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Socio-economic costs of osteoarthritis: A systematic review of cost-of-illness studies

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ABSTRACT

Objective: The burden of illness that can be attributed to osteoarthritis is considerable and ever increasing. The aim of this systematic review is to analyze currently available data derived from cost-of-illness studies on the healthcare and non-healthcare costs of osteoarthritis.
Methods: PubMed, *Index Medicus Español* (IME), and the Spanish Database of Health Sciences [*Índice Bibliográfico Español en Ciencias de la Salud* (IBECS)] were searched up to the end of April 2013. This study adhered to the PRISMA guidelines. Articles were reviewed and the study quality assessed by two independent investigators with consensus resolution of discrepancies.
Results: We identified 39 studies that investigated the socio-economic cost of osteoarthritis. Only nine studies took a social perspective. Rather than estimating the incremental cost of osteoarthritis, nine studies estimated the total cost of treating patients with osteoarthritis without a control for comorbidity. The other 30 studies determined the incremental cost with or without a control group. Only nine studies assessed a comprehensive list of healthcare resources. The annual incremental healthcare costs of generalized osteoarthritis ranged from €705 to €19,715. The annual incremental non-healthcare-related costs of generalized osteoarthritis ranged from €432 to €11,956.
Conclusions: The study concludes that the social cost of osteoarthritis could be between 0.25% and 0.50% of a country's GDP. This should be considered in order to foster studies that take into account both healthcare and non-healthcare costs.

Introduction

Osteoarthritis has the highest frequency of all rheumatic diseases and is one of the most prevalent chronic diseases [1–11]. Although its prevalence increases with age, it affects an increasingly significant number of people in the active population. The number of people with osteoarthritis is on the rise because of an ageing population and the increased prevalence of risk factors such as obesity and reduced physical activity. According to the method used in the Global Burden of Disease [12] study, progressive ageing of the population could make osteoarthritis the ninth cause of disability-adjusted life years (DALYs) in developed countries by the year 2020.

The total number of years lived with disability (YLDs) worldwide caused by knee and hip osteoarthritis increased by 60.2% between 1990 and 2010, and by 26.2% per 1000 people, meaning osteoarthritis has moved up from 15th to 11th in the list of the most frequent causes of disability [13]. In 2010, these two joints alone were responsible for 2.2% of all YLDs on a global scale and 2.7% in the United States (accounting for 0.7% and 1.2% of all DALYs, respectively) [14,15]. These numbers represent an underestimation of osteoarthritis' burden, as they do not include the corresponding data for all other joints aside from knees and hips.

Osteoarthritis is responsible for a very high number of primary healthcare visits as well as knee and hip replacement operations, plus hospital costs in general [1]. However, the socio-economic burden of osteoarthritis is not only limited to the direct costs of healthcare use but also includes significant non-healthcare-related costs. These take the form of productivity losses and the cost of formal and informal care associated with the limited independence of people with osteoarthritis.

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All authors had full access to all the data included in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Cost-of-illness studies generate a monetary estimate of the economic impact or cost resulting from the illness, including both direct healthcare costs and non-healthcare-related costs plus labor productivity losses [16]. These studies thus provide an indication of the potential social benefits that would be obtained if the disease were to be prevented or treated more effectively. Until recently, the cost of osteoarthritis received surprisingly little interest and most studies did not deal with osteoarthritis independently, but as part of a group of rheumatic diseases.

Until March 2013, only two systematic reviews of the cost of osteoarthritis were published [17,18]. When the first review was published in 2001 [17], it was limited to Europe, and only one study had been published. The second systematic review [18], which was the only one published until April 2006 that could be considered systematic and comprehensive, mentioned only 10 studies on the cost of osteoarthritis published between 1992 and 2003, five of which estimated only direct healthcare costs. In this second systematic review [18], the cost figures for each study, which were incorrectly adjusted with a 3% discount rate, fluctuated greatly (by up to a factor of 10 for the same country) and were difficult to compare with other studies and data from other countries. In order to transform the observed cost figures for different years to comparable monetary units for a given year, original figures should be adjusted by price changes—i.e., inflation—using a price index or the GDP deflator. A discount rate is not appropriate for this goal given that discounting rates measure time preference—tradeoffs among costs and benefits occurring at different times—but not price changes.

Despite the high social burden of the disease, more recent, non-systematic and incomprehensive reviews [19–21] underline the lack of knowledge about the cost of osteoarthritis in countries such as the United Kingdom [21], the wide range of different criteria used to make healthcare and non-healthcare cost estimates [19], and the limited number of studies available that actually provide reliable, up-to-date estimates of the percentage of GDP attributable to osteoarthritis [22].

The aim of this article is to present the results of an up-to-date, comprehensive and systematic review of osteoarthritis cost-of-illness studies published up to March 2013.

Methods

This systematic review of osteoarthritis cost-of-illness studies concentrated on international scientific literature published between January 1992 and March 2013. Inclusion criteria determined that all the cost studies that estimated the healthcare costs and/or non-healthcare costs associated with osteoarthritis published in either English or Spanish would be reviewed. Excluded from the review were any articles that did not refer to osteoarthritis separately or that consisted of financial assessments, review articles, editorials and opinion pieces or letters, works about methodologies, and texts not published in scientific journals.

