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# Burden of osteoarthritis in the Netherlands: a scoping review

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## **REVIEW**

Burden of osteoarthritis in the Netherlands: a scoping review

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#### **ABSTRACT**

Objective: To provide an overview of societal burden of osteoarthritis (OA) in the Netherlands. Methods: Medline (via Ovid) and Embase databases were searched in September 2022 for all publications providing prevalence/incidence, cost or health-related quality of life (HRQoL) data of OA (all sites) in the Netherlands.

Results: Twenty-eight original studies were included in this scoping review; twelve reporting prevalence/ incidence data of OA, seven reporting data on the economic burden of OA and twelve reporting HROoL data of patients with OA. Most of the available data were from Dutch national cohorts. The prevalence of knee OA ranged from 6% to 18% across studies, from 4% to 7% for hip OA and from 12% to 56% for hand OA. OA was shown to be associated with impairment in work participation and long-term requirement of health care utilization, translating into substantial medical costs and societal costs of lost productivity. All studies comparing HRQoL among persons with OA with control persons showed a significantly lower HRQoL in patients with OA after adjustment for age, sex, and various risk factors.

Conclusions: OA is a highly prevalent disease in the Dutch population and is responsible for a significant economic and health burden.

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#### **KEYWORDS**

Osteoarthritis: prevalence: incidence; economic burden; health-related quality of life; the Netherlands

## 1. Introduction

Osteoarthritis (OA) is a common, degenerative, and debilitating joint disease characterized by pain and functional impairment and is one of the leading causes of global disability [1]. The knee and hip are the two joints that are most frequently affected by this condition. The global prevalence of knee OA is estimated at 3.8% and hip OA at 0.85%, with a higher prevalence in women compared to men [1]. The incidence of OA is rising due to the increase in life expectancy and in the prevalence of obesity [2,3]. OA is associated with significant utilization of healthcare resources, and impairs health-related quality of life (HRQoL) of patients. In a systematic literature review published in 2016 including 28 large sample studies measuring the worldwide economic and/or health burden of OA, Xie et al. [4] reported important impairments in patient's HRQoL as well as considerable per-patient costs for OA with total annual average direct costs of OA comprised between US\$1,442 to US\$21,335 and total average indirect costs ranged from US\$238 to US\$29,900 (all costs adjusted to year 2015). Even though summaries of international data are worthwhile to be informed on the worldwide burden of OA, health-care decisions and resource allocation are usually made at a national level. Therefore, providing country-specific data concerning prevalence, costs and HRQoL of patients suffering from OA is important for national decision-making. For this reason, we aimed to perform a scoping review to identify and summarize relevant data on the prevalence and incidence of OA, on the costs associated with OA, and on the HRQoL of patients suffering from OA in the Netherlands. To our knowledge, no meta-research studies have been made to synthesize the burden of OA in the Netherlands. Reporting country-specific burden of OA is important when estimating the health and budget impact of the disease and when planning to develop health economic models to assess costeffectiveness of strategies for prevention and various treatment. In addition to providing an overview of the economic and health burden of OA in the Netherlands, the scoping review also intends to identify the current knowledge gaps in this area.

## 2. Methods

The proposed scoping review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA2020) extension for scoping reviews [5]. The completed PRISMA checklist is available in Appendix 1. A protocol was developed and published in Open Science Framework (https://osf.io/vgx4n/). This scoping review also followed the five-step framework by Arksey and o'Malley [6] and guidance from the Joanna Briggs Institute scoping review methodologies (https://jbi.global/scoping-review-network /resources). Covidence software (i.e. Covidence is a web-based collaboration software platform that streamlines the production



## Article highlights

- Twenty-eight original studies were identified throught a scoping review process to inform about societal burden of osteoarthritis (OA) in the Netherlands
- OA is a highly prevalent disease in the Dutch population
- OA is associated with restrictions in work participation and substantial health care consumption, translating into costs of the lost productivity and healthcare costs
- OA is responsible for a major health burden

of systematic and other literature reviews) was used to manage search results, including deduplication, abstract and title screening, and full-text screening. Data extraction was performed using Microsoft Excel.

## 2.1. Literature search

A scientific literature search was conducted in Medline (via Ovid) and Embase databases until September 2022 to identify English or Dutch language scientific studies reporting burden of osteoarthritis (excluding studies on degenerative disorders of the spine) that provided original data on prevalence/incidence, cost or HRQoL. A combination of terms of Medical Subject Headings (MeSH) and keywords was used in the search strategy (the complete search strategies for Ovid and Scopus, developed by CB, who is experienced in bibliographic research, are available in the Appendix 2).

Additionally, a manual search within the bibliography of relevant papers was also performed to complete the bibliographic search. We also conducted forward references searching of included studies using Web of Science to identify other relevant research that has referenced any article of interest.

## 2.2. Study selection

Two reviewers (CB and NL) independently screened titles and abstracts of the de-duplicated search output to exclude irrelevant articles. In the second step, the reviewers read the full text of each non-excluded article to determine eligibility for inclusion in this scoping review. Disagreements during both stages were resolved by consensus.

Studies meeting the following criteria were included:

- Original published and peer-reviewed studies (crosssectional, prospective, retrospective, case control, cost studies, baseline data from randomized controlled trials) providing prevalence and/or incidence data, costs data, quality of life data or utilities of patients with OA (any approaches to diagnose OA accepted) at any sites (except spine).
- Systematic reviews and/or meta-analyses on the theme:
- Population cohorts performed in the Netherlands;
- Studies published in English or Dutch language [7].

Non-original studies such as letters, commentary, opinion or protocols were excluded. We also excluded studies that reported costs directly linked to a surgery (i.e. knee replacement) and not to OA itself.

## 2.3. Data extraction

Data were extracted by the two independent reviewers according to a standardized data extraction form. Disagreements between reviewers were resolved by consensus. The following data were extracted: Authors, year of publication, study design, outcome(s) reported, objective of the study, inclusion/exclusion criteria of the study, name of the cohort study (if available), description of the population, site of OA, ascertainment/approach of diagnosis and main results.

## 2.4. Synthesis of results

A narrative synthesis of results was presented for each aspect (i.e. prevalence/incidence, costs and HRQoL) for the different OA sites (knee, hip, hand) when possible. For each section, a summary of the evidence is provided to better understand the current state of the art. This summary comprises 1. What is known; 2. What are the weaknesses of knowledge; 3. What is not known. No meta-analysis was undertaken. Consistent with methodology of scoping reviews, no quality assessment of individual studies was performed.

#### 3. Results

A total of 759 references were identified through the search strategies. After deduplicates, 438 references were screened for eligibility based on their titles/abstracts and 63 of them were further assessed based on their full texts. From those 63 studies, 28 fulfilled our inclusion criteria and were included in this scoping review. The list of excluded studies and their reasons of exclusion is available on our Open Science Framework deposit (https://osf.io/vgx4n/). Flowchart of study selection is available in Figure 1.

Included studies were published between 1989 and 2022. Only original studies were identified (i.e. no systematic reviews, no meta-analyses). Twelve studies reported prevalence/incidence data of OA in the Netherlands [8–19], seven reported data of economic burden of OA [20–26] and twelve reported HRQoL data of patients with OA [12,20,26–35]. Knee OA, hip OA, hand OA, ankle OA or combinations were investigated throughout these studies.

Nineteen of the 28 studies (68%) of the individual studies reported data from one of the seven main cohorts: the Population-based Netherlands Epidemiology of Obesity (NEO) study, the Hand OSTeoArthritis in Secondary care (HOSTAS) study, the Dutch, population based, musculoskeletal complaints and consequences (DMC3) cohort study, the Cohort Hip and Cohort Knee (CHECK) study, the Epidemiological Preventive Organisation Zoetermeer (EPOZstudy), the Longitudinal Aging Study Amsterdam (LASA) included in the larger European Project on OSteoArthritis (EPOSA) and the Rotterdam study. These different cohorts are described in Table 1.

## 3.1. Prevalence/Incidence data of OA in the Netherlands

Twelve scientific studies reported prevalence data of OA in the Netherlands [8–19] and three of them reported also incidence data of OA in the Netherlands [9,17,19] (Table 2). Information on prevalence of OA were obtained mainly from cross-

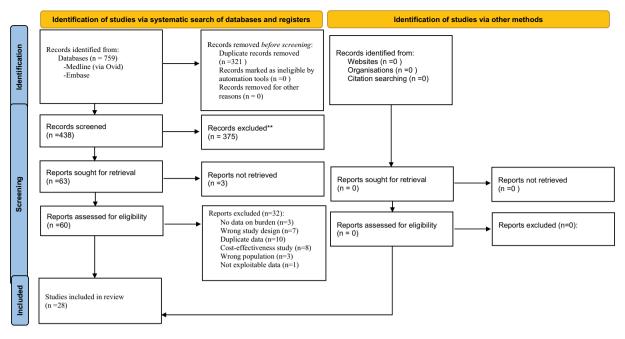


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) flowchart of study selection.

sectional analysis of cohort studies (n = 9). Most of time, studies reported prevalence data for knee [8–14], hip [8,10,11,14,17] and hand OA [8,10,11,13,15,16,19]. Only one study provided data of prevalence of OA in any sites (combined knee, hip and hand OA) [10] and three studies reported prevalence data for different combinations of OA (i.e. knee or hip [19], hip or hand [11], knee and hand [13]) (Appendix 3).

