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Disparities in healthcare services in women with endometriosis with public vs. private health insurance

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**Title: Disparities in healthcare services in women with endometriosis with public vs. private health insurance**

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**Condensation:** We report significant differences in utilization trends of endometriosis-related healthcare services and drug prescriptions based on socioeconomic parameters, indicative of health disparities in this population.

**Short title:** Endometriosis Health Disparities

**AJOG at a Glance:**

- A. This cross-sectional study was conducted on utilization data from woman with endometriosis who were members of a health insurance company that provides both public and private coverage in Puerto Rico.
- B. The significance of this investigation was to identify disparities in access to health care for women with endometriosis based on socioeconomic status.
- C. This study uncovered differences between public and private health insurance utilization trends, and provides evidence for a possible role of socioeconomic status in access to health care services for women with endometriosis.

## Abstract

**BACKGROUND:** Health disparities research's goals are to identify facilitators and barriers to health care utilization to help eliminate health inequalities. There are few studies on disparities in health care access and utilization trends for endometriosis patients that may lead to differences in appropriate care based on socioeconomic status.

**OBJECTIVE:** This retrospective cross-sectional study was conducted to compare health services utilization patterns and prevalence of co-morbidities of women with endometriosis with public (government-based) vs. private (purchased or provided by employer) health insurance.

**STUDY DESIGN:** A total of 342 de-identified datasets (171 randomly-selected cases per study group) from women with endometriosis 14-50 years-old, members of one health insurance company that provides both public and private health insurance coverage in Puerto Rico were analyzed. Patients were defined as having at least one endometriosis-related medical claim (ICD-9-617.xx; International Classification of Diseases, Ninth Revision, Clinical Modification) during the three-year study period.

**RESULTS:** Medical service (e.g., hospital, laboratory, pathology and radiology) utilization trends were 3 times lower in the public vs. the private sector. Women in the public sector were 3.5 less likely to have a laparoscopy, 2.7 times more likely to be prescribed opioid/narcotics, and were the only study subjects reporting emergency room use. Ob/Gyn services were utilized >2-fold less by women in the public (29.5%) vs. the private sector (70.5%) ( $p=0.087$ ).

**CONCLUSION:** We report significant differences in the utilization trends of endometriosis-related medical services and prescriptions, indicating differences in health care access based on socioeconomic parameters. Our results support development of public health programs to promote access to health care for endometriosis patients irrespective of socioeconomic status and promote health disparity research in other health care systems.

**Keywords:** Endometriosis, Health Disparities, Access to care, Medical claims, Health economics

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## INTRODUCTION

Endometriosis is a common gynecological diagnosis, affecting 5-10% of women worldwide who are deeply affected by their characteristic symptoms: pelvic pain and infertility<sup>1,2</sup>. This condition is often diagnosed during the decades of life when women are expected to be most productive and able to become pregnant if desired<sup>3-5</sup>. Although endometriosis is a well-established cause of physical and mental distress, and despite it being a common gynecologic diagnosis, surgical diagnosis takes on average seven years, and more in low resource settings<sup>6-8</sup>. Currently, there is no cure for endometriosis, but those with a diagnosis could receive surgical and hormonal

treatments, often in combination with alternative medicine approaches, to alleviate their symptoms<sup>9-11</sup>. If undiagnosed and untreated, the chronicity and severity of symptoms will negatively impact all aspects of a woman's life<sup>3,12</sup>. Prompt diagnosis and appropriate clinical management of this disease can prevent its effects on quality of life and psychological disorders (e.g., mood disorders, anxiety, and depression)<sup>13</sup>. Perhaps the main diagnostic challenge is the need for surgery for direct visualization, and ideally biopsy, of the ectopic endometriotic implants<sup>4</sup>. Barriers to early diagnosis have been recognized and include access to health care that in some countries is directly linked to socioeconomic status<sup>14-16</sup>.

The National Institute of Health (NIH) refers to health disparities as differences in the frequency, morbidity and mortality of diseases among groups of people or individuals that may be due to biological differences, socioeconomic factors (e.g., access to care), or cultural issues<sup>17,18</sup>. Regardless of the cause, health disparities pose negative impact on the health of the disadvantaged populations<sup>19,20</sup>. The National Healthcare Disparities Report (NHDR) from the Agency for Healthcare Research and Quality (AHRQ) states that health care resource utilization can be used to measure access to care and to assess whether barriers to access may constitute a determinant of health in certain conditions<sup>a,21</sup>. In the case of endometriosis, few studies have been conducted to assess differences in access to care within a geographic region based on socioeconomic status<sup>22-24</sup>. Experts agree that endometriosis care should be provided in the context of centers of expertise or centers of excellence, but unfortunately these do not exist in

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<sup>a</sup> United States Department of Health and Human Services and Agency for Healthcare Research and Quality. "National Healthcare Disparities Report, 2008. Chapter 3, Health Care Utilization". Retrieve on January 25, 2017

most countries, and certainly not in Puerto Rico, limiting the type and quality of health care received by the patients and ultimately determining clinical outcomes<sup>5,25</sup>. To prevent the complications and impact on quality of life and mental health of women with endometriosis it is urgent to implement programs to target early detection, to reduce and manage the burden of the disease<sup>26</sup>. But first, it is critical to identify the barriers to access to quality medical care which would facilitate accurate and prompt diagnosis and treatment.

There are reports that Hispanic populations in the United States (US) have lower rates of access to healthcare providers<sup>27</sup>. Historically this population confronts difficulties in accessing medical services as shown by low utilization of services, lack of access to centers of expertise, and high trends of Emergency Room (ER) use<sup>28-31</sup>. The present study was conducted to identify if there are disparities in access to health care for women with endometriosis in Puerto Rico, a representative Hispanic population, based on a socioeconomic measure: their ability to purchase a private health insurance plan. The long-term goal of this study is to provide data on disparities in health care access and utilization trends that may lead to differences in appropriate care based on socioeconomic status, and to identify facilitators and barriers to care and health care utilization that can help eliminate health inequalities. Puerto Rico's health insurance system is roughly composed by private insurance providers and a Medicaid supported, capitated, public insurance arrangement<sup>b,32</sup>. The main difference between these two models is the gatekeeping: in the public system the primary physician oversees granting

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<sup>b</sup> Departamento de Salud de Puerto Rico: Secretaría Auxiliar de Planificación y Desarrollo. Retrieved from <http://www.salud.gov.pr/Dept-de-Salud/Pages/Unidades-Operacionales/Secretaria-Auxiliar-de-Planificacion-y-Desarrollo.aspx> on January 25, 2017



access to specialists and sub-specialists. Despite the complexity of these systems, Puerto Rico's population enjoys one of the highest health insurance coverage rates of any US jurisdiction: 94% in 2014 in comparison with US mainland (88%)<sup>c</sup>. Since the mid 90's, there have been medical insurance companies which have covered both private and public, governmentally-sponsored patients. Only 36% of Puerto Ricans received health insurance through a commercial insurance provided, with premiums paid by an employer or the consumer<sup>d</sup>. In this study, we seized access of utilization data from one of these companies that served both populations to compare and assess disparities in endometriosis care in Puerto Rico.