The articles were independently reviewed by both authors of this study. The following databases were searched: PubMed, *Index Medicus Español* (IME), and the Spanish Database of Health Sciences [*Índice Bibliográfico Español en Ciencias de la Salud* (IBECS)]. Earlier literature reviews were used to confirm that all relevant references had been included, as were other sources such as Google Scholar. This study adhered to the PRISMA guidelines. Articles were reviewed and the study quality assessed by two independent investigators with consensus resolution of discrepancies.

The search strategy focused on the following keywords: (cost* OR economic* OR expenditure* OR resource* OR informal care* OR indirect cost* OR social cost* OR labour impact* OR sick leave) AND (arthrosis* OR osteoarthritis). In the case of Spanish IME and IBECS searches, the terms used were (coste* OR recursos) AND artrosis [(cost* OR resources) AND arthrosis/osteoarthritis].

Based on the cost figures from the studies, the annual cost in euros for the year 2011 was estimated by applying the price variation index of each economy (GDP deflator) to adjust to base year 2011 and then applying the corresponding exchange rates for each currency with respect to the euro. We use market exchange rates, as in a previous survey for osteoarthritis costs [18], in order to convert cost figures of a country in national currency terms to a common currency, although they may not always buy the same amount of goods and services in each country.

Results

The initial search identified 1153 articles: of which 954 were in PubMed, 50 in IME and IBECS, 140 were mentioned in the references of other reviews, and nine were found in other sources. After reviewing the abstracts, 62 of these were excluded as repetitions, and another 1005 did not meet the inclusion criteria. Of the remaining 86 articles, another 47 were excluded after reviewing the entire text because they did not meet the criteria, thus giving a final total of 39 publications that complied with the inclusion criteria and were therefore included in this review [23–61] (Fig.).

Synthesis of the literature

The main characteristics relative to the context, population, and method of osteoarthritis cost estimation used in the selected studies are summarized in Table 1. Of the 39 cost studies included in this review, 22 (56%) are from the United States, three are from Canada, two are from Spain, two are from Australia, and two are from Singapore; the remaining seven studies correspond to single, one-off studies in the different countries. Most of the studies selected were conducted after the year 2000 (87%) and 25 of them (64%) are relatively recent, since they were published between 2006 and 2013.

Cost measurement in 11 studies (28%) was based on incremental cost estimates of osteoarthritis patients compared with a control group, in a further 19 studies (49%) the authors quoted an incremental cost estimate but did not use a control group, while the remaining nine studies simply calculated the total cost for all patients with osteoarthritis.

Table 2 describes the different types of resources assessed as either healthcare or non-healthcare-related costs, plus the method for assessing the latter.

Of the 39 studies, only three included all of the healthcare and non-healthcare-related costs that can be attributed to osteoarthritis. In 18 of the studies, only direct healthcare costs were estimated, while four studies assessed only non-healthcare costs. A total of 14 studies included both healthcare and non-healthcare costs, but only partially, as they omitted some costs relevant to the disease.

Labor productivity losses due to work absences were assessed in 16 studies, while 11 reported the cost of formal care (care provided by a paid carer) and ten studies reported on the cost of informal care (care provided by friends and family).

Healthcare costs per patient

Table 3 provides a summary of mean annual healthcare costs per patient (in 2011 euros) classified by the patients' type of osteoarthritis in each of the studies selected for this review (generalized, knee, hip, and type not given). Table 4 provides