Approach to diagnose OA varied across studies. For case definition of hip and knee OA, ICPC codes L-89 or L90 were used [9,17] as well as ACR clinical classification [10–13]. An old study also used the Atlas of Standard Radiographs to identify knee OA based on radiographs [8]. Two studies also used population self-reported OA to establish OA prevalence [11,14]. For hand OA, the ACR clinical classification [10,11,13] was used as well as the radiographic presence of K-L K-L  $\geq$  2 in two of three joints groups [15,16,19]. One study did not provide information about the criteria used for the assessment of OA [18].

Prevalence of *knee OA* was reported in 7 out of the 12 studies [8–14]. Another study reported prevalence of hip or knee but did not reported the prevalence of knee OA separately [18]. The oldest prevalence reported was reported in the study of Van Saase in 1989 [8] and the most up-to-date data were reported by Arslan et al. in 2019 [9]. Knee OA prevalence ranged from 2.88% in the study of Arslan et al. [9] to 18.2% in the EPOSA study [10,11].

The study of Arslan et al., including a representative sample of the Dutch population, reported a prevalence of codified knee OA (ICPC code L90) of 2.88% in 2008 and of 6.15% in 2019, highlighting an increase of this prevalence across time. The same authors also reported data on incidence and also showed an increase of incidence with a incidence of 4.88 per 1,000 person year in 2008 versus 6.04 per 1,000 person year in 2019. In 2003, Picavet et al. also provided data over prevalence of knee OA on a sample representative of the adult (≥25 years) population, reporting a prevalence of knee OA in 1998, based

on ACR clinical classification criteria, of 10.1% in men and 13.6% in women. Two additional studies reported prevalence of OA within the EPOSA project, which used a subsample of older persons aged 65–85 years [10,11]. Using the ACR clinical classification, a prevalence of 18.2% for knee OA was reported in the study addressing the largest sample [11]. Finally, two studies reported prevalence of knee OA from the NEO study, a population-based cohort including 6,643 adults participants with an oversampling of overweight and obesity. Surprisingly, those two studies, reporting results of the baseline measurement of the NEO study, reported a slightly different prevalence of knee OA (10% [13] versus 15% [11]), despite a similar diagnostic approach and a similar sample size.

Prevalence of hip OA was reported in five studies [8,10,11,14,17] conducted between 1978 [8] and 2019 [17]. One additional study reported prevalence of hip or knee but did not report the prevalence of hip OA separately [18]. Range of reported hip OA prevalence across those five studies was 4–7%. As for knee OA, only one study provided prevalence data on a representative sample of the global Dutch population and reported a prevalence of hip OA of 4% [17]. Picavet et al. [14] reported a slightly higher prevalence from a representative adult (≥25 years) Dutch population, with a hip OA prevalence of 10% in women and of 4% in men (about 6.75% when combining both sexes). Finally, two separate manuscripts reported prevalence of hip OA at 7% in the NEO study.

Prevalence of *hand OA* was reported in 7 studies [8,10,11,13,15,16,19] conducted between 1989 [8] to 2011 [11]. Prevalence data across studies ranged from 11.6% [10] to 56% [15]. However, heterogeneity in terms of diagnostic approach and site of hand OA was noticed. Three studies used the ACR clinical classification for the identification of hand OA and reported, respectively, a prevalence of 29.4% (Van der Pas et al. EPOSA study [11], participants aged 65–85 years), 11.6% (Castell [10], EPOSA study, restricted sample with only 483 participants) and

Table 1. Description of the 7 national Dutch cohorts identified through the literature search that provided data on prevalence, HRQoL or costs of OA in the

Full name	Abbreviation	Short description or objective of the cohort	Information about study sample
The Longitudinal Aging Study Amsterdam	LASA	Ongoing cohort study of predictors and consequences of changes in physical, cognitive, emotional and social functioning in older persons. The LASA is included in the larger European Project on OSteoArthritis (EPOSA) study, which involves six European cohort studies. References included in the scoping review Epidemiology: 2 [10,11]; Costs: 0; HRQoL: 0	The LASA sample was selected from population registers in 11 municipalities in the Netherlands and includes individuals aged 65–85 years.
The Netherlands Epidemiology of Obesity study	NEO	Population-based prospective cohort study designed for extensive phenotyping to investigate pathways that lead to obesity-related diseases. <i>References included in the scoping review</i> Epidemiology: 2 [12,13]; Costs: 0; HRQoL: 3 [31,35], 52]	The NEO study is oversampled with overweight and obese persons.Men and women between 45 and 65 years with a self-reported BMI ≥27 kg/m2 living in the greater area of Leiden (the Netherlands) were eligible to participate. In addition, all inhabitants aged between 45 and 65 years from 1 municipality (Leiderdorp) were invited to participate irrespective of their BMI, allowing for a reference BMI distribution comparable to the general Dutch population. Men and women between 45 and 65 years with a self-reported BMI ≥27 kg/m2 living in the greater area of Leiden (the Netherlands) were eligible to participate. In addition, all inhabitants aged between 45 and 65 years from 1 municipality (Leiderdorp) were invited to participate irrespective of their BMI, allowing for a reference BMI distribution comparable to the general Dutch population.
The Rotterdam study	/	Ongoing population based cohort studying determinants of chronic disabling disease.  References included in the scoping review Epidemiology: 3 [15,16,19]; Costs:0; HRQoL: 0	
The Dutch population based Musculoskeletal Complaints and Consequences cohort study	DMC3 study	Not described.  References included in the scoping review Epidemiology: 1 [14]; Costs: 0; HRQoL: 1 [33]	The DMC study is composed with random sample of 8000 people aged ≥25 years taken from the population register of 1998, identical to the general surveys of Statistics Netherlands (response rate 52% for women and 42% for men)
The Epidemiological Preventive Organisation Zoetermeer	EPOZstudy	Population survey conducted between 1975 and 1978 to study the prevalence and determinants of rheumatic and cardiovascular diseases.  References included in the scoping review Epidemiology: 1 [8]; Costs: 0; HRQoL: 0	All inhabitants in two districts of Zoetemeer were invited to participate (response rate of 76.1%)
The Cohort Hip and Cohort Knee	CHECK study	Dutch prospective 10-year follow-up study initiated to study progression of OA in participants with early symptomatic OA of knee or hip <i>References included in the scoping review</i> Epidemiology: 0; Costs: 3 [21,22,25]; HRQoL: 1 [34]	Participants aged 45–65 years with pain and/or stiffness of the knee and/or hip referred by general practitioners were invited to participate.
The Hand Osteoarthritis in Secondary Care	HOSTAS	Ongoing observational cohort on primary hand OA aiming at investigating determinants of outcome and utility of clinimetric instruments in primary hand OA <i>References included in the scoping review</i> Epidemiology: 0; Costs: 1 [20]; HRQoL: 1 [31]	Consecutive patients from the Leiden University Medical Center (LUMC) outpatient clinic were included between June 2009 and October 2015 (mean age ±60 years).

BMI= Body Mass Index; OA= osteoarthritis.

8% (Visser et al. [13] NEO study, oversampling overweight and obese participants). Using radiographic K-L grades ≥ 2 for the classification of hand OA, Teunissen et al. [19] analyzed baseline data of the Rotterdam study (first 1991 and second 2001 cohorts included) and reported a prevalence of caropometacarpal OA of 25.3% and trapezioscaphoid OA of 14.5%. Authors did not reported directly incidence rates of OA but mentioned that the age-adjusted incidence was generally higher in females compared to males for caropometacarpal OA (4 years OR = 1.59 [95%CI 1.05;2.41] and 12 years OR = 1.59 [95%CI 1.27;2.00]) and trapezioscaphoid OA (4 years OR = 1.76 [95%CI 0.91:3.44] and 12 years OR = 2.09 [95% 1.41;3.09]). Still using data from the Rotterdam study, Dahaghin et al. [16] reported a prevalence of hand OA in 1993 of 28.3% and Kwok et al. [15] further reported a prevalence of hand OA of 56% in the sample 6 years later.

Only one study [10] provided data of prevalence of OA in any sites (combined knee, hip and hand OA). Authors reported a prevalence of people suffering from OA of 26.2% in a population with a mean age of 75 years. Other studies presented prevalence data for different combinations of OA sites; Schellevis et al. [18] reported a prevalence of knee 'or' hip OA of 29.3% in older adults (>65 years); Van der Pas et al. [11] reported a prevalence of hip 'or' hand OA of 25.9% and Visser et al. [13] reported a prevalence of knee 'and' hand OA of 4%.

