The Impact of Evolving Diagnostic Guidelines on Clinical Characterization of Endometriosis

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Background

Endometriosis is a chronic gynecological condition characterized by growth of endometrial tissue outside the uterus.[1,2] Marked by a heterogeneous set of symptoms that vary widely among women, the complex disorder can impact a range of body systems and often involves chronic pain, dysmenorrhea, dyspareunia, dysuria, and fatigue. In 2022, clinical guidelines shifted toward a more multimodal approach to diagnosis, emphasizing assessment of indicative symptoms and the use of diagnostic imaging such as transvaginal sonography and magnetic resonance imaging as a complement to laparoscopic surgery.[3-5] This shift in clinical guidelines acknowledges high variability in diagnosing endometriosis and aims to enhance accuracy and expedite diagnosis. It also suggests prior characterizations may not accurately reflect the full composition, care patterns, and spectrum of experiences associated with endometriosis. This study aimed to investigate how changes in clinical guidelines might impact patterns of diagnosis.

Methods

We performed an observational cohort study of women aged 15-49 years diagnosed with endometriosis between January 1, 2013, and December 31, 2023. Data sources included United States (US) insurance claims data from the Merative™ MarketScan® Commercial Database (CCAE), Merative™ MarketScan® Multi-State Medicaid Database (MDCD), Optum® de-identified Electronic Health Record data set (Optum® EHR), and Columbia University Irving Medical Center electronic health record (CUIMC EHR). We standardized each dataset using the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM).[6,7]

We compared five cohort definitions: women diagnosed with endometriosis based on (i) surgical confirmation (Cohort A); (ii) imaging and guideline-recognized symptoms (Cohort B); (iii) guideline-recognized symptoms, regardless of imaging (Cohort C); (iv) guideline-recognized symptoms and/or pelvic pain (Cohort D); and (v) guideline-recognized symptoms, pelvic pain, and/or abdominal pain (Cohort E). We restricted our analysis to participants with at least one year of continuous observation prior to cohort entry.

We examined age at diagnosis, proportion of patients shared among and unique to each cohort, and the prevalence of conditions, medications, and procedures documented prior to receipt of diagnosis. Among participants identified by multiple cohort definitions, we also assessed differences in cohort entry date. We examined pairwise differences between cohorts using Chi-squared and z-tests with Bonferroni correction to account for multiple comparisons.

Results

During the review period, we identified 491,048 women with endometriosis across the CCAE (N=236,594), Optum® EHR (N=181,743), MDCD (N=70,426), and CUIMC EHR (N=2,285) datasets. Only 15-20% of cases were captured by all 5 phenotypes. More than one-fourth (26-30%) were only captured by symptom-based definitions (Cohorts C-E). Women were 1% Asian, 7-8% Black/African American, and 37-40% white depending on data source; 52-55% were of unknown race and 3% were of Hispanic/Latina ethnicity. As findings were consistent across data sources, remaining data presented are from our largest EHR dataset (**Figure 1**).