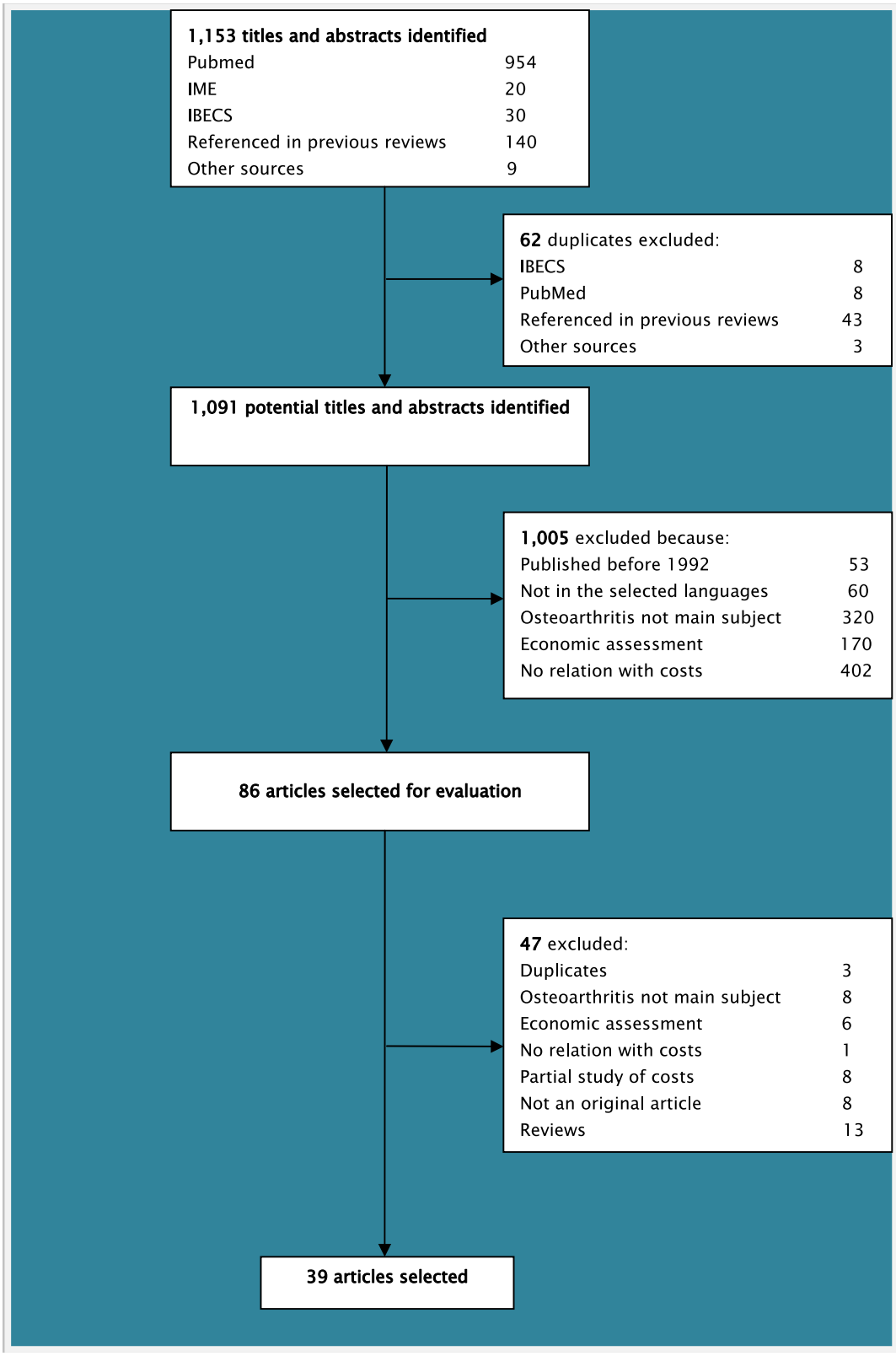

Fig. PRISMA flow diagram of the search strategy.

summaries (mean and range) for total healthcare annual cost per patient and for the healthcare incremental annual cost per patient by type of osteoarthritis and by perspective.

In the two studies carried out in the United States that estimated the total healthcare cost for patients with generalized osteoarthritis, annual total costs of €7300 [34] and €9399 [41] were observed from the perspective of the private insurer and the employer, respectively. In the studies that estimated the incremental cost of osteoarthritis, the annual incremental cost ranged from €705 [40] to €19,715 [51]. The lowest figures for incremental

Table 1
Summary of the main characteristics of the selected studies

Type of variable	Variable	Characteristics	No. of articles	Percentage
Context	Country	United States	22	56
		Canada	3	8
		Australia	2	5
		Spain	2	5
		Singapore	2	5
		Germany	1	3
		Belgium	1	3
		South Korea	1	3
		France	1	3
		Hong Kong	1	3
		Italy	1	3
		New Zealand	1	3
		Netherlands	1	3
	Year of publication	Before 2000	5	13
		Between 2001 and 2005	9	23
		Between 2006 and 2010	12	31
		Between 2011 and March 2013	13	33
Population	Population group	Economically active population alone	7	18
		Economically inactive population alone	1	3
		Economically active and inactive population	12	31
		Not given	19	49
	Age group	Under 65 years	18	44
		Over 65 years	16	39
		Not given	7	17
	Diagnostic method	Radiology	65	15
		Symptomatic or clinical both	25	64
		Not given	8	21
	Type of osteoarthritis	Generalized	8	19
		Knee	6	14
		Hip	2	5
		Not given	27	63
Method	Perspective	Social	9	21
		Public health insurance	5	12
		Private health insurance	9	21
		Employer	4	10
		Patient	4	10
		Not given	11	26
	Epidemiological approach	Prevalence	7	18
		Incidence	0	0
		Not given	32	82
	Measurement of costs	Total cost per patient	9	23
		Incremental cost, without control group	19	49
		Incremental cost, with control group	11	28
	Analysis of costs	Bottom up[a]	36	92
		Top down[b]	3	8

[a] The bottom-up methodology identifies all relevant cost components and values each cost component for *all individual* patients.
[b] The top-down methodology identifies all relevant cost components and values each cost component for *average* patients.

costs (between €705 and €1041) were collated in a Spanish study [40] with reduced or zero hospitalization costs for the lowest estimates. The results presented in Table 3 show a significantly lower cost when patients do not require hospitalization or surgery, whereas the cost is much higher in studies in which hospitalization costs represent a very large proportion of the incremental cost. For example, in a 2002 study in France by Le Pen et al. [47], the cost per hospitalized patient was observed to be more than 30 times greater than the cost per non-hospitalized patient. A similar pattern is presented in the results of studies that do not stipulate the type of osteoarthritis. Similarly, major differences were noted between studies with regard to the type of resources included and the percentage of spending representing medicine consumption.

