Supplement

Table S1. Search Strategy Using MEDLINE and EMBASE for Cost-of-illness Studies in Rheumatoid Arthritis

	Query	Results
Search filter for economic studies from Scottish Intercollegiate Guidelines Network (SIGN)		
1	Economics.af.	999167
2	"costs and cost analysis".af.	50521
3	Cost allocation.af.	2844
4	Cost-benefit analysis.af.	175670
5	Cost control.af.	92905
6	Cost savings.af.	92926
7	Cost of illness.af.	52485
8	Cost sharing.af.	11976
9	"deductibles and coinsurance".af.	2107
10	Medical savings accounts.af.	1193
11	Health care costs.af.	118202
12	Direct service costs.af.	1239
13	Drug costs.af.	35774
14	Employer health costs.af.	1159
15	Hospital costs.af.	48982
16	Health expenditures.af.	27664
17	Capital expenditures.af.	2918
18	Value of life.af.	9518
19	Exp economics, hospital.af.	11293
20	Exp economics, medical.af.	10963
21	Economics, nursing.af.	4266
22	Economics, pharmaceutical.af.	3028
23	Exp "fees and charges".af.	9333
24	Exp budgets.af.	61612
25	(low adj cost).af.	181669
26	(high adj cost) .af.	80703
27	(health?care adj cost$).af.	80964
28	(fiscal or funding or financial or finance) .af..	2312342
29	(cost adj estimate$).af.	20117
30	(cost adj variable) .af.	813
31	(unit adj cost$).af.	17841
32	(economic$ or pharmacoeconomic$ or price$ or pricing) .af.	2520189
33	Or/1-32	4692540
33	rheumatoid arthritis.sh.	189714
34	33 and 34	7494
35	limit 35 to yr="2000 - 2019"	6867
36	Not editorials	6655
37	Not conference paper and abstract	4537
38	Not review	3154
39	Not letter	3031

	Query	Results
40	Not animals	2981

Table S2. CHEERS checklist—modified version for COI study*

Section/item	Item No	Recommendation	Modified Recommendation
Title and abstract			
Title	1	Identify the study as a COI study or use more specific terms such as direct costs, indirect costs (productivity loss), and economic burden.	
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and data source), results, and conclusions.	
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	
		Present the study question and its relevance for health policy or practice decisions.	
Methods			
Target population and subgroups	4	Describe characteristics of the population and subgroups analysed, including why they were chosen.	
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	
Population (optional)	7	If the target population is compared with a matched population, describe the characteristics and how they have been matched.	
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	
Cost components	9	Describe what cost components are taken into account and their relevance to the perspective of the study.	
Estimating resources and costs	10	Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	
Currency, price date, and conversion	11	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	
Choice of model (optional)	12	If presented, describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	
Assumptions (optional)	13	If presented, describe all structural or other assumptions underpinning the decision-analytical model.	
Analytical methods	14	Describe all analytical methods supporting the COI study. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; and methods for handling population heterogeneity and uncertainty.	
Results			
Study parameters (optional)	15	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for	

Section/item	Item No	Recommendation	Modified Recommendation
		distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	
Cost	16	Report mean values for the main categories of estimated costs, as well as mean difference between the matched groups if been compared.	
Characterising uncertainty	17	Describe the uncertainty of the estimated cost (such as confidence interval, standard deviation, and sensitivity analysis), together with the impact of methodological assumptions (such as discount rate, study perspective).	
Characterising heterogeneity	18	If applicable, report differences in costs that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	
Discussion			
Study findings, limitations, generalisability, and current knowledge	19	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	
Other			
Source of funding	20	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the study. Describe other non-monetary sources of support.	
Conflicts of interest	21	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	

* *The CHEERS checklist is designed to assess good reporting of economic evaluations, items regarding to choice of model, assumptions and parameters are kept as optional for few COI studies use model-based approach. Also, items specific to economic evaluation, such as comparator, outcome measurement, and effectiveness are replace by population (optional for studies with matched population), cost components, and cost.*

Table S3. Characteristics of included studies, arranged by region, country, and year