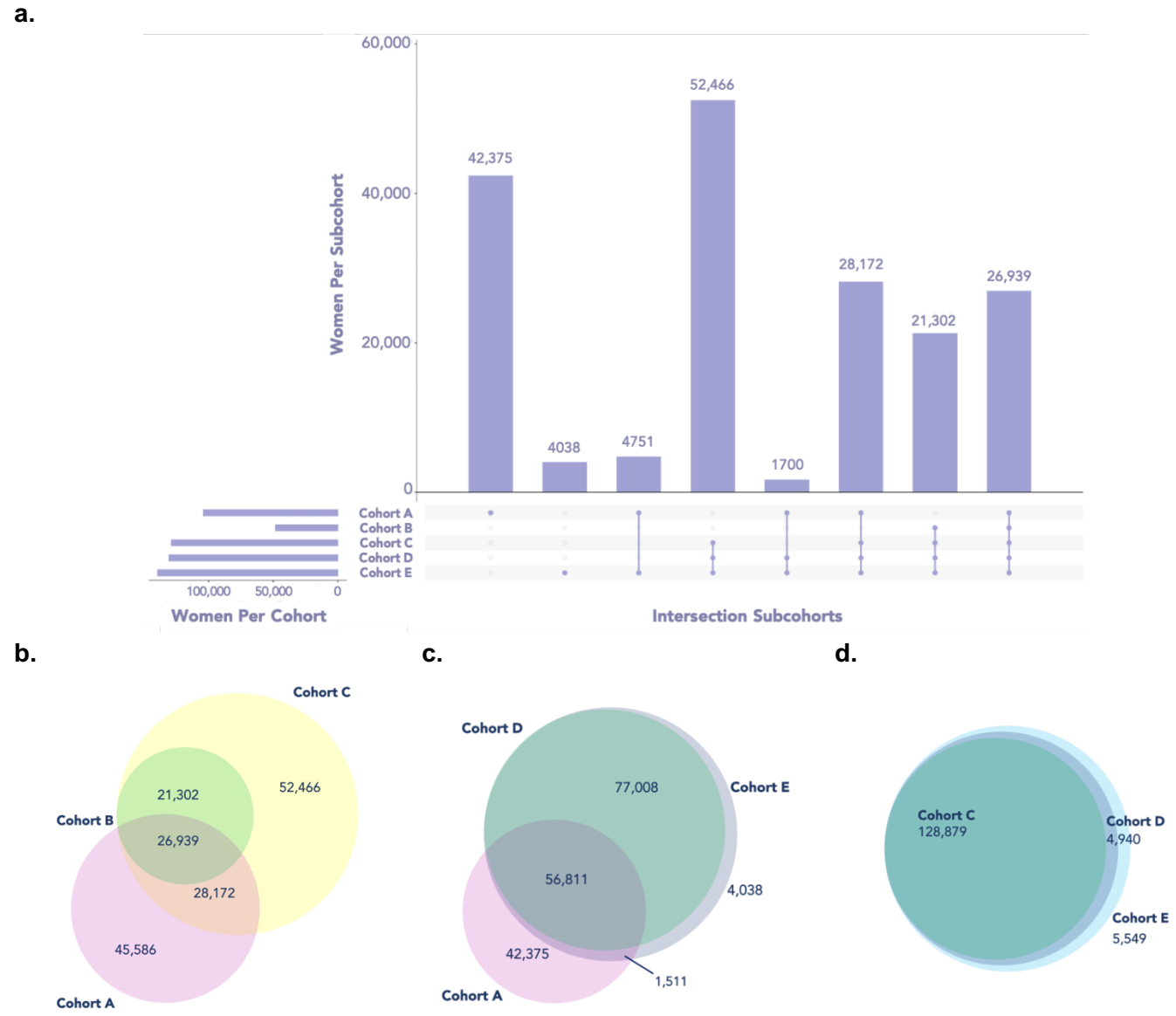

Figure 1a-d. Patient Set Overlap Among Study Cohorts in Optum EHR Dataset. a) UpSet plot illustrating intersections across all cohorts. b) Venn diagram of Cohorts A, B, and C. c) Venn diagram of Cohorts A, D, and E. d) Venn diagram of Cohorts C, D, and

Notably, women with a diagnosis of endometriosis based on surgical confirmation were older at time of diagnosis compared to women diagnosed based on imaging and symptoms (mean age = 38 years [SD = 8] in Cohort A vs 35 years [SD = 9] in Cohort B; p<0.001). We found a similar trend when comparing age at diagnosis between Cohort A and Cohorts C-E (mean age = 36, average SD = 8) with a mean age difference of 2 years (p<0.001 for all comparisons). In contrast, for most women diagnosed with endometriosis, there was little-to-no difference in date of cohort entry between Cohorts A and B (**Figure 2;** median difference = 0 days, IQR = 0-45 days). Similarly, we found almost no difference between entry into Cohort A and Cohorts C-E (median difference = 0 days for all, IQR = 0-15 days for Cohort C, 0-14 days for Cohort D, and 0-13 days for Cohort E).