The highest figures for the mean annual cost and the incremental cost of knee and hip osteoarthritis correspond to studies carried out in the United States [34] and Singapore [43], in both of which a large proportion of the cost resulted from hospitalization and surgical operations.

Despite having identified 39 studies investigating the cost of osteoarthritis, only nine of them [29,35,39,40,43,45,51,54,61] were comprehensive in that they assessed most of the healthcare resources used by patients with this disease (visits to doctors and specialists, hospitalization, medicines, and diagnostic tests) while simultaneously estimating the incremental cost of osteoarthritis without confusing it with the healthcare costs due to other causes that a similar osteoarthritis-free patient would have. Pinto et al. [35] estimated incremental costs per patient in New Zealand in 2008 and 2009 of €1179 and €1247, respectively, for a sample of 50 patients. Xie et al. [43] estimated the incremental cost per patient to be €2855 for a sample of 1179 subjects in Singapore for the year 2003, which is several times higher for patients who have undergone arthroplasty. A study by Woo et al. [51] in Hong Kong calculated an incremental cost of €1320 per patient with mild osteoarthritis, €4377 for severe osteoarthritis, and €19,715 for patients who required joint replacements. In Belgium, Rabenda et al. [45] reported an incremental cost per patient of €616 in a 2003–2004 study. In a Spanish study in 2003, Loza et al. [40] estimated a per-patient incremental cost of €930 for all types of patients, with a range varying between €743 and €1081, depending on the level of osteoarthritis severity. In the four

Table 2
Characteristics of costs measurement and assessment in the selected studies

Cost measurement and assessment	Resources assessed	No. of articles	Percentage
Healthcare costs	Primary care visits	31	79
	Visits to specialists	25	64
	Diagnostic tests	21	54
	Visits to emergency services	17	44
	Hospitalization (with or without surgery)	30	77
	Medicines	30	77
	Equipment	15	38
	Other (transport, alternative medicine, etc.)	19	49
	No details given	2	5
Non-healthcare costs[a]	Productivity losses due to absenteeism	16	41
	Productivity losses due to presenteeism	3	8
	Formal care	11	28
	Informal care	10	26
Non-healthcare cost assessment method	Productivity losses	16	41
	Human capital	15	38
	Friction costs	0	0
	Not given	1	3
	Informal care	10	26
	Replacement costs	9	23
	Not given	1	3
Total costs of osteoarthritis	Healthcare costs alone	18	46
	Non-healthcare costs alone	4	10
	Healthcare and partial non-healthcare costs	14	36
	Healthcare and full non-healthcare costs	3	8

[a] Studies with full non-healthcare costs are those that jointly estimate costs of productivity losses due to absenteeism, formal care, and informal care. Studies that estimate only partial non-healthcare costs are those that at least estimate costs of productivity losses due to absenteeism.

studies conducted in the United States [29,39,54,61], the estimated incremental cost per patient was notably higher than in the other studies, with means ranging from €3094 [39] to €5935 [29], Another US study [54] clearly demonstrated that the cost is very high during immediate pre- and post-operative periods and that healthcare cost estimates are highly affected by the proportion of patients who undergo surgery.

Non-healthcare-related costs per patient

Table 5 presents a summary of non-healthcare-related costs per patient (in 2011 euros) in each of the studies selected for this review. It includes results for both the annual total cost per osteoarthritis patient and the incremental cost of osteoarthritis. Also, Table 4 provides summaries (mean and range) for total non-healthcare annual cost per patient and for non-healthcare incremental annual cost per patient by type of osteoarthritis and by perspective.

From those 16 studies reporting productivity losses (Tables 2 and 5), eight studies estimated productivity losses due to absenteeism for employees, so productivity losses estimates are only due to missing working days [24,27,29,33,36,41,42,45]. Other eight studies [40,43,48–51,56,59] also estimated productivity losses due to absenteeism for a mix of employees and people that stopped working due to osteoarthritis. In this latter case, absenteeism productivity losses include missing working days for those still employed and for those with permanent work disability who quit their job. Unfortunately, estimated costs for those two groups are not reported separately in any of these studies.

The incremental non-healthcare costs of osteoarthritis in studies that included various types of osteoarthritis range from €432 [51] to €11,956 [48] per year. These figures vary greatly between countries and are much lower when the cost of productivity losses due to work absences is not included. Similarly, when the studies in which the type of osteoarthritis is not stated were also considered, non-healthcare-related costs were seen to vary greatly based on the type of resources assessed in the study (absenteeism, presenteeism, formal care, etc.). The proportion of non-healthcare costs that forms part of the total cost also varies greatly between countries and depends on the type of healthcare and non-healthcare resources assessed in each study. In one study on the cost of knee osteoarthritis in the Netherlands [27] that included healthcare and non-healthcare costs and an assessment of productivity losses, non-healthcare-related expenditure comprised up to 83% of the total cost. In one of the few studies that assessed the cost of reduced workplace productivity (presenteeism) carried out in the United States in 2009 [24], direct healthcare costs and productivity losses were found to increase rapidly with the severity of the osteoarthritis experienced by an active population. In the 2009 study [24], non-healthcare-related costs accounted for between 55% and 75% of the cost of osteoarthritis in the active population.

