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Citation for published version (APA):

Nielen, J. T. H., Boonen, A., Dagnelie, P. C., van den Bemt, B. J. F., Emans, P. J., Lafeber, F. P. J. G., van Spil, W. E., de Vries, F., & Welsing, P. M. J. (2018). Disease burden of knee osteoarthritis patients with a joint replacement compared to matched controls: a population-based analysis of a Dutch medical claims database. *Osteoarthritis and Cartilage*, *26*(2), 202-210. https://doi.org/10.1016/j.joca.2017.11.012

Document status and date:
Published: 01/02/2018

DOI:
10.1016/j.joca.2017.11.012

Document Version:
Publisher's PDF, also known as Version of record

Document license:
Taverne

Please check the document version of this publication:

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Osteoarthritis and Cartilage 26 (2018) 202–210

Osteoarthritis and Cartilage

Disease burden of knee osteoarthritis patients with a joint replacement compared to matched controls: a population-based analysis of a Dutch medical claims database

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ARTICLE INFO

Article history:
Received 24 March 2017
Accepted 23 November 2017

Keywords:
Knee osteoarthritis
Knee arthroplasty
Knee replacement
Incidence rate
Health care costs

SUMMARY

Objective: On a population level, the incidence of knee prostheses (KPs) has increased, but excess health care costs per patient, compared to matched controls without a KP, in the years surrounding these procedures and their determinants are largely unknown. We therefore aimed to provide estimates of age- and sex-specific incidence of KPs, revision KPs, and prosthesis complications in patients with knee osteoarthritis (OA) and to determine excess health care costs in the years surrounding surgery compared with matched controls.
Methods: All KPs in OA patients in the Achmea Health Database were identified as well as up to four controls. Incidence rates of KPs, revisions, and complications from 2006 to 2013 were determined. Annual health care cost and excess costs (over matched controls) preceding, during, and after surgery were calculated and their determinants were evaluated.
Results: The increased incidence of KPs, revisions, and complications was strongest in younger age categories and men. The average costs per patient were relatively stable between 2006 and 2012. KP patient's annual health care costs increased towards the year of surgery. After surgery, costs decreased, but remained higher as compared to costs prior to surgery. High post-surgery costs were mainly associated with subsequent revisions or additional KPs, but costs were also higher in females, lower age categories, and lower social economic status.
Conclusion: These results underscore the increasing burden and medical need associated with end-stage OA, especially in younger age categories. Improvement of guidelines tailored to individual patient groups aimed at avoiding complications and revisions is required to counteract this increasing burden.
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Introduction

Osteoarthritis (OA) is a progressive disease generally associated with joint pain and decreased functioning. Based on general practitioners (GP) registries, it is estimated that in 2011 approximately 1.2 million people in the Netherlands had (a history of) an OA diagnosis, making it one of the most common musculoskeletal conditions in the Dutch population[1]. In the same year the incidence of this disease was estimated at 9.9/1000 persons. OA is generally

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https://doi.org/10.1016/j.joca.2017.11.012
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more prevalent in women (88.5/1000 persons) compared to men (53.8/1000 persons)[1]. In newly diagnosed patients, the knee is most frequently affected (32%)[1]. In severe cases of knee OA, replacement of the joint with a knee prosthesis (KP) is considered to be an effective option to improve functioning, reduce pain, and consequently improve health-related quality of life[2].

In the Netherlands, the incidence of KPs was reported to have increased with 30% from 20,559 in 2010 to 26,754 in 2014, and the number of revisions increased with 57% from 1619 in 2010 to 2541 in 2014[3]. Similarly, in the United States (US) the prevalence of total KPs has increased over the years[4]. Moreover, one study suggested a shift towards undergoing this surgical procedure at a younger age, but this has not been confirmed by other studies[4]. Furthermore, there is limited research on health care costs associated with KPs. Previous studies suggest an increase in mean health care costs in the years prior to the surgery, followed by a peak in the first year after surgery. From the second year onward, health care costs appear to stabilize after a marked reduction compared to the first year after surgery[5,6]. Furthermore, to the best of our knowledge only one previous study has evaluated these costs with reference to cost in a control population in a period ranging from 1 year pre-surgery to 1.5 years post-surgery[7]. However, long-term effects remain unknown. Additionally, it is unclear which patient characteristics are likely to influence these costs. Knowledge of these determinants may provide insight into current clinical practice and may be relevant for future budget allocation.

Therefore, we aimed to provide estimates of the age- and sex-specific incidence of KPs, revision KPs, and prosthesis complications in patients with knee OA over calendar time. Furthermore, we aimed to determine health care costs (i.e., all medical costs reimbursed by the health insurer) over calendar time, distinguishing costs in a 7-year period preceding, during, and in the 7 years following arthroplasties. Overall as well as excess costs compared with matched controls, and determinants of high excess cost were evaluated.

Methods

Data source

The Netherlands has a singular health care system. All residents are fully insured for medical care regardless of income or socio-economic status, although a deductible (which has ranged between €150 and €385 per annum over the past decade) applies to adults. All health insurance companies in the Netherlands have the same basic health insurance package which covers most medical services, including KPs. Supplementary insurance packages may be added by each individual.

The Achmea Health Database (AHD), previously known as the Agis Health Database, records claim for medical care provided to five million people who have health insurance policies with Achmea Insurance Company. These records include information on patients, health care professionals, and the provided health service. The first two pertain to demographic data. The latter includes information regarding health services provided by GP, drug prescriptions anatomical therapeutic chemical (ATC-coding), and information regarding hospital care based on the diagnosis related groups (DRG) coding system as well as care with other health care providers that is insured. Achmea is the main health insurance company in the central part of the Netherlands and its insured population is representative for the Dutch urban population[8].

