factor was only associated with urinary complications model only in participants without diagnostic delay.

Taken together, these studies represent the first use of factor analysis to classify lesion location in endometriosis and explore associations of lesion location factors with current classification systems, demographics, presenting symptom, and surgical complications. These studies demonstrate the potential of considering lesion location factor groupings within the classification of endometriosis subtypes. Prior studies have either not considered lesion location in their studies of endometriosis, not considered how locations may group together, or have used other classification systems which are often limited. While these results are novel,

there are limitations as well. This cross-sectional dataset was collected using social media groups, which may not be representative of all people with endometriosis, the survey was limited to surgical diagnosis of disease which also limits generalizability, and all lesions may not have been found or reported during surgery or participants may not recall all locations. Endometriosis patients have been previously found to have high levels of knowledge of their disease and have accurate reporting of their disease which alleviates some concerns about recall bias. However, these analyses were strengthened by a broad survey based on a validated measure of endometriosis characteristics, symptoms, and outcomes which included additional questions on race, sex, gender, and sexuality which have not been previously explored. The survey also engaged a wide base of social media groups with a wide range of experiences that were not restricted to a single hospital or catchment area.

These findings have a multitude of implications for future research. This research is important to clinicians as well as patients. Clinicians may be able to use this research to target surgeries as well as develop interdisciplinary teams and further surgical planning tools which may result in better outcomes for their patients as more successful surgeries. This includes the use of patient profiles and demographics as well as presenting symptoms in potential surgical planning tools, including prediction of potential complications. It also underscores the need for interdisciplinary teams in endometriosis treatment, especially when considering surgical complications. Future analyses should be conducted to validate these lesion location factors in other populations and using other methods such as surgical records rather than self-report. Future studies should also consider longitudinal follow up of participants from both onset of symptoms to outcomes after surgery and any subsequent surgery. Further efforts should be

made to include racialized and minoritized groups based on race, gender, and sexuality. In conclusion, endometriosis represents a large disease burden, which is not currently being addressed adequately, and needs better interventions and diagnostic tools that are less invasive and more accessible to those with the disease. This study has taken a novel approach to begin to address these critical needs and sets the stage for future investigations to replicate and expand on these results.

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APPENDICES

**APPENDIX A
IRB APPROVAL FOR STUDY**

Approval Notice

Initial Review – Expedited Review

March 10, 2022

Kelly O'Shea, MPH

Epidemiology and Biostatistics

Phone: (312) 413-9193

RE: **Protocol # 2021-1374**

“Heterogeneity of Symptoms, outcomes, and characteristics in Patients undergoing Treatment for Endometriosis (SPiTE)”

PIs must complete a [COVID-19 Human Subjects Research Review Worksheet](#) for a protocol COVID safety assessment prior to initiating or re-starting any research activities that require in-person contact between research subjects and staff during the COVID-19 pandemic.

For additional information about this process, please refer to the [Human Subjects Research Review page on the OVCR website](#). If you need assistance, questions may be directed to research@uic.edu.

Dear Dr. O'Shea:

Members of Institutional Review Board (IRB) #1 reviewed and approved your research protocol under expedited review procedures 45 CFR 46.110(b)(1) on March 8, 2022. You may now begin your research.

Your research meets the criteria for approval under the following category: 7

APPENDIX A (continued)

Protocol reviewed under expedited review procedures 45 CFR 46.110 Category: 7

Please note the following information about your approved research protocol:

<u>Protocol Approval Date:</u>	March 8, 2022 - March 8, 2023
<u>Approved Subject Enrollment #:</u>	1500
<u>Performance Sites:</u>	UIC, INSERM (France)
<u>Sponsor:</u>	School of Public Health
<u>Institutional Proposal (IP)#:</u>	Not available
<u>Grant/Contract No:</u>	Not available
<u>Grant/Contract Title:</u>	Not available
<u>Research Protocol(s):</u>	
	a) Protocol document; Version 1.2; 03/02/2022

Documents that require an approval stamp or separate signature can be accessed via [OPRS Live](#). The documents will be located in the specific protocol workspace. You must access and use only the approved documents to recruit and enroll subjects into this research project.

Recruitment Material(s):

- a) Do you have endometriosis tearaway; Version 2; 01/10/2022
- b) Recruitment language; Version 2; 01/10/2022
- c) The SPiTE endo study social media; Version 2; 01/10/2022
- d) Social media moderator message; Version 2; 01/10/2022
- e) Do you have endometriosis flyer; Version 2; 01/10/2022

APPENDIX A (continued)

Informed Consent(s):

- a) Spite endo study informed consent; Version 4; 03/10/2022
- b) Research involves activities related to screening, recruitment, or determining eligibility per 45 CFR 46.116(g)

Please remember to:

→ **Use only the IRB-approved and stamped consent document(s) when enrolling new subjects.**

→ Use your **research protocol number** (2021-1374) on any documents or correspondence with the IRB concerning your research protocol.