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Europe			
Radner 2014, Austria[1]	N=356 11.5 years, 79.8% female, 59.9 years	Cross-sectional survey, taking into account both direct and indirect costs	RA clinic at a hospital
Westhovens 2005, Belgium[2]	Early, n=48 0.5 years, 65% female, 59.2 years Late, n=85 12.5 years, 79% female, 55.5 years	Cross-sectional survey on early (< 1 year) and late RA patients, taking into account direct costs on societal perspective	A multicentre longitudinal study from private rheumatology practices and university hospitals
Klimes 2014, Czech[3]	N=261 14.5 years, 84.3% female, 56.38 years	Cross-sectional survey, taking into account both direct and indirect costs on societal perspective	At the centre for treatment of rheumatic diseases
Kruntoradova 2014, Czech[4]	N=77 7.4 years, 64.9% female, 45.3 years	Cross-sectional survey, taking into account indirect costs on societal perspective	Three specialised centres for the treatment of rheumatic diseases
Sogaard 2010, Denmark[5]	N=3,704 75% female, 60.6 years	Cross-sectional survey taking into account indirect costs	A cohort of patients from 11 hospital-based rheumatologic clinics
Kobelt 2008, France[6]	N=1,487 18 years, 83.5% female, 62.7 years	Cross-sectional survey, taking into account both direct and indirect costs on payer's and societal perspective	Anonymous mail survey from all members of a national patient association (ANDAR)
Loppenthin 2017, Denmark[7]	N=25,547 72.3% female, 24% 60-69 years	Retrospective database analysis, taking both direct and indirect costs into account on societal perspective	National Patient Registry (NPR)
Flipon 2009, France[8]	N=180, 71.1% female	Cross-sectional survey, taking into account both direct costs and indirect on payer's perspective	Survey based on patients in the French Very Early rheumatoid Arthritis (VErA) cohort

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Beresniak 2011, France[9]	NA	Direct costs-modelling of RA according to disease activity categories on payer's perspective	Resource utilization and unit costs estimated through expert opinion and simulated using distribution ranges for each item
Chevreul 2014, France[10]	N=813 214 days, 76.8% female, 47.6 years	Retrospective database analysis and survey data of patients on distinct DMARDs treatment, taking into account direct costs on payer's perspective	A multicentre, prospective study of patients with early arthritis (ESPOIR Cohort)
Beck 2015, France[11]	N=862, 80.3% female	Retrospective database analysis of patients on biologic treatments, taking into account direct costs on payer's perspective	Administrative claims data from the DCIR and PMSI databases
Fautrel 2016, France[12]	Not reported	Retrospective database analysis, taking into account direct costs on payer's perspective	A national claim database (EGB)
Martikainen 2016, Finland[13]	N=7,831 4 years (median), 71% female, 46 years	Retrospective database analysis, taking into account indirect costs on societal perspective	Health insurance database
Ruof 2003, Germany[14]	N=338 8.4 years, 76% female, 58.4 years	Retrospective database analysis, taking into account both direct and indirect costs on payer's perspective	Health insurance database (AKON) and regional physicians' association (KVN)
Hulsemann 2005, Germany[15]	N=136 77% female, 57.4 years	Cross-sectional survey to determine out-of-pocket expenditures, taking into account direct costs on patients' perspective	A multicentre randomised controlled prospective trial
Merkesdal 2005, Germany[16]	N=234 8 years, 76% female, 53 years	Cost data derived from questionnaires of patients matched with payer's database, taking into account indirect costs on societal perspective	A multicentre randomised controlled prospective trial matched with a health insurance database (AKON)

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Kirchhoff 2011, Germany[17]	N=180 8.5 years, 69% female, 53 years	Cross-sectional survey, taking into account both direct and indirect costs on societal perspective	A multi-centre clinical trial on RA
Huscher 2015, Germany[18]	N=3,327 10.3 years, 75.8% female, 63.1 years	Retrospective database analysis, taking into account both direct and indirect costs on societal perspective	The National Database of the Collaborative Arthritis Centres (NDB)
Ziegelbauer 2018, Germany[19]	N=678 57.5% female 51.1 years	Retrospective database analysis of patients on TNFi treatment, taking direct costs into account	German statutory health insurance funds database
Horvath Cs 2014, Hungary[20]	N=976, 87% female	Retrospective database analysis in long-term care settings, taking into account direct costs on payer's perspective	The National Health Insurance Fund Administration (NHIFA)
Della Rossa 2010, Italy[21]	N=34 14 years, 67.6% female, 66.5 years	Cross-sectional survey, taking into account both direct and indirect costs on societal perspective	RA patients in Pisa
Verstappen 2007, Netherlands[22]	<2/ 2-6/ 6-10/ >10 years, n=73/ 214/ 114/ 60 0.9/ 4/ 7.7/ 19 years 77%/ 73%/ 62%/ 78% female 54/ 58/ 61/ 60 years	Cross-sectional survey, taking into account direct costs on payer's perspective.	A cross-sectional study of the Utrecht Rheumatoid Arthritis Cohort study group (SRU)
Kvamme 2012, Norway[23]	N=1,152 6 years, 72% female, 57 years	Retrospective database analysis of patients on DMARDs or biologic treatments, taking into account both direct and indirect costs on societal perspective	A Norwegian DMARD register (NOR-DMARD). Patients were from five rheumatology departments in hospitals
Malinowski 2016, Poland[24]	N=8,800	Retrospective database analysis, taking into account indirect costs on payer's perspective	The Social Insurance Institution database

