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Health resource use and costs of symptomatic knee

and/or hip osteoarthritis

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29 **Abstract**

30

31 **Background:** Data on the economic consequences of hip and knee osteoarthritis (OA) are
32 scarce. We aimed to estimate the annual direct and indirect costs for patients followed for hip
33 and/or knee OA in the KHOALA cohort.

34 **Methods:** The KHOALA cohort, set up from 2007 to 2009, is a French multicenter study of
35 878 individuals with symptomatic knee/hip OA who were 40 to 75 years old. Resources used
36 were collected annually for 5 years. Costs were assigned by using official sources and
37 expressed in 2018 euros per patient.

38 **Results:** The mean annual total costs per patient over the 5-year study period were $2,180 \pm$
39 $5,305\text{€}$. The mean annual direct medical costs per patient were $2,120 \pm 5,275\text{€}$ and mean
40 annual indirect costs per patient $180 \pm 1,735\text{€}$ for people of working age. Costs increased
41 slightly over the study period. Drugs were the largest cost share, representing over 50% of all
42 direct costs. However, the proportion attributable to OA drugs accounted for only 10.5% of
43 drug costs. The second cost share was hospitalizations; hip and knee prosthetic surgery
44 accounted for 27% of surgery hospitalization costs. Health professional visits were the third
45 cost share, accounting for 3% of direct medical costs. The median costs induced could be as
46 high as 2 billion €/year (IQR 0.7–4.3) in France.

47 **Conclusion:** Hip and knee OA costs were substantial and increased over the study period in
48 France. However, the costs attributable to OA represented only a small fraction of overall
49 costs

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52 **Word count: 245**

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56 ***Introduction***

57 Osteoarthritis (OA) is one of the most frequent musculoskeletal diseases, often resulting in
58 severe functional disability (1). The prevalence of symptomatic knee and hip OA ranges from
59 10% to 20% depending on the population studied and the methods used to elicit these
60 estimates (2). The prevalence of radiographically knee OA in 2010 was estimated to be 3.8%
61 (3). The age-standardised prevalence of radiographically hip OA in 2010 was 0.85% (3). In
62 the United States, the annual incidence of symptomatic knee OA is estimated at 17% and
63 symptomatic hip OA 10% (4,5). In Europe, the prevalence of radiological hip and knee
64 symptomatic OA in people 40 to 75 years old was estimated at 1.9% and 4.7%, respectively,
65 for men and 2.5% and 6.6% for women (2). The overall ageing of the population as well as
66 the increasing prevalence of obesity will be associated with an increased prevalence of lower-
67 limb OA and its functional consequences on affected patients, for an impending public health
68 issue in society (6).

69 The mean total costs associated with knee and/or hip OA range from €500 to €10,900 per year
70 (5). There is a substantial heterogeneity in the methods used to assess the costs of OA (7).
71 Depending on the population studied (community or hospital recruitments, patient profiles,
72 socioeconomic status) and mode of diagnosis (symptomatic vs radiographic OA), OA cost
73 estimates were reported with a multiplication factor between the lowest and highest estimates
74 of 22 for hip and knee OA and even 65 for all-site OA (7). For more accurate estimates from
75 an epidemiologic and public health perspective, we need to assess health resource use in a
76 representative and large population sample with extended follow-up.

77 The Knee and Hip Osteoarthritis Long term Assessment (KHOALA) cohort is a French
78 multicenter, population-based prospective cohort of prevalent cases of symptomatic hip and
79 knee OA; it was the continuation of a population-based survey aiming to estimate the
80 prevalence of hip and knee OA independent of access to care by patients (2,8). Patients were

81 included between 2007 and 2009, then followed regularly to collect information on general
82 and joint health as well as health resource use (2,8).

83 Here we aimed to estimate the annual direct and indirect OA costs incurred by patients in the
84 KHOALA cohort over 5 years to describe their distribution in terms of cost components.