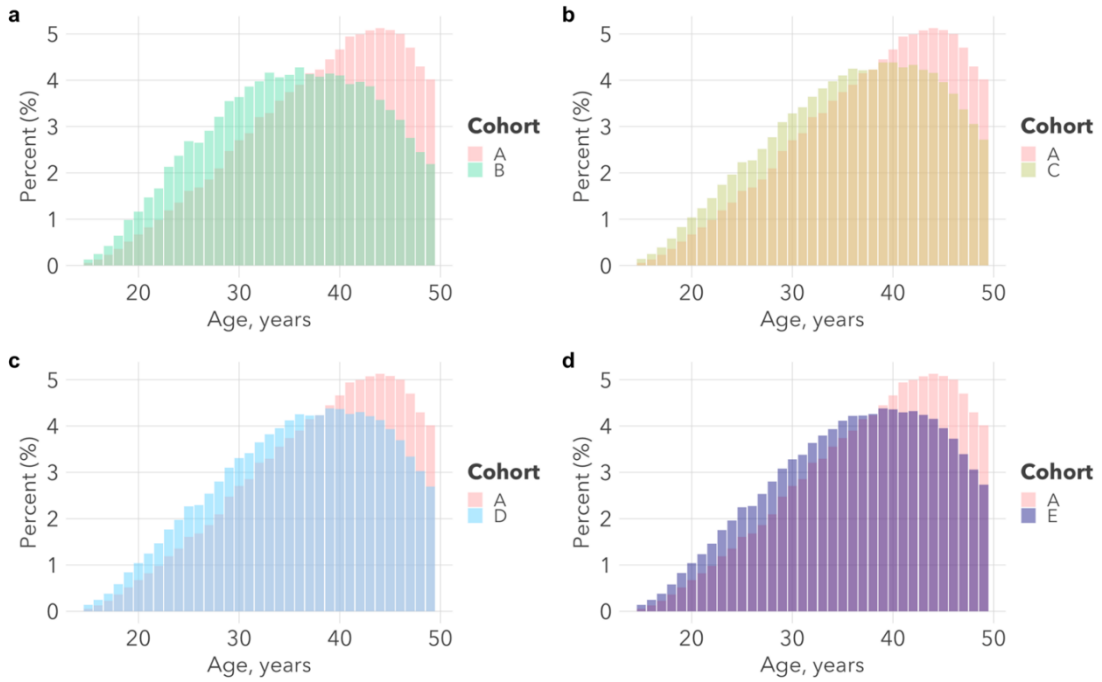

Figure 2a-d. Age at Diagnosis of Endometriosis (Optum EHR Dataset)

Pain was most commonly reported (91% of Cohort A, 100% of Cohorts B-E). Localized pain of the abdomen and pelvis (69%-70% of women in Cohort A, 83%-90% in Cohorts B-E) were documented without mention of guideline-based symptoms in 2-5% of all cases (14,795 women total). Among guideline-recommended treatments, women in Cohorts B-E were more likely to receive hormones and related agents (44% in Cohort A, 61% in Cohort B, 50-51% in Cohorts C-E), including hormonal contraceptives for systemic use (50% in Cohort A, 67% in Cohort B, 56-57% in Cohorts C-E). Opioid use was common among all cohorts, especially women in Cohort A (96% in Cohort A, 82% in Cohort B, 77-78% in Cohorts C-E). Women diagnosed based on imaging and symptoms made more emergency room (ER) visits (**Table 1**; 41% of women in Cohort B vs 30% in Cohort A, p<0.001; mean visits = 1.4, SD = 4.3 in Cohort B vs mean visits = 0.8, SD=3.2 in Cohort A; p<0.001). While nearly half of women (45%) in Cohort A had at least one hospitalization prior to diagnosis (mean = 0.6, SD=1.1), this was the case for only one-fourth (26%) in Cohort B (mean = 0.4, SD=1.8). Similar trends held when comparing Cohorts C-E to Cohort A.

Table 1. Healthcare Utilization (Optum EHR Dataset)

Encounter Type	**Characteristic**	**Cohort A** (N = 100,697)	**Cohort B** (N=48,241)	**Cohort C** (N = 128,879)	**Cohort D** (N = 133,819)	**Cohort E** (N = 139,368)
Outpatient Visits	n (%)	100,362 (100)	47,755 (99)	126,060 (98)	130,889 (98)	136,191 (98)
	mean (SD)	17.4 (16.7)	20.5 (18.8)	17.1 (17.6)	16.8 (17.4)	16.4 (17.3)
	median (IQR)	13 (6-23)	15 (8-27)	12 (5-23)	12 (5-22)	11 (5-22)
ER Visits	n (%)	30,560 (30)	19,738 (41)	43,170 (34)	44,118 (33)	44,949 (32)
	mean (SD)	0.8 (3.2)	1.4 (4.3)	1 (3.9)	1 (3.8)	0.9 (3.8)
	median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)
Inpatient Visits	n (%)	45,459 (45)	12,287 (26)	32,564 (25)	33,599 (25)	34,830 (25)
	mean (SD)	0.6 (1.1)	0.4 (1.8)	0.4 (1.5)	0.4 (1.5)	0.4 (1.4)
	median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)

Abbreviations: EHR, electronic health record. ER, emergency room. IQR, interquartile range. SD, standard deviation.

Conclusion

Overlap among women identified by all five cohort definitions represented only 15-20% of all endometriosis cases, reflecting the heterogeneous presentation of the disease and importance of expanding diagnostic criteria. Cohorts derived from updated clinical guidelines identified patients who were younger at time of diagnosis. Our analysis further revealed higher rates of ER visits among women diagnosed based on imaging and a larger number of hospitalizations among patients diagnosed via laparoscopy. Nearly one-fourth of cases were also consistently identified only when using symptom-based phenotypes, suggesting that imposing surgery or imaging-related constraints to diagnosis may miss a substantial portion of women. Additionally, a sizable percentage of women presented with only pelvic and/or abdominal pain and none of the guideline-recognized symptoms. These findings underscore the continued need for improved access to timely and appropriate care, particularly among those who may present with non-classical symptoms, demonstrate different care-seeking preferences, or lack access to surgical intervention. Nonetheless, limitations associated with secondary use of insurance claims and EHR data should be considered, including reliance on clinical codes that do not necessarily capture all diagnostic guideline criteria for endometriosis.

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