→ Review and comply with the [policies](#) of the UIC Human Subjects Protection Program (HSPP) and the guidance [Investigator Responsibilities](#).

Please note that the UIC IRB has the right to ask further questions, seek additional information, or monitor the conduct of your research and the consent process.

Please be aware that if the [scope of work](#) in the grant/project changes, the protocol must be amended and approved by the UIC IRB before the initiation of the change.

We wish you the best as you conduct your research. If you have any questions or need further help, please contact the OPRS office at (312) 996-1711 or me at (312) 355-3949. Please send any correspondence about this protocol to OPRS via [OPRS Live](#).

APPENDIX A (continued)

Sincerely,

Eddie Mendoza

IRB Coordinator, IRB # 1

Office for the Protection of Research Subjects

cc: Mary Ellen Turyk,

Ronald C. Hershow, Epidemiology and Biostatistics, M/C 923

OVCR Administration, M/C 672

APPENDIX B
DEMOGRAPHICS FOR TOTAL SAMPLE INCLUDING THOSE WITH NO LESION LOCATIONS

TABLE XXIII DEMOGRAPHICS FOR TOTAL SAMPLE INCLUDING THOSE WITH NO LESION LOCATIONS (N = 898)

Variable	N (%)
Number of Locations	
1	280 (29.3)
2	192 (20.1)
3+	426 (44.5)
Missing	59 (6.2)
Right Ovary	
Selected	316 (33.0)
Not Selected	641 (67.0)
Left Ovary	
Selected	316 (33.0)
Not Selected	641 (67.0)
Unknown Ovary	
Selected	156 (16.3)
Not Selected	801 (83.7)
Right Fallopian Tube	
Selected	173 (18.1)
Not Selected	784 (81.9)
Left Fallopian Tube	
Selected	160 (16.7)
Not Selected	797 (83.3)
Unknown Fallopian Tube	
Selected	90 (9.4)
Not Selected	867 (90.6)
Uterus	
Selected	482 (50.4)
Not Selected	475 (49.6)
Vagina	
Selected	85 (8.9)
Not Selected	872 (91.1)

**TABLE XXIII DEMOGRAPHICS FOR TOTAL SAMPLE INCLUDING THOSE WITH NO LESION
LOCATIONS N =898 (continued)**

Variable	N (%)
Pouch of Douglas	
Selected	179 (18.7)
Not Selected	778 (81.3)
Digestive Tract	
Selected	257 (26.9)
Not Selected	700 (73.2)
Abdominal Wall	
Selected	280 (29.3)
Not Selected	677 (70.7)
Bladder	
Selected	200 (20.9)
Not Selected	757 (79.1)
Ureters	
Selected	92 (9.6)
Not Selected	865 (90.4)
Kidney	
Selected	25 (14.2)
Not Selected	821 (85.8)
Uterosacral Ligaments	
Selected	136 (14.2)
Not Selected	821 (85.8)
Round Ligaments	
Selected	60 (6.3)
Not Selected	897 (93.7)
Diaphragm	
Selected	37 (3.9)
Not Selected	920 (96.1)
Other Location	
Selected	74 (7.7)
Not Selected	883 (92.3)
Have Surgical Reports	
Yes	524 (54.8)

TABLE XXIII DEMOGRAPHICS FOR TOTAL SAMPLE INCLUDING THOSE WITH NO LESION LOCATIONS (N = 898) (continued)

Variable	N (%)
No	375 (39.2)
Missing	58 (6.1)
Race	
White	747 (78.1)
Other Race	51 (5.3)
Black	43 (4.5)
AAPI	107 (11.2)
Missing	9 (0.9)
BMI	
< 18.5	59 (6.2)
18.5 - 24.9	350 (36.6)
25-29.9	266 (27.8)
>=30	269 (28.11)
Missing	13 (1.4)
Diagnostic Delay	
Incidental or < 1 Year	121 (12.6)
1-5 Years	192 (20.1)
6-10 Years	157 (16.4)
11-15 Years	118 (12.3)
> 15 years	190 (19.9)
Missing	179 (18.7)
Early Menarche	
Before Age 12	195 (20.4)
Age 12 or Later	668 (69.8)
Missing	94 (9.8)
Number of Pregnancies	
0	466 (48.7)
1	98 (10.2)
2+	303 (31.7)
Missing	90 (9.4)
Gender	
Ciswoman	903 (94.4)