## 3.2. Economic burden of OA

Seven studies [20–26] reported the economic burden of OA including (the impact on) work participation (n = 4) with [20– 23] or without costs [21,22], healthcare utilization (n = 2)[25,26], costs of healthcare utilization (n = 1) [24] and indirect or productivity costs (n = 3) [20,23,24] caused by OA (Table 3). Hand, hip and knee OA were addressed in one, five, and six studies, respectively. Data were obtained from cohort studies

(n=5) [21–25] or baseline data from randomized controlled trials (n=2) [20,26]. The sample size varied from 117 [30] to 1399 participants [34]. For the classification criteria of OA, ACR clinical criteria as well as the radiographic presence of K-L were used in most studies [21–26]. None of the seven studies presented comparative results between patients with OA and a control group without OA.



What is known: OA is a common disease in the Dutch population, is more common in women than in men and increases with age. The prevalence of knee OA ranged from 6% to 18% across studies and of hip OA from 4% to 7%. The lowest prevalence was observed in a representative sample of the Dutch population and the highest prevalence was observed in a representative sample of the older Dutch population aged 65–85 years. The prevalence of hand OA ranged from 12% to 56%.



What are the weaknesses of knowledge: There is heterogeneity in the classification criteria for OA, especially for hand. In addition, the area of the hand in which OA was measured varied widely between studies, making comparison between studies difficult. Also, the majority of epidemiological studies are obtained from routine primary care codified data. As Arslan et al. have shown in their studies [9,17], this leads to a serious underestimation of the true prevalence of OA. Narrative data could be added to codified data to better reflect the actual prevalence.



What is not known: None of the studies reported the prevalence of hand OA in a population representative sample of the Dutch adult population. The most recent available data on prevalence were obtained in 2019. There is a lack of data reporting prevalence of OA at any site or of specific combinations of joint sites.

Four studies reported the impact of OA on work participation as 'natural units'. In both studies of Bieleman et al. [21,22], data were reported on present working status, sick leave and work adaptation; the knee & hip OA study by Hardenberg et al. [23] on sick leave, and the hand OA study by Terpstra et al. [20] on unpaid and paid work restrictions, unpaid work replacement by others, inefficiency at work and sick leave. Two studies by Bieleman et al. [21,22] indicated that the baseline work participation rate (51%) of Dutch people with early hips/knees OA was similar to general Dutch population, but a decrease was captured during 2 years follow-up (46%). In addition, 12% and 14% of workers reported sick leave and work adaptions at baseline, respectively, and a further increase by 6% was captured for work adaptions at 2 years. Subjects who stopped working were on average 4.2 years older than those who continued working. In addition, female sex and lower education level were related to lower participation. Societal factors appear to have had more effect on work participation than health status. Hardenberg et al. [23] reported that knee and hip OA was associated with an average sick leave episode of 186 and 159 calendar days per patient over 3 years (2015–2017), respectively. In the study of Terpstra et al. [20], 45% of patients (with hand OA) who have to perform unpaid work, reported others had to take over such tasks because of hand OA. Absence from paid work (sick leave) in those employed, work restrictions and unproductive hours while at work due to hand OA at work was reported by 7%, 66% and 15% of patients, respectively.

Costs of productivity loss associated with restricted work participation were presented in three studies. Hardenberg et al. [23] reported, using information reported by occupational physicians that an average sick leave episode of knee (186 days) and hip (159 days) OA was associated with €15,550 and €12,482 in costs over 3 years (2015-2017), respectively. These costs are particularly high among male workers and workers with a higher number of weekly working hours. The average annual costs (2015-2017) for the Dutch workforce due to sick leave for knee and hip OA were estimated at €26.9 million and €13.8 million, respectively. Hardenberg et al. [23] also indicated that sick leave (i.e. absenteeism) costs decreased for hip and not for knee OA during 2015-2017. As every OA patient may not visit an occupational physicians, authors acknowledged a potential underestimation of the actual sick leave-related costs in their study. In another study, Hermans et al. [24] estimated the total knee-related productivity costs of conservatively treated symptomatic knee OA patients with paid employment in the Netherlands at €772 per patient per month. Higher pain intensity during activity and performing physically loading work were significantly associated with productivity loss. In a third study [20], the total estimated work-related societal costs (i.e. societal costs of paid labor productivity loss quantifying by lost hours due to paid work absenteeism and presenteeism – in the form of extra hours to catch up with unproductive hours at work caused by OA) per patient with hand OA were estimated at €94 per 2 weeks (€2452 per year).

With regard to health care utilization, Pelle et al. [26] evaluated the short-term effects of use of an app (the app proposes a list of five pre-formulated goals to a healthier lifestyle, based on machine learning techniques fed by data collected in a personal profile, aiming to promote health behaviors, better self-management, and optimal use of non-surgical treatment options). It suggests the number of second line healthcare visits (i.e. orthopedic surgeon, rheumatologist, or physician therapist) increased after OA, visits to physical therapist were most common.

Hoogeboom et al. [25] included in a study on care utilization comprising analgesic use, supplement use, contact with a General Practitioner (GP), contact with a Health Professional (HP), contact in secondary care, and alternative medicine use and indicated that analgesic use, contact with a GP, and contact with an HP were most frequently used health care by patients with knee and/or hip OA at baseline. Individuals with early symptomatic OA rely in the first 2 years mainly on analgesics, contacting with a GP significantly decreased while supplement use increased during 2 years follow-up. Education, ethnicity and familiarity with care are strongly associated with more health care use, suggesting health care use should be optimized by taking the health needs of patients in OA into consideration and by minimizing the influence of predisposing factors.

For *medical costs* related to OA, Hermans et al. [24] reported that the total knee-related medical costs of conservatively treated symptomatic knee OA patients with paid employment in the Netherlands were €149 (median €137, IQR €72–198) per patient per month. Visits to primary care professionals physical therapist and general practitioner were

Table 2. Characteristics of 12/28 studies reporting prevalence data for OA in the NL.

Reference	Study design and cohort name	Population	Sites of OA and classification criteria	Main prevalence results
Arslan, 2022 [17]	Prospective cohort; IPCI database	N= approximatively 2.5 millions age : ≥ 30 years % women: NA	Hip OA  Classification criteria: codified hip OA (ICPC code L89) + algorithm developed to identify patients with narratively diagnosed hip OA (see FT for more details)	Codified hip OA:  Prevalence2008: 2.07% (95% CI 2.06-2.08) 2019: 4.01% (95% CI 4.00-4.02)  Incidence 2008: 3.74 per 1,000 person-year 2019: 3.22 per 1,000 person-year  Narrative diagnosis of hip OA:  Prevalence in 2008: 1.96% (95CI 1.96-1.97) 2019: 3.33% (95% CI 3.32-3.34)  Incidence: 2008: 2.72 per 1,000-person year (95%CI 2.68-2.75) 2019: 3.86 per 1,000 person-year
Arslan, 2022[9]	Prospective cohort; IPCI database	N= approximatively 2.5 millions age: ≥ 30 years % women: NA	Knee OA  Classification criteria: codified knee OA (ICPC code L90) + algorithm developed to identify patients with narratively diagnosed knee OA (see FT for more details)	(95% Cl 3.82-3.89)  Codified knee OA  Prevalence: 2008: 2.88% (95%Cl 2.87-2.89); 2019: 6.15% (95%Cl 6.14-6.17)  Incidence: 2008: 4.88 per 1,000 person-year ; 2019:6.04 per 1,000 person-year  Narrative diagnosis of knee OA  Prevalence: 2008: 2.92% (95%Cl 2.91-2.93) 2019: 5.60% (95%Cl 5.58-5.61)  Incidence: 2008: 4.42 per 1,000 person-years (95%Cl 4.38-4.46) 2019: 6.21 per 1,000 person-year (95%Cl 6.16-6.26)
Castell, 2015 [10]	Cross-sectional: baseline data of the EPOSA study	N=483 Age (mean (SD)): 74.9 (5.6) years % women: 54.9%	Hand, Hip & knee OA Classification criteria: ACR clinical classification	6.20) Prevalence in 2011: Any sites: 26% (95% Cl 22.1-29.9) Hand OA: 11.6% (95% Cl 8.7-14.5) Hip OA: 6.9% (95% Cl 4.6-9.2) Knee OA: 18.3% (95% Cl 4.9-21.7)
Dahaghin, 2005 [16]	Cross sectional: baseline data of the Rotterdam study	N= 3,906 participants, Age (mean (SD)): 66.6 (7.3) years % women: 58.3%	Hand OA  Classification criteria: Radiographic – presence of  K-L ≥ 2 in two of three groups (distal interphalangeal, proximal interphalangeal, first carpometacarpal plus trapezioscaphoid)	Prevalence (baseline measurements of the Rotterdam study conducted between 1990 and 1993): Right hand: 21.5%, left hand 20.6%, right or left hand:
Kwok, 2011 [15]	Cross sectional: data at the 6-year follow-up of the Rotterdam study	N=3,430 participants, Age (mean): 66 years% women: 56%	Hand OA  Classification criteria: Radiographic – presence of  K-L ≥ 2 in two of three groups (distal interphalangeal, proximal interphalangeal, first carpometacarpal plus trapezioscaphoid)	28.3% Prevalence (6-year follow-up of the Rotterdam study occurred between 1996 and 1999): All: 56%
Loef, 2020 [12]	Cross-sectional: baseline data of the NEO study	N=6,643 Age (mean (SD)): 56(6) years % of women: 56%	Knee OA Classification criteria: ACR clinical classification	Prevalence (baseline data of the NEO study who recruited participants from 2008 to 2012): Overall: 15% Women: 18.3% Men: 10.4%
Picavet, 2003 [14]	Prospective cohort, DMC study	N=3,664 participants Age: 47% aged 25-44, 34.6% aged 45-64 and 18.4% aged 65 + % of women: 51%	Knee OA & Hip OA  Classification criteria: self-reported (survey)	Prevalence knee OA in 1998:  Men: 10.1%±1.5 Women: 13.6%±1.5 Prevalence hip OA in 1998: Men: 3.9±0.9% Women 9.6±1.3%

Table 2. (Continued).