## MATERIALS AND METHODS

### *Study design*

This is a cross-sectional study, based on medical billing codes indicating a diagnosis of endometriosis (ICD-9-617.xx). This secondary data set was obtained from one major Health Insurance Company (HIC) that provided services to the government and also to private individuals and employers in Puerto Rico. The dataset, which was devoid of identifiers, included medical billing data on medical, procedures and pharmacy services spanning three full years between 2004 and 2006. During those years, this HIC had a total of 1,409,567 combined members (public and private). Although the HIC included members from all municipalities, for this study we only analyzed data of members from two geographical regions of Puerto Rico in which this HIC provided both public and

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<sup>c</sup> Puerto Health Care Infrastructure Report, January 2017, [www.urban.org](http://www.urban.org)

<sup>d</sup> Levis-Peralta et al. 2016. *Description of the State Health Care Environment: Puerto Rico State Health Innovation Plan*. Rio Piedras: Puerto Rico Department of Health. <https://docplayer.net/40857316-R-e-p-o-r-t-description-of-the-state-health-care-environment-prepared-for-funding-statement-prepared-by-authors-graphic-design-citation.html> Accessed 10/16/18

private health insurance plans (**Figure 1**). All protocols used in this study were approved by the Ponce Health Sciences University (PHSU) Institutional Review Board (IRB) as an Exempt protocol.

### *Study universe*

This study was conducted on a randomly-selected sample from the original dataset of 1,409,567 clients of a single health insurance company. An endometriosis patient was defined as a female aged 14 to 50, who had at least one endometriosis medical claim during the study period. Only cases from Southern and Southeastern Puerto Rico were analyzed to allow for comparisons of public vs. private utilization trends. Data from three full years of coverage was selected from subjects meeting the inclusion criteria, checked for missing data, and transferred into SPSS®20 version (SPSS, Chicago, IL) for statistical analysis. A total of 2,378 female subjects with at least one endometriosis-related claim regardless of type of health insurance coverage were eligible for this study. Epi Info 7 was used a priori to calculate the sample size and power. A total of 342 subjects (171 per group) had 80% power,  $\alpha = 0.05$ , 95% of Confidence Interval (CI), and an effect size of 0.5 to observe differences between health insurance sectors. Next, we randomly selected 171 patients from each insurance sector as the sample to be analyzed. **Figure 2** depicts the process used in selecting the study participants.

The type of data collected was quantitative and included age, sex, town of residence and the endometriosis-specific ICD-9-CM codes (International Classification of Diseases, Ninth Revision, Clinical Modification) from 617.0 to 617.9. We also obtained

the surgical procedures data or CPT (Current Procedural Terminology codes for that same period. In addition, this dataset included ICD codes for co-morbid conditions. Available data (claims, places of services, doctor and specialist visits, surgeries, prescriptions and co-morbid conditions) was described using frequency distributions or simple descriptive analysis and reported as percent (%), means, mode, or median, and standard deviation ( $\pm$ SD). Variables such as age, municipalities, line of coverage, place of services, type of services, laboratories (i.e., blood tests, X-RAYS, and MRI), ER visits, hospital admissions, length of stay, endometriosis lesion site were included in these analyses. The dataset did not include clinical information such as endometriosis severity by disease staging, symptomatology nor follow up clinical data. This population may or may not have had a surgical-related procedure to diagnose endometriosis during those years. Also, they may or may not have been treated for endometriosis (with hormones, NSAID's, narcotics, among others) during that time period.

### *Study outcomes*

The primary outcome of this study was the total number of endometriosis-related medical claims in each type of health insurance (public or private) during the 3-year study period. Secondary outcomes were used to determine the endometriosis prevalence and the healthcare resource utilization (e.g., place of services, type of services, hospitalization, ER use, type of surgery, LOS, drug prescription, prevalence of co-morbid conditions). Outcomes were compared between the two groups of insurance coverage to determine if there were health care disparities based on subjects sociodemographics.

### *Data analysis*

Data met the normal distribution assumptions, and they were analyzed with parametric tests. T-tests were used to assess significant differences between the means and median costs of medical and pharmacological events of the two study groups. When expected cases were less than five observations, the Fisher's exact test was applied. Paired t-test was used to explore difference between two related variables, and the independent t-test was conducted to assess the differences and the level of significance between the type of insurance coverage (government-based vs. private insurance coverage). Each sector was analyzed and compared with binary variables including the number of medical claims. For differences between groups means such endometriosis lesion and procedures, an analysis of variances (ANOVA) was used. The Levene's Test (F) allowed to note if there was an equality of variance; a non-significant F ( $>0.050$ ) means that groups are assumed to have similar variance. Correlations were run to explore possible association between variables, followed by a Pearson's Correlation Coefficient (r) to study the strength of the association between continuous variables (e.g., age, LOS, costs for medical and pharmacological claims), or Pearson's chi-squared test ( $\chi^2$ ) to examine the differences between two categorical variables, in this case, type of health insurance coverage (government-based versus private) and other variables (e.g., hospitalizations, type of services, place of services, comorbidities).

Logistic regression analysis was used to adjust for the potential confounding effect of variables (age and geographical region). Odds ratios (OR) were used to measure the

association between type of health insurance coverage and prescription type, being the exposure 'public coverage' and the outcome 'treatment'. ORs were also used to measure the association between type of health insurance coverage and the risk of comorbid conditions, being the exposure 'public coverage' and the outcome 'comorbidity'. The 95% confidence intervals (95%CI) were used as a proxy for statistical significance. Significant ORs were included in multivariate models to adjust for covariates, and adjusted for possible confounders: such as age (<21, ≥21), and region (East and Southeast). The Cochran-Mantel-Haenszel (CMH) statistical test was used to determine the significance of the AOR. The Breslow-Day two-sided test was performed a priori to determine the homogeneity between variables. A non-significant Breslow-day test suggests that a summary OR or AOR are valid. A value <0.05 was considered statistically significant.

## RESULTS

A total of 2,378 women had claims related to endometriosis (ICD-9-617.xx) in the complete database covering all towns in Puerto Rico. Of those, 744 were between 14-50 y/o and their town of residence was in the two selected geographical regions. To find differences between the public and the private sector, a total of 342 women with endometriosis were randomly selected from this cohort, and equally distributed between public (n=171) and private (n=171) health insurance sectors. No missing data were detected in the final dataset.

Based on medical claims from 2005, we estimate the prevalence of women with endometriosis in Puerto Rico at 7.4%, for a total of approximately 70,045 affected women between 10-50 years old (Based on data from the 2000 Census; www.census.gov). The characteristics of all women with endometriosis in our cohort are described in **Table 1**. Women ages were similar between groups, with an average of 32.8 y/o  $\pm$  8.5 for the whole cohort. Also similar was the proportion of women in the public vs. the private sector. Therefore, we conclude that these two groups are comparable. There was a significantly higher proportion of individuals in the private sector with  $\geq 10$  medical claims in the study period. The average number of medical claims in the three years of the study were significantly lower in the public ( $2.7 \pm 2.7$ ) than in the private ( $5.5 \pm 6.7$ ) sector ( $p < 0.001$ ). The number of medical claims ranged from 1 to 16 (median = 1) in the public sector compared to a range of 1 to 35 (median = 3) in the private sector.