**TABLE XXIII DEMOGRAPHICS FOR TOTAL SAMPLE INCLUDING THOSE WITH NO LESION
LOCATIONS (N = 898) (continued)**

Variable	N (%)
Other	40 (4.1)
Missing	14 (1.5)
Sexuality	
Heterosexual/Straight	698 (72.9)
Other	242 (25.3)
Missing	17 (1.8)
Age Diagnosed	
Less than 18	47 (4.9)
18 - 35	610 (63.7)
36-45	125 (13.1)
46 and up	27 (2.8)
Missing	148 (15.5)
Income Levels	
60k +	585 (61.1)
30k to 59K	214 (22.4)
Less than 30k	158 (16.5)
Employment	
Employed Full Time	552 (57.7)
Employed Part Time	140 (14.6)
Unemployed, Student, Retired, or Homemaker	209 (21.8)
Disabled	56 (5.2)
Education	
Bachelor's Degree or Higher	665 (69.5)
Some College	242 (25.3)
High School Degree and Less	50 (5.2)
Smoking Status	
Never Smoker	685 (71.6)
Started at 18 or older	123 (12.9)
Started Before 18	148 (15.5)
Missing	1 (0.1)
Alcohol Use	
Non-Drinker	413 (43.2)

**TABLE XXIII DEMOGRAPHICS FOR TOTAL SAMPLE INCLUDING THOSE WITH NO LESION
LOCATIONS (N = 898) (continued)**

Variable	N (%)
Light Drinker	398 (41.6)
Moderate/Heavy Drinker	143 (14.9)
Missing	3 (0.3)
Lived in Rural Area > 1 Year	
Never	624 (65.2)
18 or Older	109 (11.4)
Before 18	215 (22.5)
Missing	9 (0.9)
Ever Breast/Chest Fed	
No	140 (14.6)
Yes	253 (26.4)
Never Pregnant	466 (48.7)
Missing	98 (10.2)
Number of Comorbidities	
0	184 (19.2)
1	110 (11.5)
2	116 (12.1)
3	128 (13.4)
4 or More	419 (43.8)
Family History⁹	
Any Family History	514 (53.7)
No Family History	158 (16.5)
Missing	285 (29.8)
Subtypes/Related Disease	
SPE	78 (8.2)
OMA	172 (18.0)
DE	66 (6.9)
Adenomyosis	59 (6.2)
Not Specified	227 (23.7)
Multiple Subtypes	296 (30.9)
Missing	59 (6.2)

**TABLE XXIII DEMOGRAPHICS FOR TOTAL SAMPLE INCLUDING THOSE WITH NO LESION
LOCATIONS (N = 898) (continued)**

Variable	N (%)
Surgical Stage	
Not Mentioned	246 (25.7)
Stage I	101 (10.6)
Stage II	140 (14.6)
Stage III	88 (9.2)
Stage IV	117 (12.2)
Unknown	207 (21.6)
Missing	58 (6.1)
Age	
Average	39.0 (SD 13.0)
Missing	81 (0.9)
Year of Diagnosis	
Average	2011 (SD 11.2)
Missing	10 (0.1)

APPENDIX C
MISSINGNESS TABLE

TABLE XXIV MISSINGNESS AND UNKNOWN TABLE

Variable	N	Percentage
Race		
Missing	8	0.89
BMI		
Missing	13	1.45
Diagnostic Delay		
Missing	121	13.47
Early Menarche		
Missing	36	4.01
Number of Pregnancies		
Missing	32	3.56
Year of Diagnosis		
Missing	11	1.22
Gender		
Missing	10	1.11
Sexuality		
Missing	15	1.67
Age		
Missing	78	8.69
Age Diagnosed		
Missing	90	10.02
Income Levels		
Missing	0	0
Employment		
Missing	0	0
Education		
Missing	0	0
Smoking Status		
Missing	1	0.11
Alcohol Use		
Missing	2	0.22
Lived in Rural Area > 1 Year		
Missing	4	0.45

TABLE XXIV MISSINGNESS AND UNKNOWN TABLE (continued)

Variable	N	Percentage
Ever Breast/Chest Fed		
Missing	40	1.45
Number of Comorbidities		
Missing	0	0
Family History		
I Don't Know	219	24.39
Missing	45	5.01
Stage Diagnosis		
I Don't Know	206	22.94
Missing	0	0
Not On Surgical Report	246	27.39
Endo Subtype		
Missing	227	25.38

VITA

Kelly O'Shea

EDUCATION

University of Illinois at Chicago December 2023 School of Public Health, Chicago, IL PhD in Epidemiology Doctoral committee: Mary Turyk, PhD (chair), Marina Kvaskoff, Caryn Peterson, PhD, Gelila Goba, MD, Li Liu, PhD Dissertation: Heterogeneity of Symptoms, Outcomes, and Characteristics of Patients in Treatment for Endometriosis	Anticipated
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University of Illinois at Chicago School of Public Health, Chicago, IL Masters of Public Health in Epidemiology	2015
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Northern Illinois University College of Liberal Arts and Sciences, DeKalb, IL BA in Anthropology Minor in Southeast Asian Studies	2010
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HONORS AND AWARDS