Study population

All patients' ≥16 years who had a KP (Supplementary Table I; DRG coding: specialty 05 diagnostic code 1801 or 1803 and treatment code 008, 019, 036, 051, 103, 104, 223, or 226) between 2006 and 2013 were included in the study. KPs include both total and partial prostheses. In order to gain insight into the excess cost associated with KPs, up to four controls from the AHD were exactly matched to each patient based on age, sex, index year, and region (first two digits of postal code) by means of cumulative sampling. Consequently, controls were not allowed to have had a KP within the entire study period. The index year was defined as the year of first KP for the cases. Patients and controls with a diagnosis of rheumatoid arthritis (RA), monoarthritis, oligoarthritis, or polyarthritis, during the study period were excluded (DRG coding: specialty 24 (rheumatology); diagnostic codes 0101, 0115, 0116, 0117).

Statistical analyses

Baseline characteristics of KP cases and matched controls were described. Age- and gender-specific incidences (per 1000 persons per year) of all KPs and complications (DRG diagnostic code 1803 without treatment code 008, 019, 036, 051, 223 or 226) associated with end-stage OA were calculated for every year between 2006 and 2013. All KPs include initial/non-revision KPs (diagnostic code 1801 and treatment code 103, 104, 223 or 226) and revision KPs (DRG diagnostic code 1803 and treatment code 008, 019, 036, 051, 223 or 226). In general, non-revision KPs included all primary KPs, and other KPs that were not registered as a revision. This could have been a primary total KP, but also a replacement of an unicondylar prosthesis by a total KP that was not registered as a revision KP. It could also have been a primary KP of the contralateral knee. The denominator for calculating incidences was the age- and gender-specific population size in the AHD database per calendar year.

In all cost-analyses, health care costs were presented as total costs and stratified by four cost categories: GP; pharmaceutical; hospital; and other costs. First, average annual health care costs per patient in the year of their first KP were calculated by calendar year. Second, average annual health care costs per patient over the observation period were calculated and stratified by year of first KP. Third, average annual health care costs per patient were calculated relative in time to the surgical procedure. Inherent to the structure of the data, for a patient who had a KP in 2013, we were able to calculate annual health care costs during and up to 7 years prior to surgery, whereas for a patient who had a KP surgery in 2006 we were able to calculate costs during and up to 7 years after surgery. As all costs were calculated using a similar approach for the matched controls (i.e., taking the date of KP for the matched OA patient as reference date for cost comparison), excess costs associated with KP surgery in OA patients could be calculated. Fourth, the presentation of excess costs was performed separately for patients with a subsequent KP (revision or subsequent KP in contralateral knee) and patients without a subsequent KP in follow-up, as these were considered to be two distinct groups with regard to economic burden. Fifth, to determine characteristics associated with excess costs, patient' characteristics (age category, gender, number of years insured with Achmea, occurrence of a subsequent revision KP, subsequent non-revision KP, and complication) were described stratified by the average annual excess cost of patients over follow-up using quartiles (Q1 being the lowest excess costs, and Q4 the highest). Kruskal–Wallis tests were conducted in order to assess differences in median values for the previously mentioned characteristics between quartiles. Sixth, the association of possible predictive variables (age, gender, number of years insured, social economic status (SES; tertiles), and time-varying variables: occurrence of a subsequent revision KP, subsequent non-revision KP, and a complication, and year relative to first KP, and calendar year) with high average yearly excess health care costs over time was examined using longitudinal logistic regression analyses (using a Generalized Estimating Equation (GEE) model for clustered response data using the genmod procedure in Statistical Analysis System (SAS)). High annual excess health care costs were defined per year as costs higher than the median excess costs over the total observation period. These associations were expressed as odds ratios (OR) with 95% confidence intervals (95% CIs), and *P*-values. Statistical significance was set at $P < 0.05$. Health care costs were expressed as non-indexed euros (€). Analyses were conducted using SAS 9.4.

Results

Baseline characteristics of all KP cases and matched controls are depicted in Table I. Distribution of age, gender, and year of inclusion per definition was comparable in cases and controls. Average number of years insured by Achmea was also similar in cases compared to controls (7.4 and 7.2 years, respectively). Eighteen percent of the cases underwent subsequent KP surgery in the study period. The first subsequent KP was mostly (79.5%) a non-revision type KP. Furthermore, less than 1.5% of the cases had a second or third subsequent KP in the study period. The second and third subsequent KPs were mostly revisions (71.6% and 87.3%, respectively). Approximately 14% of the cases had a prosthesis complication that did not require surgery. Detailed information regarding the type of subsequent KPs in study period is depicted in Supplementary Fig. 1.

