

Review Article

Economic Burden of Endometriosis: A Systematic Review

Katharina C. Koltermann^{1*}, Christina Dornquast¹, Andreas D. Ebert², and Thomas Reinhold¹

¹Institute of Social Medicine, Epidemiology and Health Economics, Charité Universitätsmedizin Berlin, Germany

²Praxis für Frauengesundheit, Gynäkologie und Geburtshilfe, Germany

***Corresponding author**

Koltermann KC, Institute for Social Medicine, Epidemiology and Health Economics, Charité – Universitätsmedizin Berlin, Luisenstr. 57, 10117 Berlin, Germany, Tel: 49 30 450 529 002; Email: Katharina-cheryl.koltermann@charite.de

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Abstract

At present, few discussions have addressed the economic burden of endometriosis. The present study aimed to update two previous reviews and to assess the current body of literature regarding the costs associated with endometriosis. We searched the PubMed, EMBASE and The Cochrane Library databases using “endometriosis”, “economics”, “costs”, “productivity”, “insurance” and “burden” as search terms to identify articles published between 2004 and 2015. To enable the performance of comparisons across reported studies, cost findings were converted to international dollars using purchasing power parities (PPPs) and then inflated to 2010 dollars using the Consumer Price Index (CPI). The search yielded 11 relevant articles. Of these articles, four evaluated direct costs, one analysed indirect costs, and six reported both direct and indirect costs. Based on the results of these studies, endometriosis was estimated to account for annual total costs of Int\$-PPP 2.193-8.475 in newly diagnosed women and Int\$-PPP 11.688-12.941 in previously diagnosed women. The indirect costs associated with this condition were much higher for previously diagnosed women than newly diagnosed women. The included articles varied considerably in terms of study design, included cost categories and methodological quality.

Although it has been ten years since seven methodological considerations for designing future endometriosis cost studies were defined, the application of these recommendations was infrequently identified in the current body of literature. As endometriosis affects women of reproductive and, thus, working age chronically, the indirect costs of endometriosis are especially high. Accordingly, future studies must better explore the manner in which costs, particularly indirect costs, accrue among women affected by endometriosis to best facilitate health and social policy interventions.

ABBREVIATIONS

PPP: Purchasing Power Parity; CPI: Consumer Price Index; SHI: Statutory Health Insurance; EM: Endometriosis; n.r.: not reported; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; e.g.: for example; US: United States; vs.: versus.

INTRODUCTION

At present, discussions regarding endometriosis, a common benign but chronic disease in women of reproductive age, have focused on the clinical burden of disease [1]. Endometriosis is defined as the presence of endometrial-like tissue outside the uterus [2-4], and is associated with highly variable severity and symptoms [5]. As endometriosis is a chronic disease with a mean time delay between onset of symptoms, diagnosis and the initiation of effective treatment of at least seven years [6], this does not only cause considerable clinical but also significant economic burden.

Healthcare payers and policy makers, however, are increasingly becoming aware of the economic burden endometriosis places on society [7]. To enable a critical and informed discussion among decision makers concerning the optimal use of the limited available resources, detailed information regarding the costs attributable to endometriosis and its associated cost drivers is needed. Two recently published analyses have evaluated the significant economic burden of deep infiltrating endometriosis of the bowel and the bladder within the German health system [8,9]. While these studies contributed to the body of literature regarding the costs, they concentrated on the costs associated with two severe endometriosis subtypes from two perspectives within the context of the German health system: first, from the hospital perspective [8], and second, from the perspective of a statutory health insurance fund [9].

The first systematic analysis and comprehensive review of healthcare costs attributable to endometriosis in general was performed in 2006 by Gao et al., reviewing 13 studies published

worldwide between 1990 and 2004 [1]. This review concluded that limited economic information on endometriosis was available; nevertheless, data suggest that the disease's burden on patients and society is considerable.

The following year, Simoens et al. performed an evaluation of 13 cost-of-illness studies published worldwide between 1990 and 2006 [10], also including the study conducted by Gao et al. [1]. Simoens et al., estimated the annual healthcare costs and costs of productivity loss associated with endometriosis to be \$ 2.801 and \$ 1.023 per patient, respectively, and extrapolated these findings to the US population, resulting in an annual cost of \$ 22 billion. They identified a need for more and better-designed longitudinal studies and identified seven considerations for the design of future cost studies of endometriosis.