For the whole study cohort of 342 women with endometriosis, there were 2,837 medical claims for endometriosis-related medical services. The most commonly utilized places of service were doctor's office (49.0%), laboratories/X-rays (30.0%), hospitals (19.3%). Emergency room (ER) utilization was only 0.2% during the 3-year study period for the whole cohort (**Table 2**). There were approximately half the total number of medical claims in the public ( $n=461$ ) vs. the private ( $n=840$ ) sector. Doctor's office visits were half as frequent in the public sector ( $n=201$ ; 31.4%) compared to the private insurance group ( $n= 429$ ; 68.6%) ( $p < 0.001$ ). Notably, only women from the public sector had claims related to ER utilization. There were significant differences in Laboratory/X-ray

utilization rates ( $p < 0.0001$ ) but no significant differences in hospital use between sectors ( $p = 0.27$ ).

Regarding utilization of services by doctor's specialty, there were a total of 1,403 claims in the whole cohort of 342 women with endometriosis, of which the most common were for Ob-Gyn (29.4%), Clinical Laboratory (24.9%), and Hospital Inpatient services (14.9%) (**Table 2**). Ob/Gyn services were utilized 2.4-fold less by the women with public health insurance coverage (29.5%) compared to the private sector (70.5%) ( $p = 0.087$ ). Pathology services represented only 4.2% of all claims, and from those the majority of claims (67.8%) were from the private sector. General practitioner services were also very low (1.1% of all claims) in the whole cohort. There were two specialty categories that were significantly higher under the public sector: Radiology services [ $n = 23$ , 59.0% vs.  $n = 16$ , 41.0%;  $p < 0.001$ ]; and surgeons [ $n = 9$ , 64.3% vs.  $n = 5$ , 35.7%]; 0.012]. The use of other medical services such as cardiologist, pediatrician, internal medicine, and infectious diseases, which represented 15% of all claims, were 10-fold higher in the private sector (90.9% vs. 9.1%). Moreover, these medical services represented 14.5% of all medical specialty claims in the private sector compared to only 3% in the public sector. Likewise, Clinical laboratory services, which represented 24.9% of all specialty claims, were significantly lower in the public sector (26.9%) vs. the private sector (73.1%) ( $p = 0.007$ ). The length of stay (LOS) median was 3 days (d) (Range: 1-6 d) for the whole cohort, and it was not different between sectors ( $2.8 \pm 1.3$  vs.  $2.9 \pm 1.9$  in public vs. private sectors, respectively ( $p = 0.638$ )).

Regarding procedures (CPT codes), only 4.7% of the total claims were surgically-related (**Table 2**). The most frequently used CPT-codes were those related to laparoscopy (CPT: 49200, 49201, 58340, 58558, 5866, 58673, and 58720; 61.6% of all procedure claims). There were very few claims for laparotomy (CPT: 49320, and 49321; 9%), and for hysterectomy (CPT: 56605, 58100, 58120, and 58150; 29.3%). Among CPT claims, the only statistically significant difference between groups was laparoscopy, which was less frequent in the public (n=18; 22.0%) vs. the private sector (n=64; 78.0%) (p=0.030).

From a total of 7,020 pharmacological claims in the 3-year study period, only 1,269 (18.1%), were directly attributed to endometriosis-related treatments (e.g., OCP's, NSAID's, Danazol/Danocrine, GnRH agonists, Narcotics, and Opioids). **Table 3** shows the percent of each endometriosis-related treatment among all therapeutic options in both groups, demonstrating significant differences in prescription rates of Danazol, NSAIDs, and Opioids/Narcotics between groups. The frequencies of Danazol/Danocrine (0.0% vs. 100%) Opioids/Narcotics (40.0% vs. 60.0%) claims were lower in women with public coverage compared to private. In contrast, NSAID's claims were higher in the public sector (54.7% vs. 45.3%). Differences between public and private sectors in the rates of prescription of OCP's, Progestins, and GnRH agonists were not statistically significant.

Next, logistic regression analysis was done to study the association between treatments and having public health insurance coverage, adjusting for age and region to account



for factors that may modify prescription decisions (**Table 4**). This analysis showed that women with endometriosis with a public health insurance coverage are 0.6 less likely to be treated with Danazol and 2.7 more likely to be prescribed Opioids/Narcotics ( $p=0.003$ ). This means that for women in the public sector prescriptions of opioids/narcotics is actually influenced by age and region.

In general, the most frequent conditions based on pharmacological claims were bacterial infections, gastrointestinal conditions, muscle conditions, and allergies (**Table 5**). Compared to the private sector, women from the public sector had significantly higher rates of claims related to urinary tract infections (64.6% vs. 35.4%), muscle-related conditions (63.2% vs. 36.8%), Vitamin/mineral deficiency (63.2% vs. 36.6%), and bone-related disorders (61.3% vs. 38.7%) ( $p<0.05$ ). In contrast, women from the private sector had significantly higher rates of claims related to migraine (13.3% vs. 86.7%), breast cancer (16.7% vs. 83.3%), mental disorders (32.3% vs. 67.7%), thyroid disorders (32.3% vs. 67.7%), skin conditions (33.6% vs. 66.4%), cold/flu (37.9% vs. 62.1%), vaginal infections (40.6% vs. 59.4%). All other claims were not significantly different between groups.

Logistic regression for Odds Ratios (OR) with 95% (CI) was used to study the association between endometriosis co-morbidities and having private insurance coverage, adjusting for age and region (**Table 6**). This analysis showed that women with endometriosis with a private health insurance coverage are more likely to have

claims related to certain co-morbid conditions. The higher ORs were found for migraine [OR: 7.0, 95%CI: 1.544 – 31.297], breast cancer [OR: 5.2, 95%CI: 1.133 – 24.322], skin-related infections [OR: 3.0, 95%CI: 1.931 – 4.784], and mental disorder (depression/anxiety) [OR: 2.5, 95%CI: 1.398 – 4.385].

## STRUCTURED DISCUSSION

### *Principal Findings*

In order to explore the possibility that endometriosis is a health disparity, we analyzed utilization data in women with endometriosis who were members of a health insurance plan in Puerto Rico providing public and private insurance coverage. To our knowledge, this is the first study to compare health services utilization trends and prevalence of co-morbidities based on correlates of socioeconomic status, namely public vs. private coverage types. This study uncovered differences between public and private health insurance utilization trends, and provides evidence for a possible role of socioeconomic status in access to health care services for women with endometriosis.

Our study was conducted with utilization data from women residing in two proximal geographical areas of Puerto Rico between 2004 to 2006<sup>33</sup>. These two regions were similar at the socioeconomic level: both had a high proportion of residents with income below the poverty level (annual median household income of \$18,660). This agrees with the poverty level of the whole island (45.6%) reported in the 2010 census<sup>e</sup>. Also, there

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<sup>e</sup> United States Census Bureau. Quick Facts. (2011). Puerto Rico Retrieved on February 10, 2017, from <http://www.census.gov/quickfacts/table/PST045216/72>

are no tertiary care hospitals in these regions<sup>f</sup>, which suggests that this population as a whole has limited access to advanced medical expertise, including laparoscopic surgeries. In this study, claims data from a single insurance company was used to determine whether there would be differences in access to care based on socioeconomic correlates. Based on these data, we calculated the prevalence of endometriosis at 7.4%, which is 3% higher than what we reported in 2008<sup>34</sup>. We speculate that this prevalence is lower than the expected prevalence of 10% due to limitations in access to care in the Island resulting from socioeconomic disparities.