Table I
Baseline characteristics of all KP cases and their controls

	Cases		Controls	
	$n = 26{,}963$		$n = 84{,}786$	
	$n = (\%)$		$n = (\%)$	
Age by category at baseline				
16–20	6	(0.0)	13	(0.0)
21–30	20	(0.1)	57	(0.1)
31–40	160	(0.6)	515	(0.6)
41–50	1190	(4.4)	4107	(4.8)
51–60	5059	(18.8)	17,372	(20.5)
61–70	9022	(33.5)	28,838	(34.0)
71–80	8466	(31.4)	25,113	(29.6)
81–85	2323	(8.6)	6697	(7.9)
>85	717	(2.7)	2074	(2.4)
Female	17,876	(66.3)	55,270	(65.2)
SES by category				
Low	8918	(33.1)	28,019	(33.0)
Medium	8912	(33.1)	27,236	(32.1)
High	8896	(33.0)	28,800	(34.0)
Missing	237	(0.9)	731	(0.9)
Year of inclusion (baseline)				
2006	23,479	(87.1)	76,262	(89.9)
2007	834	(3.1)	2580	(3.0)
2008	176	(0.7)	483	(0.6)
2009	1763	(6.5)	4269	(5.0)
2010	175	(0.6)	350	(0.4)
2011	191	(0.7)	310	(0.4)
2012	207	(0.8)	299	(0.4)
2013	138	(0.5)	233	(0.3)
Years insured with Achmea in study period (mean, SD)	7.4	(1.4)	7.2	(1.7)
First subsequent KP in study period	4746	(17.6)	–	–
Revision	975	(20.5)*	–	–
Second subsequent KP in study period	345	(1.3)	–	–
Revision	247	(71.6)*	–	–
Third subsequent KP in study period	55	(0.2)	–	–
Revision	48	(87.3)*	–	–
Fourth subsequent KP in study period	11	(0.0)	–	–
Revision	10	(90.9)*	–	–
Fifth subsequent KP in study period	3	(0.0)	–	–
Revision	3	(100.0)*	–	–
Complications other than revision	3877	(14.4)	–	–

Detailed information regarding type of subsequent KPs in follow-up is depicted in Supplementary Fig. 1.
* Percentage of patients where first/second/third subsequent KP in study period was a revision.

The incidence rates of all KPs, revisions, and complications were higher in women compared to men. Furthermore, the incidence rates of all KPs, revision, and complications were highest in the population aged 60–85 years. The relative increase in incidence rates of all KPs, revision, and complications from 2006 to 2013 was strongest in men, and in younger age categories (<60 years). The relative increase over time was strongest for complications not requiring surgery (Fig. 1, Table II).

Average annual health care costs and excess costs during year of surgery were stable between 2006 and 2012 [Fig. 2(a)] and increased in 2013 by approximately €10,000. Average annual health care costs and excess health care cost for cases over the patient observation period decreased between 2006 (€11,837 and €6021, respectively) and 2012 (€9417 and €5070, respectively). In 2013 average annual health care costs and excess health care cost for cases over the observed period (11,347 and 7074, respectively) increased compared to previous years [Fig. 2(b)].

Average annual health care costs and excess costs in cases slightly increased up to the year of surgery and were highest in the year of surgery (€29,211 and €24,353, respectively). Excess costs in the year of surgery were largely attributable to increased hospital costs. Health care costs subsequently decreased in the first year after surgery, but excess costs did not reach the level of the years prior to KP. In the years following KP, health care costs and excess costs stabilized at a level higher than the years prior to surgery. However, from the sixth year after KP onwards, the health care costs and excess cost gradually increased [Fig. 3(a)]. Excess costs of cases with and cases without a subsequent KP (either revision or new primary KP) in the study period remained higher than the excess costs in the years prior to surgery [Fig. 3(b)].

The percentage of patients in lower age categories, that are female, with revision KPs, with subsequent non-revision KPs, and with complications increased with increasing excess cost quartiles. The average number of years insured with Achmea during follow-up was lower in higher excess cost quartiles. These differences were statistically significant based on Kruskal–Wallis tests ($P < 0.05$) (Supplementary Table II). Over time, revisions, other subsequent KPs, and complications were significantly associated with high average annual excess health care costs. Male gender, high SES, and number of years insured were associated with low average annual excess costs. Higher age categories were associated with significantly decreased excess health care costs. Prior to the KP the years towards the year of surgery were increasingly associated with higher excess health care costs. There was no clear trend for calendar year, except 2013, which was associated with high excess annual health care costs (Table III).

Discussion

In the present study, we evaluated the age- and sex-specific incidence of KPs, revision KPs, and prosthesis complications in patients with knee OA over calendar time. Furthermore, we determined health care costs and excess health care costs associated with these procedures. We showed that the incidence of KPs, revision KPs, and complications increased over time. The strongest relative increase was seen for complications. Over time, there was an increasing incidence of these procedures at a younger age, and a stronger increase in men compared to women. Higher excess health care costs were associated with subsequent KPs, revision KPs, complications, younger age, and the year relative to surgery. Although these excess costs are mainly related to hospital costs, which may be a direct result of these operations, excess costs

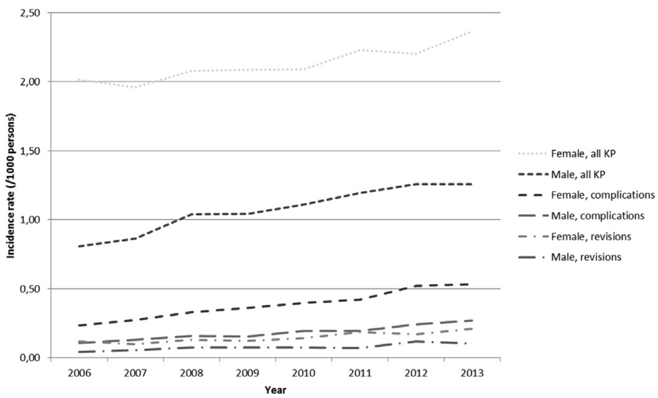

Fig. 1. Incidence rates of all KPs, revision KPs, and complications.

increased in other cost categories as well. Low costs were associated with male gender and the number of years insured by Achmea.