One decade later, an update of these two reviews would be valuable. Accordingly, the aim of the present study was to evaluate the current body of knowledge regarding the economic burden associated with the severe chronic disease, endometriosis, using the two previous reviews as a framework for its assessment. Since healthcare systems are in a permanent transition, the new information provided by the present study may be helpful to identify ongoing knowledge gaps in research and areas in which further research is particularly needed.

MATERIALS AND METHODS

The study was a systematic review of literature on the economic burden of endometriosis published between 2004 and 2015. It was performed to update the findings of Gao et al. [1]. and Simoens et al. [10]. Like these predecessors, the present study attempts to explore the overall economic impact of endometriosis by determining cost levels and cost drivers, the direct costs associated with specific treatments, and the indirect costs associated with societal productivity loss due to this chronic disease.

Systematic literature search and selection criteria

The systematic literature search was conducted using the following online databases: EMBASE, PubMed and the Cochrane Library. For the initial search, the following inclusion criteria were predefined: a) full-text articles published in peer-reviewed journals; b) studies published in English, German or Spanish; c) studies published between 1st January 2004 and 30th March 2015; d) human studies of patients with endometriosis; and e) original research articles reporting costs attributable to endometriosis. Reviews were excluded from the study.

According to the previous review conducted by Gao et al. [1], the following search terms were defined and used to search the abovementioned databases: "endometriosis", "economics", "costs" and "productivity". Additionally, we included the terms "burden" and "insurance", as those terms led to relevant results in an orientative search. As the focus of this study was on costs and not on quality of life, "treatment", "pain" and "quality of life", which had been used as search terms in the study conducted by Gao et al. [1], were not considered in the present study.

The articles identified during the initial searches of the relevant databases were combined into one dataset, and

duplicates were subsequently identified and excluded. Two researchers (KCK and CD) independently reviewed the titles and abstracts of each of the articles. Articles not meeting the inclusion criteria were excluded. For the remaining publications, two reviewers (KCK and CD) checked the full texts for eligibility. Disagreements within the selection process were resolved through consensus-based discussion or the opinion of a third reviewer (TR). Articles meeting the inclusion criteria underwent detailed review, and important findings were extracted.

Data extraction and analysis

Data on study design, data collection, study sample, epidemiological approach, perspective, scope of included costs, time horizon, year of costing, country and currency were extracted from each article. We determined whether the cost values reported were attributable to endometriosis only or all-cause total costs. If in addition to the all-cause cost estimates of endometriosis patients also the costs within the average female population were reported, the costs attributable to endometriosis only were estimated as the mean difference between the all-cause costs of both populations.

For included studies with a documented time horizon longer than one year, annual costs per case were evaluated. To enable assessment across studies, reported costs were assigned to the following categories based on their type and relevance to the healthcare of endometriosis patients: direct healthcare costs, direct non-healthcare costs and indirect costs. If no total value for cost categories was reported but, for example, the costs of individual procedures were indicated, then weighted mean costs per patient were calculated using individual procedure costs and patient numbers. If information for a cost category was not reported but could be calculated based on the incremental costs presented in the reported cost categories, the calculated data were included in the evaluation. Transportation costs and the cost of supporting household activities were assessed within the direct non-healthcare cost categories. Indirect non-healthcare cost values were categorized as lost productivity or lost leisure time, if reported.

To evaluate costs across a variety of countries and time periods, the extracted cost values were converted to international dollars using purchasing power parities (PPPs) [12] and then inflated to 2010 international dollars using the Consumer Price Index (CPI) [13], as this was the last costing year assessed within the eligible articles. Thus, differences of pricing across countries were standardized using PPPs. If no costing year was reported, the median year within the observational period was adopted as base year.