85

86 **Participants and Methods**

87 **Participants**

88 Individuals who were 40 to 75 years old and had uni- or bilateral symptomatic hip and/or
89 knee OA (American College of Rheumatology [ACR] criteria (9,10)) with Kellgren and
90 Lawrence (KL) stage ≥ 2 (11) were recruited from a French national prevalence survey for the
91 multicenter KHOALA cohort study (2). The cohort and its methodology for data collection
92 were previously described (2,8). Individuals were recruited from two-stage population-based
93 national prevalence survey conducted in France from April 2007 to March 2009 (2). Patients
94 have been recruited through a population-based poll aiming to assess knee and/or hip OA
95 prevalence, independently of any visit to a physician. Briefly, the survey involved a random
96 sample of households in six French regions obtained by random digit phone dialing and the
97 next-birthday method in each household. OA diagnosis was confirmed by a rheumatologist.
98 All people with OA identified were invited to participate in the 10-year KHOALA cohort
99 prospective study. Inclusion criteria were both sexes; age 40 to 75 years; uni- or bilateral
100 symptomatic hip and/or knee OA; clinical diagnosis confirmed and fulfilling ACR criteria for
101 knee (10) and hip OA (9); and KL stage ≥ 2 on standard X-rays (11). Individuals were
102 excluded if they had prosthesis for the symptomatic joint, previous osteotomy, severe
103 comorbidity leading to significant deterioration of functional abilities and quality of life or
104 major healthcare consumption, isolated patello-femoral OA, or other joint disease. The cohort
105 study was approved by the Medical Ethics Committee CPP Est III and was registered at

106 ClinicalTrials.gov (NCT00481338). All participants gave their written informed consent
107 before inclusion in the study.

108

109 **Health resource use data**

110 This study is an analysis of data for the first 5-year cohort (2008-2012). Data were collected
111 by use of a validated self-reported questionnaire including consultations with physicians
112 (general practitioners, rheumatologists, orthopedic surgeons and other specialists) and other
113 health professionals (physiotherapists, nurses, occupational therapists, podiatrists, dentists,
114 speech therapists and alternative medicine practitioners), drug use, imaging [radiography (X-
115 ray), CT scan, MRI, bone densitometry, scintigraphy and other work-ups], hospitalizations,
116 biological investigations [i.e. 25-(OH) D3 levels, serum creatinin, parathormone, sensitive C-
117 reactive protein, erythrocyte sedimentation rate, leucocyte count, platelet count, hemoglobin
118 concentrations, albumin and coagulation parameter], technical aids and transportation. This
119 method had previously demonstrated good agreement with administrative data in people with
120 OA (12). The questionnaires were administered every year, exploring a period of 3 months for
121 consultations, drugs, biological investigations, imaging, technical aids and transportation and
122 12 months for hospitalizations. If necessary, health resource use was annualized. The original
123 questionnaire is available in supplemental data.

124

125 **Direct medical costs and indirect costs assessment**

126 Estimation of direct medical costs included all costs incurred via the National Health
127 Insurance System (NHIS) and private supplementary health insurance and by patients. For
128 specialists, general practitioners, nurses and physiotherapists, an average consultation fee was
129 estimated by using the 2015 general classification system for treatments (13–15)..
130 Transportation, lab and imaging work-ups as well as technical aids were estimated according

131 to the 2015 social health insurance reimbursement fee of the Classification Commune des
132 Actes Médicaux (www.ameli.fr/accueil-de-la-ccam/index.php) or the Nomenclature des Actes
133 de Biologie Médicale
134 (http://www.codage.ext.cnamts.fr/codif/nabm/index_presentation.php?p_site=AMELI)
135 (14,16,17).

136 Drugs were grouped according to their international nonproprietary names, and their costs
137 were calculated by estimating the mean fee per milligram or per dose, according to the Vidal
138 2016 database (18). If dosage data were missing, standard dosages were imputed taking into
139 account the patient's weight when applicable. According to the therapeutic class, we
140 differentiated drugs related to OA (analgesics, non-steroidal anti-inflammatory drugs
141 [NSAIDs], symptomatic slow-acting drugs, corticosteroids, corticosteroid infiltration and
142 viscosupplementation) or not.

