

SYSTEMATIC REVIEW OPEN ACCESS

Time to Diagnose Endometriosis: Current Status, Challenges and Regional Characteristics—A Systematic Literature Review

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ABSTRACT

Background: Endometriosis diagnosis reportedly faces delays of up to 10 years. Despite growing awareness and improved guidelines, information on the current status is limited.

Objectives: To systematically assess the published evidence on the status of time to diagnosis in individuals with endometriosis, with respect to the definition of time to diagnosis, geographical location and patient characteristics.

Search Strategy: MEDLINE (via PubMed) and Embase were searched for publications reporting time to diagnosing endometriosis since 2018. No restrictions to population or comparators were applied. All publications were screened by two independent reviewers.

Selection Criteria: Search results were limited to primary publications of randomised controlled trials, non-randomised trials and observational studies. Case reports, secondary publications and grey literature were excluded. No restrictions were made regarding language, provided that an English title and abstract were available.

Data Collection and Analysis: Publications were assessed with respect to time to diagnosis, diagnostic methods, study type, study country and potential bias.

Main Results: The 17 publications eligible for inclusion in this literature review were all observational studies. The publications reported diagnosis times between 0.3 and 12 years, with variations depending on the definition of time to diagnosis (overall, primary, or clinical), geographical location and characteristics of the included study population. Evidence was of poor to good quality overall.

Conclusions: Diagnostic delay is still present, primarily driven by physicians, and this review underscores the need for standardised definitions, increased awareness and targeted diagnostic interventions.

1 | Introduction

Endometriosis research has gained considerable interest over the last decades. Despite growing interest, numerous challenges still remain, including the lack of universal diagnostic criteria, the difficulty of identifying a definite diagnosis due to the diverse

symptomatology and diagnostic challenges, the ongoing normalisation of underlying endometriosis symptoms by both the health care provider and patient and many more [1–3]. These factors contribute to a delay between the onset of first symptoms and a definite diagnosis, ultimately delaying effective treatment. The delay can have profound implications for patients, contributing to

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potentially worsened symptoms [4, 5], impaired quality of life [6, 7] and increased healthcare costs [8]. As the diagnostic delay seems to be a catalyst for many challenges in the endometriosis research field currently investigated, reducing the diagnostic delay is key.

Diagnostic delay in endometriosis is a well-known phenomenon, with studies consistently reporting prolonged intervals of up to 7–10 years between the symptom onset and confirmed diagnosis [8]. A 1997 study observed a decreased time to diagnosis from 9.21 to 4.63 years over 15 years [5]. A recent study in the United States noted a mean time from symptom onset to diagnosis of 4.4 years, suggesting a potentially shorter diagnostic journey in contemporary healthcare settings [9]. In recent years, efforts have been made to raise awareness about endometriosis and reduce delays through initiatives such as awareness campaigns [10], patient advocacy groups [11] and educational programs for healthcare professionals [12]. Numerous (inter)national organisations have published guidelines on the diagnosis of endometriosis: the American College of Obstetricians and Gynecologists [13], the European Society of Human Reproduction and Embryology [14], the Royal Australian and New Zealand College of Obstetricians and Gynaecologists [15] and the UK National Institute for Health and Care Excellence [16]. These guidelines aim for increased awareness among healthcare providers about the diagnostic criteria of endometriosis and thus may lead to earlier recognition and referral of affected individuals for specialist evaluation. Additionally, the standardisation of diagnostic protocols outlined in these guidelines may streamline the diagnostic process, reducing unnecessary delays caused by variations in clinical practice.

Given these numerous advancements, the increased awareness and research interest in the field of endometriosis, our aim was to assess the current status of time to diagnosis, focusing on studies published from 2018 onwards. More specifically, we aimed to quantify the current time to diagnosis in different geographical regions and population groups (e.g., comorbidities, symptoms, ethnicity and gender).

2 | Methods

2.1 | Literature Search

A pre-specified protocol (PROSPERO ID: CRD42023453141) was followed for this study which adhered to the current Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Appendix S2). A comprehensive literature search using MEDLINE (via PubMed) and Embase was performed to identify (non-) randomised trials, observational longitudinal and cross-sectional studies, case reports and case series from January 1, 2018 to May 16, 2023, the day of conducting the search. By focusing on studies published from 2018 onwards, we aimed to capture the most current data, reflecting the contemporary clinical environment and patient experience with respect to time to diagnosis. The complete search string is provided as Supporting Information (Appendix S1). In summary, a combination of MeSH (medical subject headings) or Emtree index terms and free text search terms were used to identify eligible publications.