RESULTS

Search results

In total, 633 articles were identified in the initial search. After the removal of duplicates and screening of the titles and abstracts of potentially relevant studies, a total of 570 articles were excluded because they failed to meet the inclusion criteria, resulting in 63 remaining articles. The full texts of these remaining articles were reviewed for eligibility and inclusion. In total, eleven articles [6,7,14-22] were selected for inclusion in the de-

tailed review and key finding analysis. The overall search process is presented in the following flow chart (Figure 1).

General characteristics

Of the included articles, two described international multicentre studies [20,21], four reported North-American evaluations (USA [14,17,22], Canada [18]) and five described studies conducted in Europe (Germany [6,19], Belgium [7,15], Austria [16]).

Nearly all the included publications were cross-sectional studies; only two studies utilized a case-control design and matched endometriosis patients to a control group [14,17]. Four articles used claims data for their analysis and evaluated costs from the payer's perspective [14,17,19,22]; the other publications assessed costs from the societal perspective and were based on survey data, of which three were conducted prospectively [7,15,20]. The time horizon of the data collection in the included studies varied from the duration of one single hospital stay to insurance claims [19,22] covering an observation period up to ten years [14]. The majority of studies measured endometriosis costs over a time period of twelve months [6,7,14-20]. Four articles evaluated only direct costs [14,17,19,22], one article analysed only indirect costs [21], and six articles reported both direct and indirect costs [6,7,15,16,18,20]. Direct healthcare costs were assessed in nine articles [6,14-20,22], while direct non-healthcare costs were analysed in four articles [7,15,18,20]. A detailed overview of the general characteristics and methodology of the selected studies is presented in Table 1.

Cost categories

Physician visits or overall outpatient care was analysed in seven of the nine articles [6,14-16,18,20,22]. These studies also

reported the costs of medication. Information regarding the costs of monitoring tests was only provided in three publications [15,18,20]. The combined costs of inpatient care were analysed in five articles [6,14,16,19,22]; four studies reported the costs of surgery [15,17,18,20], and four studies described the costs of hospitalization and/or emergency visits [14,15,18,20]. Costs of infertility treatment were evaluated by two studies [15,16]. Three articles reported other treatment costs [15,18,20]. Two studies considered informal care and transportation costs [15,20]. Costs of household activities were taken into account by four studies [7,15,18,20], and two publications also considered out-of-pocket payments [16,18]. Costs of disease-related lost productivity were provided in seven articles [6,7,15,16,18,20,21], but only one study took the costs of lost leisure time into account [18].

COSTS

Within the assessed studies, three study populations categories became apparent: (1) newly diagnosed women; (2) women diagnosed with endometriosis before the study period; (3) women with an unknown diagnosis status. This categorization facilitated the comparison of costs across the heterogeneous studies. Table 2 shows the individual costs reported within the included studies after standardization to 2010 international dollars using PPPs (Int\$-PPP). The total cost estimates varied considerably across the evaluated articles. The total costs reported in studies analysing newly diagnosed patients ranged from Int\$-PPP 2.193 to Int\$-PPP 8.475. The total costs identified for patients previously diagnosed with endometriosis varied between Int\$-PPP 11.688 and Int\$-PPP 12.941. Within the two studies in which the diagnosis status of the evaluated women was unclear, the total costs of Int\$-PPP 7.273-11.688 were estimated. In one retrospective survey with unclear selection criteria, direct healthcare costs were more than two times higher than indirect costs [16]. However, in general, indirect costs made up the largest proportion of total costs in studies considering several types of costs [6,15,16,18-20]. In one study, indirect costs were up to 3.5 times higher than direct costs [15].

DISCUSSION AND CONCLUSION

Discussion

The objective of the present study was to evaluate the body of international literature regarding the economic burden of endometriosis. Eleven articles published between 2004 and 2015 were identified. The analysed articles varied considerably in their study design and applied heterogeneous methodological approaches. Overall, the studies tended to focus on the costs of treatment for associated symptoms rather than addressing the overall costs of endometriosis. That said, seven studies also assessed indirect costs related to endometriosis, and six studies considered the costs of direct medical care in inpatient or ambulatory settings in their analyses. The results of the present study suggest there to be a considerable difference in annual costs depending on how long a woman was diagnosed. The standardized annual total costs identified for newly diagnosed women varied between Int\$-PPP 2.193 and Int\$-PPP 8.475. Patients previously diagnosed with endometriosis had total costs of Int\$-PPP 11.688-12.941 per year. Overall, indirect costs were mostly described for women who had been diagnosed with endometriosis for some