143 For each hospitalization, a primary diagnosis or action code was assigned according to the
144 reason for the hospitalization reported by participants. This coding enabled the identification
145 of the closest corresponding Diagnosis-Related Group and the associated fees for the year
146 2015 as reported by the Technical Agency for Information on Hospital Care (*Agence*
147 *Technique de l'Information sur l'Hospitalisation*) (19). The attribution to OA was determined
148 by the authors on the basis of the reason for hospitalization.

149 Indirect costs were calculated in terms of the number of days off work per year due to knee
150 and/or hip OA as reported by participants. The costs associated with one day of sick leave
151 corresponded to the mean daily salary of a French employee, on the basis of the national
152 global domestic product (GDP) per capita in 2016.

153 Total costs were the sum of direct medical costs and indirect costs.

154

155

156 **Statistical analysis**

157 Patient characteristics at baseline and health resource use for each year of follow-up are
158 described by mean (SD) or number (%) at baseline. Yearly costs are described by mean for
159 each year (year 1, 2, 3, 4 and 5) and/or median (interquartile range [IQR]) if non-normal
160 distribution. To assess the median annual total costs of hip and knee OA in the 40 to 75-year-
161 old population, standardized prevalence estimates calculated according to the French age and
162 sex distribution for 2006 (www.insee.fr/fr/statistiques) were used (2). All statistical analyses
163 involved using SAS v9.4, (SAS Institute, Inc., Cary, NC).

164

165 **Results**

166 **Patient characteristics**

167 In total, 878 individuals were included in the KHOALA cohort, 222 with hip OA (mean age
168 61.2 ± 8.8 years), 607 knee OA (mean age 62.0 ± 8.5 years) and 49 both hip and knee OA
169 (mean age 64.7 ± 8.0 years). Baseline characteristics of the 878 participants are in Table 1.
170 Radiographic disease severity for KL (11) stages 2, 3 and 4 represented 69.8%, 26.1% and
171 4.1%, respectively, of hip OA patients and 44.5%, 30.3%, and 25.2%, respectively, of knee
172 OA patients. Mean Functional Comorbidity Index (FCI) (20) was 3 ± 1.5 for hip OA; $3.1 \pm$
173 1.6 for knee OA and 3.1 ± 1.4 for hip and knee OA. Mean duration after first symptoms is
174 higher compared to mean duration after diagnosis. Mean body mass index (BMI) was $26.9 \pm$
175 4.4 for patients with hip OA, 30.3 ± 6.2 for those with knee OA and 29.8 ± 6.2 for those with
176 both hip and knee OA.

177

178 **Health resource use**

179 The proportions of patients using healthcare resources are shown in Table 2. General
180 practitioners have a central role. Only 20% of patients consult a rheumatologist. Most of

181 health care use is stable over 5 years. The decrease in the number of patients is due to loss-to-
182 follow-up (refusal to prosecute (60%), death (22%), other (18%)).

183

184 **Costs**

185 *Direct medical costs*

186 The mean and median annual direct medical costs per patient over 5 years were 2,120€ and
187 980€ (IQR 395–2,350) respectively. The mean annual direct medical costs per patient were
188 1,515€ in year 1; 1,945€ in year 2; 1,935€ in year 3; 3,270€ in year 4; and 2,140€ in year 5.
189 Although OA mean direct medical costs increased by 41% at the end of the follow-up, the
190 median decreased by 33% from 515€ in year 1 to 345€ in year 5. This decrease was explained
191 by the fact that 50% of the patients accounted for 89% of the total direct medical costs over
192 the 5 years. The mean annual direct medical costs per patient over 5 years were 1,805€ for hip
193 OA; 2,230€ for knee OA; and 2,195€ for hip and knee OA (Table 3).