For the scope of our search, all publications related to individuals diagnosed with endometriosis and reported information

on diagnosis time were targeted. Identified publications were screened independently by two reviewers based on title and abstract, before conducting a full text assessment on the remaining publications. The following inclusion and exclusion criteria were applied for the search. Publications that focused on individuals of all ages diagnosed with endometriosis could be included. All methods for diagnoses were accepted (e.g., based on clinical symptoms, laparoscopy, etc.), provided that the diagnosis was confirmed by the treating physician. Publications were included regardless of interventions or comparators if they allowed an assessment of diagnosis time. Included publications were limited to primary publications (such as original research articles or conference abstracts), whereas secondary publications (e.g., narrative reviews, systematic reviews, or meta-analyses), grey literature (e.g., government reports, graduate dissertations, unpublished clinical trials, etc.) and anecdotal evidence (e.g., case reports) were excluded. Articles of all languages were included, provided that an English title and abstract were available for screening of search results. Eligible publications in languages other than English were assessed with an automated translation using Google translate. Publications were included or excluded according to unanimous votes of both reviewers. Any discrepant findings were resolved in discussion.

A flowchart depicting the screening process is provided in Figure 1. A qualitative and narrative synthesis of included publications was performed. The following information was extracted from each publication: reported diagnosis time, study design, overall sample size, study country/–ies, gender, population of interest, time of data collection, diagnostic methods and specialty of the diagnosing physician. Ethics approval was not required for the scope of the systematic review.

2.2 | Bias Assessment

The risk of bias was critically assessed by two independent reviewers for a synoptic view and a subsequent discussion of bias across included publications. The following appraisal tools were used depending on the study type: the critical appraisal skills programme (CASP) tool [17] for cohort studies and the critical appraisal tool for cross-sectional studies (AXIS) [18].

2.3 | Presentation of Overall Time to Diagnosis

Mean and/or median time to diagnosis was presented as reported in single publications. In case only ranges were reported, mean years until diagnosis were calculated by first determining the midpoints of each range. Each midpoint was then multiplied by the number of participants in that range to obtain a weighted sum and was then divided by the total sample size.

2.4 | Definition of Diagnostic Delay

The authors classified diagnosis time according to three definitions: (1) the time between the onset of first symptoms until diagnosis of endometriosis by a physician (i.e., overall diagnosis time), (2) the time between the onset of first symptoms until the first related physician visit (i.e., primary diagnosis time) and (3)

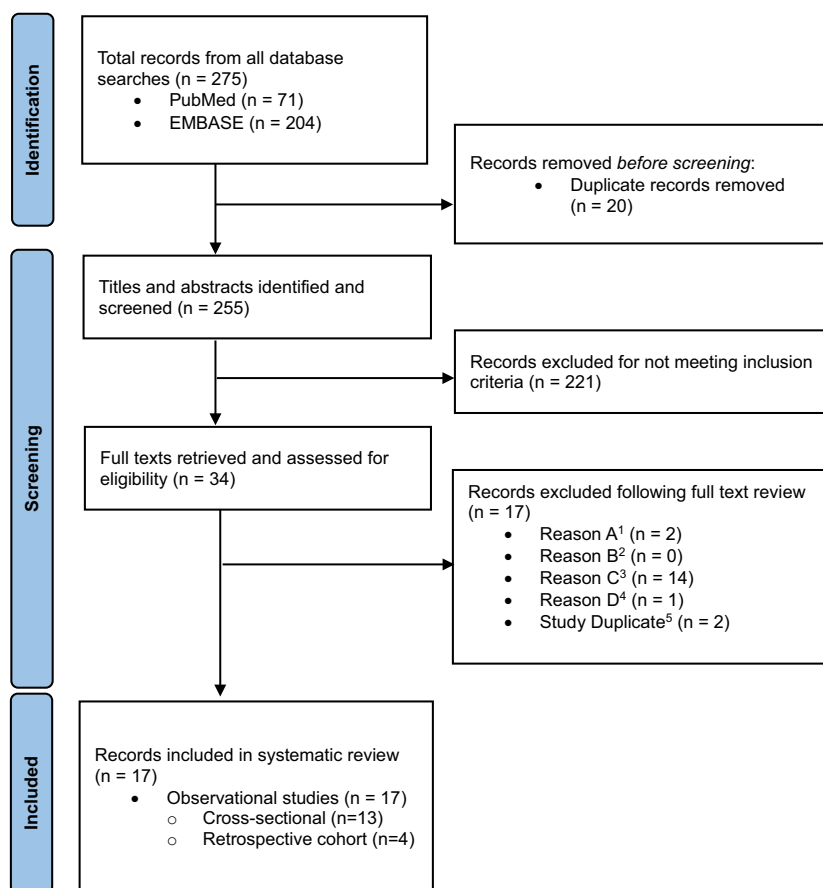


FIGURE 1 | Flowchart of search process and study selection according to PRISMA guidelines. Multiple reasons allowed. ¹A: Population (i.e., persons not diagnosed with endometriosis); ²B: Intervention (i.e., publications with and without interventions that do not allow an assessment of diagnosis time); ³C: Outcome (i.e., publications that do not allow an assessment of diagnosis time); ⁴D: Study type (i.e., case reports); ⁵Several records reporting on the same study results.

the time between the first physician visit and diagnosis of endometriosis (i.e., clinical diagnosis time).