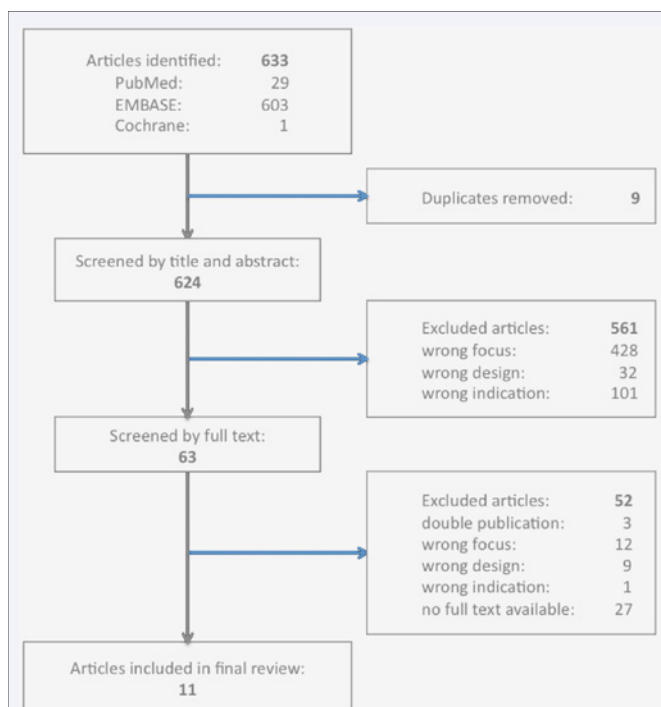


Figure 1 Flowchart – Literature screening process.

Table 1: General characteristics and methodology of included articles.

Reference	Year of costing	Design	Data collection	Sample	Time horizon	Perspective	Scope of included costs	Country / currency
Fuldeore_2015 (14)	2010	Case control study	Longitudinal, retrospective claims data analysis	37,570 matched pairs of EM patients vs. controls without EM	10 years: the 5 years before and 5 years after diagnosis. (2000 to 2010)	Payer	Direct costs	USA / US dollars
Klein_2014 (15)	2009	Cross sectional study	Prospective survey	134 women with EM-associated symptoms	2 months	Society	Direct and indirect costs	Belgium / Euros
Prast_2013 (16)	2009	Cross sectional study	Retrospective survey	73 EM patients	1 year	Society	Direct and indirect costs	Austria / Euros
Fuldeore_2011(17)	2009	Case control study	Longitudinal, retrospective claims data analysis	15,891 newly diagnosed EM patients vs. 63,564 population controls (Match: 1 EM vs. 4 controls)	24 months: 12 months prior through 12 months following the index date. Cost data: 12 months following the index date.	Payer	Direct costs	USA / US dollars
Levy_2011 (18)	2009	Cross sectional study	Retrospective survey	27 EM patients and 18 physicians	1 year	Society	Direct and indirect costs	Canada / Canadian dollars
Oppelt_2012(19)	2006	Cross sectional study	Retrospective claims data analysis	21,244 inpatients with EM as initial diagnosis	Hospital admission	Payer	Direct costs	Germany / Euros
Simoens_2012 (20)	2009	Cross sectional study	Prospective survey	909 EM patients	Data collection: 2 months; Results: extrapolated to 1 year	Society	Direct and indirect costs	10 countries / Euros
Simoens_2011 (7)	n.r.	Cross-sectional study	Prospective survey	394 EM patients with surgical treatment	30 months (6 months prior to surgical treatment and at 6, 12, 18 and 24 months following treatment)	Society	Direct and indirect costs	Belgium / Euros
Nnoaham_2011 (21)	2007 hourly labour cost	Cross-sectional study	Retrospective survey	1,418 inpatients from 16 hospitals in 10 countries: 1) Women with EM; 2) symptomatic control (women without EM); and 3) sterilization control (women without EM)	4 weeks	Society	Indirect costs	10 countries/ US dollars
Brandes_2009(23)	2003	Cross-sectional study	Retrospective survey	479 members of EM association & 257 rehab patients with EM as initial diagnosis	12 months	Society	Direct and indirect costs	Germany / Euros
Mirkin_2007(22)	2003	Cross-sectional study	Retrospective claims data analysis	30,325 member years of women with EM diagnosis	Relevant claim	Payer	Direct costs	USA / US dollar