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Miranda 2012, Portugal[25]	N=351 8.2 years, 84% female, 59 years	Cross-sectional survey, taking into account direct costs on societal perspective	A cohort of RA patients (FRAIL Study)
Leon 2016, Spain[26]	N=1,095, 74% female, 62 years	Retrospective database analysis, taking into account direct costs on payer's perspective	A cohort of RA and spondyloarthritis patients (EMAR-II) study
Jacobsson 2007, Sweden[27]	N=613 16.7 years (median), 73.9% female, 66 years	Cross-sectional survey, taking into account both direct and indirect costs on societal perspective	RA patients living in Malmo
Hallert 2014, Sweden[28]	N=125 6 years, 67% female, 55 years	Cross-sectional survey on patients after 6 years follow-up of early RA, taking into account both direct and indirect costs on societal perspective	A longitudinal prospective multicentre TIRA study
Eriksson 2015, Sweden[29]	Prevalent, n=49,829 9.7 years, 73% female, 65.1 years Incident, n=2,695 69% female, 61.9 years	Retrospective database analysis, taking into account both direct and indirect costs on societal perspective	The Swedish National Patient Register and the Swedish Rheumatology Quality Register.
Johansson 2015, Sweden[30]	Moderate, n=1,638 10 years, 74% female, 56 years High, n=1,870 10 years, 75% female, 60 years	Retrospective database analysis of patients grouped into moderate and high disease activity by DAS28, taking into account direct costs	The Swedish Rheumatology Quality Register, primarily on early arthritis and patients on biologic treatments
Hallert 2016, Sweden[31]	N=340 70.3% female, 59 years	Cross-sectional survey on early RA patients, taking into account both direct and indirect costs on societal perspective	A longitudinal prospective multicentre study (TIRA2)

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Malhan 2010, Turkey[32]	N=562	Literature review of patients on DMARDs or TNFi treatment, taking into account direct costs on payer's perspective	Patient data taken from a reference article; cost data collected from hospital bills, social security institution price lists, and Ministry of Health drug price list.
Malhan 2012,Turkey[33]		Expert opinions, taking into account both direct and indirect costs on societal perspective	A panel of experts chosen from 20 clinics at tertiary healthcare institutions nationwide
Baser 2013, Turkey[34]	Prevalent, n=1,920 83.5% female, 53.9 years old Incident, n=693 80% female, 52.1 years	Retrospective database analysis of patients grouped into prevalent and incident cases, taking into account direct costs on payer's perspective	Turkish national health insurance database (MEDULA)
North America			
Fautrel 2007, Canada[35]	N=121 79.3% female, 63% between 40-64 years	Cross-sectional survey on patients and general population, taking into account both direct and indirect costs on societal perspective	Patients recruited from their treating physicians; general population enrolled from random digit dialling for people living in Quebec
Barnabe 2013, Canada[36]	N=1,086 13.6 years, 72.1% female, 55.1 years	Retrospective database analysis of patients on biologic treatments, taking into account direct costs on societal perspective	The Alberta Biologics Pharmacosurveillance Program (ABioPharm) linked with provincial health care administrative database
Tarride 2013, Canada[37]	N=233 75.5% female, 58.9 years	Cross-sectional survey on patients linked retrospective database analysis, taking into account direct costs	Canadian Community Health Survey (CCHS) linked to the Ontario Health Insurance Program (OHIP)

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Thanh 2013, Canada[38]	N=1,222 13 years, 69% female, 52 years	Retrospective database analysis of patients on DMARDs or TNFi treatment, taking into account indirect costs on societal perspective	The Alberta Biologics Registry
Ohinmaa 2014, Canada[39]	N=1,086 13.6 years, 72.1% female, 55.1 years	Retrospective database analysis of patients on biologic treatments, taking into account direct costs on societal perspective	The Alberta Biologics Pharmacosurveillance Program (ABioPharm) linked with provincial health care administrative database
Yelin 2007, USA[40]	N=4,801	Retrospective database analysis, taking into account direct costs	A national probability sample of households (MEPS)
Kessler 2008, USA[41]	N=333 72.4% female, 52.9% 45–59 years	Cross-sectional survey, taking into account direct costs on employer's perspective	Samples from manufacturing firm (MF) employees and commercially insured subscribers
Joyce 2009, USA[42]	RA/+CVD/+depression/ +both above n=8,916/608/716/58 77%/55%/88%/81% female, 50.9/58.7/49.6/53 years	Retrospective database analysis of RA patients with co-morbidities, taking into account direct costs on payer's perspective	The PharMetrics Patient-Centric Database
Birnbaum 2010, USA[43]	Privately insured/ Medicare/ Medicaid n=14,317/ 12,157/ 6,415 33.3/ 42.9/ 38.5 months, 70.4%/ 70.6%/ 76.6% female, 49.8/ 70.7/ 45.3 years	Retrospective database analysis, taking into account both direct and indirect costs on societal, employer, patients' and payer's perspectives	Indirect costs from Ingenix Employer Database; direct costs from the Medicare 5% Standard Analytic and Florida Medicaid claims databases