Reference	Study design and cohort name	Population	Sites of OA and classification criteria	Main prevalence results
Schellevis, 1993 [18]	Cross-sectional Seven general Dutch practice (15 GPs)	N= 23,534 Age: 0-24 years: 35.6%, 25-44 years: 35.8%, 45-54: 19.3%, ≥65 years: 9.3% % of women: 51.2%	Hip & Knee OA  Classification criteria: no information provided	Prevalence hip or knee OA in 1988: <65 years: 1.7% (95%Cl 1.2-2.2) >65 years: 29.3% (95% Cl22.6-37.3)
Teunissen, 2022 [19]	Cross sectional: baseline data of the Rotterdam study	N= 7,792 % women: 56.2% Mean age (median, IQR): 65.3 (60.2- 72.5) years	Thumb OA (carpometacarpal + trapezioscaphoid) Classification criteria: Radiographic, K-L grade ≥2	Prevalence, first (1991) and second (2001) cohort were combined: Carpometacarpal: 25.3% Trapezioscaphoid: 14.5%
Van der Pas, 2013 [11]	Cross-sectional baseline data of the EPOSA study	N= 2,942 Age (mean (SD): 75.2 (5.7) years % of women: 55.2% mean	Knee, Hip & Hand OA  Classification criteria: ACR clinical classification  + self-reported	Prevalence in 2011: Clinical OA: Knee OA: 18.2% Hip OA: 6.7% Hand OA: 11.3% Hip or hand OA: 25.9% Self-reported OA: Knee OA: 26.2% Hip OA: 19.1% Hand OA: 29.4% Hip or hand OA: 48.9%
Van Saase, 1989[8]	Cross-sectional: baseline data of the Zoetermeer survey	N= 6,585 Age: > 20 years (mean age not reported) % women: 52.8%	Hand, feet, hip, knee & shoulder OA Classification criteria: radiographic (grading system for radiological OA according to the Atlas of Standard Radiographs)	Prevalence in 1978: Large number of prevalence data both for mild and severe OA of different sites, stratified by sex and by 13 different age groups <sup>a</sup> Prevalence increased with age and was highest for lumbar spine (peak: 71-9%, women 67.3%), and distal interphalangeal joints of the hands (peak: men 64-4%, women 76%)
Visser, 2014 [13]	Cross-sectional: baseline data of the NEO study	N= 6,334 Age (median and IQR): 56 (50-61) years % women: 55%	Knee & Hand OA  Classification criteria: ACR clinical classification	Prevalence (baseline data of the NEO study who recruited participants from 2008 to 2012): Knee OA: 10% (95%CI 9-11) Hand OA: 8% (95%CI 7-8) Knee & hand OA: 4% (95%CI 4-5)

Abbreviations: NA: not available; OA: osteoarthritis; ICPC: International Classification of Primary Care; GP: General Practitioner; SD: Standard Deviation; IQR: interquartile range; K-L: Kellgren and Lawrence; IPCI: The Integrated Primary Care Information database (database that contains electronic health records from Dutch general practice of approximatively 2.5 million patients)

Additional notes:

the main component of the total medical costs, with an average total costs of €62 (median €31, IQR €9–96) per patient per month. The mean total costs for secondary care (orthopedic surgeon) were €33 (median €24, IQR €24–48) per patient per month. Other medical costs included drug costs, aids and diagnostic imaging costs.

## 3.3. HRQoL burden of OA in the Netherlands

Twelve studies reporting HRQoL data for Dutch patients with OA were identified in this scoping review among [12,20,26–35] which six were cross-sectional studies [12,20,29,31,33,35], one was a prospective study [34], one was a case control study [32] and four were randomized controlled trial for which only baseline data of participants were used [26,27,29,30] (Table 4). Regarding sites of OA, four studies studied only knee OA [12,20,24,30,35]; three studies knee and hip OA [26,33,34]; one ankle OA [32]; another study studied hand OA and hand and knee OA [31] and the remaining three studies included a sample of patients suffering from OA localized in multiple sites (i.e. generalized OA) [27–29].

In most of the studies (7/12, 58.3%), the Short Form-36 (SF-36) questionnaire was used to measure HRQoL of patients [20,27,31–35]. The other tools used were the quality of life domain of the patient reported outcome measure Knee Injury and Osteoarthritis Outcome Score (KOOS) (3/12 studies [12,26,30], 25%) and the Sickness Impact Profil (SIP) Questionnaire (2/12 studies [28,29], 16.7%). Three additional studies (3/12 studies [26,30,33], 25%) used the Euroquol-5 dimension (EQ-5D) questionnaire and provided a utility score.

Half studies presented data of HRQoL only for patients suffering from OA and did not therefore provide a comparison of HRQoL between patients with OA and a control group without OA [26,27,29,30,33,34]. The other half studies presented data of HRQoL for patients with OA and compared those data to a control group, without OA [12,20,28,31,32,35]. In studies including only OA patients, sample size varied from 117 [30] to 979 participants [34]. In studies including both patients with or without OA, sample sizes varied from 191 [32] to 6,643 participants [31].

Four out of the six studies that compared a sample of patients with OA to a sample of control patients without OA highlighted a significant lower HRQoL in patients with OA [12,28,31,32], even after adjustment for age, sex and various risk factors. However,

<sup>&</sup>lt;sup>a</sup>The amount of data reported in the paper is impossible to summary. See the full-text paper for detailed prevalence data.

among those studies, Loef et al. reported no significant reduction of MCS of the SF-36 between patients with/without hand or hand&knee OA [31] based on the results of the NEO study. Two additional studies reported lower scores for patients with knee OA but did not reported the results of the statistical tests to estimate the difference between groups [20,35].

Six other studies reported HRQoL for patients with OA without any comparison with a control group [22,26,27,29,30,33,34]. Using the EQ-5D questionnaire, utility values of  $0.70\pm0.23$  in patients with knee OA [30] and of 0.71 in patients with hip and knee OA [26] were reported. A third study on hip and knee OA [33] also used the EQ-5D tool and reported values for each domain of the EQ-5D and compared them between patients with knee and hip OA. Generally, patients with hip OA reported better values in

each domain of the EQ-5D compared to patients with knee OA. Using the SF-36, a study on knee & Hip OA [34] reported PCS values of  $45.6\pm7.9$  and MCS values of  $53\pm8.6$ . In generalized OA (i.e. shoulder, elbow, hand, neck, spine, hip, knee or foot OA) Cupertus et al. [27] reported PCS values of  $37.4\pm6.9$  and MCS values of  $47.8\pm10.5$ . Authors also indicated that scores were worst for subscales including physical function, physical role limitations, bodily pain and vitality; and that highest scores were obtained for subscales of mental health and emotional role limitations. The same observation was reported by Picavet et al. [33] who also reported scores for all domains of the SF-36 for patients with knee OA and with hip OA. Generally, all SF-36 values of patients with knee OA were worse than those for patients with hip OA.

Table 3. Characteristics of the 7/28 studies reporting economic data for OA in the Netherlands

Reference	Study design and cohort references	Population	Sites of OA and Classification criteria	Economic burden	Methods to calculate costs	Mair result
Bieleman, 2013 [22]	Prospective cohort: baseline data of the CHECK study	N = 926 Age: (mean): 58 year % of women: 79%	Knee & Hip OA Classification criteria: Radiographic, K&L rating score	Work participation (present or last job, work hours, working history, present working status, sick leave, physical work demands)	2 years followers follower	rtion in rk: s. 46% sick vs. f2) tations: s. 20% elated tatus: ee
Bieleman, 2010 [21]	Prospective cohort: baseline data of the CHECK study		Knee & Hip OA Classification criteria: Radiographic, K&L rating score	work participation (present or last job, work hours, working history, present working status, sick leave)	Participation paid won OA related leave: por prevalen year prevalen 12% Work adapt 14% Predictors rework participation increasir female solower ecolevel were related to participation on work participation work participatio	rk: 519 sick sick ence 2% ence tations elated tition: ng age ex, an ducatic re to low factors factors to have

Table 3. (Continued).