Abbreviations: EM: Endometriosis; n.r.: Not Reported

time; these costs were much higher than those of women newly diagnosed and resulted in the identification of higher total costs. This is not a surprising finding, as women with endometriosis are generally of reproductive and, therefore, working age. Hence, the disease causes a remarkable productivity loss.

Comparison with previous reviews

The review conducted by Gao et al. identified hospitalizations, especially those related to surgical intervention, as the main

direct cost-drivers for endometriosis [1]. Furthermore, the authors reported that only a few studies assessed the costs of direct medical care in inpatient or ambulatory settings, and the availability of studies assessing indirect costs associated with endometriosis was especially limited. The results of the present study showed that recent studies have more frequently considered indirect costs and do not only focus on direct inpatient costs of endometriosis. Nevertheless, intangible costs are difficult to assess in monetary form and have not yet been measured.

Table 2: Results - Annual costs case in International \$ PPP by time point of diagnosis.

Reference	EM Sample (Total Sample, N)	Data source	Patient characteristics	Attributable costs vs. costs per patient	Direct Healthcare costs (Int\$-PPP)	Direct Non-Healthcare costs (Int\$-PPP)	Indirect costs (Int\$-PPP)	Total costs (Int\$-PPP)
Newly diagnosed; data before diagnosis								
Nnoaham_2011 (21)	n=745 women (N=1.418)	Retro-spective question-naire	18-45 years; mean age: 32,5 years	Attributable costs	-	-	3.719 ^c	3.719 ^c
Newly diagnosed; data before and after diagnosis								
Fuldeore_2015 (14)	n=37.570 women (N=75.140)	Claims data	18-45 years:	Overall costs ^a	2.631 ^e	-	-	2.631 ^e
Fuldeore_2011 (17)	n=15.891 women (N=79.455)	Claims data	18-45 years; mean age: 36,4 years	Attributable costs	8.475	-	-	8.475
Levy_2011 (18)	n=27 women (N=45)	Retro-spective question-naire	18-49 years; mean age: 36,4 years	Attributable costs	924	60	3.416	4.401
Simoens_2011 (7)	n=180 women (N=180)	Retro-spective question-naire	mean age: 31 years	Attributable costs	n.r. ^d	n.r. ^d	-	2.193 ^e
Newly diagnosed; data after diagnosis								
Mirkin_2007 (22)	n=40.150 member years (N=6,220,349 member years)	Claims data	18-55 years; mean age n.r.	Overall costs ^a	3.386 ^a	-	-	3.386 ^a
Already diagnosed, data of treatment								
Klein_2014 (15)	n=134 women (N=134)	Prospective question-naire	21-44 years ^b ; mean age: 33 years	Attributable costs	2.650	237	8.801	11.688
Oppelt_2012 (19)	n=21.244 women (N=21.244)	Claims data	30-45 years; mean age n.r.; SHI + privately insured	Attributable costs	3.947	-	8.800	12.747
Simoens_2012 (20)	n=909 women (N=909)	Prospective questionnaire	15-67 years ^b ; mean age: 36,1 years	Attributable costs	4.206	227	8.508	12.941
Unclear selection (diagnosis, treatment, time point unclear)								
Prast_2013 (16)	n=73 women (N=73)	Retro-spective question-naire	Mean age: 36 years; SHI only	Attributable costs	6.748	-	2.535	9.283
Brandes_2009 (23)	n=736 women (N=736)	Retro-spective question-naire	Mean age: 36 years	Attributable costs	2.762	-	4.510	7.273

^a = attributable costs calculated as the difference between EM patients and general population costs; ^b = no inclusion criteria reported except for age; ^c = mean calculated based on data from 10 reported countries; ^d = values reported for individual time points but not the total study period; ^e = mean annual value over the total study period.