In this study, we found incidence rates of KPs and revisions that were higher than the previously reported national rates reported by the Dutch Arthroplasty Register (in Dutch: Landelijke Registratie Orthopedische Implantaten (LROI)). In their report, the number of KPs has increased with 30% from 20,558 in 2010 to 26,754 in 2014[3]. This corresponds with an incidence rate of 1.24/1000 persons in 2010 to 1.59/1000 persons in 2014 (based on 16.6 and 16.8 million inhabitants in 2010 and 2014, respectively[9]). The number of revisions has increased with 57% from 1619 in 2010 to 2541 in 2014, corresponding to an incidence rate of 0.10/1000 persons in 2010 to 0.15/1000 persons in 2014[3]. Several aspects should be accounted for when comparing these figures to the results in our study. First, our definition of all KPs included total, unicondylar, patellofemoral, and revision KPs, whereas revisions were excluded from the LROI definition of a KP. Second, the use of different types of data sources may also partly explain why we found higher incidence rates. In this study, we classified KPs based on the DRG coding system, whereas the LROI report is based on registration by health care providers. Consequently, if a wrong DRG code was used (1801 instead of 1803) a revision may have been classified as a non-revision in our study. Third, the lower number of KPs or revisions in the LROI report may be due to the fact that not all medical facilities performing KP surgeries were included, especially in the years prior to 2012. It is estimated that approximately 10% of the KPs in 2010 were not included in the LROI report[10]. In 2014 this is estimated to be 3% of all KPs[3]. Lastly, the hospitals that were included in this study may differ from those in the LROI study. The AHD is representative for an urban population, whereas the LROI included (90–97% of the) hospitals nationwide.

Similar to other studies, KPs were mostly conducted in females and in the population aged >60 years, while the incidence rates show a stronger increase in men and patients at a younger age[3,4]. The relatively strong increase in complications may be partly due to an increased number of KPs. Additionally, as the relative increase of KPs and complications is strongest in the age categories <60 years, possibly younger persons at higher risk for surgical complications but with strong preference for surgical treatment of their knee problem undergo KP surgery. In addition, younger patients likely remain more physically active after surgery, putting the prostheses are under more stress, possibly leading to more complications. Overall, our study shows the same trends compared to existing reports. However, absolute numbers may be different due to the use of dissimilar definitions.

Average annual health care costs and excess costs during year of surgery were stable between 2006 and 2012 and increased in 2013 with approximately €10,000. This substantial increase may be due to a reallocation of health care budget from the 'Algemene Wet Bijzondere Ziektekosten' (AWBZ) to the 'Zorgverzekeringswet' (ZW) in 2013 where e.g., some rehabilitation related care became part of ensured care and thus registered in AHD[11]. Average annual cost over the observation period ranged between 11,837 and 9417, which is in line with previous studies reported in a recent review on the economic consequences of lower-limb OA[12].

Trends in health care costs relative to year of surgery found in this study were largely comparable to two previous studies. In those studies, there was an increase of annual health care cost towards year of surgery and costs stabilized after the year of surgery[5,6]. This steady increase of cost towards the year of surgery may be caused by an increased need of medical care (e.g., GP visits, drug use) due to progression of OA eventually leading to the surgical procedure. This suggestion is partly confirmed by the study by Berger *et al.*, which has shown that the use of analgesic and anti-inflammatory drugs increases in the 2 years preceding the surgical procedure[5]. Due to a relative short follow-up, the increase from the sixth year onwards found in the present study was not reported in previous studies[5,6]. Graver *et al.* reported the highest cost in first year after surgery, whereas in our study health care costs were highest in the year of surgery. This difference was due to the fact that in the study by Graver *et al.* the surgical costs were categorized in the first year after surgery rather than the year of surgery itself[6]. In our study, the excess costs after the year of surgery did not reach the level of the years prior to KP in both patients with and without a subsequent surgery. This is in contrast to a previous study that reported no difference in total costs in the post-surgery period compared to the pre-surgery period in patients without a subsequent KP[7].

High annual health care costs were associated with younger age, female gender, a subsequent (revision or non-revision) KP in follow-up, and a complication in the follow-up. Due to additional surgical or less invasive additional procedures, it was expected that subsequent KPs and complications in the follow-up would result in higher costs. Younger age was an independent determinant of higher excess costs, possibly because controls in these age categories are more likely to be relatively healthy compared to the controls in older age categories. Moreover, patients in the older population are more likely to have a comorbidity that is contraindicated with KP surgery. The presence of these contraindicating comorbidities could lead to a control population that has relatively high health care costs. Furthermore, functionality levels set or expected by health care professionals as well as patients may be higher in younger age categories compared to older patients. Additional care needed to achieve these levels could result in relatively higher health care costs in younger patients. Additionally, if surgeries are being performed at a younger age, the likelihood of undergoing a subsequent surgery may increase as more people will outlive their prosthesis. Furthermore, the patients that undergo surgery at a younger age are possibly less severe cases, which has been suggested to reduce cost-effectiveness of this procedure[13]. The inverse association between number of years insured and health care costs may indicate that patients with stable health (and consequently less costs) are more likely to be satisfied with their insurer and therefore less likely to switch to another insurance company.