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Bonafede 2012, USA[44]	N=26,911 71.7% female, 59.7 years	Retrospective database analysis, taking into account direct costs on societal perspective	The MarketScan Commercial Claims and Encounters (Commercial) Database and the Medicare Supplemental and Coordination of Benefits (COB) Database
Kawatkar 2012, USA[45]	N=5.8 million 61.1% female, 19.3% 45–54 years	Retrospective database analysis, taking into account direct costs on payer's perspective	A national probability sample of households (MEPS)
Simons 2012, USA[46]	N=34,145 80.4% female, 50.6% 40–64 years	Retrospective database analysis, taking into account both direct and indirect costs	A national probability sample of households (MEPS)
Kleinman 2013, USA[47]	N=2,705 61.4% female, 45.1 years	Retrospective database analysis, taking into account both direct and indirect costs on employer's perspective	US employees' administrative health care and payroll data in an employer-sponsored health insurance plan
Gunnarsson 2015, USA[48]	N=90,046 76.3% female, 38.8% 45–54 years	Retrospective database analysis, taking into account indirect costs	A national probability sample of households (MEPS)
Zhou 2016, USA[49]	Switched to another TNFi, N=1,169 81.3% female, 49.3 years	Retrospective database analysis of patients on different strategies of TNFi treatment, taking into account direct costs	A US employer-based insurance claims database.
Curtis 2017, USA[50]	N=4,593 11.8 years, 74.4% female, 70.6 years	Retrospective database analysis, taking into account direct costs	A disease registry across 40 states (Corrona) linked to administrative data from Medicare
Grabner 2017, USA[51]	TNFi treatment responders, n=2,337 70.8% female, 52.3 years	Retrospective database analysis of patients on different strategies of TNFi treatment, taking into account direct costs on payer's perspective	Members of 14 large U.S. commercial health plans represented in the HealthCore Integrated Research Database

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Chen 2018, USA[52]	N= 115,867 79.4% female, 75.2 years	Retrospective database analysis, taking into account direct costs	Medicare fee-for-service (FFS) claims database
Strand 2018, USA[53]	N= 2527 71.1% female, 56.9 years	Retrospective database analysis of patients on biologic treatments, taking both direct and indirect costs into account	OptumHealth Care Solutions database
Asia			
Aggarwal 2006, India[54]	N=101 8.1 years, 89% female, 43.2 years	Cross-sectional survey, taking into account direct costs	RA clinic at a tertiary care hospital
Xu 2014, China[55]	N=829 9.2 years, 78.6% female, 53.3 years	Cross-sectional survey, taking into account both direct and indirect costs on societal perspective	RA clinics at 21 tertiary care hospitals
Hu 2018, China[56]	N=133 68% female, 60.4 years	Cross-sectional survey, taking into account both direct and indirect costs on societal perspective	RA clinics at 2 referral hospitals
Lee 2007, Hong Kong[57]	N=147 12.6 years, 76.9% female, 54.7 years	Retrospective database analysis, taking into account direct costs on payer's perspective	RA clinic at a general hospital
Zhu 2011, Hong Kong[58]	N=144 10.8 years ,73% female, 49 years	Cross-sectional survey linked to retrospective database, taking into account both direct and indirect costs on societal perspective	RA clinic at a general hospital
Tanaka 2010, Japan[59]	N=6,823 11.4 years, 83.3% female, 58.4 years	Retrospective database analysis, taking into account direct costs on societal perspective	A disease registry database (IORRA) from RA clinic at Tokyo Women's Medical University
Tanaka 2013, Japan[60]	N=5,265 12.9 years, 83.9% female, 59.5 years	Cross-sectional survey linked to retrospective database analysis, taking into account direct costs on societal perspective	A disease registry database (IORRA) from RA clinic at Tokyo Women's Medical University

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
Sruamsiri 2018, Japan[61]	N=250 9.8 years, 59% female, 52.1 years	Cross-sectional survey, taking into account indirect costs	A nationwide online survey of RA patients
Sruamsiri 2018, Japan[61]	N= 6,153 77% female, 59.2 years	Retrospective database analysis, taking into account direct costs	Hospital claims data from Medical Data Vision Co., Ltd. (MDV)
Kwon 2012, South Korea[62]	N=151,472 77.2% female, 53.1 years	Retrospective database analysis, taking into account direct costs on societal perspective	The national claims database
Lang 2016, Taiwan[63]	Prevalent, n=30,013 Female: male ratio 3.8 Incident, n=2,714 Female: male ratio 3.1	Retrospective database analysis, taking into account direct costs	The National Health Insurance Research Database (NHIRD)
Wang 2016, Taiwan[64]	N=41,269 78.1% female, 59.4 years	Retrospective database analysis for direct costs and a cross-sectional survey for indirect costs	The National Health Insurance Research Database (NHIRD) and 140 patients identified at RA clinics in four hospitals.
Shi 2018, Taiwan[65]	N=110, 645 84% female, 55.5 years	Retrospective database analysis, taking into account direct costs	The National Health Insurance Research Database (NHIRD)
Osiri 2007, Thailand[66]	N=158 10.3 years, 95.6% female, 53.2 years	Cross-sectional survey, taking into account both direct and indirect costs on societal perspective	RA clinic in a major tertiary care facility
Osiri 2013, Thailand[67]	N=684 6.3 years (DMARDs treatment), 90.8% female, 55.2 years	Retrospective database analysis of patients on DMARDs treatment, taking into account direct costs on societal perspective	RA clinic in a major tertiary care facility
Latin America & Australasia			
Chermont 2008, Brazil[68]	N=100 11 years, 92% female, 51 years	Cross-sectional survey linked to retrospective database analysis, taking into account direct costs on societal perspective	RA clinic in a tertiary reference centre.