### *Results*

Endometriosis is a multi-systemic disease that requires the attention of various medical specialists beyond their primary physician. Our study showed that women with endometriosis from the public sector had significantly lower average number of overall medical claims than those with private health insurance (2.7 vs. 5.5, respectively). Also, there was a significantly lower proportion of subjects with  $\geq 10$  medical claims in the women public sector group during the study period. Moreover, this group had less access to medical specialists (i.e., Ob/Gyn, anesthesiologists, and pathologists) compared to those with private health insurance coverage. Women in the public sector had lower rates of hospital-related services and were the only with ER claims. These results suggest that this cohort utilizes the ER in lieu of visiting a doctor's office, adding costs to the health system. These results are in accord with previous studies showing that being insured decreases the likelihood of emergency room visits for

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<sup>f</sup> Pan American Health Organization (2007). Monitoring and Analyzing Health Systems: Change/Reform Process. *Health System Profile Puerto Rico*, Washington D.C. Retrieved from: [www1.paho.org/hq/dmdocuments/2010/Health\\_System\\_Profile-Puerto\\_Rico\\_2007.pdf](http://www1.paho.org/hq/dmdocuments/2010/Health_System_Profile-Puerto_Rico_2007.pdf).

gynecologic conditions<sup>35</sup>. Possible solutions include increasing awareness about the role of gynecologists as the medical specialty with the appropriate training to diagnose and manage pelvic pain. Furthermore, the fiscal consequences pertaining to misuse of ER resources validate the need to promote gynecologists as the primary care providers for all women of reproductive age in publicly insured health systems<sup>35</sup>. Unfortunately, in some settings patients belonging to governmental insurance needing specialized evaluation regarding reproductive health require a referral by their general practitioner who often have minimal training in gynecological pathologies<sup>36</sup>. Moreover, in a capitated system, referrals are not especially encouraged since they lead to increase expenditure of capitation funds, a clear conflict of interest in detriment of the women's health. Definitely, facilitating access to specialists and establishment of referral centers or centers of expertise will decrease ER use and thus costs to the health system<sup>35</sup>.

Laparoscopy surgery was a common procedure for both groups, although the proportion of laparoscopy claims among all surgical procedures was lower in the public sector. Also, the number of laparoscopy claims was 3.5 lower in the public sector, indicating that this group had less access to what is still considered the gold standard for diagnosis of endometriosis<sup>37</sup>. Another worrisome finding was that the proportion of hysterectomies was two times higher in the public sector. It would be important to follow up on this finding in a larger sample to determine the specific ages, whether salpingo-oophorectomies were done, and to obtain the pathology reports of the hysterectomies in order to define what were the indications for this procedure. There were twice as many claims of a surgical intervention for endometriosis than claims for pathology during the

same period, despite professional guidelines supporting the need for histological examination to support the diagnosis of endometriosis<sup>38</sup>. The average LOS in both groups was consistent with the literature<sup>39</sup> and considered long for a condition that can be diagnosed and managed in an outpatient basis.

Regarding pharmacological treatment claims, NSAIDs were the most common claim in the whole cohort, and also more frequently prescribed in the public vs. private sector. OCP's/Progestins, which represent an inexpensive and safe alternative to manage dysmenorrhea and pelvic inflammation, were prescribed at the same frequency in both groups. Significant differences were also observed for Danazol/Danocrine and for opioids and narcotics, more frequently prescribed in the private sector. While Danazol/Danocrine is FDA approved as treatment for endometriosis, it is not considered optimal treatment due to its androgenic side effects. Interestingly, logistic regression analysis shows that women with endometriosis with public health insurance coverage are more likely to be prescribed opioids/narcotics after adjusting for age and region. This indicates that the odds of being prescribed opioids/narcotics in the public sector is actually influenced by age or region or both, confounding the prescription decision process for these women. Narcotics are not recommended for the treatment of chronic pelvic pain since they cause substantial morbidity and mortality. Experts have raised concern about the prevalent use of opioid treatment for CPP and are calling for additional training for medical doctors as a measure to also prevent opioid use disorders<sup>40</sup>.

Notably, in general the use of GnRH agonists and OCPs/Progestins was very low in both groups, suggesting that patients are being treated with non-hormonal treatments and probably relying on over-the-counter (OTC) analgesics (e.g., acetaminophen and paracetamol) for pain management. Another explanation could be that there is a large population of patients who are seeking to conceive and do not use medication that will halt ovulation in their attempt to conceive. We are aware that 30-50% of endometriosis patients will experience infertility. Yet, this research design cannot ascertain this group of patients. Currently, there is no cure for endometriosis, but those with a diagnosis should receive surgical and hormonal treatments to alleviate their symptoms<sup>9</sup>. If undiagnosed and untreated, the chronicity and severity of symptoms will negatively impact all aspects of a woman's life.

Previous studies have shown higher rates of comorbid conditions in women with endometriosis<sup>41-43</sup>, a common finding in patients with chronic conditions<sup>9</sup>. This study also explored possible differences in the frequency of co-morbidity claims between women with endometriosis with public vs. private insurance coverage. Our analysis, based on total pharmacological claims, showed significant differences in the prevalence of co-morbidities between sectors, despite them sharing demographic and socioeconomic characteristics. In general, our results are in accord with previous data on co-morbidities, and showed higher rates of bacterial infections, gastrointestinal conditions muscle-related conditions, and allergies among women with endometriosis. Women from the public sector had significantly higher rates of muscle-related conditions, urinary

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<sup>9</sup> Institute of Medicine. 2001. a. Coverage Matters: Insurance and Health Care. Washington, DC: National Academy Press

infections, and vitamin/minerals deficiency, while women in the private sector were more likely to have claims related to mental health disorders, migraines and breast cancer. Interestingly, there were few reports of some of the most frequent co-pathologies in chronic pelvic pain along with endometriosis such as painful bladder syndrome, interstitial cystitis, or irritable bowel syndrome in this cohort. These findings could be explained by healthcare access issues that precluded referrals to subspecialists (urologists, gastroenterologists). If present, these conditions should be identified during routine visits to a primary doctor, leading to prompt referrals, diagnosis and treatment before they turn into more complicated and costly conditions. In support of this possibility, this study showed significant differences in the frequency of doctor's visits between groups, with less than half claims in the public compared to the private sector (31% vs. 69%). Also, visits to general practitioners were very infrequent in the whole cohort, representing only 1.1% of all doctor's visits.

### *Clinical Implications*

This study showed that in women with endometriosis with a public health insurance plan medical utilization trends, Ob-Gyn service utilization, and rates of laparoscopic intervention were lower. At the same time, these women were more likely to be prescribed opioid/narcotics, and were the only reporting emergency room use. Evidently, disparities in access to health care based on socioeconomic status may lead to higher physical and emotional impact as well as long-term costs in this patient population, a possibility that needs to be addressed in future follow up studies. Puerto Rico's national health care system has a dualistic medical services delivery

model, in which the clinical gatekeepers of the governmentally insured female patients are rarely formally trained ObGyn's. In contrast, private insurance patients, have no access barriers to proper ObGyn services. The endometriosis patients' dichotomy described in our research highlights the need for ObGyn's to be recognized as women's primary physicians in the PR governmental health system. Our Medicaid based public system is well underfunded due to our disadvantaged territorial condition. This financial situation could be inducing insurance-related stakeholders to restrict expending, and to rely on non-ObGyn's for female care. The approach of these non-ObGyn physicians to a complex condition such as endometriosis may deviate from standards of care both because of lack of resources and knowledge. A recent example of this restriction was the historical lack of contraceptive use of long-acting reversible contraception, which was identified and corrected during the 2016 Zika outbreak<sup>44</sup>. If PR's ObGyn's receive the opportunity to consistently and invariably evaluate and treat publicly insured women suffering endometriosis, perhaps we may observe clinical management uniformity across both health delivery systems, public and private.