This study has several strengths. To the best of our knowledge, it is the first study looking at excess costs and factors influencing these costs in OA patients preceding, during, and after KP surgery over a longer period. Furthermore, misclassification of surgical procedures could have a substantial impact on hospital budgets. In the case of primary KP surgery associated with OA it is required to register the code for the underlying disease along with the code for

Table II
Age- and sex-specific incidence rate (per 1000 person years) of all KPs, revisions, and complications associated with OA within study period

	Age group	2006		2007		2008		2009		2010		2011		2012		2013	
		No.	IR	No.	IR	No.	IR	No.	IR	No.	IR	No.	IR	No.	IR	No.	IR
All KPs																	
Male	≤40	6	0.01	8	0.02	12	0.03	11	0.02	24	0.05	25	0.05	13	0.03	12	0.02
	41–50	32	0.16	35	0.17	52	0.25	83	0.33	88	0.35	85	0.35	113	0.45	111	0.44
	51–60	198	1.05	221	1.17	249	1.34	314	1.46	366	1.71	344	1.62	403	1.85	432	1.94
	61–70	281	2.15	335	2.36	417	2.79	478	2.77	487	2.76	582	3.29	646	3.54	637	3.38
	71–80	286	3.41	290	3.31	336	3.80	368	3.78	380	3.83	393	3.92	376	3.66	411	3.85
	81–85	67	2.80	67	2.64	86	3.37	76	2.75	81	2.86	72	2.49	78	2.62	64	2.08
	>85	22	1.53	17	1.08	25	1.51	23	1.24	13	0.67	23	1.15	21	1.00	15	0.68
	All	892	0.81	973	0.86	1177	1.04	1353	1.04	1439	1.11	1524	1.19	1650	1.26	1682	1.26
Female	≤40	8	0.02	6	0.01	9	0.02	15	0.03	16	0.03	20	0.04	19	0.04	20	0.04
	41–50	48	0.25	57	0.29	75	0.38	111	0.47	114	0.49	141	0.61	143	0.60	169	0.70
	51–60	339	1.88	343	1.91	374	2.11	444	2.23	459	2.32	566	2.88	579	2.85	620	2.98
	61–70	655	4.97	648	4.54	756	5.07	884	5.24	934	5.44	961	5.58	1053	5.95	1139	6.28
	71–80	886	8.44	870	8.05	852	7.93	911	7.93	872	7.54	878	7.61	838	7.17	976	8.17
	81–85	279	6.73	275	6.50	267	6.35	277	6.25	246	5.56	229	5.16	225	5.02	216	4.75
	>85	86	2.29	80	2.01	84	2.04	93	2.10	85	1.87	79	1.70	51	1.08	53	1.10
	All	2301	2.01	2279	1.96	2417	2.08	2735	2.09	2726	2.09	2874	2.23	2908	2.20	3193	2.37
Total		3193	2.82	3252	2.82	3594	3.12	4088	3.13	4165	3.20	4398	3.42	4558	3.46	4875	3.62
Revision KPs																	
Male	≤40	1	0.00	0	0.00	1	0.00	1	0.00	0	0.00	1	0.00	1	0.00	4	0.01
	41–50	5	0.02	7	0.03	8	0.04	11	0.04	5	0.02	7	0.03	16	0.06	15	0.06
	51–60	10	0.05	18	0.10	25	0.13	30	0.14	36	0.17	26	0.12	54	0.25	40	0.18
	61–70	13	0.10	14	0.10	28	0.19	32	0.19	35	0.20	34	0.19	53	0.29	51	0.27
	71–80	15	0.18	20	0.23	19	0.22	17	0.17	17	0.17	17	0.17	25	0.24	21	0.20
	81–85	1	0.04	3	0.12	4	0.16	6	0.22	2	0.07	2	0.07	3	0.10	5	0.16
	>85	3	0.21	1	0.06	1	0.06	0	0.00	1	0.05	4	0.20	2	0.10	1	0.05
	All	48	0.04	63	0.06	86	0.08	97	0.07	96	0.07	91	0.07	154	0.12	137	0.10
Female	≤40	1	0.00	1	0.00	4	0.01	1	0.00	2	0.00	3	0.01	7	0.01	2	0.00
	41–50	5	0.03	2	0.01	10	0.05	11	0.05	14	0.06	19	0.08	18	0.08	23	0.10
	51–60	21	0.12	31	0.17	27	0.15	30	0.15	36	0.18	63	0.32	47	0.23	78	0.38
	61–70	42	0.32	31	0.22	50	0.34	61	0.36	65	0.38	88	0.51	76	0.43	91	0.50
	71–80	48	0.46	34	0.31	36	0.33	39	0.34	45	0.39	55	0.48	58	0.50	71	0.59
	81–85	15	0.36	12	0.28	15	0.36	15	0.34	22	0.50	8	0.18	15	0.33	14	0.31
	>85	2	0.05	5	0.13	12	0.29	5	0.11	3	0.07	2	0.04	7	0.15	7	0.15
	All	134	0.12	116	0.10	154	0.13	162	0.12	187	0.14	238	0.18	228	0.17	286	0.21
Total		182	0.16	179	0.16	240	0.21	259	0.20	283	0.22	329	0.26	382	0.29	423	0.31
Complications																	
Male	≤40	3	0.01	3	0.01	3	0.01	4	0.01	1	0.00	2	0.00	5	0.01	6	0.01
	41–50	14	0.07	16	0.08	18	0.09	14	0.06	23	0.09	30	0.12	24	0.10	39	0.16
	51–60	26	0.14	34	0.18	40	0.21	53	0.25	57	0.27	73	0.34	90	0.41	104	0.47
	61–70	16	0.12	42	0.30	50	0.33	71	0.41	89	0.50	77	0.44	107	0.59	113	0.60
	71–80	43	0.51	43	0.49	49	0.55	43	0.44	60	0.61	58	0.58	65	0.63	74	0.69
	81–85	12	0.50	10	0.39	10	0.39	10	0.36	16	0.56	6	0.21	19	0.64	20	0.65
	>85	6	0.42	1	0.06	8	0.48	6	0.32	4	0.21	5	0.25	6	0.29	3	0.14
	All	120	0.11	149	0.13	178	0.16	201	0.15	250	0.19	251	0.20	316	0.24	359	0.27
Female	≤40	2	0.00	3	0.01	5	0.01	9	0.02	10	0.02	7	0.01	8	0.02	9	0.02
	41–50	5	0.03	12	0.06	18	0.09	21	0.09	36	0.15	35	0.15	38	0.16	56	0.23
	51–60	39	0.22	55	0.31	63	0.36	76	0.38	104	0.52	105	0.53	142	0.70	159	0.76
	61–70	87	0.66	99	0.69	113	0.76	130	0.77	154	0.90	164	0.95	245	1.38	280	1.54
	71–80	79	0.75	90	0.83	125	1.16	159	1.38	140	1.21	157	1.36	182	1.56	163	1.36
	81–85	37	0.89	40	0.95	38	0.90	55	1.24	51	1.15	53	1.20	52	1.16	34	0.75
	>85	17	0.45	21	0.53	22	0.54	26	0.59	23	0.51	23	0.50	24	0.51	19	0.39
	All	266	0.23	320	0.28	384	0.33	476	0.36	518	0.40	544	0.42	691	0.52	720	0.53
Total		386	0.34	469	0.41	562	0.49	677	0.52	768	0.59	795	0.62	1007	0.76	1079	0.80