Table S3. Continued

Study reference (Author, Year, Country)	Study population (mean duration of disease, gender, mean age)	Study design	Data source
De Azevedo 2008, Brazil[69]	N=192 9.79 years, 85.9% female, 47.37 years	Cross-sectional survey, taking into account indirect costs on societal perspective	RA clinic in a tertiary reference centre.
Alvarez-Hernandez 2012, Mexico[70]	N=320 17 months, 89.3% female, 42.7 years	Cross-sectional survey, taking into account both direct and indirect costs on patients' perspective	11 institutional and private centres in five major cities
Cross 2006, Australia[71]	N=70 25.9 years, 84.3% female, 62.7 years	Cross-sectional survey, taking into account direct costs	The Arthritis Cost and Outcome Project, patients were recruited from public and private outpatient clinics

Abbreviations: RA, rheumatoid arthritis; DAS28, Disease Activity Score-28; WPAI, Work Productivity and Activity Impairment questionnaire; WTP, willingness to pay; DMARDs, disease modified anti-rheumatic drugs; TNFi, tumour necrosis inhibitor; CVD, cardiovascular disease; USA, United States of America.

Table S4. Cost components of direct costs measured among included studies

Author	Country	Cost year	Drug cost	Inpatient [a]	Outpatient [b]	Diagnostic examination [c]	Devices and adaptation	Non-medical [d]
Europe								
Radner et al. 2014	Austria	NR	+	+	+	+	+	+
Westhovens et al. 2005	Belgium	2000	+	+	+		+	+
Klimes et al. 2014	Czech	2013	+	+	+	+		
Loppenthin et al. 2018	Denmark	2006	+	+	+			
Flipon et al. 2009	France	2003	+	+	+	+		+
Kobelt et al. 2008	France	2005	+	+	+	+	+	+
Chevreul et al. 2014	France	2007	+	+	+	+		+
Beresniak et al. 2011	France	2008		+	+	+	+	+
Fautrel et al. 2016	France	2010	+	+	+	+	+	+
Beck et al. 2015	France	2012	+	+	+	+		+
Ruof et al. 2003	Germany	2001	+	+	+	+	+	+
Kirchhoff et al. 2011	Germany	2002	+	+	+			+
Hulsemann et al. 2005	Germany	2004	+	+	+		+	+
Huscher et al. 2015	Germany	2011	+	+	+	+		
Ziegelbauer et al. 2018	Germany	NR	+	+	+			
Horvath Cs et al. 2014	Hungary	2012		+	+			
Della Rossa et al. 2010	Italy	NR	+		+	+		+
Verstappen et al. 2007	Netherlands	2003	+	+	+	+	+	+
Kvamme et al. 2012	Norway	2010	+	+	+	+		
Miranda et al. 2012	Portugal	2010	+	+	+	+	+	+
Leon et al. 2016	Spain	2010	+	+	+	+		+
Jacobsson et al. 2007	Sweden	2004	+	+	+		+	+
Eriksson et al. 2015	Sweden	2010	+	+	+			
Hallert et al. 2014	Sweden	2012	+	+	+	+		
Johansson et al. 2015	Sweden	2012	+	+	+			

Table S4. Cost components of direct costs measured among included studies

Author	Country	Cost year	Drug cost	Inpatient [a]	Outpatient [b]	Diagnostic examination [c]	Devices and adaptation	Non-medical [d]
Hallert et al. 2016	Sweden	2013	+	+	+	+		
Malhan et al. 2010	Turkey	NR	+	+	+	+	+	
Malhan et al. 2012	Turkey	2011	+	+	+			
Baser et al. 2013	Turkey	NR	+	+	+	+	+	+
North America								
Fautrel et al. 2007	Canada	2002	+	+	+	+	+	
Tarride et al. 2013	Canada	2002		+	+	+		
Barnabe et al. 2013	Canada	2008		+	+			
Ohinmaa et al. 2014	Canada	2008		+	+			
Yelin et al. 2007	USA	2003	+	+	+		+	+
Kessler et al. 2008	USA	2005	+	+	+			
Birnbaum et al. 2010	USA	2005	+	+	+		+	+
Joyce et al. 2009	USA	2006	+	+	+	+		
Kawatkar et al. 2012	USA	2008	+	+	+			+
Bonafede et al. 2012	USA	NR	+	+	+			+
Simons et al. 2012	USA	NR	+	+	+		+	+
Kleinman et al. 2013	USA	2010	+	+	+			
Chen et al. 2018	USA	2013	+	+	+			
Zhou et al. 2016[49]	USA	2012	+	+	+			
Grabner et al. 2017	USA	2014	+	+	+	+		
Strand et al. 2018	USA	2014	+	+	+	+		+
Curtis et al. 2017	USA	2016	+	+	+			
Asia								
Aggarwal et al. 2006	India	NR	+	+		+		+
Xu et al. 2014	China	2005	+	+	+	+		+
Hu et al. 2017	China	2013	+	+	+			