Total population cost

Only five of the 39 studies included in this review presented some kind of global extrapolation of total osteoarthritis healthcare costs, or the total cost including non-healthcare costs (even if they were only partially represented), in a specific country and for a given period [39,40,47,51,57].

The study by Le Pen et al. [47] estimated that the healthcare costs (doctor visits, medicines, and hospitalizations) for patients with osteoarthritis accounted for around 1.7% of France's total healthcare expenditure in 2002. This figure was calculated using various macroeconomic hypotheses in order to attribute the cost of doctor visits, medicines, and hospitalizations that were due to osteoarthritis. Through a similar approach, Mathers and Penm [57] estimated Australia's total annual healthcare cost for osteoarthritis to be $624 million between 1990 and 1994, equivalent to 21% of the healthcare costs resulting from all musculoskeletal diseases in Australia (in the given period).

A study [39] of US data corresponding to the 1996–2005 period estimated the incremental cost attributable to osteoarthritis by applying a regression model to individual data that controlled for

Table 3
Summary of mean healthcare costs per patient (€/patient/year)

Type of osteoarthritis	Measurement of costs	Study country	Study year	Primary care visits	Visits to specialists	Diagnostic tests	Emergencies	Hospitalization	Medicines	Equipment	Other	No details given	Perspective	Annual cost per patient (in 2011) (€)	% Hospital costs	% Medicine costs
Generalized	Total cost per patient with osteoarthritis	USA	2001–2008 [34]	X	X		X	X	X	X	X		Private health insurance	7300	20.2	20.2
		USA	2003–2004 [41]	X	X	X	X	X	X				Employer	9399	27.7	25.5
	Incremental cost of osteoarthritis	New Zealand	2008–2009 [35]	X	X	X	X	X	X				Public health insurance	1247	56.9	5.9
		New Zealand	2008–2009 [35]	X	X	X	X	X	X				Public health insurance	1179	60.1	7.6
		USA	2007 [37]	X		X	X	X					Private health insurance	4552	39.9	n/a
		Spain	2003 [40]	X	X	X		X	X	X	X		Social	930	22.3	9.0
		Spain	2003 [40]	X	X	X		X	X	X	X		Social	743	0.0	2.0
		Spain	2003 [40]	X	X	X		X	X	X	X		Social	705	0.0	2.9
		Spain	2003 [40]	X	X	X		X	X	X	X		Social	740	0.0	2.5
		Spain	2003 [40]	X	X	X		X	X	X	X		Social	1081	0.0	2.2
		Singapore	2003 [43]	X	X	X		X	X	X	X		Social + patient	7645	46.8	0.4
		Singapore	2003 [43]	X	X	X		X	X	X	X		Social + patient	2855	53.0	0.4
		Hong Kong	Not given [51]	X	X	X		X	X	X	X		Social	1320	4.7	11.6
		Hong Kong	Not given [51]	X	X	X		X	X	X	X		Social	4377	26.5	4.6
		Hong Kong	Not given [51]	X	X	X		X	X	X	X		Social	19,715	80.9	1.0
Knee	Total cost per patient with osteoarthritis	USA	2001–2008 [34]	X	X		X	X	X	X	X		Private health insurance	7675	19.0	21.1
		Italy	2000–2001 [49]	X	X	X		X	X	X	X		Social	838	34.2	9.4
	Incremental cost of osteoarthritis	Netherlands	2009–2010 [27]	X	X	X			X	X			Not given	1810	n/a	5.4
		Singapore	2003 [43]	X	X	X		X	X	X	X		Social + patient	11,293	46.2	0.1
		Spain	2001 [44]	X	X	X			X		X		Social	528	n/a	15.7
Hip	Total cost per patient with osteoarthritis	USA	2001–2008 [34]	X	X		X	X	X	X	X		Private health insurance	6525	22.5	17.9
	Incremental cost of osteoarthritis	Singapore	2003 [43]	X	X	X		X	X	X	X		Social + patient	15,499	47.1	1.5
Not given	Total cost per patient with osteoarthritis	USA	2005–2008 [23]	X	X	X	X	X	X	X	X		Private health insurance	7225	18.9	20.0
		USA	2005–2008 [23]	X	X	X	X	X	X	X	X		Private health insurance	27,417	85.1	1.7
		USA	2005–2008 [23]	X	X	X	X	X	X	X	X		Private health insurance	8283	29.9	18.2
		Germany	2003–2005 [31]	X				X	X		X		Not given	1608	11.6	46.3
		USA	2001–2008 [38]						X			X	Employer	6915	n/a	11.0
		USA	1999–2005 [42]	X	X	X	X	X	X				Private health insurance/ employer	6779	29.7	16.1