surgery. It is therefore expected that classification of OA (based on DRG code 1801) as underlying indication for a non-revision KP is highly accurate. There were some limitations as well. First, the definition of revisions and complications based on DRG could have resulted in an overestimation of revisions and complications due to OA. Revisions and complications were based on DRG code 1803. In contrast to code 1801, this code does not specify the primary underlying disease for KP surgery. If a RA-like disease was the primary underlying disease for KP, additional (e.g., pharmaceutical) costs associated with this disease could affect the analysis. In order to limit this misclassification, we excluded patients with a diagnosis of RA, monoarthritis, oligoarthritis, or polyarthritis in the entire study period. Second, this study is based on claims data from one health insurance company in the Netherlands. The population insured by this company is representative for the Dutch urban population only, limiting the generalizability of these results[7]. Furthermore, costs were expressed as non-indexed €, therefore inflation has not been taken into account. However, costs are based on yearly negotiated tariff per DRG as reimbursed by the health insurer. As these costs indirectly account for inflation, it is not meaningful to further adjust for inflation. Lastly, we were unable to adjust for comorbidities in our regression analysis, resulting in potential residual confounding. However, the main results of our regression analysis are not expected to change substantially after adjustment for comorbidities.

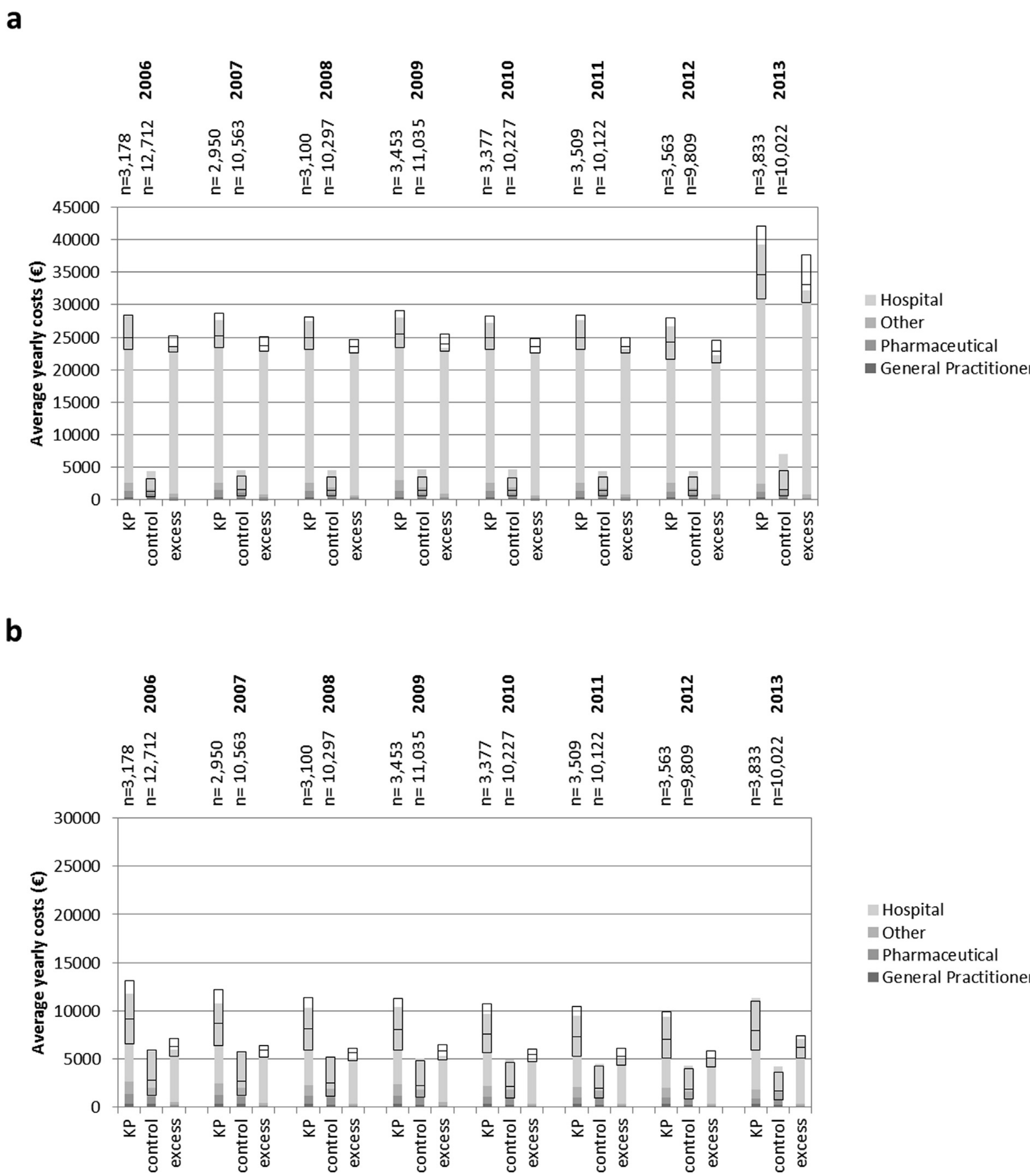

Fig. 2. (a) Average health care costs in the year of first surgery per calendar year categorized by cost category. (b) Average yearly health care costs over the observation period stratified by year of first surgery categorized by cost category. Box plots show Q1, median, and Q3 values of total yearly costs.