3 | Results

3.1 | Search Results

The literature search was performed in both PubMed and Embase on May 16, 2023. The used search strings (see Appendix S1) resulted in a total of 275 publications (PubMed: 71; Embase: 204). After excluding duplicate entries, 255 publications remained for abstract screening, of which 221 were excluded. Full texts of the remaining 34 publications were then screened again, of which 17 remained for data extraction. An overview of the screening process is provided in Figure 1 together with the main reasons for exclusion of full texts. A comprehensive list of all publications is given in Appendix S3 (Table S1).

3.2 | General Findings

All 17 publications included in this review were observational studies and encompassed two design types, namely,

cross-sectional and retrospective cohort designs. The geographical distribution of included studies was confined to Western high-income nations. Four were based in the United Kingdom [19–21], of which one also comprised Ireland [22], four in the United States [23–26], three in Australia [27–29] and one each in Germany [30], France [31], Italy [32], Canada [33] and New Zealand [34]. One publication did not specify the geographical location [35]. The included sample sizes ranged from 49 to 11 793 individuals with a physician-confirmed endometriosis diagnosis. A summarised overview of included publications is provided in Table 1. Methods used to diagnose endometriosis varied between publications and included laparoscopy, histological confirmation, surgical confirmation (surgery unspecified), empirical/clinical evaluation, physician-suspected, imaging or not specified. In 13 out of 17 publications, the diagnostic confirmation method was self-reported by the study participants.

Despite variations in study methodologies, settings and diagnostic methods, there was minimal heterogeneity observed among the populations studied. Where specified, the majority of included participants were white, highly educated women, aged 30 years or older and presented with multiple symptoms such as pelvic pain, infertility, dysmenorrhea and menstrual or cycle-related gynaecological problems leading to diagnosis or at the

TABLE 1 | Summarised overview of included publications.

Author and year	Study type (data source)	Baseline characteristics				Study country/-ies	Symptoms prior to diagnosis/at onset	Symptom profile included participants	Diagnosis methods	Overall diagnosis time	Primary diagnosis time	Clinical diagnosis time	Diagnosing physician specialty
		Time of data collection	Sample size	Time of data available (Yes/No)?	Gender								
Bullo et al. 2020	Observational cross-sectional study (online survey)	N = 131	Not available	No	Female	UK and Ireland	Pelvic pain, menstruation-related pain	Not specified	Method not specified, selection from the Language of Endo-metriosi's social media platforms	Not available	8.6 years	Not available	
Tewhaiti-Smith et al. 2022	Observational cross-sectional study (online survey)	N = 620	Mar-May 2021	Yes (age, occupation, ethnicity, education, income, gyn history)	Female	Aotearoa New Zealand	Severe dysmenorrhoea (88.7%) Non-cyclical pelvic pain (64.4%) Ovulation pain (46.1%) Chronic fatigue (46.3%) Cyclical/perimenstrual symptoms (40%) Deep dyspareunia (27.9%) Subfertility (7.3%)	Pelvic pain with periods in the last 3 months Occasionally (5.8%) Often (10.5%) Always (83.6%)	Laparoscopy	2.9 years (±4.0) for those with endometriosis	5.8 (±5.7) years Before 2005; 8.4 years (±7.0) 2005–2012; 5.3 years (±4.0) After 2012; 2.0 years (±1.9)	Not specified	
Markowitz et al. 2023	Observational cross-sectional study (retrospective chart review)	N = 152	Jan 2017–Dec 2020	Yes (BMI)	Female	Not Available	Not specified	Not specified	Laparoscopy	Not Available	Obese: 18.4 months (IQR 3.1–42.8) Overweight: 9.0 months (IQR 2.5–23.2) Normal and underweight: 3.8 months (IQR 1.1–17.0)	Physicians from an academic tertiary hospital	
Nicolaus et al. 2020	Observational cross-sectional study (postal survey)	N = 266	Jan 2016–Dec 2017	Yes (age, gyn history)	Female	Germany	With infertility N = 76 Without infertility N = 106 Chronic pelvic pain (91.8%) Dyspareunia (53.3%) Dysmenorrhea (47.3%) Dyschezia (46.7%) Dysuria (24.7%)	Not specified	Histologically confirmed	Not available	<1 year (13.5%–16.9%) 1–5 years (29.8%–31.0%) 6–10 years (12.7%–19.2%) > 10 years (37.5%–39.4%)	Not specified	

(Continues)

TABLE 1 | (Continued)