Table S4. Cost components of direct costs measured among included studies

Author	Country	Cost year	Drug cost	Inpatient [a]	Outpatient [b]	Diagnostic examination [c]	Devices and adaptation	Non-medical [d]
Lee et al. 2007	Hong Kong	2003	+	+	+	+		
Zhu et al. 2011	Hong Kong	2006	+	+	+	+	+	+
Tanaka et al. 2010	Japan	2007	+		+	+	+	
Tanaka et al. 2013	Japan	2007	+	+	+		+	+
Sruamsiri et al. 2018	Japan	2016	+	+	+			
Kwon et al. 2012	South Korea	2009	+	+	+	+		
Lang et al. 2016	Taiwan	2011	+	+	+			
Wang et al. 2016	Taiwan	2011	+	+		+	+	
Shi et al. 2018	Taiwan	2016	+	+	+			
Osiri et al. 2007	Thailand	2001	+	+	+	+	+	+
Osiri et al. 2013	Thailand	2009	+		+	+		
Latin America								
Chermont et al. 2008	Brazil	2002	+	+	+	+	+	+
Alvarez-Hernandez et al. 2012	Mexico	2005	+	+	+	+	+	+
Australasia								
Cross et al. 2006	Australia	NR	+	+	+	+	+	

[a] Inpatient costs include costs of hospitalisation, surgery, and emergency room visit.

[b] Outpatient costs include costs of visits to physicians and other healthcare professionals, such as nurse, OT, PT etc.

[c] Diagnostic examination includes costs of imaging and laboratory tests.

[d] Non-medical costs include costs of informal care, home help, and transportation etc.

Table S5. Cost components of indirect costs measured among included studies

Author	Country	Cost year	Method	Absenteeism [a]	Work disability [b]	Others
Europe						
Radner et al. 2014	Austria	NR	HCA/FCA	+	+	
Kruntoradova et al. 2014	Czech	2010	FCA	+	+	Productivity impairment
Klimes et al. 2014	Czech	2013	FCA	+	+	
Loppenthin et al. 2018	Denmark	2006	NR	+	+	Foregone earnings
Sogaard et al. 2010	Denmark	2007	HCA	+		Presenteeism
Martikainen et al. 2016	Finland	2013	HCA	+	+	
Flipon et al. 2009	France	2003	NR		+	
Kobelt et al. 2008	France	2005	HCA	+	+	
Merkesdal et al. 2005	Germany	2001	HCA/FCA	+	+	
Kirchhoff et al. 2011	Germany	2002	HCA/FCA	+	+	Work loss
Ruof et al. 2003	Germany	2003	NR	+	+	
Huscher et al. 2015	Germany	2011	HCA/FCA	+	+	
Della Rossa et al. 2010	Italy	NR	HCA	+		
Kvamme et al. 2012	Norway	2010	HCA/FCA	+		
Malinowski et al. 2016	Poland	2012	HCA	+	+	
Miranda et al. 2012	Portugal	2010	HCA	+		Work day lost by the companion
Jacobsson et al. 2007	Sweden	2004	NR	+	+	Loss of leisure time
Eriksson et al. 2015	Sweden	2010	HCA/FCA	+	+	
Hallert et al. 2014	Sweden	2012	HCA	+	+	
Hallert et al. 2016	Sweden	2013	HCA	+	+	
Malhan et al. 2012	Turkey	2011	HCA	+	+	
North America						
Fautrel et al. 2007	Canada	2002	HCA/WTP			
Thanh et al. 2013	Canada	2010	HCA	+		
Birnbaum et al. 2010	USA	2005	NR	+	+	
Simons et al. 2012	USA	NR	NR	+		Workforce participation/ income loss
Gunnarsson et al. 2015	USA	2008	NR	+		

Table S5. Cost components of indirect costs measured among included studies

Author	Country	Cost year	Method	Absenteeism [a]	Work disability [b]	Others
Kleinman et al. 2013	USA	2010	NR	+	+	
Strand et al. 2018	USA	2014	HCA	+		
Asia						
Xu et al. 2014	China	2005	HCA	+		
Hu et al. 2017	China	2013	HCA	+		
Zhu et al. 2011	Hong Kong	2006	HCA	+		Unemployment/ days off from household work or daily activities
Sruamsiri et al. 2017	Japan	2016	NR	+		Presenteeism
Wang et al. 2016	Taiwan	2011	NR	+		Presenteeism
Osiri et al. 2007	Thailand	2001	NR	+		
Latin America						
De Azevedo et al. 2008	Brazil	2005	HCA	+		
Alvarez-Hernandez et al. 2012	Mexico	2005	NR			Job loss/ third party help

Abbreviations: HCA, human capital approach; FCA, friction cost approach; WTP, willingness to pay.