194

195 *Indirect costs*

196 The mean annual indirect costs per patient over 5 years were 60€ (180€ for the 554 patients
197 who were still on the market place). These costs were 95€ in year 1; 65€ in year 2; 40€ in year
198 3; 70€ in year 4; and 45€ in year 5. Hip and knee OA patients did not differ in indirect costs:
199 60€ for hip OA; 65€ for knee OA and 40€ for hip and knee OA (Table 3).

200

201 *Total costs*

202 The mean and median (IQR) annual total costs per patient over 5 years were 2,180€ and
203 1,115€ (400–2,385), respectively. They ranged from 1,615€ in year 1; to 2,010€ in year 2;
204 1,975€ in year 3; 3,340€ in year 4; and 2,190€ in year 5 (Figure 1). The mean annual total

205 costs per patient over 5 years were 1,865€ for hip OA; 2,295€ for knee OA; and 2,235€ for
206 hip and knee OA (Table 3).

207

208 **Costs over 5 years by patient characteristics (Table 3)**

209 The affected joint, KL stage and FCI seemed associated with consumption of care. Indeed, the
210 mean annual total costs over 5 years were increased for patients with knee OA and increased
211 KL grade and FCI but not body mass index.

212

213 **Cost share (or cost structure) and costs attributable to OA**

214 The estimated costs of health resource use are shown in supplemental data. Drugs were the
215 largest cost share, representing over 50% of all direct medical costs across the years. Annual
216 drug costs ranged from 905€ in year 1 to 1,760€ in year 4 and 1,130€ in year 5. However, the
217 proportion attributable to OA-specific agents (analgesics, NSAIDs, symptomatic slow-acting
218 drugs, corticosteroids, corticosteroid infiltration and viscosupplementation) accounted for
219 only 10.5% of drug costs over 5 years (i.e., annual mean of 110€ per patient and per year).

220 Hospitalizations were the second largest component of health resource utilization. Costs of
221 OA-related hospitalizations in medicine accounted for 9% of the total hospitalizations costs
222 over 5 years (i.e., annual mean 20€ per patient and per year). Direct medical costs of OA-
223 related hospitalizations in surgery accounted for 43% of surgery hospitalization costs over 5
224 years (i.e., annual mean 280€ per patient and per year). Hip and knee prosthetic surgery was
225 the main reason for surgery (23%) but accounted for 27% of surgery hospitalization costs
226 over 5 years (i.e., annual mean 177€ per patient and per year). The other reasons for surgery
227 were less frequent but more expensive (according to the 2015 coding of the Technical Agency
228 for Information on Hospitalization).

229 Health professional visits were the third direct medical cost component of health resource
230 utilization, mainly for physiotherapy. They accounted for 3% of direct medical costs over 5
231 years (i.e., annual mean 150€ per patient and per year). Physiotherapy accounted for 1% to
232 2% of the direct medical costs over 5 years (i.e., annual mean 8€ per patient and per year).
233 Annual cost distribution per resource user and average annual direct medical costs per patient
234 and per resource are available in supplemental data.

235

236 **The economic burden of hip and knee OA in France**

237 On standardization to the French population 40 to 75 years old, the prevalence of hip and
238 knee symptomatic and radiological OA was 2.5% and 6.5% for men and 1.0% and 2.7% for
239 women, respectively [i.e. 1.8 million patients in 2017 (2)]. From these prevalence estimates,
240 the median annual total costs of hip and knee OA in the 40- to 75-year-old population would
241 be approximately 2 billion €/year (IQR 0.7–4.3), with direct medical costs of 1.7 billion
242 €/year (IQR 0.7–4.2).

243

244 ***Discussion***

245 This study described costs related to healthcare use among a representative sample of
246 individuals with symptomatic hip and/or knee OA over 5 years. The mean and median annual
247 total costs per patient over 5 years were 2,180€ and 1,115€ (IQR 400–2,385) respectively.
248 Direct medical costs accounted for 97% of the total cost. Our findings highlight the burden of
249 drugs, which represented the largest cost component among KHOALA patients.