Author and year	Study type (data source)	Baseline characteristics				Symptom profile included participants	Diagnosis methods	Overall diagnosis time	Primary diagnosis time	Clinical diagnosis time	Diagnosing physician specialty	
		Time of data collection	available (Yes/No)?	Gender	Study country/-ies							
Ghai et al. 2020	Observational cross-sectional study (postal survey)	2014	Yes (gyn history)	Female	UK	Menstrual cramps (73.3%) Trying to conceive > 12 months (48%)	Not specified	Laparoscopy with a confirmatory histology	Median time 8 years (Q1-Q3: 3-14) Women with rectovaginal endometriosis: Median time of 11 years (Q1-Q3: 4-16) Women with superficial endometriosis: median 5 years (Q1-Q3: 1-11) Women that experienced menstrual cramps during adolescence: median 11 years (Q1-Q3: 4.25-16) Women that did not experience menstrual cramps during adolescence: median 2 years (Q1-Q3: 1-5)	From GP to gynaecologist: 1 year (Q1-Q3: 0-4) From gynaecologist to diagnosis: 0 years (Q1-Q3: 0-1) The perceived attitudes of the health professional to pain also influenced the diagnosis. Women who felt their pain were not taken seriously by their GP experienced a twofold time from first symptom(s) to diagnosis (median 12, Q1-Q3: 5.25-15.75 vs. 6, Q1-Q3: 1-13) Those who felt that their gynaecologist did NOT acknowledge their symptoms experienced a median diagnosis time from their initial consultant to a diagnosis of 1 year (Q1-Q3: 0-4.5 vs. 0, Q1-Q3: 0-1)	3 years (Q1-Q3: 0-10)	Gynaecologists

(Continues)

TABLE 1 | (Continued)

Author and year	Study type (data source)	Sample size	Time of data collection	Baseline characteristics		Study country/-ies	Symptoms prior to diagnosis/at onset	Symptom profile included participants	Diagnosis methods	Overall diagnosis time	Primary diagnosis time	Clinical diagnosis time	Diagnosing physician specialty
				available (Yes/No)?	Gender								
Karavadra et al. 2021	Observational cross-sectional study (triphasic design: online survey , semi-structured interviews, focus groups with healthcare workers)	N = 1252 replied to the online questionnaire N = 16 (took part in semi-structured interviews) N = 15 (Healthcare workers participated in focus groups)	Not available	No	Female	UK	Not specified	Not specified	5.5 years	Not available	Not available	Not available	Not specified
Armour et al. 2020	Observational cross-sectional study (online survey)	N = 409 responses were received of which N = 340 have endometriosis N = 67 have chronic pelvic pain without endometriosis diagnosis	Feb 2017- Apr 2017	Yes (age, ethnicity, relationship status, occupation, education, gyn history)	Not specified	Australia	Severe dysmenorrhea (89.4%) Deep Dyspareunia (32.3%) Pelvic pain (78.7%) Ovulation pain (46.7%) Cyclical or perimenstrual (38.1%) Infertility (7.6%) Chronic fatigue (38.8%)	Pelvic pain with periods in last 3 months (85.9%) Pelvic pain with intercourse (69.1%)	8 years	2.9 years (±4.4)	4.9 years (±5.7)	Not specified	
Whitfield et al. 2022	Observational cross-sectional study (retrospective chart review)	N = 9413	N/A	No	Not specified	UK	Abdominal pain (61%) Mental health symptoms (34%) Irregular menstruation (32%)	Not specified	3.7 years Subgroups by age in paper	Not available	Not available	Not specified	
Surrey et al. 2020	Observational cohort study (retrospective chart review)	N = 11 793 n = 4446 short delay (≤ 1 year) n = 3179 intermediate delay (1-3 years) n = 4168 long delay (3-5 years)	Jan 2004-Jul 2016	Yes (age, origin, gyn history, comorbidities)	Not specified	US	Dyspareunia, pelvic pain, abdominal pain, dysmenorrhea, infertility	Not available	Mean: 763.9 ± 631.0 days (2.09 ± 1.77 years) Mean short delay: 90.2 days Mean intermediate delay: 733.4 days Mean long delay: 1505.9 days	Not available	Not available	Not specified	

(Continues)

TABLE 1 | (Continued)