	Ctudy docian				Methods	
Reference	Study design and cohort references	Population	Sites of OA and Classification criteria	Fconomic burden	to calculate costs	Main results
Reference Hardenberg, 2022 [23]	references  Cohort study: database from a large occupational health service	Population  N = 1,399  Age: 5% aged < 45, 9% aged 45–49, 15% aged 50–54, 30% aged 55–59, 36% aged 60–64, 5% aged ≥ 65  % of women: 43%	Sites of OA and Classification criteria  Knee & Hip OA  Classification criteria: CAS, with L642 for knee OA (ICD code M17) and L641 for hip OA (ICD code M16)	Absenteeism episode & costs (employer's perspective using HCA)	costs  Knee OA:  Mean sick lepisode: calendar per patii 3 years  Mean annu for the I workforc €26.9 m Hip OA: Mean sick lepisode: calendar per patii 3 years Mean sick lepisode: costs: € Mean annu for the I workforc €13.8 m Predictors re sick leav costs are particula among I workers workers wi a higher number	186 days ent over leave 5,550 al costs Dutch tee: illion leave 159 days ent over ck leave €12,482 tal costs Dutch tee: illion leave type type type type type type type typ
Hermans, 2012 [24]	Cross sectional study: baseline data of an RCT * <sup>a</sup>	N = 117 Age (mean (SD)): 53.2 (7.4) years % of women: 43%	Knee OA Classification criterias:K-L grade of 1–3 and with a minimum NRS for pain score of 2	Productivity costs and medical costs	hours Knee-relate productiv costs: €722 (medi €217, IQ 1,041) p patient   month Knee-related medical €149 (medi €137, IQ 198) per per mor Predictors ra productiv More pain activity, performi physicall intensive	ian R €0- er oper  d costs: ian R €72- patient ith elelated to vity loss: during ing



## Table 3. (Continued).

	6. 1. 1. 1				Methods	
	Study design and cohort				to calculate	Main
Reference	references	Population	Sites of OA and Classification criteria	Economic burden	costs	results
Reference Hoogeboom, 2012 [25]	references  Prospective cohort: baseline and follow-up data of the CHECK study	N = 1,002	Sites of OA and Classification criteria  Knee & Hip OA  Classification criteria: Radiographic, K&L rating score	Health care use (analgesic use, supplement use, contact with a GP, contact with a HP, contact in secondary care, and alternative medicine use)	Hip, Knee, H Knee OA (baseline analgesic us 29% and contact witt 32%, 38% 36% contact witt 26%, 18% 20% These three care use reported often at baseline. Hip, Knee, H Knee OA follow-up contact witt significar decrease supplement increasec other treatr modalitie remainec Predictors re health co analgesic us was the stronges predictor analgesic us as the stronges contact witt at T0 was stronges	dip and  TO): se: 38%, 1 47% h a GP: % and h a HP: % and e health were most  dip and (2-year o T2): h a GP ntly d t use d ment es d stable elated to are use: se at TO  t f for t use at h a HP es the
Pelle, 2019 [26]	Cross sectional study: baseline data of an RCT * <sup>b</sup>	N = 427 Age (mean (SD)): 62.1 (7.3) years % of women: 72%	Knee & Hip OA Classification criteria: self-reported (having a painful knee and/or hip, knee and/or hip pain >15 days of the past month, morning stiffness <30 min (knee) and/or <60 min (hip))	Health care use (The number of secondary health care consultations (i.e. orthopedic surgeon, rheumatologist, physician assistant))	predictor contact v a HP afte The number of secon- healthcai (i.e. orth- surgeon, rheumate or physic therapist increased OA, visite physical therapist most cor	r of with er T2 er d line re visits opedic ologist, cian d after s to

Table 3. (Continued).

Reference	Study design and cohort references	Population	Sites of OA and Classification criteria	Economic burden	Methods to calculate Main costs results
Terpstra, 2022 [20]	Cohort study: baseline data of HOSTAS study	N = 381 Age (mean (SD)): 61 (8) years % of women: 84%	Hand OA Classification criteria: ACR clinical criteria, K&L rating score	Work participation (unpaid and paid work restrictions, unpaid work replacement by others, inefficiency and absence during paid work) Productivity costs	Work participation: Replacement of unpaid work: 171 out of 381 patients (45%) Paid work absenteeism: 13 out of 181 (7%) Paid work unproductive hours: 28 out of 181 (15%) paid work restrictions: 120 out of 181 (66%) Productivity costs: €94 (95% CI 59 to 130) per 2 weeks (€2452, 95% CI 1528 to 3377 per year)

Abbreviations: OA osteoarthritis; SD standard deviation; CI confidence interval; ACR American College of Rheumatology; K&L Kellgren-Lawrence. System; HCA Human Capital Approach; RCT random controlled trial; GP general practitioner; HP health professional. Additional notes: <sup>a</sup> RCT investigating the cost-effectiveness of intraarticular hyaluronic acid in addition to usual care, registered at the Dutch trial register. <sup>b</sup>RCT examining the effectiveness of the dr. Bart app on the number of self-reported consultations in secondary health care over half a year.

c Dr. Bart app is a standalone eHealth application developed to enhance self-management and to actively involve people with OA in managing their own disease.

## 4. Discussion

As essential for policy-making on resource allocation, this scoping review mapped the evidence on the prevalence or incidence of osteoarthritis in the Netherlands, the economic burden of osteoarthritis in the Netherlands, and the impact of osteoarthritis on the health-related quality of life of Dutch people affected by this disease. This scoping review allowed us to identify seven population-based cohort studies developed in the Netherlands. The development of such cohorts of individuals seems essential to understand a disease, to assess its association with risk factors or consequences, and thus to define the individual or societal burden of a disease.



**What is known:** OA is associated with restrictions in work participation and substantial health care consumption, translating into costs of the lost productivity and healthcare costs. Increasing age and lower education level were related to lower work participation, higher productivity loss and higher health care consumption.



What are the weaknesses of knowledge: Domains of work participation (work disability, sick leave, presenteeism) and the categories of health care services/uses were defined/selected differently in different studies, making the comparison between those studies difficult.



What is not known: There is a general lack of studies on direct and types (including generalized OA) and specifically a lack of studies comparing work restrictions, resource utilization and associated costs to the general population. Studies reporting costs of unpaid work (e.g. household work and informal care) are also missing. Although not all cohorts included a representative sample of the population, they have provided data on the prevalence of OA and confirmed that OA is a chronic, prevalent disease that continues to impose a significant burden on patients and health care systems.

## 4.1. Prevalence of OA in the Netherlands

Based on the data from the population-based cohort studies, a prevalence of knee OA ranging from 6% to 18%, a prevalence of hip OA ranging from 4% to 7% and a prevalence of hand OA ranging between 12% and 56% was reported. The high prevalence of hand OA is probably biased by the sample of studies reporting hand OA, as all of these studies included older individuals and none of them was based on a representative sample of the population. This prevalence should therefore be interpreted with caution. In addition to the 12 studies included in this scoping review, the 2019 Global Burden of the Disease (GBD) study [1] provides comprehensive and systematic assessments of age- and sexspecific incidence, prevalence, mortality, life-years lost, lifeyears lived with disability, and disability-adjusted life-years (DALYs) for 369 diseases, including osteoarthritis, in 204 countries and territories from 1990 to 2019. Because the 2019 GBD study is not a population cohort performed in the Netherlands, it was not identified by our search strategy. Nevertheless, this study provides prevalence data as it integrated all available data, including published data, gray literature data, survey data, and hospital and clinical data. Using



data from the 2019 GBD study [1], the age-standardized prevalence rate of osteoarthritis in the Netherlands was 4.16% in 1990, compared with 4.38% in 2019, representing a change in absolute numbers of 66.67% and an estimated annual percentage change of 5% [36]. Higher changes in absolute number between 1990 and 2019 were highlighted for knee OA



What is known: The burden of OA in terms of HRQoL and value for health (utility) are supported by a large number of studies published in Dutch populations.



What are the weaknesses of knowledge: Heterogeneity in the scales used to measure HRQoL prevents a clear quantitative synthesis (e.g. meta-analysis) of the data. Data on value/preference for health (utility) was scare and. no data are available on utility loss compared to the general population. Only one longitudinal study was identified, all others were cross-sectional studies, which limits the causal relationships that can be drawn between HRQoL and OA.



What is not known: This scoping review did not identify studies reporting QALY or DALY across the lifetime of patients with OA with different type not generalized OA in the NL. The Dutch Healthcare Institute recommends the use of QALY in cost-effectiveness analyses. Only one study used a subdomain of a specific PROM instrument to estimate HROoL and no studies used a disease specific HRQoL. Studies providing comparison of HRQoL of OA patients with normative values of health population are also missina.

(+72.01%) and hip OA (+74.15%) compared to hand OA (+54.1%) [36]. Regarding annual incidence of OA, the GBP indicated an incidence of 9.15% in 2019 (ranging from 0% in population younger than 30 years to 11.9% for population aged 70 to 74 years) [37].

