Data Driven Approach to Enhancing Efficiency and Value in Healthcare

Richard E. Guerrero Ludueña

Appendix A

Predicting the burden of revision knee arthroplasty: simulation of a 20-year horizon

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Predicting the Burden of Revision Knee Arthroplasty: Simulation of a 20-Year Horizon

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ABSTRACT

Objectives: To estimate future utilization scenarios for knee arthroplasty (KA) revision in the Spanish National Health System in the short- and long-term and their impact on primary KA utilization. **Methods:** A discrete-event simulation model was built to represent KA utilization for 20 years (2012–2031) in the Spanish National Health System. Data on KA utilization from 1997 to 2011 were obtained from the minimum data set. Three scenarios of future utilization of primary KA (1, fixed number since 2011; 2, fixed age- and sex-adjusted rates since 2011; and 3, projection using a linear regression model) were combined with two prosthesis survival functions (W [worse survival], from a study including primary KA from 1995 to 2000; and B [better survival], from the Catalan Registry of Arthroplasty, including primary KA from 2005 to 2013). The simulation results were analyzed in the short-term (2015) and the long-term (2030). **Results:** Variations in the number of revisions depended on both the primary utilization rate and the survival function applied, ranging from increases of 8.3% to 31.6% in the short- term and from 38.3% to 176.9% in the long-term, corresponding to scenarios 1-B and 3-W, respectively. The prediction of increases in overall surgeries ranged from 0.1% to 22.3% in the short-term and from 3.7% to 98.2% in the long-term. **Conclusions:** Projections of the burden of KA provide a quantitative basis for future policy decisions on the concentration of high-complexity procedures, the number of orthopedic surgeons required to perform these procedures, and the resources needed.

Keywords: burden of illness, health care utilization, osteoarthritis, simulation models.

Introduction

Knee osteoarthritis is a frequent cause of musculoskeletal pain in older adults and can impair mobility and quality of life. In Spain, as in other countries, its incidence has increased as a result of population ageing and the growing prevalence of risk factors, mainly obesity [1,2].

When the disease is severe and conservative treatment fails, knee arthroplasty (KA) is a highly effective procedure [3,4]. Some studies have shown that despite KA's high cost, it is highly cost-effective from the societal perspective over the entire lifespan [5]. In recent years, rates of KA have increased in most Western countries because of ageing, reduced surgical risk, and broader criteria for surgery [6,7].

A key point in effectiveness assessment is the survival of knee prostheses, and guidelines recommend a minimum of 90% survival 10 years after surgery [8]. Besides effectiveness assessment, it is important to take into account the future burden of revision KA and its impact on the availability of resources for primary KA in the coming years.

Predictions of future demand for nonelective health services are important for decision makers, especially nowadays when there are increasing constraints on health provision. Specifically, present elective primary KAs are expected to influence the future demand for KA surgeries because of the not always lifelong duration of prostheses causing a need for urgent revision.

Health care organizations face challenges in efficiently accommodating increased patient demand with limited resources and capacity [9]. Discrete-event simulation models are increasingly being applied in the analysis of health care systems and have been accepted by health care decision makers as a viable tool for

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improving health resource planning [10]. Few authors, however, have used discrete-event simulation models for the arthroplasty process [11–13] and none to plan the future resources needed to meet the demand for revision KA. Only a few studies have evaluated international temporal trends for total joint replacements [3,14,15]. One of them showed that in the United States alone, the growth in demand for joint replacement surgery is projected to exceed available surgical and economic resources if the historic growth rates continue in the next two decades [3]. For predictions in Sweden, studies used a model with an upper asymptote and led to more conservative predictions [15,16]. None of them, however, used prosthesis survival to predict the burden of revision KA. The growth in demand for total knee surgery has major implications for national health care delivery systems, given the many years required to train surgeons and the equally complex task of planning hospital capacity. Thus, reliable projections of the demand for arthroplasties are crucial for policymakers in government, education, and industry. Importantly, reliable projections for revision arthroplasties would be particularly useful because these interventions consume greater economic resources than do primary procedures.

Thus, the aim of this study was to estimate future scenarios of revision KA utilization in the Spanish National Health System in the short- and long-term and their impact on primary KA utilization according to different scenarios of utilization and prosthesis survival.

Methods

Methodology based on discrete-event simulation models consists of defining a conceptual model to represent the reality to be analyzed, estimation of the necessary parameters, and computer programming to run the model and obtain results. The present discrete-event simulation model was developed to estimate the impact of primary KA on revision KA for the next 20 years (to 2031) in the Spanish health system. Discrete-event simulation was chosen because of its potential to include continuous survival time and the need to model the waiting list as a queue, even though a waiting list analysis was out of the scope of the study. Previous studies predicting the burden of KA used regression models based on historical data and took into account population ageing projections. Nevertheless, none of them used prosthesis survival to predict the burden of revision KA.

Conceptual Model

Figure 1 shows a schematic representation of the conceptual model. The model was built to represent the process from a primary KA to a revision KA or death. New patients in the model represented demand for primary KA, had their own characteristics, such as age and sex, and were included on a waiting list. Primary KA surgery applied to patients on the waiting list according to the estimated number of primary KAs. Each patient who underwent primary KA was assigned a survival time for the prosthesis. If the prosthesis survival was shorter than the lifetime, the patient returned to the waiting list with the highest priority. All patients needing revision had their operation. Patient death could occur at any time, representing exit from the model. Re-revision was not considered.