Author and year	Study type (data source)	Baseline characteristics				Symptoms prior to diagnosis/at onset	Symptom profile included participants	Diagnosis methods	Overall diagnosis time	Primary diagnosis time	Clinical diagnosis time	Diagnosing physician specialty	
		Time of data collection	Sample size	Time of data available (Yes/No)?	Study country/-ies								Gender
O'Hara et al. 2022	Observational cross-sectional study (online survey)	Nov 2017- Jan 2018	N = 620 n = 601 responded to diagnostic delay question	Yes (age, origin, education, relationship status, language, insurance, occupation, gyn history)	Australia	Female	GSWH survey comprising list of symptoms*	Pelvic pain with periods (65.8%), pelvic pain with intercourse (61.1%), pain at other times (82.7%)	Surgical	Mean: 6.4 ± 5.8 years	Not available	Not available	Not specified
Bontempo et al. 2020	Observational cross-sectional study (online survey)	April 2017	N = 758 n = 601 completed the survey	Yes (age, race, marital status, education, income, origin, gyn history)	US	Not specified	List of symptoms**	Infertility (47.1%), average worst pain level (0-100) 88.6	Surgical (self-reported)	Mean: 8.6 ± 6.5 years	Not available	Not available	Not specified
Singh et al. 2020	Observational cross-sectional study (online survey)	Dec 2018- Jan 2019	N = 30000 n = 1686 with endometriosis diagnosis and symptoms before diagnosis	Yes (age, ethnicity, origin, gyn history)	Canada	Female	List of symptoms***	Same list of symptoms*** data divided into ever experienced and currently experienced symptoms	Surgical (30.8%) Empirical (32.7%) Physician-suspected (56.4%) (all self-reported)	Mean: 5.4 years	Mean: 3.1 years	Mean: 2.3 years	Obstetrician (53.0%) Primary care physician (19.0%) General surgeon (17.0%) Infertility specialist (7.3%) Urologist (1.1%) Other specialist (2.5%)
Fernley et al. 2021	Observational cross-sectional study (analysis of publicly accessible online autobiographical accounts)	Jun 2019-Aug 2019	N = 49 accounts	No	Australia	Female	Not specified	Not specified	Not specified	<1 year (n = 4) 2-5 years (n = 12) >6 years (n = 27) 11-20 years (n = 12)	Not available	Not available	Not specified
Zhang et al. 2021	Observational cohort study (retrospective chart review)	2015-2020	N = 198 n = 184 white patients n = 14 black patients	Yes (race)	US	Female	Not specified	Pelvic pain (87.3%), dysmenorrhea (72.5%)	Surgical	Mean: 40.6 ± 56.9 months White patients (Mean): 40.3 ± 56.8 months Black patients (Mean): 43.7 ± 60.9 months	Not available	Not available	Not specified

(Continues)

TABLE 1 | (Continued)

Author and year	Study type (data source)	Sample size	Time of data collection	Baseline characteristics		Study country/-ies	Symptoms prior to diagnosis/at onset	Symptom profile included participants	Diagnosis methods	Overall diagnosis time	Primary diagnosis time	Clinical diagnosis time	Diagnosing physician specialty
				available (Yes/No)?	Gender								
Pino et al. 2023	Observational cross-sectional study (online survey)	N=940 n = 689 symptomatic and completed questionnaire	Oct 2014–Jun 2019	Yes (age, origin, education, gyn history)	Female	Italy	Dysmenorrhea, dyspareunia, pelvic pain	Severe pain symptoms, 654 out of 689 patients (93.7%) scored at least 7 on the NRS pain intensity scale when the was at its worst in their lifetime	Surgical (+ histology; n = 344) Imaging (US/MRI, n = 332) Clinical (n = 17)	Mean: 11.4 ± 7.7 years 9–19 years old: 14.8 years (IQR: 10,19) 20–30 years old: 6.9 years (IQR: 1, 11) > 30 years old: 2.9 years (IQR: 0.5, 3) Further sub-groups in full text (number of symptoms (1, 2 or 3) and severity of symptoms (<7 or higher or equal than 7))	Not available	Not available	Not specified
Aubrey et al. 2023	Observational cross-sectional study (consultation survey)	N = 84 n = 57 included for diagnostic delay assessment	Jun 2017–Jun 2019	Yes (age, origin, BMI, occupation, gyn history)	Not specified	France	Not specified	Dysmenorrhea, abdominal pain outside of menses, transit disorder, rectorrhagia, pain on defecation, hematuria, dysuria, dyspareunia, infertility	Surgical (+ histology), 2% Imaging (Ultrasound/MRI), 42%/56%	Median: 12 years (min: 0, max: 33) Subgroup analysis by region and physician specialty in full text	Median: 4 years (min: 0, max: 27) Subgroup analysis by region and physician specialty in full text	Median: 8 years (min: 0, max: 33) Subgroup analysis by region and physician specialty in full text	Gynaecologist (n = 46) General practitioner (n = 11)
DI Vasta et al. 2018	Observational cross-sectional study (online survey)	N = 402 n = 270 adolescents replied to diagnostic delay n = 101 adults replied to diagnostic delay	Nov 2012–Mar 2016	Yes (age, race, BMI, education, gyn history)	Females	US	Pain, infertility	Pelvic pain, abdominal pain, dysmenorrhea, urinary or bowel movement habit changes, gastrointestinal symptoms	Surgical	Median in adolescents: 2 years (min: 0, max: 7) Median in adults: 5 years (min: 0, max: 26)	Median in adolescents: 1 year (min: 0, max: 7) adults: 1 year (min: 0, max: 17)	Not available	Not specified