In addition to the scientific literature, the Netherlands Institute for Health Services Research (NIHSR) also provides prevalence and incidence data based on registered data from hundreds of primary care providers throughout the country. Assuming that people with ailments and conditions would eventually visit their general practitioner and/or other primary care providers, this institute hypothesized that the figures recorded by these general practitioners would provide an adequate picture of health in the Netherlands. According to this Institute, the prevalence of knee OA in 2021 in the Netherlands is of 4.35% (https:// www.nivel.nl/nl/nivel-zorgregistraties-eerste-lijn/cijfers-overaandoeningen/jaarcijfers-aandoeningen-

huisartsenregistraties). This prevalence is higher in women compared to men (i.e. 5.44% vs.3.25%). The annual incidence for 1000 persons is of 2.5 (men 1.9; women 3.1). Numbers reported by this Institute for hip OA are lower with a total prevalence of 2.77% (men 2.05%, women 3.48%) and a total annual incidence for 1000 persons of

Table 4. Characteristics of 12/28 studies reporting HRQoL data for OA in the Netherlands.

Reference	Study design and cohort references	Population	Sites of OA and Classification criteria	Tool used for HRQoL	Main results
Cuperus, 2015 [27]	Cross-sectional Baseline data from a RCT <sup>*a</sup>	N = 147 (all with OA)Age (mean): 60 years% of women: 85% Age (mean): 60 years % of women: 85%	Generalized OA Classification criteria: objective signs of OA in at least two joints + clinical symptoms in ≥ 3 out of 8 joint area	SF-36 (range 0–100)	Component scores (mean (SD)): SF-36 PCS: 37.4 (6.9) SF-36 MCS: 47.8 (10.5) Subdomains: Lowest (i.e. worse)scores obtained for Physical function: 37.4 (7.7); Physical role limitations: 39.0 (8.3); Bodily pain: 40.0 (6.6) and; Vitality: 40.3 (5.5) Highest (i.e. best) scores obtained for the subscales mental health: 47.7 (8.6) and emotional role limitations: 45.4 (12.0)
De Bock, 1996 [29]	Cross-sectional Baseline data from a RCT <sup>*b</sup>	<ul> <li>N = 198 patients (all with OA)Age (aggregate mean of two groups): 66.5 years% of women: 83.8%</li> <li>Age (aggregate mean of two groups): 66.5 years</li> <li>% of women: 83.8%</li> </ul>	Peripheral OA: knee, hip, hand & wrist, elbow, feet & ankle Classification criteria: ICHPPC-02 criteria	Sickness Impact Profile (range 0– 23)	Total score (aggregate mean of two groups): 9.67 Physical dimension (aggregate mean of two groups): 9.04 Psychological dimension (aggregate mean of two groups): 6.81
De Bock, 1996 [28]	Cross-sectional Patients recruited from Dutch general practitioners records	N = 575 (195 with OA, 380 controls without OA)Age (mean (SD)): NA % of women: NA Age (mean (SD)): NA % of women: NA	All OA Classification criteria: ICHPPC- 02 criteria	Sickness Impact Profile (range 0– 23)	Age group 41–60 years (mean (SD)): OA = 7.04 (7.06); no OA = 3.7 (5.04), $p < 0.01$ Age group 61–75 years (mean (SD)): OA = 8.6 (6.52); no OA = 5.0 (6.89), $p < 0.01$ Age group >75 years (mean (SD)): OA = 14.4 (10.29); no OA = 8.9 (8.45), $p < 0.01$
Hermans, 2012[24]	Cross-sectional Baseline data from a RCT <sup>*c</sup>	N = 117 (all with OA)Age (mean (SD): 53.2 (7.4) years% of women: 53% Age (mean (SD): 53.2 (7.4) years % of women: 53%	Knee OA Classification criteria: K-L grade of 1–3 + numeric rating scale for pain score of 2	EQ5D (range 0-1) KOOS QoL subscale (range 0- 100)	EQSD(mean (SD)): 0.70(0.23) Koos QoL subscale(mean (SD)): 33.3(18.6)



Table 4. (Continued).

Reference	Study design and cohort references	Population	Sites of OA and Classification criteria	Tool used for HRQoL	Main results
Loef, 2019 [31]	Cross-sectional baseline data of the NEO study and the HOSTAS study	NEON = 6,334 (8% with hand OA, 4% with hand/knee OA, 78% of controls without OA)Age (mean): 56 years% of women: 55% HOSTASN = 538 (all with OA)Age (mean): 61 years% of women: 86% N = 6,334 (8% with hand OA, 4% with hand/knee OA, 78% of controls without OA) Age (mean): 56 years % of women: 55% HOSTAS N = 538 (all with OA) Age (mean): 61 years % of women: 86%	Hand OA + hand & knee OA Classification criteria: ACR clinical criteria	SF-36 (range 0–100)	NEO study:  Component scores (mean (SD)): PCS: No hand/knee OA = 55.1(7.6) Hand OA = 52(8.7); Hand/knee OA = 45.9(9.7)  (p < 0.05 compared to controls MCS: No hand/knee OA = 51.1  (8.8); Hand OA = 51.3 (8.9); Hand/knee OA = 51.7 (9.4) (p > 0.05 compared to controls) Subdomains: Significant reduced HRQoL score for hand OA compared to controls for subdomains GH, BF, and PP; significant reduced Qol scores for hand/knee OA compared to controls for subdomains GH, BP, VT, PP and RF. No significant reduction for the other domains. HOSTAS cohort: Component scores (mean (SD)): PCS: Hand OA = 46.5(8.1); hand/knee OA = 42.1(7.7) MCS: Hand OA = 45.1(7.7), hand/knee OA = 46.5(6.6) BP: Hand OA = 45.1(7.7), hand/knee OA = 42.6(6.7) VT: Hand OA = 47.5(8.8), hand/knee OA = 44.6(6.7) VT: Hand OA = 47.8(8.8), hand/knee OA = 43.3(9.2) RFP: Hand OA = 47.8(10.2), hand/knee OA = 44.5(10.4) MH: Hand OA = 51.1(9.1), hand/knee OA = 49.4(8.3) SF: Hand OA = 51.1(9.5), hand/knee OA = 47.1 (9.5) RFE: Hand OA = 51.1(9.5), hand/
Loef, 2020 [12]	Cross-sectional baseline data of the NEO study	N = 6,643 (15% with OA)Age (mean): 56 years% of women: 56% Age (mean): 56 years % of women: 56%	Knee OA Classification criteria: ACR clinical criteria	KOOS QoL subscale (range 0– 100)	knee OA = 49.6(10.3)  Clinical knee OA associated with highest odds of worse KOOS scores in all subscales. Largest ORs found for the subscale pair in men 13.79 (9.61; 19.79) and for the subscale QOL in womer
Paget, 2021 [32]	Case-control sub- study of the PRIMA trial (efficacy of platelet-rich plasma injections for ankle OA)	N = 191 (100 with OA and 91 controls without OA)Age (mean): 56 years% women: 39.8% Age (mean): 56 years % women: 39.8%	Ankle OA Classification criteria: severity of ankle OA pain on a VAS ≥40 mm during daily activities + X-rays with ≥grade 2 talocrural OA on the van Dijk classification.	SF-36 (range 0–100)	9.45 (7.06; 12.65).  Component scores (median (IQR)): PCS: Ankle OA = 45 (40–50) No OA = 52 (44–55), p = 0.003 MCS: Ankle OA = 43 (39–47) No OA = 53 (47–56), p < 0.001
Pelle, 2019 [26]	Cross sectional baseline data of an RCT * <sup>d</sup>	N = 427 (all with OA)Age (mean): 62.1 years% of women: 71.7% Age (mean): 62.1 years % of women: 71.7%	Knee & Hip OA Classification criteria: self-reported OA	EQ5D-3 L (range 0–1) + KOOS quality of life subscale (range 0– 100)	EQ-5D (aggregate mean of two groups): 0.71 Koos QoL: 38.1