	Canada	1999–2000 [50]	X	X	X		X	X	X	X		Social	3270	25.0	43.7
Incremental cost of osteoarthritis	USA	2009 [24]	X			X	X					Social	631	49.2	n/a
	USA	2009 [24]	X			X	X					Social	1294	54.2	n/a
	USA	2009 [24]	X			X	X					Social	3308	61.8	n/a
	USA	2006–2009 [25]	X	X		X	X	X				Not given	8206	44.9	8.8
	USA	2006–2009 [26]	X	X		X	X	X				Not given	5109	67.0	14.2
	USA	2006–2009 [26]	X	X		X	X	X				Not given	4806	66.3	17.4
	Canada	2000–2001 [28]	X		X		X					Public health insurance	1117	45.3	n/a
	USA	2007 [29]	X	X		X	X	X		X		Not given	9732	53.9	7.5
	USA	2007 [29]	X	X		X	X	X		X		Not given	5935	24.0	12.4
	USA	2008 [32]	X	X	X	X	X	X	X			Private health insurance	5855	36.8	12.8
	USA	2009 [33]	X			X	X					Not given	1143	44.6	n/a
	USA	1996–2005 [39]	X	X	X		X	X				Patient	532	n/a	n/a
	USA	1996–2005 [39]	X	X	X		X	X				Patient	1057	n/a	n/a
	USA	1996–2005 [39]	X	X	X		X	X				Private health insurance	3094	n/a	n/a
	USA	1996–2005 [39]	X	X	X		X	X				Private health insurance	3705	n/a	n/a
	Belgium	2003–2004 [45]	X	X	X	X	X	X		X		Social	616	11.0	15.1
	USA	1997–2003 [46]	X	X		X	X	X		X		Private health insurance	969	53.9	11.7
	USA	1996 [52]									X	Private health insurance	4573	n/a	n/a
	USA	1996 [52]									X	Private health insurance	1449	n/a	n/a
	Australia	1994 [53]	X		X		X	X	X			Patient	256	0	38
	Australia	1994 [53]	X		X		X	X	X			Patient	512	2	37
Incremental cost of osteoarthritis	USA	1992–1994 [54]	X	X	X	X	X	X				Public health insurance	567	43	32
	USA	1992–1994 [54]	X	X	X	X	X	X				Public health insurance	761	15	49
	USA	1992–1994 [54]	X	X	X	X	X	X				Public health insurance	15,372	95	2
	USA	1992–1994 [54]	X	X	X	X	X	X				Public health insurance	1117	65	19
	USA	1975–1987 [55]	X		X		X	X	X	X		Not given	1592	68	0
	USA	1992 [56]							X			Social	101	n/a	n/a
	USA	1991–1993 [58]	X				X	X	X	X		Private health insurance	2954	n/a	7
	USA	1991–1993 [58]	X				X	X	X	X		Private health insurance	2051	n/a	2
	USA	1997 [60]	X	X			X	X	X	X		Not given	2094	4	57
	USA	2000–2001 [61]	X	X	X	X	X	X		X		Not given	4592	33	9

Table 4
Summary of costs per patient (€/patient/year)

	Total annual cost per patient		Incremental annual cost per patient	
	Mean	Range	Mean	Range
By type of osteoarthritis				
Generalized				
Healthcare costs	8350	7300–9399	3622	705–19,715
Non-healthcare costs	3748	–	2524	432–11,956
Knee				
Healthcare costs	4257	838–7675	4175	528–11,293
Non-healthcare costs	1519	–	4774	2296–8772
Hip				
Healthcare costs	6525	–	15,499	–
Non-healthcare costs	–	–	–	–
Not given				
Healthcare costs	8785	1226–27,417	3068	101–15,372
Non-healthcare costs	2056	2066–2045	1704	69–7212
By perspective[a]				
Social				
Healthcare costs	2054	838–3270	4077	101–19,715
Non-healthcare costs	1782	1519–2045	1875	191–7212
Public health insurance				
Healthcare costs	–	–	3466	567–15,372
Non-healthcare costs	–	–	–	–
Private health insurance				
Healthcare costs	10,172	6525–27,417	3529	1449–5855
Non-healthcare costs	2066	–	–	–
Employer				
Healthcare costs	7698	6779–9399	–	–
Non-healthcare costs	1938	2066–3748	380	360–399
Patient				
Healthcare costs	–	–	4405	256–15,499
Non-healthcare costs	–	–	2897	69–11,956
Not given				
Healthcare costs	1608	–	4502	1143–9732
Non-healthcare costs	–	–	3224	719–8772

All values are in 2011 euros.

[a] Counting for any type of osteoarthritis here.

comorbidity and socio-demographic characteristics. The same study estimated the aggregate annual expenditure attributable to osteoarthritis paid by insurers and patients to be $185.5 billion in the United States for the year 2007 (63.6% of which corresponded to women). In a Spanish cost-of-illness study that analyzed individual patient data for the year 2003 [40], and which only partially considered non-healthcare-related costs, the economic burden of osteoarthritis was estimated to be equivalent to 0.5% of the GDP for 2007. One cost-of-illness study conducted in Hong Kong [51] estimated that osteoarthritis healthcare and non-healthcare-related costs amounted to 0.28% of the country's GDP.