*Pelvic pain; Pelvic mass; Painful periods; Heavy periods; Infertility; Ovarian cyst; Painful intercourse; Pain on opening bowels; Bleeding from back passage when opening bowels; Bowel upset e.g.: constipation, diarrhoea; Pain on passing urine; Blood in urine; Other urinary problems.
 **Back pain; Bloating; Blood in the stool; Blood in the urine; Chest pain; Constipation; Cramping; Cysts; Diarrhea; Dysmenorrhea; Dyspareunia; Excessive bleeding; Fatigue; Flank pain; Frequent urination; Headache; Infertility; Joint pain; Leg pain; Nausea; Painful bowel movements; Painful urination; Pelvic pain; Rectal pain; Weight gain.
 ***Menstrual pelvic pain or cramping; Non-menstrual pelvic pain or cramping; Dyspareunia; Fatigue, weariness, or anemia; Heavy menstrual bleeding (e.g.: spotting between periods); Passage of clots; Irregular periods (timing and/or duration); Pelvic pressure; Lower back pain; General abdominal pain; Constipation, bloating, or diarrhea; Difficulty having bowel movement; Frequent urination or urinary urgency; Infertility; Depressed feelings or mood swings; Dizziness during period; Anxiety or stress; Complications during pregnancy and labour.

time of study conduct. If information was available, focus was exclusively on study populations with a female gender identity.

The data extraction revealed variations in diagnosis times ranging from 0.3 to 12 years. The overall time to diagnosis ranged from 5 to 12 years, the primary time to diagnosis ranged from 1 to 4 years and the clinical time to diagnosis ranged from 0.3 to 8.6 years. More details on the reported time to diagnosis per country can be found in Figure 2. Due to the difference in the interpretation of time to diagnosis based on the study design, it was decided to report results for cross-sectional and cohort studies separately.

3.3 | Cross-Sectional Studies

Thirteen publications investigated time to diagnosis using a cross-sectional study design, wherein the endometriosis diagnosis was predominantly self-reported by participants, indicating that they were diagnosed by a physician or stated that their diagnosis was confirmed through, e.g., laparoscopy or other diagnostic methods that can only be performed by a healthcare practitioner. Among these studies, 11 reported a mean or median overall diagnosis time. The overall mean time to diagnosis ranged from 5.4 to 11.4 years, and the median time varied between 5 and 12 years. Six publications reported primary diagnosis time: The mean primary diagnosis time ranged from 2.9 to 3.1 years. The reported median primary diagnosis time varied between 1 and 4 years. Seven studies reported a clinical

diagnosis time, which ranged from 2.3 to 8.6 years. Median clinical diagnosis time varied between 3 and 8 years.

3.4 | Retrospective Observational Studies

Four publications used a retrospective cohort study design, in which time to diagnosis was identified via retrospective chart review and available diagnostic codes for endometriosis and endometriosis-related symptoms. Due to the study design, we could only assess clinical diagnosis time for these publications. Mean clinical diagnosis time ranged from 2.1 to 3.7 years, and the median diagnosis time varied between 0.3 and 1.5 years.

3.5 | Quality and Bias Assessment

Quality and bias assessment of the included studies was conducted using the CASP [17] and AXIS [18] tools for the retrospective cohort and the cross-sectional studies, respectively. The studies were evaluated based on criteria such as study design, sample size, methodology and reporting quality. Common biases assessed included selection bias and reporting bias. The results of bias assessment are summarised in Appendix S4 (Tables S1 and S2). In summary, the assessment of eligible publications revealed a range from poor to fair quality for the cross-sectional studies. For the retrospective cohort studies, assessment revealed a range from fair to good quality.