[a] Absenteeism includes the costs of work hour loss, short-term and long-term sick leaves.

[b] Work disability includes the costs of early retirement and disability pensions.

Table S6. Quality assessment by modified CHEERS checklist

Recommendations	Yes	No	Not applicable	%
1. Title	67	5	0	93%
2. Abstract	59	13	0	82%
3. Background and objectives	69	3	0	96%
4. Target population and subgroups	62	9	0	87%
5. Setting and location	71	1	0	99%
6. Study perspective	50	22	0	59%
7. Population	12	0	60	17%
8. Time horizon	67	5	0	93%
9. Cost components	61	11	0	85%
10. Estimating resources and costs	70	2	0	97%
11. Currency, price date, and conversion	63	9	0	88%
12. Choice of model	1	0	71	1%
13. Assumptions	1	0	71	1%
14. Analytical methods	57	15	0	79%
15. Study parameters	1	0	71	1%
16. Cost	72	0	0	100%
17. Characterising uncertainty	51	21	0	71%
18. Characterising heterogeneity	52	20	0	72%
19. Study findings, limitations, generalisability, and current knowledge	68	4	0	94%
20.Source of funding	55	17	0	76%
21. Conflicts of interest	45	27	0	63%

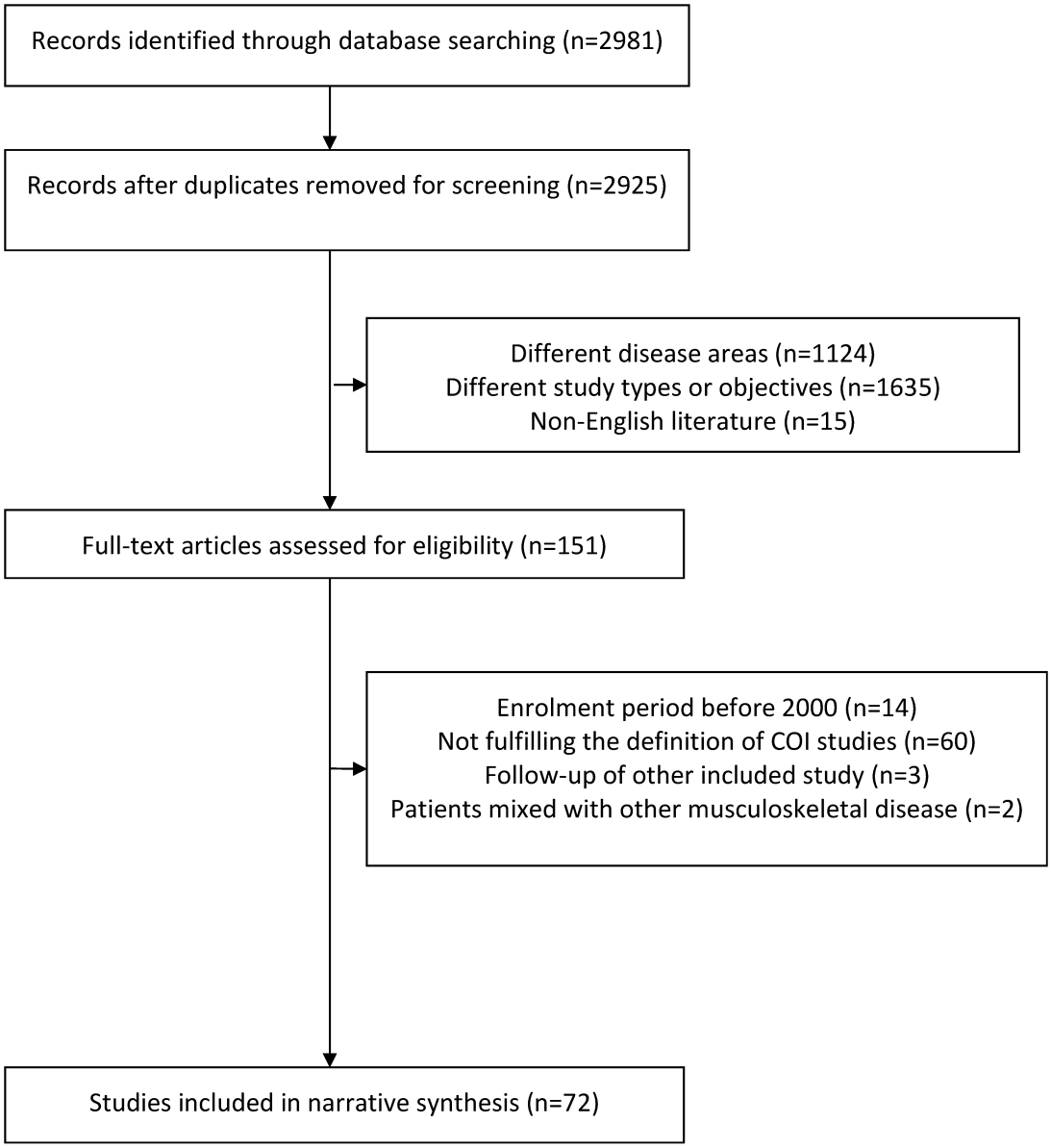

Figure S1. PRISMA flow diagram

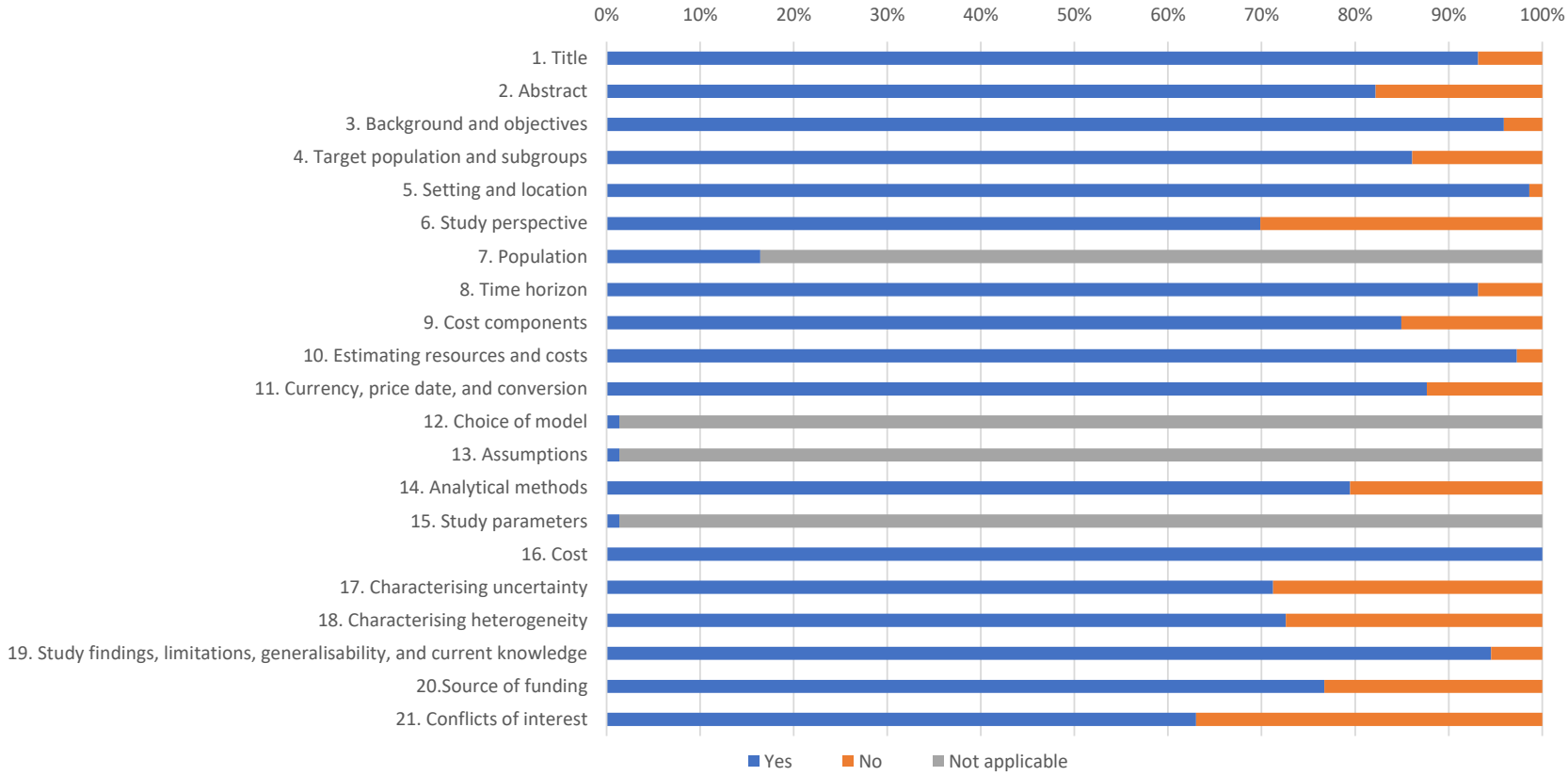

Figure S2. Bar chart illustrating quality assessment of included studies by using modified CHEERS checklist, as percentage of adequately reported items.

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