Abbreviations: EM: endometriosis; Int\$-PPP: international dollar, calculated using purchasing power parity; n.r.: not reported; PPP: purchasing power parity; SHI: statutory health insurance.

In 2007, Simoens et al. [10]. proposed the following seven methodological considerations for the design of future cost studies of endometriosis: 1) use of case-control designs to better distinguish endometriosis and its main symptoms; 2) provision of a detailed report of the profile of included patients and special focus on adolescent patients (also underlined by Gao et al. [1]), 3) use of an incidence-based approach (also considering recurrence); 4) prospective collection of primary data; 5) focus on direct non-healthcare costs and indirect costs; 6) measurement of costs based on actual resource use, not administrative charges; and 7) performance of comparisons between various approaches

to surgical diagnosis and treatment and between medical and surgical approaches.

Ten years later, the results of the present study provide the opportunity to consider the extent to which these seven methodological considerations have been considered in the current international literature and demonstrate that a number of these recommendations remain infrequently applied. Of the eleven included articles, only two utilized a case-control study design [14,17], and only one included adolescent patients [20]. Furthermore, none of the included studies used an incidence-

based approach; two prospective studies collected questionnaire data [15,20], and four [7,15,18,20] and seven studies [6,15,16,18-21] reported direct non-healthcare costs and indirect cost values, respectively. Six articles estimated all or at least some costs using administrative tariffs [6,15,16,19,20,22], and none of the studies compared medical and surgical approaches or different treatments. But as the combination of surgical and histological verification of endometrial glands and/or stroma is considered to be the gold standard for the diagnosis and surgery is the gold standard treatment of endometriosis [5] it is not surprising, that the focus of the included studies was on the surgical approach and, hence, did not full fill the seventh consideration. Therefore, these data suggest that only direct non-healthcare costs and indirect costs were the subject of current evaluations.

In addition to the two previously conducted reviews, other more recent review studies are present in the existing body of literature. Prast et al. [16] also briefly compared the costs reported in different publications but did not conduct a full review. Furthermore, in another cost review conducted by Brandes [23], a systematic approach was not used to identify relevant articles. The recent review conducted by Soliman et al. [24], also updated the two previous reviews conducted by Gao et al. [1], and Simoens et al. [10], but used different search terms to identify articles published up to 2013, leading to the identification of articles that were different from those included in the present study. In that study, a different approach was applied, which was focused more on the identification of costs in different countries? The estimated total direct costs varied from \$ 1.109 per patient per year in Canada to \$ 12.118 per patient per year in the USA. Unlike the present study, the authors did not account for the potential impact of time point of diagnosis on the evaluated costs.

Strengths and limitations of the present study

To update the findings of the two previous reviews of the costs of endometriosis, an extensive systematic search in relevant international databases was performed, and the identified studies were assessed using established methods.

The present review focused on common international and peer-reviewed databases. The application of a systematic methodology is one advantage of this study. Other important strengths of the present study were its focus on the time point of data collection and consideration the time point of diagnosis. As the procedure used for the diagnosis of endometriosis is, in general, invasive and often combined with surgical treatment, its effect on costs remains clear. The time point of diagnosis is not equivalent to the duration of illness, as mean time until diagnosis can be up to ten years [21,25,26], at least this measure provides some indication of its extent.

Limitations of the present study do exist and should be acknowledged. First, the comparability of cost values across different countries is limited. Furthermore, a diverse range of cost types was considered in the included studies. The authors attempted to account for different price levels between countries through the use of PPPs and the CPI [12]. More fundamentally, however, the comparability across studies was limited due to the evaluation of different healthcare systems and country-specific differences in resource consumption [27]. The approach

used in this study could not account for all the differences between national healthcare systems. This limitation needs to be considered when interpreting the results of this study or considering their relevance or generalizability to other health systems.

Second, limiting the present review to articles published in English, German and Spanish language may have also biased our results. Finally, based on these data, it is evident that endometriosis and its consequences should also be further examined in low- and middle-income countries.