### *Research Implications*

Our findings should prompt additional studies conducted in other populations, countries, and health care systems for validation. Also, we expect that our results spearhead changes in public policy to solve the inequities uncovered and ensure "equal access to available care for equal need, equal utilization for equal need, equal quality of care for all"<sup>45</sup>.



### *Strengths and Limitations*

This study is limited to the data provided by one health insurance company for a specific three-year study period. It is possible that data from other periods can differ. Also, the results obtained could only be specific to the studied population; because of cultural, ethnic, sociodemographic and political issues these results may not be generalizable. We recognize that the dataset is ten years old, however the management of endometriosis has not changed significantly in this time period. In addition, the temporality of the co-morbidities in relation to the diagnosis of endometriosis could not be determined, nor could we establish the sequence of the claims before 2004. Therefore, it was not possible to predict if endometriosis preceded a comorbid condition, or vice-versa, or if evaluation by primary care physicians or laparoscopic diagnosis were done before the study period. Being uninsured or underinsured is generally associated with less access to health care services, poorer quality of care, and ultimately worse health outcomes<sup>46</sup>. Since we did not have access to the medical records or follow up data from these patients, correlations of claims data with endometriosis severity, symptomatology or general health status could not be conducted. Although our process of randomly selecting patients in each study group ensured that they consist of a representative sample, it is possible that there are other differences between groups which could result in the different outcomes observed. For these reasons, this study cannot conclude that less access to health services results in poorer general health and endometriosis-related health outcomes. Additional studies will be necessary to make causal claims about the benefits, quality and effectiveness of care under one sector over the other. Despite these limitations, this study uncovered substantial differences in

health care services utilization for women with endometriosis, and provides strong evidence for a possible role of socioeconomic factors in the observed differences in access to care.

### Conclusions

Based on the definition of health disparities of the National Institutes of Health, we conclude that there are endometriosis-associated health disparities in Puerto Rico. We speculate that uninsured or underinsured women with endometriosis will be 1) more likely to have poor health status, 2) less likely to receive medical care, 3) more likely to be diagnosed later, and 4) more likely to have a poor quality of life<sup>47,48</sup>. More studies are necessary to assess whether the observed disparities result in the detriment of the health and wellbeing of those who do not receive appropriate care based on their socioeconomic status.

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## TABLES

**Table 1.** Endometriosis-related medical claims by health insurance coverage type

	<b>Public</b> <b>N = 171</b> <b>N (%)</b>	<b>Private</b> <b>N = 171</b> <b>N (%)</b>	<b>p-value</b>
Age (years old)*	32.4 ± 7.9	33.2 ± 9.1	0.386
<i>Region</i>			
<i>East</i>	83 (41.5)	117 (59.5)	<b>&lt;0.001</b>
<i>Southeast</i>	88 (62.0)	54 (38.0)	
<i>Total number of endometriosis-related medical claims: <b>2,837</b></i>	<b>939</b>	<b>1898</b>	
<i>Average number of endometriosis-related medical claims per person per year**</i>	2.7 ± 2.7	5.5 ± 6.7	<b>&lt;0.001</b>
<i>Median</i>	<b>1</b>	<b>3</b>	
<i>(Range)</i>	(1-16)	(1-35)	
<i>Number of subjects in each claim frequency category</i>			<b>&lt;0.001</b>
1-3 claims	128 (56.6)	98 (43.4)	
4-6 claims	28 (46.7)	32 (53.3)	
7-9 claims	9 (40.9)	13 (59.1)	
≥ 10 claims	6 (17.6)	28 (82.4)	

Statistically significance was set at an alpha level of  $p \leq 0.050$ .

\*Mean ± SD age differences and claims were calculated by T-test statistical analyses.

\*\* Mean ± SD was calculated for claims, with their median and range.

\*\*\* Mean  $\pm$  SD, median and range were calculated for claims, with the analysis exclusion of five identified outliers outside of interquartile range (percentiles: 25, 50, 75).

- Subject characteristics were described using frequency distributions or simple descriptive statistics and are reported as percent (%).
- For variables with less than five in a cell, Fisher' exact test was used. For all other variables chi-square value was used.

**Table 2.** Frequency of healthcare utilization services among all claims of women with endometriosis by health insurance coverage

Healthcare utilization services	Total Number of claims per category (%)	Public (N=171) Number of claims (%)	Private (N=171) Number of claims (%)	p-value
<i>Place of services</i>				
Doctor's office	640 (49)	201 (31.4)	439 (68.6)	<b>&lt;0.001</b>
<b>Hospital-related</b>	251 (19.3)	<b>119 (47.4)</b>	<b>132 (52.3)</b>	0.27
<b>Emergency Room<sup>c</sup></b>	21 (0.2)	21 (100)	0 (0.00)	N/A
Laboratory/X-Rays	389 (30)	120 (30.8)	269 (69.2)	<b>&lt;0.001</b>
Total	1,301	461	840	
<i>Doctor's specialty</i>				
Primary care/Generalist	15 (1.1)	4 (26.7)	11 (73.3)	0.608
OB-GYN	413 (29.4)	122 (29.5)	291 (70.5)	0.087
<b>Laboratory</b>	349 (24.9)	<b>94 (26.9)</b>	<b>255 (73.1)</b>	<b>0.007</b>
<b>Radiologist</b>	39 (2.8)	<b>23 (59.0)</b>	<b>16 (41.0)</b>	<b>&lt;0.001</b>
<b>Surgeon<sup>b</sup></b>	14 (1.0)	<b>9 (64.3)</b>	<b>5 (35.7)</b>	<b>0.012</b>
<b>Non-specified Hospital inpatient</b>	209 (14.9)	<b>103 (49.3)</b>	<b>106 (50.7)</b>	<b>&lt;0.001</b>
Anesthesiologist	151 (10.8)	52 (34.4)	99 (65.6)	0.662
<b>Pathology</b>	59 (4.2)	<b>19 (32.2)</b>	<b>40 (67.8)</b>	<b>&lt;0.001</b>
<b>Others-specified</b>	154 (11.0)	<b>14 (9.1)</b>	<b>140 (90.9)</b>	<b>&lt;0.001</b>
Total	1,403	440	963	
<i>Procedures</i>				
<b>Laparoscopy</b>	82 (62)	<b>18 (22.0)</b>	<b>64 (78.0)</b>	<b>0.030</b>
Laparotomy <sup>b</sup>	12 (9)	4 (33.3)	8 (66.7)	0.972
Hysterectomy	39 (29)	16 (41.0)	23 (71.4)	0.271
Total	133	38	95	
<b>Total number of claims</b>	<b>2,837</b>	<b>939</b>	<b>1,898</b>	

Subject characteristics were described using frequency distributions or simple descriptive statistics and reported as percent (%).

Statistically significant was set at an alpha level of 0.05 (p-value  $\leq$  0.050)

<sup>b</sup>For variables with less than five in a cell Fisher' exact test was used. For all other variables chi-square test was used.

<sup>c</sup>T test not appropriate for values of 0.

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**Table 3.** Frequency of endometriosis-related treatment claims in women with endometriosis with public vs. private health insurance coverage in Puerto Rico.