## Table 4. (Continued).

Reference	Study design and cohort references	Population	Sites of OA and Classification criteria	Tool used for HRQoL	Main results
Picavet, 2004 [33]	Cross sectional baseline data of the DMC <sub>3</sub> study	N=3,664 (14.9% with knee OA and 9.66% with hip OA)Age: 47% aged 25-44, 34.6% aged 45-64 and 18.4% aged 65+% of women: 51% Age: 47% aged 25-44, 34.6% aged 45-64 and 18.4% aged 65+% of women: 51%		SF-36 (range 0–100) and EQ5D (range 0–1)	Knee OA (mean (SD)):  SF-36 PF: 67.6(1)  SF-36 RP 61(1.9)  SF-36 BP: 62.7(1.1)  SF-36 GH: 60.1(1)  SF-36 SF: 75.7(1.1)  SF-36 SF: 75.7(1.1)  SF-36 RE: 80.4(1.6)  SF-36 MH: 72(0.9)  EQ5D (Percentage with problem in each domains (standard error)):  EQ5D Mobility: 44.1(1.7)  EQ5D Sefl care: 10 (1.0)  EQ5D Usual activities: 40.9(2)  EQ5D Pain/discomfort: 71.1  (2.5)  EQ5D Anxiety/depression: 28.3  (1.9)  Hip OA (mean (SD)):  SF-36 PF: 62.4(1.4)  SF-36 RP: 52.8(2.5)  SF-36 BP: 59.1(1.5)  SF-36 SF: 73.2(1.5)  SF-36 SE: 80.5(2.1)  SF-36 MH: 73.5(1.2)  EQ5D Mobility: 56.3(2.3)  EQ5D Sefl care: 14.8 (1.3)  EQ5D Usual activities: 51.9(2.7)  EQ5D pain/discomfort: 76.6(3.2)  EQ5D pain/discomfort: 76.6(3.2)  EQ5D pain/discomfort: 76.6(3.2)  EQ5D Dain/discomfort: 76.6(3.2)
Terpstra, 2021[20]	Cross-sectional baseline data of the NEO study	N = 6,212 (14% with knee OA)Age (mean) : 56 years% women: 55% Age (mean) : 56 years % women: 55%	Knee OA Classification criteria: ACR clinical criteria	SF-36 (range 0–100)	(2.6)  Component scores (mean (SD)):  PCS: Knee OA = 47.7(9.5)  No knee OA = 54.8(7.8)  MCS: Knee OA = 51.6(9.6)  No knee OA: 51.1(8.8)  Statistical difference between
Visser, 2015 [35]	Cross-sectional baseline data of the study NEO study	N = 1,262 (16% with knee OA)Age (mean) : 56 years% women: 56% Age (mean) : 56 years % women: 56%	Knee OA Classification criteria: ACR clinical criteria	SF-36 (range 0–100)	groups NA  Component scores (mean (SD)): PCS: Knee OA = 46.9(9.5) No knee OA = 54.2(7.9) MCS: Knee OA = 51.2(9.9) No knee OA = 51.5(8.5) Statistical difference between groups NA
Wesseling, 2013 [34]	Prospective 10-year CHECK cohort study	<ul> <li>N = 979 (all with OA)Age (mean):</li> <li>56 years% women = 79% of women</li> <li>Age (mean): 56 years</li> <li>women = 79% of women</li> </ul>	Knee & Hip OA Classification criterias: pain or stiffness of the knee or hip. Severity of OA scored according to K-L.	SF-36 (range 0–100)	Component scores (mean (SD)): PCS: 45.6 (7.9) MCS: 53 (8.6)

Abbreviations: NA: not available; OA: osteoarthritis; RCT: randomized controlled trial; GP: General Practitioner; SD: Standard Deviation; IQR: interquartile range; ACR: American College of Rheumatology; QoL: quality of life; K-L: Kellgren and Lawrence.

Cohorts descriptions: NEO: The Netherlands Epidemiology of Obesity study is a population-based prospective cohort study with an oversampling of persons with

overweight or obesity; HOSTAS study: the Dutch population based Musculoskeletal Complaints and Consequences cohort study (DMC) is composed with a random sample of 8000 people aged ≥25 years taken from the population register of 1998, identical to the general surveys of Statistics Netherlands: the CHECK study: Dutch prospective 10-year follow-up study initiated to study progression of OA in participants with early symptomatic OA of knee or hip. Additional notes..

<sup>&</sup>lt;sup>a</sup>RCT comparing the effectiveness of two multidisciplinary non-pharmacological treatment programs for patients with generalized OA.

<sup>&</sup>lt;sup>b</sup>RCT comparing Nabumetone 1000 mg 2dd versus Piroxicam 20 mg 1dd in persons with symptomatic OA.

cRCT investigating the cost-effectiveness of intraarticular hyaluronic acid in addition to usual care.

d RCT comparing the short-term effects of the dr. Bart app compared to usual care.

1.6 (men 1.3, women 2.0). It is relevant to highlight, once again, that Arslan et al. [9,17] have demonstrated that prevalence data obtained from routine primary care data may be underestimated. As reliable estimates are needed for health policy maker to respond to the increasing demand for health care relating to OA, Arslan et al. [9,17] shown that the addition of narrative data could provide a more realistic picture of the current burden of OA. Nevertheless, the use of such data may be challenging due to data protection and to the fact that coding systems may differ between countries.

Compared to worldwide data on overall prevalence of OA (i.e. estimated at 3.8% for knee OA and 0.85% for hip OA) [1], prevalence in the Dutch population seems a bit higher. Prevalence data obtained from population-based cohorts included in this scoping review were also a bit superior than prevalence data obtained from the NIHRS. The reason is that most of the cohort studies identified by our scoping review included adults population, children being excluded from the figures.

## 4.2. Economic burden of OA in the Netherlands

OA, as the 15th highest cause of years lived with disability worldwide, is no doubt associated with substantial costs (consisting of direct medical costs and indirect productivity costs) due to the health care consumption and restrictions in work participation such as sick leave (absenteeism) and sickness/ productivity loss while at work (presenteeism). The impact of OA on work force participation can be reflected in various aspects from requiring more assistance at paid work to withdrawal from the work force, the heterogeneity was also identified in our review, making it difficult to quantify the general work participation loss in the Netherlands.

OA is nevertheless a costly disease in economic terms because of its far higher prevalence given two main factors: aging and obesity. Approximately one-third of direct OA expenditures are allocated for medications, much of which goes toward pain-related agents [38]; hospitalization and surgery costs account for the largest part of direct costs. Besides scientific literature identified in this scoping review, vzinfo.nl reported data estimated by the Dutch National Institute for Public Health and the Environment [39]. They estimated the direct medical costs for OA in the Netherlands in 2019 at €1.1 billion (€495 million and €446 million for knee and hip OA, respectively). Most of the expenditures relates to hospital care. This corresponds to 19.3% of the costs for musculoskeletal diseases, and 1.1% of the total annual health care costs. Compared to other chronic diseases, OA is associated with greater indirect costs (productivity costs) which is largely attributable to the effects of disability and related restrictions in work participation. This is confirmed by the study of Hermans et al. [24] as productivity costs accounted for 83% of the total knee-related costs of conservatively treated symptomatic knee OA patients with paid employment in the Netherlands. In addition, it was indicated that performing physically intensive

work were significantly associated with more productivity loss and higher productivity costs. However, we found welldocumented information on direct and indirect OA-related costs in the Netherlands are largely scarce, the lack of evidence on indirect costs possibly prevails because no reliable national registries for sick leave and absenteeism data, more information are expected to be provided by future studies.

## 4.3. Burden of OA in health-related quality of life

OA is associated with significant physical disabilities and psychological disorders like depression, anxiety or sleep disturbance [1,40,41]. It is therefore not surprising to observe a negative impact of OA on HRQOL, as highlighted by a recent systematic literature review and meta-analysis [42]. A previously published meta-analysis of 6 studies [42] (7094 patients with any OA, 12100 healthy controls) using the SF-36 questionnaire to measure HRQoL revealed a significantly impaired state in each dimension of HRQoL for OA patients in comparison to the general population. Authors of this meta-analysis also showed that physical health is more likely to be affected by OA than mental health (mean difference (MD) between patients with OA and healthy controls of -31.24% (95%CI -43.49;-18.99) for physical function vs MD of -12.55% (95%CI -18.1;-7.00) for mental health) [42]. Due to strict inclusion criteria used by authors (i.e. restriction to cross-sectional studies, to studies provided results of the 8 domains of the SF-36, to studies reporting results as mean ± SD, etc.), none of the 6 studies comparing a group of patients with OA to a healthy controls group identified through our scoping review, was included in the MA of Yan et al. [42]. Nevertheless, results from those 6 studies seems concordant to those provided by Yan et al. [42], with a significant reduction in HRQoL of patients suffering from OA, mainly for the physical component score of the SF-36. Another interesting point to discuss is the fact that none of the studies included in our scoping review directly reported quality-adjusted life years (QALYs) for OA patients, which is one of the HRQoL indicator expressed as an unique measure of utility assigned to different health states [43]. Only two studies [26,30] from our scoping review provided a global utility score from the EQ-5D questionnaire for patients with OA (respectively 0.70 and 0.71) but the cross-sectional design of the study does not allow the computation of cumulative QALYs over time. In the US, Losina et al. [44] estimated a mean losses of 1.71 QALYs per person with OA. A gap of evidence in the estimation of QALYs for Dutch people suffering from OA from Dutch cohort studies is therefore identified. This observation is also valid for disability-adjusted life year (DALYs), a time-based measure that combines years of life lost due to premature mortality. The 2019 data reported by the GBD study highlighted a worldwide DALYs of hip osteoarthritis of 1.04 million and an age-standardized DALY rate of 12.57 per 100,000 person. The higher DALYs of hip OA were observed in the U.S.A., China and India. Data for the Netherlands were above the Mondial mean (i.e. 7,428 DALYs; age-standardized DALYs rate of 23,44 per 100,000 persons). Since we did not identify population cohorts in the Netherlands reporting DALYs, the comparison with the GBD study is therefore not possible. Finally, we observed that most of studies performed in the Netherlands used a generic HRQoL questionnaire (such as the SF-36, the EQ5D or the KOOS tool), partly due to the fact that the Dutch Healthcare Institute recommends the use of QALY in cost-effectiveness analyses. By definition, a specific HRQoL questionnaire is specific to a disease, more able to detect subtle effect of the disease on the HRQoL and therefore more sensitive to change. Further studies using specific instruments to measure HRQoL in Dutch patients suffering from OA may complement the available evidence. Policymakers can play a pivotal role in promoting the adoption of standardized tools, facilitating more robust and consistent assessments of quality of life in knee osteoarthritis. Addressing these research gaps and considering the implications for policymakers will not only enhance our understanding of the disease burden but also contribute to more informed decision-making, ultimately improving the quality of care and outcomes for patients with knee osteoarthritis.