Notwithstanding, as knee OA is associate with obesity and obesity also with other comorbidities it would be interesting to see which comorbidities and to what extend they are associated with pre- and post-surgery excess costs. However, as previously mentioned data on comorbidities were not available.

The results of this study show that in the Netherlands, the incidence of KPs, revision KPs, and complications has markedly increased over the period 2006–2013. Similar to other studies there was an increased incidence of these procedures at a younger age, and a stronger increase in men compared to women. Average annual health care costs per patient were relatively stable between 2006 and 2012, but increased strongly in 2013, most likely due to an administrative change (i.e., reallocation of budget). Annual health care cost increase towards year of surgery, likely caused by an increased need for medical care due to progression of OA. In patients without, but especially in patients with a subsequent KP, annual excess health care costs after surgery reached higher levels compared to the period prior to surgery. This suggests that in persons with high risk for post-surgery revisions or complications, expected health benefits and surgical risks should be carefully balanced. High health care costs were mainly associated with subsequent KPs and revision KPs. Complications not leading to

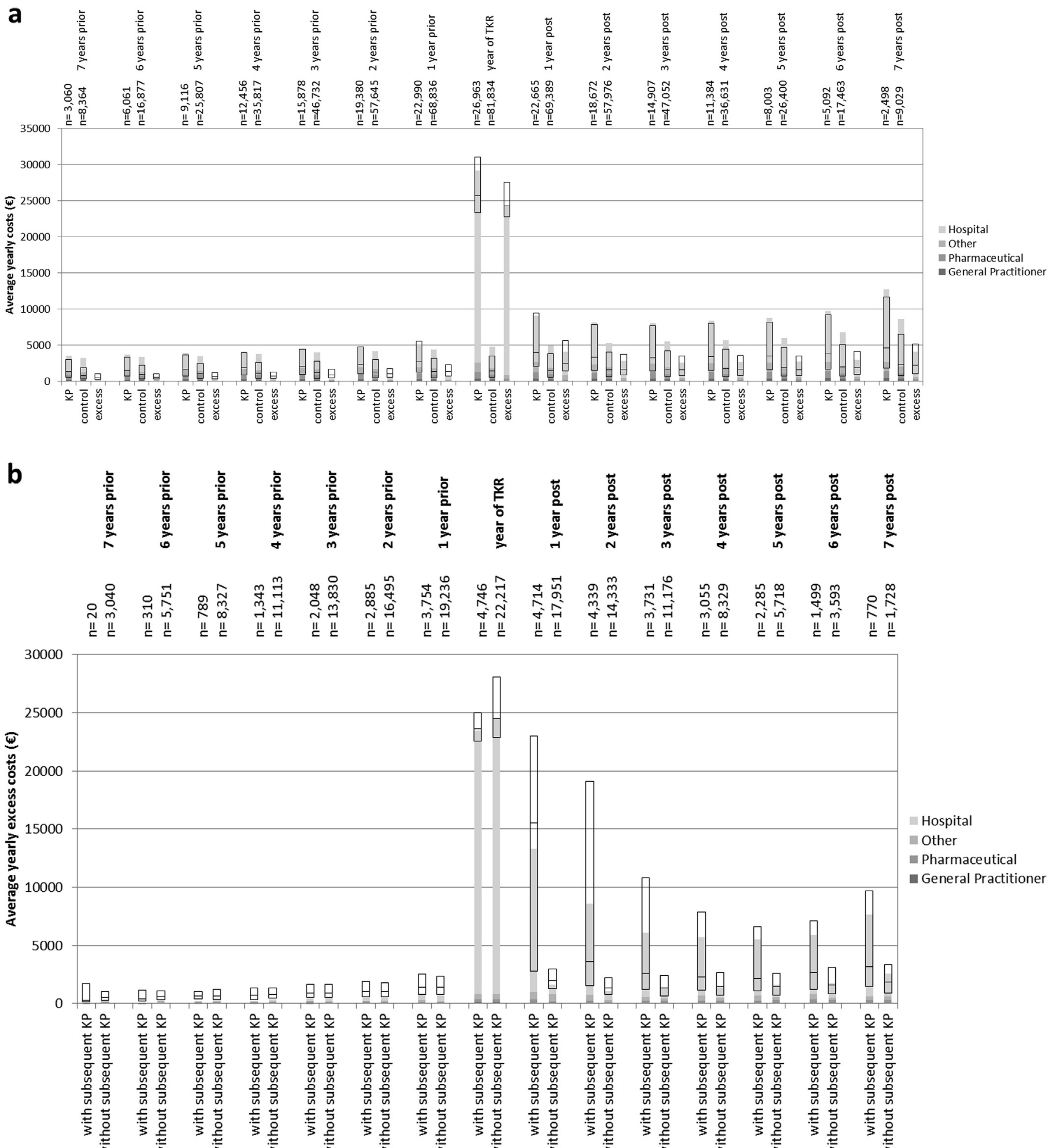

Fig. 3. a) Average yearly health care costs of all cases and controls and excess costs per year per patient categorized by type. (b) Average yearly excess health care costs of cases with or without a subsequent KP per year relative to year of first KP categorized by type. Plots show Q1, median, and Q3 values of total yearly costs. Year of KP is year of first KP.