Methodological differences of the included articles

As previously discussed, relevant articles published over the last decade have not substantially improved upon the methodological approaches used in previous studies. Strength of the current research, however, is the identification of more information on direct non-healthcare costs and indirect costs of endometriosis. Furthermore, two multinational studies were performed, enabling the performance of an international overview of the burden of this disease.

Overall, the methodological approaches of the included articles were highly heterogeneous. The following key considerations were not taken into account by several studies:

The first aspect was the time horizon of the included studies. Ten years ago, Simoens et al. [10], reported that their identified studies failed to adequately account for the chronic nature of endometriosis. In the present study, three identified articles, two claims data analyses [14,17] and one prospective survey [7], evaluated the study population for longer than one year. That said, as most of the studies reported data collected at only one time point that was generally one year after diagnosis or treatment, cost values reported at several time points could not be compared. This information could, therefore, not be considered in the present evaluation. To account for the chronic nature of endometriosis, studies assessing a longer observational period and information obtained at several time points are needed.

Second, the studies included in the present review gathered data from the following diverse data sources: four studies collected data from claims databases [14,17,19,22]; five study collected data via retrospective patient questionnaires [6,7,16,18,21], one of which was retrospective study included a physician survey [18]; and two prospective studies collected data via patient surveys [15,20]. While a strength of retrospective claims data analyses in general is that it provides comprehensive information on the use of healthcare resources, this type of analysis may be limited by missing data and the incorrect coding of claims. The reliability of survey data depends on the manner in which cost data were generated. If cost data were reported as costs or charges, as indicated by resource use billed for actual reimbursement, the information may be trustworthy. If, on the other hand, cost estimates were calculated by multiplying patient-reported resource use with unit charges or costs, the reliability of data may be hindered by patients' limited ability to recall healthcare resource use [7].

Related to this potential limitation, the third methodological aspect was the imprecise differentiation between the use of

real costs or national tariffs as cost information. Some articles were unclear regarding whether true costs were reported or administrative charges to estimate relevant costs. As stated by Simoens et al. [10], charges tend to apply to certain institutions and, hence, cannot be generalized to other institutions or even countries.

Finally, when synthesizing the included studies, cost values could only be correctly assigned to standardized cost categories when the reported cost data were clearly defined in the original article. Some articles were relatively similar in their definition of cost categories, but this was not the case for all studies. For example, it was not clear whether infertility treatment was included in the category “prescribed drugs” or was not estimated when the costs associated with this treatment were not reported as their own category. Additionally, it was unclear whether laparotomy was categorized as a surgical or a diagnostic procedure, which would be dependent upon the therapeutic approach applied. Likewise, there was some ambiguity as to whether over-the-counter drugs were included in the category “medication” or if this category only included prescribed drugs. Similar problems could be observed in the differentiation between monitoring and diagnostic tests.

CONCLUSION

Endometriosis places a substantial economic burden on affected women and the healthcare system. As previously described by Simoens et al. in 2007 [10], the chronic nature of endometriosis and the costly medical and surgical treatment required for this disease account for this high economic burden. Additionally, as endometriosis chronically affects the quality of life and the ability to work of women of reproductive and, thus, working age, also the indirect costs associated with this disease are especially high. Furthermore, the time delay between onset of symptoms and diagnosis appears to be particularly strongly related to this burden, and physicians should be more aware of the symptoms of this disease in order to focus on adequate treatment.

Ten years after seven methodological considerations for designing future cost studies of endometriosis were defined by Simoens et al. [10], we found that these recommendations remain infrequently applied in the current body of literature. Accordingly, future studies should realize the importance of utilizing an optimal and comparable methodological design to better determine “when”, “where”, “why” and “how” various types of costs accrue among endometriosis patients. These studies must better explore the manner in which costs, particularly indirect costs, accrue among women affected by endometriosis to best facilitate health and social policy interventions.

CONFLICTS OF INTEREST

This research did not receive any specific grants from funding agencies in the public, commercial or not-for-profit sector. No potential conflicts of interest relevant to this article exist for KCK, TR, CD and ADE. In the past, ADE acted as a consultant for Bayer Pharma Germany, Takeda Pharma Germany, Gedeon Richter and Jenapharm.

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