<b>Endometriosis treatment</b>	<b>Total number of claims per category</b>	<b>Public (N =171) Number of claims (%)</b>	<b>Private (N = 171) Number of claims (%)</b>	<b>p-value</b>
OCP's/Progesterone	80	41 (51.3)	39 (48.8)	0.798
<b>Danazol/Danocrine*</b>	8	<b>0 (0.0)</b>	<b>8 (100.0)</b>	<b>0.007</b>
GnRH	35	15 (42.9)	20 (57.1)	0.372
<b>NSAID's</b>	<b>212</b>	<b>116 (54.7)</b>	<b>96 (45.3)</b>	<b>0.026</b>
<b>Opioids/Narcotics</b>	115	<b>46 (40.0)</b>	<b>69 (60.0)</b>	<b>0.008</b>
Total	450	218	232	

Statistically significant was set, at an alpha level of 0.05 ( $p\text{-value} \leq 0.05$ )

\*For variables with less than five in a cell, Fisher' exact test was used. For all other variables chi-square test was used.

**Table 4.** Association of treatment with public health insurance coverage in women with endometriosis from Puerto Rico.

<b>Endometriosis treatment</b>	<b>OR crude</b>	<b>AOR (95%CI)</b>	<b>p-value</b>
OCP's/Progesterone	1.0	2.2 (0.326-15.541) <sup>a</sup>	0.748
<b>Danazol/Danocrine*</b>	<b>0.5</b>	<b>0.6 (0.511-0.650)</b>	<b>0.002</b>
GnRH	1.2	2.8 (0.555-14.470) <sup>f</sup>	0.365
NSAID's	0.7	1.5 (0.387-5.814) <sup>a</sup>	0.156
<b>Opioids/Narcotics</b>	<b>1.4</b>	<b>2.7 (1.403-5.247)<sup>ar</sup></b>	<b>0.003</b>

Statistically significant was set, at an alpha level of 0.05 (p-value  $\leq$  0.050)

This Logistic Regression was adjusted by age and region

**Table 5.** Endometriosis-related co-morbid conditions among women with endometriosis insured by a government-based or private insurance coverage in Puerto Rico.

<b>Co-morbid conditions</b>	<b>Public N= (%)</b>	<b>Private N= (%)</b>	<b>p-value</b>
Skin-related infections	45 (33.6)	89 (66.4)	<b>&lt;0.001</b>
Muscle-related	72 (63.2)	42 (36.8)	<b>0.001</b>
Cold and Flu	44 (37.9)	72 (62.1)	<b>0.001</b>
Mental disorders	21 (32.3)	44(67.7)	<b>0.002</b>
Urinary infections	51 (64.6)	28 (35.4)	<b>0.003</b>
Migraine*	2 (13.3)	13 (86.7)	<b>0.006</b>

Vitamin and Minerals deficiency	43 (63.2)	25 (36.6)	<b>0.015</b>
Vaginal Infections	41 (40.6)	60 (59.4)	<b>0.024</b>
Bone-related disorders	46 (61.3)	29 (38.7)	<b>0.026</b>
Breast cancer*	2 (16.7)	10 (83.3)	<b>0.035</b>
Thyroid disorders	10 (32.3)	21 (67.7)	<b>0.038</b>
Neuropathic pain*	5 (26.3)	14 (73.7)	0.056
Eye-related conditions	10 (34.5)	19 (65.5)	0.081
Allergies	68 (44.7)	84 (55.3)	0.082
STD's	7 (35.0)	13 (65.0)	0.167
Heart disease*	10 (32.3)	4 (28.6)	0.171
Hypertension	35 (57.4)	26 (42.6)	0.204
Hyperlipidemia *	4 (30.8)	9 (69.2)	0.258
Diabetes	9 (39.1)	14 (60.9)	0.280
Hyperprolactinemia *	3 (33.3)	6 (66.7)	0.502
Motion sickness	18 (54.5)	15 (45.5)	0.583
Fungal infections	35 (47.9)	38 (52.1)	0.692
Ear-related conditions	17 (53.1)	15 (46.9)	0.710
Asthma/COPD	28 (48.3)	30 (51.7)	0.773
Bacterial infections	134 (50.2)	133 (49.8)	0.896
Gastrointestinal disorders	65 (50.4)	64 (49.6)	0.911
Skin cancer*	2 (66.7)	1 (33.3)	0.999
Fertility*	0 (0.0)	1 (100.0)	0.999
Incontinence*	1 (50.0)	1 (50.0)	0.999
Others	6 (21.4)	22 (78.6)	<b>0.002</b>

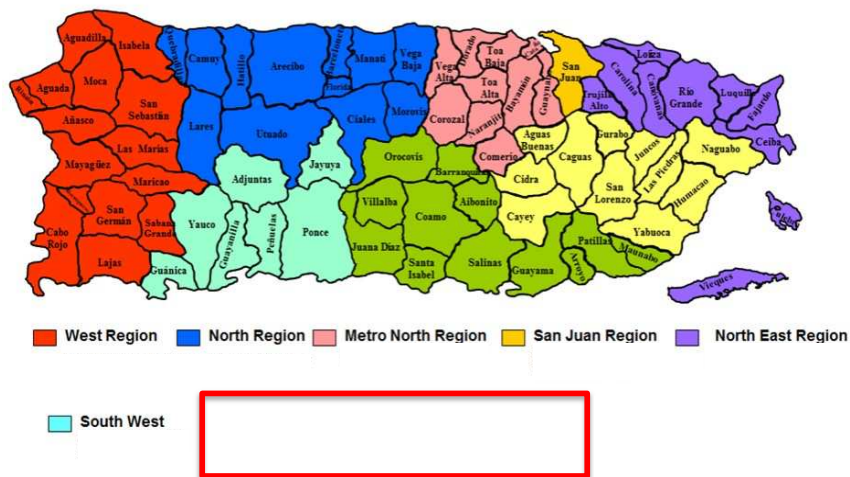
Statistically significant was set, at an alpha level of **0.05** (p-value  $\leq$  0.050)

\*For variables with less than five in a cell, Fisher' exact test will be use. For all other variables chi-square test was used

## FIGURES

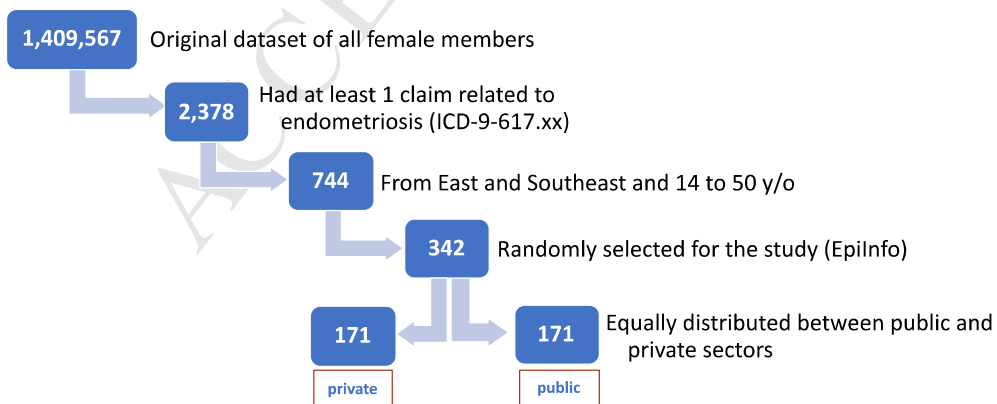
**Figure 2:** Health care regions in Puerto Rico

**Figure 1:** Health care regions in Puerto Rico



**Figure 2:** Diagrammatic representation of process used to select study participants

Figure 2: Study population



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**Table 1.** Endometriosis-related medical claims by health insurance coverage type

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Median (Range)	<b>1</b> (1-16)	<b>3</b> (1-35)	
Number of subjects in each claim frequency category			<b>&lt;0.001</b>
1-3 claims	128 (56.6)	98 (43.4)	
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- a. Subject characteristics were described using frequency distributions or simple descriptive statistics and are reported as percent (%).
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- c.