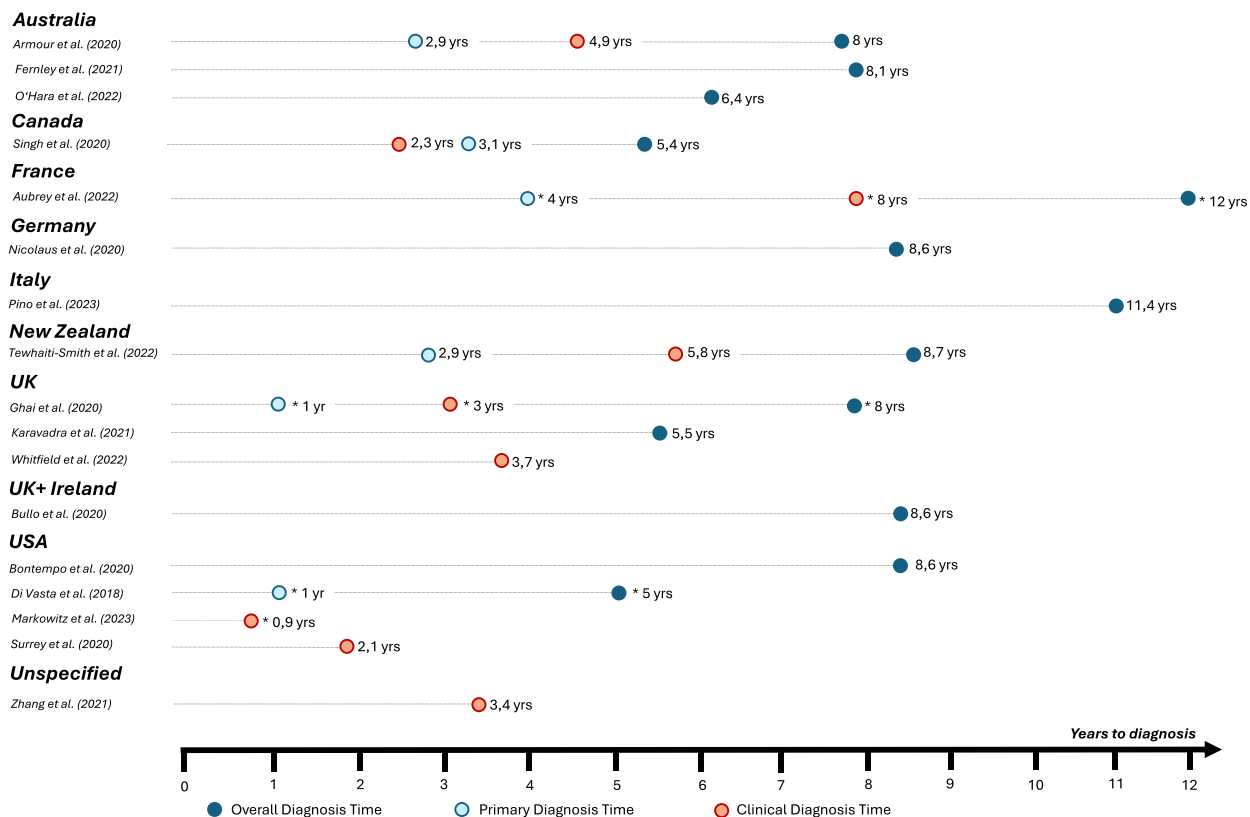


FIGURE 2 | Diagnosis time distributions per country and publication included in this systematic review. The average time to diagnosis is presented as the mean. Instances where the median diagnosis time is reported are marked with an asterisk (*).

4 | Discussion

4.1 | Main Findings

We reviewed publications from January 1, 2018 to May 16, 2023, identifying 17 studies for data extraction. Despite a comprehensive search strategy, few studies addressed current diagnosis time, especially in specific populations like different ethnicities, gender identity groups, or non-Western countries. This gap highlights the need for more research on diagnostic procedures and time to diagnosis across diverse endometriosis populations.

Diagnostic delays were still observed in this systematic review. Seventeen studies reported diagnosis times with varied definitions and study designs, making comparisons difficult. To address this, we categorised delays into three groups: overall, primary and clinical diagnosis times. The time to diagnosis showed significant variation, with mean and median times ranging from 0.3 to 12 years. This variation depended on how time to diagnosis was defined, the geographical location of the study and the characteristics of the study populations.

The overall time to diagnosis varied from 5 to 12 years. These findings align with previously published studies conducted on endometriosis and diagnostic delay between 2010 and 2018, reporting the time of first symptoms to diagnosis between 5 and 13 years [7, 12, 36–39]. These findings and comparison with previous literature highlight that diagnostic delays have remained a persistent issue over the past decade despite advancements and increased awareness. Additionally, it highlights that improvements observed in the 1997 study [40] may not fully reflect the current landscape.

The primary diagnosis time highlights that patients wait 1–4 years in seeking medical attention after experiencing first symptoms. Factors contributing to this delay include a lack of awareness of symptoms [10] or symptom normalisation [41], fear of diagnosis, socioeconomic status, access to healthcare and cultural beliefs [42]. The variation in primary diagnosis times suggests that there are substantial differences in how quickly people seek medical help across regions and populations.

The clinical diagnosis time ranged from 0.3 to 8.6 years, indicating a considerable time between the initial consultation with a healthcare provider and receiving a confirmed diagnosis. Contributing factors may include misinterpretation of symptoms, symptom normalisation [43], lack of access to specialised diagnostic tools or expertise [44], healthcare system inefficiencies and diagnostic challenges due to complex or rare conditions [25, 45]. The wide range of clinical times to diagnosis could further suggest disparities in healthcare infrastructure, resources and expertise across different regions and healthcare settings. Despite existing (inter-)national guidelines, healthcare systems and their qualities vary considerably between countries, and therefore, a more standardised approach is necessary in diagnosing endometriosis.

Five of the selected publications reported differences between patient subcategories, in which longer diagnosis times were seen in individuals who were overweight or obese compared to normal weight individuals [25], who were younger when presenting

first symptoms [21, 26, 32], who had infertility compared to those without infertility [26], who had multiple comorbidities [26] and who were black compared to white individuals [35]. Another qualitative publication reported a twofold time to diagnosis for those who felt their pain not being taken seriously by the general practitioner [19]. Given that these findings were only observed in single studies, it is not possible to draw consistent conclusions. Further research on various patient characteristics and impact on diagnosis time is warranted to corroborate these observations.