## 4.4. Strength and limitations

This is the first time that an exhaustive synthesis of the burden of osteoarthritis at the Netherlands national level is conducted. Even though summaries of international data are worthwhile to be informed on the worldwide burden of OA, health-care decisions and resource allocation are usually made at a national level. Therefore, providing countryspecific data concerning prevalence, costs and HRQoL of patients suffering from OA is important for national decision-making.

Although we carefully followed the PRISMA-ScR statement, there are some limitations to this work that should be taken into account. First, we only investigated two different bibliographic databases. Even if we supplemented our search with a manual search to identify the maximal available evidence, we may have missed some studies providing burden data of OA in the Dutch population. Second, data extraction was performed by only one researcher. Although a second reviewer carefully checked all data extracted, we could be prone to bias in collection of data. Third, we did not measure the quality of all individual studies involved in this scoping review. The large heterogeneity of included study designs prevent us to appraise the quality of included studies using a standardized tool. Nevertheless, quality appraisal of individual studies included in a scoping review is not mandatory, and therefore this methodological weakness of our work is limited. Four, we chosen not to include papers that reported costs data related to surgery. By excluding these studies, we might have overlooked valuable insights into the economic burden of knee osteoarthritis and the cost-effectiveness of surgical interventions. Surgical treatments, including joint replacement, are important aspects of disease management and can significantly impact healthcare resource allocation. Due to the specific focus of our scoping review on prevalence, incidence, and health-related quality of life, we made a strategic decision to exclude studies that primarily examined surgical costs. Although this decision limits the scope of our review, it allows us to concentrate on the broader burden of osteoarthritis and its impact on population Future research could consider conducting a separate review specifically focusing on the economic aspects of surgical interventions for osteoarthritis in the Netherlands.

## 5. Conclusion

The findings of this scoping review may have important implications for national health policy decision-making and resource allocation in the Netherlands. The prevalence and economic burden of osteoarthritis revealed in this study highlight the significant impact of this disease on individuals and the healthcare system. The high prevalence rates, particularly for knee and hip osteoarthritis, underscore the need for targeted interventions and allocation of resources to address the growing burden. These findings can inform policymakers in developing strategies that focus on prevention, early diagnosis, and effective management of osteoarthritis. Additionally, the negative impact of osteoarthritis on health-related quality of life emphasizes the importance of integrating patientcentered outcomes in policy discussions. By considering the physical disabilities, psychological disorders, and diminished quality of life associated with osteoarthritis, policymakers can prioritize interventions that aim to improve patients' overall well-being. Ultimately, these insights can contribute to the development of comprehensive and evidence-based policies that address the burden of osteoarthritis and promote better health outcomes for individuals in the Netherlands.

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## **Declaration of interest**

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

## **Authors contribution**

C Beaudart, M Hiligsmann and A Boonen conceived the study and developed the search question. Protocol was developed by C Beaudart and reviewed by M Hiligsmann and A Boonen. Once the protocol was approved, C Beaudart ran the search strategy. Study selection and data



extraction were done by C Beaudart and N Li. First draft of the manuscript was written by C Beaudart. All authors read and approved the final draft.

## Availability of data

All data are available upon request.

## **Reviewer disclosures**

Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

## Registration

A protocol was developed and published in Open Science Framework (https://osf.io/vgx4n/).

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## **Appendix 1**

## Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-Scr CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3
Objectives  4 Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g. population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.			3
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g. a Web address); and if available, provide registration information, including the registration number.	3
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g. years considered, language, and publication status), and provide a rationale.	4
Information sources*	7	Describe all information sources in the search (e.g. databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	3–4
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	Appendix
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e. screening and eligibility) included in the scoping review.	4
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g. calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	4
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	NA
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	4
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	4–5
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	5
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	NA
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Click here to enter text.
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	5–11
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	11
Limitations	20	Discuss the limitations of the scoping review process.	15



#### (Continued).

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	15–16
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	Title page

JBI = Joanna Briggs Institute: PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews. Where sources of evidence (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.

- \*.A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g. quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with information sources (see first footnote).
- †.The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.
- ‡.The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of 'risk of bias' (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g. quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colguhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467-473. doi: 10.7326/M18-0850.

## **Appendix 2**

Search Strategy:Ovid MEDLINE(R) - September 2022

- (1) exp Osteoarthritis/
- (2) osteoarth×.ti,ab,kf.
- (3) degenerative arthritix.ti,ab,kf.
- (4) (arthroses or arthrosis).ti,ab,kf.
- (5) or/1-4
- (6) 'costs and cost analysis'/or 'cost of illness'/or 'global burden of disease'/or exp health care costs/or Cost-Benefit Analysis/or Health Expenditures/or Economics, Medical/or Economics, Pharmaceutical/
- (7) (cost or costs or costing or costly or expenditure or resource\* or economic\* or economy or pharmacoeconomic\* or informal care or labor impact\* or sick leave).ti,ab,kf.
- (8) Absenteeism/
- (9) 'Quality of Life'/
- (10) (quality adj2 life).ti,ab,kf.
- (11) (utilities or utility or ICER or eq-5d or HRQoL or SF-36 or 'eurogol 5-dimension' or gol).ti,ab,kf.
- (12) incidence/or prevalence/
- (13) burden.ti,ab,kf.
- (14) or/6-13
- (15) Netherlands/
- (16) netherlands.mp.
- (17) holland.mp.
- (18) dutch.mp.
- (19) or/15-18
- (20) 20 5 and 14 and 19

## Search Strategy:EMBASE - September 2022

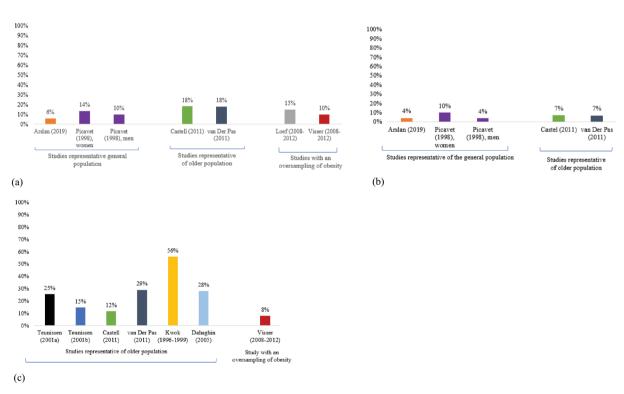
- #25. #22 AND #23 AND #24
- #24. #20 OR #21
- #23. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
- #22. #1 OR #2 OR #3 OR #4 OR #5
- #21. netherlands:ab,kw,ti OR holland:ab,kw,ti OR dutch:ab,kw,ti
- #20, 'netherlands'/de
- #19. prevalence:ab,kw,ti OR incidence:ab,kw,ti OR burden:ab,kw,ti
- #18. 'incidence'/de
- #17. 'prevalence'/de
- #16. (quality NEAR/2 life):ab,kw,ti
- #15. utilities:ab,kw,ti OR utility:ab,kw,ti OR icer:ab,kw,ti OR 'eq 5d':ab,kw,ti OR hrgol:ab,kw,ti OR 'sf 36':ab,kw,ti OR 'eurogol 5-dimension':ab,kw,ti OR galy:ab,kw,ti OR galys:ab,kw,ti OR gol:ab,kw,ti
  - #14. 'quality of life'/de



#13. (((cost:ab,kw,ti OR costs:ab,kw,ti OR costing:ab,kw,ti OR costly:ab,kw,ti OR expenditure:ab,kw,ti OR resource\*:ab,kw,ti OR economic\*:ab,kw,ti OR economic\*:ab,kw,ti OR economic\*:ab,kw,ti OR labour:ab,kw,ti OR labour:ab,kw,ti OR burden:ab,kw,ti OR absenteeism:ab,kw,ti OR productivity:ab,kw,ti OR labour:ab,kw,ti OR burden:ab,kw,ti OR absenteeism:ab,kw,ti OR productivity:ab,kw,ti

- #12. 'cost effectiveness analysis'/de
- #11. 'pharmacoeconomics'/de
- #10. 'cost effectiveness analysis'/de
- #9. 'expenditures'/de
- #8. 'absenteeism'/de
- #7. 'disease burden'/de
- #6. 'cost'/de
- #5. arthrosis:ab,kw,ti
- #4. arthroses:ab,kw,ti
- #3. (degenerative NEAR/1 arthritis):ab,kw,ti
- #2. osteoarthr\*:ab,kw,ti
- #1. 'osteoarthritis'/de

Appendix 3. Prevalence of knee OA (A), hip OA (B) and hand OA (C) reported in scientific studies (classified by year of reported data on prevalence)



Teunissen (a)=Carpometacarpal OA; Teunissen (b)=Trapezioscaphoid OA.

Because of the way data were provided in the Study of van Saase (1978), it was impossible to synthetise them within those graphs. Data from this study were therefore not used.