Chateaubriand Fellowship Embassy of France in the United States	2021
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Epidemiology-Biostatistics Department Award University of Illinois at Chicago	2022
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Graduate Student Council Travel Award University of Illinois at Chicago	2018
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RESEARCH EXPERIENCE & PROFESSIONAL DEVELOPMENT

<i>Associate Director of Evaluation and Tracking</i> Center for Clinical and Translational Sciences University of Illinois at Chicago	2020-Present
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<i>Chateaubriand Fellow</i> ComPaRe – Endometriosis INSERM, Paris, France	2021-2022
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<i>Assistant Director of Evaluation and Tracking</i> Center for Clinical and Translational Sciences University of Illinois at Chicago, Chicago, IL	2018-2020
<i>Research Specialist for Evaluation and Tracking</i> Center for Clinical and Translational Sciences University of Illinois at Chicago, Chicago, IL	2017-2018
<i>Research Coordinator for Perinatal Psychiatry</i> The Asher Center Northwestern University, Chicago, IL	2016-2017
<i>Data Analyst for Texas Medicaid</i> Valance Health, Chicago, IL	2015-2016
<i>Epidemiology and Program Evaluation Intern</i> Keep Your Heart Healthy Chicago Department of Public Health, Chicago, IL	2013-2015
MEMBER IN PROFESSIONAL ORGANIZATIONS	
Society for Epidemiologic Research, Member	2022—Present
Society for Perinatal Pediatric and Perinatal Epidemiologic Research, Member	2022—Present
CTSA Translational Science Benefits Model Working Group, Member	2022—Present
American Evaluators Association, Member	2017 – Present
American Public Health Association, Member	2018—2022
UIC SPH Committee on Research, Student Member	2018—2019
SERVICE	
<i>Abstract Reviewer</i>	
UIC SPH Research Article Award	2023
American Public Health Association	2019—2020
TEACHING EXPERIENCE	
<i>Guest Lectures</i>	
“Endometriosis”	2023
EPID : Chronic Disease Epidemiology University of Illinois at Chicago (Graduate Audience)	

“What We Do in the Surveys”

2022

Master Class Series Project Management: In The Field
(Professional Audience)

PUBLICATIONS

Impact of a Clinical and Translational Science Awards Hub on Faculty Research Grant Productivity. **K O'Shea**, J Soo, T Johnson. Journal of Clinical and Translational Sciences 2022

Bipolar Disorder and Psychotropic Medication: Impact on Pregnancy and Neonatal Outcomes KL Wisner, D Sit, **K O'Shea**, DL Bogen, CT Clark, E Pinheiro, A Yang, Journal of Affective Disorders 2019

Validity of the WHIPLASHED as a Tool to Identify Bipolar Disorder in Women DR Mahmoud, A Yang, JD Ciolino, SD Fisher, D Sit, E Pinheiro, T Pendergrast, **K O'Shea**, KL Wisner, and CT Clark, Journal of Affective Disorders 2019

CONFERENCE PRESENTATIONS AND PUBLISHED ABSTRACTS

(**O'Shea, K** = presenter, Other = Co-Author presenter)

O'Shea, K., Konda, S., Kvaskoff, M., Liu L., Peterson, C., Goba, G., Turyk, M. (2023 April 17). Factor Analysis in the Categorization of Endometriosis Lesion Location from the SPiTE study [Poster Session]. 5th Annual UIC Women's Health Research Day, Chicago, IL , USA.

O'Shea, K., Krogen, M., Johnson, T. (2021 November 8 - 13). A Comparison of CTSA Pilot Applicants Subsequent Productivity [Paper Presentation]. American Evaluation Association, Virtual.

Soo, J., **O'Shea, K.**, & Johnson, T. (2018, October 31–November 3). Influence of CTSAs on Faculty Productivity [Paper Presentation]. American Evaluation Association, Cleveland, OH, USA.

O'Shea, K., Pendergrast, T., Kolia, M., Stika, C., George, A., Avram, M., Rasmussen-Torvik, L., Ciolino, J., & Wisner, K. L. (2017, April 6). Optimal Medication Management of Mothers with Depression (OPTI-MOM) [Poster Session]. 13th Annual Lewis Landsberg Research Day, Chicago, IL, USA.

Pendergrast, T., O'Shea, K., Kolia, M., Clark, C., Fisher, S., & Wisner, K. L. (2017, November 7–10). Assessing, Stress, Health, Emotion, and Response (ASHER) Registry [Poster Session]. 3rd Biennial Perinatal Mental Health Conference, Chicago, IL, USA.