surgical intervention, female gender, and lower age were also associated with high health care cost, but to a lesser extent. These results underscore the high, increasing burden and medical need associated with end-stage OA, especially in younger age categories, females and patients with a lower SES. Furthermore, as health care costs in the post-surgery period remain higher than pre-surgery, the long-term health gain achieved by these procedures may be disputed. Possibly by tailoring treatment more to specific sub-populations with OA, e.g., younger patients, females, and patients with lower SES, health care costs can be decreased and cost-effectiveness of interventions increased[13]. Alternative treatment options aiming more at preserving the joint rather than replacing it,

Table III
Odds of exceeding the median (€4656) average yearly excess health care cost in years around first KP for potential predictors of high costs based on a multivariate longitudinal logistic regression model

	OR	95% CI	*P*-value
Intercept	0.36	0.27–0.48	<0.0001
Male	0.92	0.89–0.96	<0.0001
Years insured	0.94	0.92–0.95	<0.0001
Revision	114.18	82.98–157.12	<0.0001
Subsequent non-revision KP	234.63	178.99–307.56	<0.0001
Complication	2.64	2.43–2.87	<0.0001
Age category (years) (overall significance $P < 0.0001$)			
<40	Reference		
41–50	0.78	0.62–1.00	0.049
51–60	0.63	0.50–0.80	<0.001
61–70	0.61	0.49–0.77	<0.002
71–80	0.67	0.54–0.84	0.001
81–85	0.66	0.52–0.83	<0.001
>85	0.68	0.53–0.87	0.002
SES category (overall significance $P < 0.0001$)			
Low	Reference		
Medium	0.90	0.86–0.94	<0.0001
High	0.86	0.82–0.90	<0.0001
Year relative to year of first KP (overall significance $P < 0.0001$)			
7 years prior to first KP	Reference		
6 years prior to first KP	1.02	0.89–1.17	0.724
5 years prior to first KP	1.15	1.00–1.31	0.042
4 years prior to first KP	1.20	1.04–1.37	0.009
3 years prior to first KP	1.38	1.21–1.58	<0.0001
2 years prior to first KP	1.43	1.24–1.64	<0.0001
1 year prior to first KP	1.70	1.48–1.95	<0.0001
Year of first KP	465.13	390.68–553.76	<0.0001
1 year after first KP	1.96	1.69–2.27	<0.0001
2 years after first KP	1.75	1.50–2.04	<0.0001
3 years after first KP	1.81	1.55–2.12	<0.0001
4 years after first KP	1.93	1.64–2.26	<0.0001
5 years after first KP	1.96	1.66–2.32	<0.0001
6 years after first KP	2.06	1.73–2.45	<0.0001
7 years after first KP	2.21	1.84–2.66	<0.0001
Calendar year (overall significance $P < 0.0001$)			
2006	Reference		
2007	1.00	0.95–1.05	0.969
2008	1.03	0.97–1.09	0.351
2009	1.07	1.01–1.13	0.031
2010	1.04	0.97–1.11	0.236
2011	1.09	1.02–1.17	0.013
2012	1.05	0.98–1.13	0.189
2013	1.47	1.36–1.60	<0.0001

thereby postponing joint replacement surgeries include optimizing pain treatment, other non-surgical treatments, or novel regenerative medicine approaches like knee joint distraction[14]. Using decision aids may also help to reach optimal decisions regarding type and timing of treatment[15]. In addition, public awareness of OA risk factors and improvement of research and clinical guidelines regarding indications for surgery and avoiding complications and revisions is required to counteract this increasing burden. The increasing incidence of KPs and associated costs in younger patients, females, and patients with lower SES warrants further research into the reasons for these trends.

Authors' contribution

All authors contributed to the conception and design of the study. FPJGL, FdV and PMJW contributed to the acquisition of data. JTHN and PMJW contributed to analysis of data. All authors contributed to interpretation of data. JTHN, AB, and PMJW drafted the manuscript and all authors contributed intellectual content in revising the article. All authors gave final approval of the version to be submitted and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interest

JTHN, PMJW, FPJGL and FdV have no conflicts of interest to declare. BJFvdB received research grants to his department from Pfizer and Roche and occasionally speakers honoraria from Pfizer, Roche, Abbvie and MSD. AB received research grants to her department from Amgen Abbvie, Pfizer and Merck and occasionally speakers honoraria from Pfizer, UCB and Sandoz. PCD has received unrestricted grants from NWO, EU and nutritional industry for research unrelated to this topic. WEvS received honoraria from Lilly as a member of its medical education advisory board, unrelated to this subject. PJE has received research grants to his department from the Dutch Reumafonds, Regentis, DSM Biomedical, Active Implants, Carbylan Biosurgery, and Stryker.

Acknowledgments

There was no funding source involved in writing this manuscript.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.joca.2017.11.012.

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