250 Worldwide, the mean estimated annual total costs for knee and/or hip OA are heterogeneous:
251 €1,000 in Europe, €6,200 in Asia (Singapore) and €10,000 in North America (7). The
252 difference in costs we observed could be related to several points. First, published studies
253 showed substantial methodological heterogeneity. Our economic study is innovative in its

254 method of recruitment and duration of follow-up. Indeed, the multi-center recruitment of
255 individuals independent of any medical consultation is a major strength because it potentially
256 allowed for including individuals who never consulted any physician (2). Regardless, OA
257 diagnosis was ascertained by physicians on the basis of clinical and radiological features.
258 Second, we included patients who had a prosthesis during follow-up. Prosthetic surgery is not
259 always included in the direct medical costs of studies even though joint surgery is considered
260 an important cost driver in hip and knee OA (7). Also, the follow-up of our study was 5 years,
261 whereas the median follow-up for previous studies was 1 year (range 3 months to 2 years) (7).
262 Third, the health resources studied in KHOALA are quite exhaustive, unlike in some studies,
263 in which costs such as physiotherapy, hospitalizations, biology and imaging are not
264 systematically included in direct cost estimates (7).

265 In terms of all elements, the KHOALA cohort can be considered representative of the reality
266 of people living with knee and hip OA.

267 The social burden of OA is expected to be high and increasing in France. Indeed, in 1993, 3
268 million people had symptomatic OA, with direct medical costs of about 0.6 billion €/year
269 (21). In 2003, 4.6 million people had symptomatic OA, with direct medical costs of about 1.6
270 billion €/year (22). These studies included patients with symptomatic general OA, including
271 those over 75 years old. From the standardized prevalence, 1.8 million people 40 to 75 years
272 old would have symptomatic and radiological hip and/or knee OA in 2017. Median annual
273 direct medical costs would be about 1.7 billion €/year (IQR 0.7–4.2). The prevalence of OA is
274 increasing with the aging of the population as well as obesity, which is becoming more
275 common (23). The costs of the disease have increased even further, owing to an increase in
276 patient demand for care and more frequent use of prosthetic surgery (24,25).

277 Previous studies reported high rates of comorbidities and healthcare utilization among OA
278 patients (26–28)

279 However, specific costs attributable to OA represented only a small fraction of overall costs.
280 Our patients had a substantial number of comorbidities, which was expected due to the
281 population demography. As a result, the main cost share was related to these comorbidities
282 rather than OA. The importance of costs attributable to OA-related comorbidities has been
283 discussed (26) but never clearly demonstrated.

284 The limitations of the study include the observational design, missing data and lack of
285 comparison. The presence of a control group (a cohort of patients matched for age, sex and
286 co-morbidities, without knee and / or hip osteoarthritis) would reduce confounding bias.
287 Moreover, use of self-reported questionnaires can imply memory bias and inaccurate data.
288 However, the observational design have the advantage of better meeting the needs of daily
289 practice and including subjects often excluded from randomized controlled trials and on a
290 larger number of subjects and time much longer observation time. Using a patient-completed
291 questionnaire was a feasible and valid way to capture health resource use and costs for
292 patients with OA as compared with data from administrative databases (12).

293 To conclude, in the KHOALA cohort, healthcare consumption costs over the first 5 years
294 after inclusion in the cohort were heterogeneous and substantial. The costs might be related to
295 a high proportion of patients with comorbidities. The follow-up of the cohort is 10 years, we
296 will can study annual direct and indirect OA costs over 10 years and if the use of the
297 replacement joints allows a costs reduction in long-term. These data are important for
298 describing the healthcare costs of a representative sample of patients with symptomatic OA of
299 the hip and/or knee recruited from the general population in France.

300

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305

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308 CG, FG and BF. All authors participated in the interpretation of the results and manuscript
309 writing. All have read and approved the final version of the manuscript for publication.

310

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312

313 **Competing interests**

314

315 **Conflict of interest:** None

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Figure Legends:

Figure 1: Average annual total costs per patient over 5 years

Supplemental data: Mean annual direct medical costs per patient and per resource