Discussion

The increase in the number of osteoarthritis cost-of-illness studies published in the last few years, especially since 2006, is very notable when compared to the results obtained in reviews [17,18] published prior to this one.

Despite the steady increase in the number of works published, our analysis of osteoarthritis cost studies highlights the fact that a significant proportion of the studies have major limitations with regard to their design and methodology, the lack of uniformity regarding the resources assessed, and the cost estimates obtained.

The clinical and socio-economic characteristics of osteoarthritis patients included in the cost-of-illness study play a very important role in the study results because the disease affects both the elderly and the active population (with an exponential increase observed starting at the age of 50 years) and because osteoarthritis manifests in diverse forms: localized (hand, foot, knee, hip, and spinal column) or generalized.

The type of osteoarthritis and its evolution and treatment plan are some of the most influential factors behind the lack of uniform criteria observed in the cost-of-illness assessments studied in this literature review. The two previous reviews also pointed toward the influence of these factors, despite analyzing considerably fewer studies. Future studies on the cost of osteoarthritis should perform a separate and/or duly stratified cost analysis of generalized osteoarthritis and of each type of localized osteoarthritis. Disease evolution and treatment type can also be very relevant when designing a study on costs, given that any over- or under-representation of hospitalization or surgery within a patient study sample can result in highly variable, incomparable cost estimates of scarcely any use when the aim is to draw conclusions about the overall cost of osteoarthritis and not the cost of surgery.

The differences and limitations observed in the design of a high number of osteoarthritis cost studies also contribute to the wide variety in cost estimates. The counterfactual selection of the study determines whether it will calculate the total cost for patients with osteoarthritis (including any use of healthcare services or non-healthcare costs that may or may not be related to the disease) or the actual cost of osteoarthritis. In the former case, it would not actually be a cost-of-illness study but also a study on the cost of patients with osteoarthritis, among other health problems that may or may not be associated with the disease.

The studies that used a control group of an osteoarthritis-free population as the counterfactual estimated the incremental cost of the disease with respect to the cost of the population without the disease, whether by comparing means or using some form of multiple regression analysis to provide an estimate of the degree of additional or incremental contributions to healthcare or non-healthcare costs arising from osteoarthritis diagnosis. Depending on the counterfactual selected to estimate the incremental cost of osteoarthritis, two types of study can be distinguished, each with distinct methodological features. Firstly, almost half of the studies analyzed did not explicitly use a control group to estimate the incremental cost. Rather, they directly measured only the differential consumption of resources directly attributable to osteoarthritis (doctor visits as a result of the disease, medicines for osteoarthritis, etc.). This method is more straightforward than the explicit use of two population groups (i.e., one interest group with osteoarthritis and one control group without osteoarthritis), but it requires very precise data systems that provide detailed identification of the reasons each patient uses each resource. In most of the retrospective studies of this type included in this review, the authors do not clearly or transparently explain the criteria for attributing visits, consultations, hospitalizations, or tests to osteoarthritis. This represents a notable limitation of the validity of the osteoarthritis cost estimates obtained.

Incremental osteoarthritis cost estimates are more accurate in studies with an osteoarthritis-free control group because they allow statistical significance tests and confidence intervals to be calculated for incremental cost estimates per person with osteoarthritis in comparison to the absence of the disease. The frequency of this type of study has increased significantly in recent years at the expense of studies without a control group.

The studies we reviewed also presented significant differences in the identification and measurement of the type of healthcare resources consumed. For example, five of the 39 studies did not include the cost of hospitalization or medicines, which means they were only partial studies on healthcare costs that cannot be compared with the results from complete studies of healthcare costs. Actually, of the 39 studies selected, only the one by Bozic et al. [23] can be considered a complete study of healthcare costs in the sense that it includes an assessment of every type of

Table 5
Summary of mean non-healthcare-related costs per patient (€/patient/year)