Large differences were also seen between countries. The overall diagnosis time was the lowest in the United States and the highest in France. The primary diagnosis time was the lowest in the United Kingdom and the United States and the highest in France. The clinical diagnosis time was the lowest in the United States and the highest in France. Since multiple publications conducted in the United Kingdom, the United States and Australia were included in this review, we could compare diagnosis times reported within the different studies. We noticed large within-country variations in diagnosis time among individuals living in these countries. In the United Kingdom, the overall diagnosis time ranged from 5.5 to 8 years, with clinical delays between 3 and 8.8 years. In the United States, the overall diagnosis time ranged from 5 to 8 years, with clinical delays between 2.1 and 3.4 years. In Australia, the overall diagnosis time varied from 6.4 to 8 years. Due to varying or unspecified descriptive information, the reasons for these differences remain unclear. Future studies need a consistent definition of diagnosis time, detailed study population descriptions and research into the interplay between patient factors, healthcare systems, provider practices and disease-specific issues to address these disparities effectively.

4.2 | Strengths and Limitations

This systematic review summarises the current status and existing challenges with regards to time to diagnose endometriosis and employed a thorough search strategy across PubMed and Embase, ensuring the inclusion of all relevant studies related to endometriosis and diagnostic delay. The review followed a pre-defined and pre-registered protocol outlining the study objectives, inclusion criteria and methods for data extraction and analysis. Adherence to established guidelines (i.e., PRISMA) ensured transparency and reproducibility of the review process. All studies from different geographical regions and diverse populations were considered. Another strength of this paper is the categorisation of time to diagnoses, which enhances comparability across various study designs and assessments, thereby increasing the robustness of our findings.

A couple of limitations should be considered when interpreting the results of this review. The majority of studies on endometriosis relied on cross-sectional, online survey data and self-reported, physician-confirmed diagnoses. This approach can introduce selection bias, as participants in online surveys and forums might not represent the broader population affected by endometriosis [46]. They may have distinct characteristics, like a greater willingness to engage online or different symptom severity, skewing the results. Moreover, many studies lacked detailed baseline

or disease characteristics of participants, limiting our ability to analyse diagnosis time in relation to these factors. The studies also included patients with diverse symptoms such as pelvic pain, infertility and other issues, complicating the analysis and generalisability of the findings. Additionally, most studies did not specify the specialties of diagnosing physicians, making it difficult to evaluate the influence of healthcare provider characteristics on diagnosis time. Despite focusing on papers from the last 5 years, some studies included data collected before 2018. Thus, their figures on diagnosis time might not accurately represent current timelines, potentially hiding any recent improvements in diagnosis speed. It should also be noted that the COVID-19 pandemic, particularly for the studies assessing time to diagnosis from 2020 onwards [25, 34, 35], likely influenced diagnosis time due to restricted healthcare access and resource reallocation. The challenges posed by the pandemic may have contributed to longer diagnostic intervals, which should be considered when interpreting the findings. However, despite including study data during the COVID-19 pandemic, the diagnosis times reported in the corresponding publications [25, 34, 35] were within the overall ranges, as observed across the other publications. Lastly, the quality assessment of eligible publications varied from poor to good, reflecting differences in study methodologies, reporting standards and potential biases. The generalisability of findings is restricted in some cases due to small sample sizes. This variability highlights the need to critically evaluate the evidence base when interpreting the review's findings.

4.3 | Interpretation

Despite medical advancements and awareness campaigns, this systematic review confirms that diagnostic delays persist across healthcare settings, challenging timely patient care. Evidence suggests minimal improvement in diagnosis times in recent years, and the overall time to diagnosis remains high. Delays involve both patients and clinicians, but this review indicates that clinical diagnosis times are more significant than primary times. This highlights a need to raise awareness about endometriosis among healthcare providers, improve access to diagnostic resources and further research early diagnostic markers or interventions.

5 | Conclusion

In conclusion, this systematic review highlights the ongoing issue of diagnostic delay in endometriosis. Both patients and physicians contribute to these delays, but longer delays typically occur on the physician's side. Our findings provide crucial insights into current diagnostic timelines but emphasise the need for a consistent definition of diagnosis time and a clear description of study populations. Understanding the factors contributing to these delays is essential for developing and implementing global interventions to reduce diagnostic delays effectively.

Author Contributions

P.D.C., M.K. and S.v.S.: contributed to the statistical methodology of the study, development of the search strategy and criteria for inclusion and

exclusion of studies, conducted the data analysis and synthesised the findings. They performed the quality assessment of included studies and interpreted the results in the context of existing literature, and contributed to preparing the figures and submission of the paper. M.K. and S.v.S.: were responsible for the systematic search and retrieval of relevant articles. P.D.C.: drafted the first version of the manuscript, and all authors contributed to the revision of the manuscript critically for important intellectual content, also contributed to the main concept and design of the study, and take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Ethics Statement

In conducting this systematic review, ethical approval was not required as the study involved the analysis and synthesis of data from previously published sources, without the involvement of new data collection or direct interaction with human subjects. This approach aligns with the standard practice in systematic reviews, which typically do not necessitate formal ethics approval. Nonetheless, all efforts were made to adhere to ethical guidelines, including ensuring the appropriate use and accurate citation of the original publications.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.