**Table 2.** Frequency of healthcare utilization services among all claims of women with endometriosis by health insurance coverage

Healthcare utilization services	Total Number of claims per category (%)	Public (N=171) Number of claims (%)	Private (N=171) Number of claims (%)	p-value
<i>Place of services</i>				
Doctor's office	640 (49)	201 (31.4)	439 (68.6)	<b>&lt;0.001</b>
<b>Hospital-related</b>	251 (19.3)	<b>119 (47.4)</b>	<b>132 (52.3)</b>	<b>&lt;0.001</b>
<b>Emergency Room<sup>b</sup></b>	21 (0.2)	21 (100)	0 (0.00)	<b>0.27</b>
Laboratory/X-Rays	389 (30)	120 (30.8)	269 (69.2)	<b>0.27</b>
Total	1,301	461	840	<b>N/A/N/A</b>
<i>Doctor's specialty</i>				
Primary care/Generalist	15 (1.1)	4 (26.7)	11 (73.3)	0.608
OB-GYN	413 (29.4)	122 (29.5)	291 (70.5)	0.087
<b>Laboratory</b>	349 (24.9)	<b>94 (26.9)</b>	<b>255 (73.1)</b>	<b>0.007</b>
<b>Radiologist</b>	39 (2.8)	<b>23 (59.0)</b>	<b>16 (41.0)</b>	<b>&lt;0.001</b>
<b>Surgeon<sup>b</sup></b>	14 (1.0)	<b>9 (64.3)</b>	<b>5 (35.7)</b>	<b>0.012</b>
<b>Non-specified Hospital inpatient</b>	209 (14.9)	<b>103 (49.3)</b>	<b>106 (50.7)</b>	<b>&lt;0.001</b>
Anesthesiologist	151 (10.8)	52 (34.4)	99 (65.6)	0.662
<b>Pathology</b>	59 (4.2)	<b>19 (32.2)</b>	<b>40 (67.8)</b>	<b>&lt;0.001</b>
<b>Others-specified</b>	154 (11.0)	<b>14 (9.1)</b>	<b>140 (90.9)</b>	<b>&lt;0.001</b>
Total	1,403	440	963	
<i>Procedures</i>				
<b>Laparoscopy</b>	82 (62)	<b>18 (22.0)</b>	<b>64 (78.0)</b>	<b>0.030</b>
Laparotomy <sup>b</sup>	12 (9)	4 (33.3)	8 (66.7)	0.972
Hysterectomy	39 (29)	16 (41.0)	23 (71.4)	0.271
Total	133	38	95	
<b>Total number of claims</b>	<b>2,837</b>	<b>939</b>	<b>1,898</b>	

Subject characteristics were described using frequency distributions or simple descriptive statistics, and reported as percent (%).

Statistically significant was set at an alpha level of 0.05 (p-value  $\leq$  0.050)

<sup>b</sup>For variables with less than five in a cell Fisher' exact test was used. For all other variables chi-square value was used.



**Table 3.** Frequency of endometriosis-related treatment claims in women with endometriosis with public vs. private health insurance coverage in Puerto Rico.

<b>Endometriosis treatment</b>	<b>Total number of claims per category</b>	<b>Public (N =171) Number of claims (%)</b>	<b>Private (N = 171) Number of claims (%)</b>	<b>p-value</b>
OCP's/Progesterone	80	41 (51.3)	39 (48.8)	0.798
<b>Danazol/Danocrine*</b>	8	<b>0 (0.0)</b>	<b>8 (100.0)</b>	<b>0.007</b>
GnRH	35	15 (42.9)	20 (57.1)	0.372
<b>NSAID's</b>	<b>212</b>	<b>116 (54.7)</b>	<b>96 (45.3)</b>	<b>0.026</b>
<b>Opioids/Narcotics</b>	115	<b>46 (40.0)</b>	<b>69 (60.0)</b>	<b>0.008</b>
Total	450	218	232	

Statistically significant was set, at an alpha level of 0.05 (p-value  $\leq$  0.05)

\*For variables with less than five in a cell, Fisher' exact test was used. For all other variables chi-square value was used.

**Table 4.** Logistic regression analysis of treatment profiles of women with endometriosis with public health insurance

<b>Endometriosis treatment</b>	<b>OR crude</b>	<b>AOR (95%CI)<sup>#</sup></b>	<b>p-value</b>
OCP's/Progesterone	1.0	2.2 (0.326-15.541) <sup>a</sup>	0.748
<b>Danazol/Danocrine*</b>	<b>0.5</b>	<b>0.6 (0.511-0.650)</b>	<b>0.002</b>
GnRH	1.2	2.8 (0.555-14.470) <sup>r</sup>	0.365
NSAID's	0.7	1.5 (0.387-5.814) <sup>a</sup>	0.156
<b>Opioids/Narcotics</b>	<b>1.4</b>	<b>2.7 (1.403-5.247)<sup>ar</sup></b>	<b>0.003</b>

Statistically significant was set at an alpha level of 0.05 (p-value  $\leq$  0.050)

<sup>#</sup>Adjusted by age (a) and region (r).

**Table 5.** Endometriosis-related co-morbid conditions among women with endometriosis insured by a government-based or private insurance coverage in Puerto Rico.

<b>Co-morbid conditions</b>	<b>Public N= (%)</b>	<b>Private N= (%)</b>	<b>p-value</b>
Skin-related infections	45 (33.6)	89 (66.4)	<b>&lt;0.001</b>
Muscle-related	72 (63.2)	42 (36.8)	<b>0.001</b>
Cold and Flu	44 (37.9)	72 (62.1)	<b>0.001</b>
Mental disorders	21 (32.3)	44(67.7)	<b>0.002</b>
Urinary infections	51 (64.6)	28 (35.4)	<b>0.003</b>
Migraine*	2 (13.3)	13 (86.7)	<b>0.006</b>
Vitamin and Minerals deficiency	43 (63.2)	25 (36.6)	<b>0.015</b>
Vaginal Infections	41 (40.6)	60 (59.4)	<b>0.024</b>
Bone-related disorders	46 (61.3)	29 (38.7)	<b>0.026</b>
Breast cancer*	2 (16.7)	10 (83.3)	<b>0.035</b>
Thyroid disorders	10 (32.3)	21 (67.7)	<b>0.038</b>
Neuropathic pain*	5 (26.3)	14 (73.7)	0.056
Eye-related conditions	10 (34.5)	19 (65.5)	0.081
Allergies	68 (44.7)	84 (55.3)	0.082
STD's	7 (35.0)	13 (65.0)	0.167
Heart disease*	10 (32.3)	4 (28.6)	0.171
Hypertension	35 (57.4)	26 (42.6)	0.204
Hyperlipidemia *	4 (30.8)	9 (69.2)	0.258
Diabetes	9 (39.1)	14 (60.9)	0.280
Hyperprolactinemia *	3 (33.3)	6 (66.7)	0.502