Type of osteoarthritis	Measurement of costs	Study country	Study year	Costs assessed					Assessment method		Perspective	Annual cost per patient (in 2011) (€)
				Productivity losses absenteeism	Productivity losses presenteeism	Formal care	Informal care	Other	Productivity losses	Informal care		
Generalized	Total cost per patient with osteoarthritis	USA	2003–2004 [41]	X		X		X	Human capital		Employer	3748
	Incremental cost of osteoarthritis	Spain	2003 [40]			X	X	X		Not given	Social	587
		Singapore	2003 [43]	X					Human capital		Social + patient	1344
		Singapore	2003 [43]	X					Human capital		Social + patient	818
		Singapore	2003 [43]	X					Human capital		Social + patient	3029
		Canada	2000–2001 [48]	X		X	X	X	Human capital	Replacement costs	Patient	11,956
		Hong Kong	Not given [51]	X		X	X		Human capital	Replacement costs	Social	432
		Hong Kong	Not given [51]	X		X	X		Human capital	Replacement costs	Social	746
		Hong Kong	Not given [51]	X		X	X		Human capital	Replacement costs	Social	1280
Knee	Total cost per patient with osteoarthritis	Italy	2000–2001 [49]	X		X	X		Human capital	Replacement costs	Social	1519
	Incremental cost of osteoarthritis	Netherlands	2009–2010 [27]	X	X		X		Human capital	Replacement costs	Not given	8772
		Spain	2001 [44]			X	X	X		Replacement costs	Social	3255
		Singapore	2005 [59]	X			X	X	Human capital	Replacement costs	Not given	2296
Not given	Total cost per patient with osteoarthritis	USA	1999–2005 [42]	X				X	Human capital		Private health insurance/ employer	2066
		Canada	1999–2000 [50]	X		X	X		Human capital	Replacement costs	Social	2045
	Incremental cost of osteoarthritis	USA	2009 [24]	X	X				Human capital		Social	777
		USA	2009 [24]	X	X				Human capital		Social	3786
		USA	2009 [24]	X	X				Human capital		Social	7212
		USA	2007 [29]	X				X	Human capital		Not given	2209
		USA	2007 [29]	X				X	Human capital		Not given	1403
		USA	2009 [33]	X	X				Human capital		Not given	3944
	Incremental cost of osteoarthritis	USA	1996–2005 [36]	X					Human capital		Employer	399
		USA	1996–2005 [36]	X					Human capital		Employer	360
		Belgium	2003–2004 [45]	X			X		Human capital	Replacement costs	Social	918
		Australia	1994 [53]			X					Patient	69
		Australia	1994 [53]			X					Patient	165
		USA	1992 [56]	X		X			Not given		Social	191
		USA	1997 [60]			X					Not given	719

healthcare resource used by osteoarthritis patients. These results confirm the continued use of very different criteria among osteoarthritis cost-of-illness studies and the enormous difficulty in making comparisons, as observed by Mittendorf et al. [62] in 2003 and Xie et al. [18] in 2007. In the case of non-healthcare cost measurements, the productivity losses resulting from work absences were assessed in fewer than half the studies, although they did not compare results using the human capital method with those using the friction cost method. Reduced productivity without missing work (i.e., presenteeism, for which it is much more difficult to collect data) was only analyzed in three studies. Similarly, only around 25% of the studies included the cost of formal and/or informal care, meaning that the other 75% failed to examine dependence, a significant cost of osteoarthritis. Finally, as mentioned by Mittendorf et al. [62], none of the studies reviewed estimated the cost of premature mortality attributable to osteoarthritis.

The lack of uniform criteria observed in the population, study design, and measurement and assessment of resources related to osteoarthritis produces per-patient cost estimates that vary greatly between countries and even within individual countries. This high variability of estimated costs persists over time, despite a marked increase in the number of studies [18,19]. In some cases, local data are also used (e.g., prices or costs that only apply regionally or to a few health centers or hospitals), along with small patient samples, short observation periods (3 months or less), and a study perspective limited to the costs borne by a private insurer or the patient. All of these factors highlight the need to present results after carrying out per-patient, cost-sensitivity analysis.

Comparison of the studies that provided a more comprehensive estimate of the incremental healthcare cost per patient (only nine out of 39) reveals slightly less variability in the results between countries and even within the same country (the United States is the only country with more than one study). This subgroup of studies confirmed that the incremental cost per patient is much higher in the United States and that the cost clearly increases along with the level of severity of the osteoarthritis [40,51]. Similarly, it confirms that the maximum cost corresponds to patients who undergo arthroplasty. Therefore, the inclusion of these patients in the study population is responsible for a significant part of the variability observed between studies and within individual studies.

An added complication when trying to obtain reliable estimates of the global or aggregate cost for a country and part of the reason why there is an absence of cost studies with an incidence-based approach is that most accurate information about the prevalence and incidence of osteoarthritis is local data.

Conclusions

The present review shows a major increase over the last 10 years in the number of studies on the cost of osteoarthritis. However, more than half of them were done in the United States, and there are many other countries with a high healthcare expenditure for which no data are available on osteoarthritis costs.

Despite the growing accumulation of information on osteoarthritis costs highlighted by this review, the analysis of the studies presented a high degree of variance in the population, the study design, and the identification and assessment of healthcare resources and non-healthcare-related resources that significantly limited the validity and comparability of results (not only between countries but also within individual countries). Notwithstanding the lack of uniformity in the approaches and criteria used in the different studies, they shared some important points concerning the relative and absolute significance of the healthcare and non-healthcare-related costs of osteoarthritis.

Firstly, the healthcare costs of osteoarthritis represented could be between 0.8% and slightly more than 1% of healthcare expenditure in the health systems of the countries studied. When non-healthcare-related costs are also considered, even when they are limited to productivity losses, the cost of osteoarthritis could be between 0.25% and 0.50% of GDP.

Secondly, the incremental healthcare costs of people with osteoarthritis compared to those without the disease exceeded €1000 in 2011 euros in most of the estimates reviewed for different countries. This figure was much higher in the United States. The incremental cost of osteoarthritis rises sharply with age and the severity of the disease and reaches a maximum when osteoarthritis-related surgery becomes necessary.

Thirdly, the current limited number of studies assessing productivity losses and the cost of formal and informal care for osteoarthritis patients show high values for these factors, such that, if the severity level of osteoarthritis and disability are elevated, these costs could easily become higher than direct healthcare costs.

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