Motion sickness		18 (54.5)	15 (45.5)	0.583
Fungal infections		35 (47.9)	38 (52.1)	0.692
Ear-related conditions		17 (53.1)	15 (46.9)	0.710
Asthma/COPD		28 (48.3)	30 (51.7)	0.773
Bacterial infections	267	134 (50.2)	133 (49.8)	0.896
Gastrointestinal disorders	129	65 (50.4)	64 (49.6)	0.911
Skin cancer*		2 (66.7)	1 (33.3)	0.999
Fertility*		0 (0.0)	1 (100.0)	0.999
Incontinence*		1 (50.0)	1 (50.0)	0.999
Others		6 (21.4)	22 (78.6)	<b>0.002</b>

Statistically significant was set, at an alpha level of **0.05** ( $p\text{-value} \leq 0.050$ )

\*For variables with less than five in a cell, Fisher' exact test was used. For all other variables chi-square value was used.

**Table 6.** Logistic regression analysis of co-morbid conditions with public health insurance coverage in women with endometriosis from Puerto Rico

<b>Other conditions</b>	<b>OR (95%CI)</b>	<b>AOR (95% CI)<sup>a</sup></b>	<b>p-value<sup>b</sup></b>
Ear-related conditions	0.9 (0.420-1.806)	-----	-----
<b>Mental disorder</b>	<b>2.5 (1.398-4.385)</b>	<b>2.5 (1.387-4.352)</b>	<b>0.003</b>
Asthma/COPD	1.1 (0.618-1.912)	-----	-----
Diabetes	1.6 (0.675-3.815)		
Motion sickness	0.8 (0.398-1.680)	-----	-----
<b>Vaginal Infections</b>	<b>1.7 (1.070-2.745)</b>	<b>1.7 (1.074-2.753)</b>	<b>0.032</b>
Gastrointestinal disorders	1.0 (0.630-1.511)	-----	-----
<b>Skin-related infections</b>	<b>3.0 (1.931-4.784)</b>	<b>3.0 (1.916-4.753)</b>	<b>&lt;0.001</b>
Bone-related disorders	0.6 (0.329-0.936)	-----	-----
Eye-related conditions	2.0 (0.907-4.466)		
STD's	1.9 (0.750-4.957)		
Vitamin and Minerals deficiency	0.5 (0.295-0.881)	-----	-----
Upper respiratory infections	<b>2.1 (1.328-3.318)</b>	<b>2.1 (1.330-3.326)</b>	<b>0.002</b>
Skin cancer	0.5 (0.045-5.534)	-----	
Allergies	1.5 (0.953-2.245)		
Hypertension	0.7 (0.398-1.218)	-----	
<b>Neuropathic pain</b>	<b>3.0 (1.042-8.411)</b>	<b>3.3 (1.020-10.042)</b>	<b>0.053*</b>
<b>Migraine</b>	<b>7.0 (1.544-31.297)</b>	<b>7.7 (1.634-35.884)</b>	<b>0.007**</b>

Bacterial infections	1.0 (0.579-1.613)	-----	-----
Fungal infections	1.1 (0.662-1.863)	-----	-----
Muscle-related	0.5 (0.282-0.711)	-----	-----
<b>Breast cancer</b>	<b>5.2 (1.133-24.322)</b>	<b>5.2 (1.1120-28.744)</b>	0.041**
Hyperprolactinemia	2.0 (0.501-8.278)		
Hyperlipidemia	2.3 (0.700-7.681)		
Fertility	-----	-----	-----
Heart diseases	0.4 (0.119-1.254)	-----	-----
Thyroid disorders	2.3 (1.028-4.943)	2.2 (1.011-4.836)	0.065***
Urinary infections	0.5 (0.274-0.776)	-----	-----
Incontinence	1.0 (0.062-16.118)	-----	-----
<b>Others</b>	<b>4.1 (1.603-10.286)</b>	3.4 (1.378-8.708)	0.008*

- a. Logistic regression for OR with 95% CI was calculated, adjusting for age, and region
- b. The p-value will be calculated for adjusted OR
- c. Variables with a small sample, adjusted OR cannot be calculated.

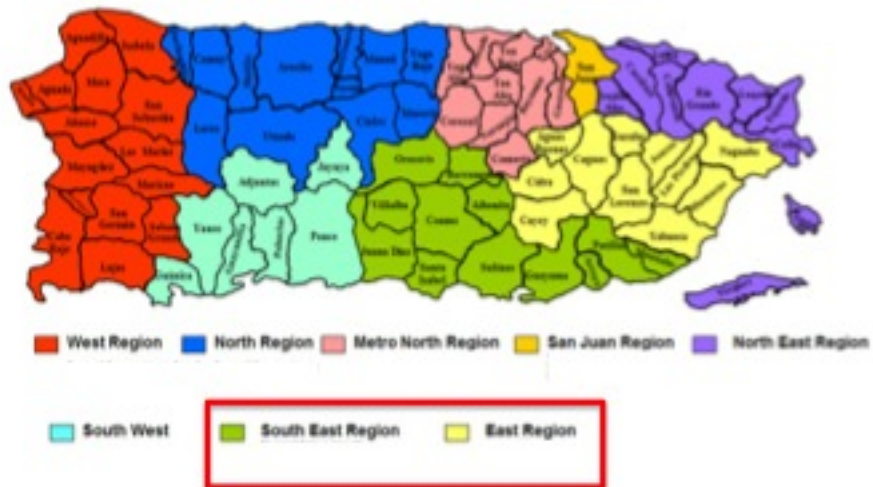
NS = Not significant

\*There was interaction by region

\*\*There was an interaction by age and region

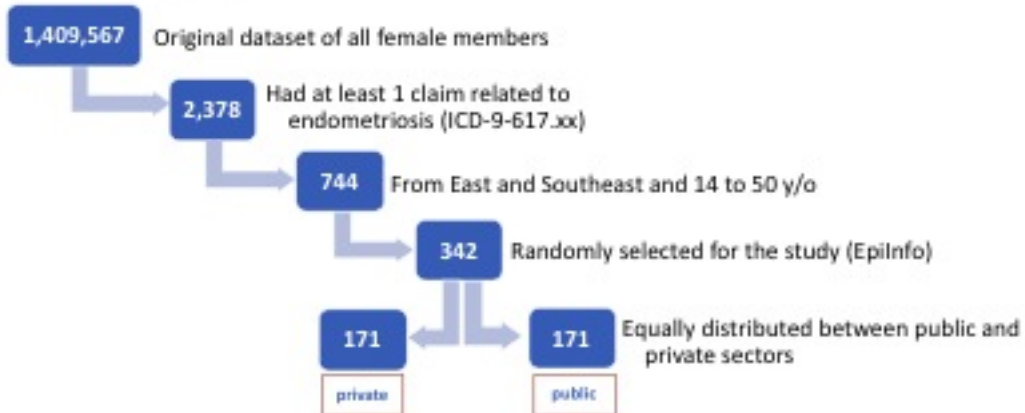
\*\*\*Confounded by age

Figure 1: Health care regions in Puerto Rico



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Figure 2: Study population



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