Parameter Estimation

Information on the sources and the values of the parameters is presented in Table 1. Population data between 1997 and 2011 were obtained from the Spanish National Institute of Statistics [17]. The lifetime distribution (probability distribution of the time until death depending on present age) was estimated through Gompertz models for men and women [18] using 2011 features on inhabitants and number of deaths [17]. See the Appendix in Supplemental Materials found at http://dx.doi.org/10.1016/j.jval.2016.02.018 for details.

The hospital discharge minimum data set of the Spanish health system was used to estimate KA utilization [19]. Data on the number of surgeries were available per year from 1997 to 2011, by sex and age group (45–64 years, 65–74 years, and ≥74 years). The *International Classification of Diseases, Ninth Revision, Clinical Modification* code 81.54 (total knee replacement) was used to identify total primary KA utilization, and codes 81.55 (revision of knee replacement, not otherwise specified) and 00.8x (00.81: revision of knee replacement, tibial component; 00.82: revision of knee replacement, femoral component; 00.83: revision of knee

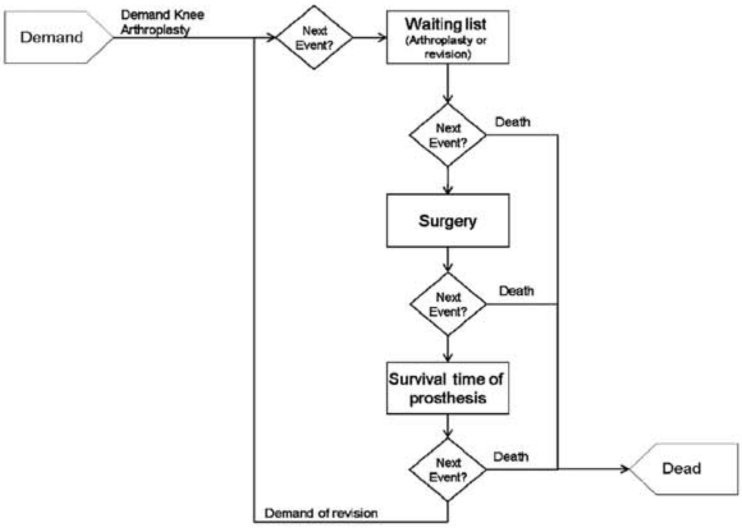

Fig. 1 – Conceptual model.

Table 1 – Model parameters: Values, distributions, and information sources.

Parameter	Source	Distribution	Value
Time (d) between primary procedures (1997–2011)	Minimum data set	Cubic regression on calendar time (t)	$-1.57 \times 10(-13) \times t^3 + 2.53 \times 10(-9) \times t^2 - 1.28 \times 10(-5) \times t + 3.02 \times 10(-2)$
Time (d) between primary procedures (2012–2030)			
Scenario 1 (low)	Minimum data set	Constant	0.0099
Scenario 2 (moderate)	INEbase	Empirical	Rate of 187.5 primary KAs per 100,000 inhabitants applied to projections of the Spanish population
Scenario 3 (high)	Minimum data set	Empirical	Linear prediction based on the relationship between the number of primary KAs and the number people ≥75 y
Proportion of KA in women	CMBD	Linear projection on calendar time (t)	$-0.0057 \times t + 0.7882$
Time to death	INEbase	Gompertz	Male: $\alpha = 6.39 \times 10(-5)$; $\beta = 8.72 \times 10(-2)$ Female: $\alpha = 2.25 \times 10(-6)$; $\beta = 0.1222$
Age of primary KA	Minimum data set	Empirical	
Prostheses survival scenario W	AIAQS report	Weibull	$\alpha = 0.75$; $\beta = 8.02 \times 10(-3)$
Prostheses survival scenario B	RACat	Weibull	Male: $\alpha = 0.4881$; $\beta = 1.03 \times 10(-4)$ Female: $\alpha = 0.6951$; $\beta = 1.3 \times 10(-3)$ Hazard ratios by age group: 3.15 (45–64 y); 2.05 (65–74 y); 1 (>74 y) for men and 2.34 (45–64 y); 1.56 (65–74 y); 1 (>74 y) for women Hazard ratios by type of arthroplasty: 1.77 (uni and fem); 1 (CR and PS); 1.71 (other types) for men and 2.38 (uni and fem); 1 (CR and PS); 1.43 (other types) for women
Distribution of type of arthroplasty	RACat	Empirical	2.5% (uni and fem); 97.4% (CR and PS); 0.1% (other types)

AIAQS, Agency for Health Quality and Assessment of Catalonia; CR, posterior cruciate ligament-retaining KA; fem, femoropatellar KA; KA, knee arthroplasty; PS, posterior-stabilized KA; RACat, Catalan Arthroplasty Registry; uni, unicompartimental KA.

replacement, patellar component; and 00.84: revision of knee replacement, tibial insert) were used to identify revision KA. See the Appendix in Supplemental Materials for details.

According to the utilization data, the proportion of KA in women decreased in Spain over time from 79% in 1997 to 70% in 2011. Using a lineal projection, we estimated this proportion from 2011 to 2031, reaching 59% in 2031. This percentage is similar to the rate observed in other countries (range 52%–67%) [20–25]. The age distribution of primary arthroplasty by sex was estimated using individual data from the Catalan Arthroplasty Registry (RACat) between 2005 and 2011 [26,27]. See the Appendix in Supplemental Materials for details.

To simulate future utilization of primary KA, we considered three scenarios under different assumptions. In "scenario 1: low primary KA utilization rate," the resources were considered constant from 2011 to 2031 and, therefore, the number of surgeries per year was unchanged during the period. In "scenario 2: moderate primary KA utilization rate," the number of surgeries was projected for the years 2012 to 2031, considering 2011 age- and sex-specific KA rates (Table 2, only for persons ≥45 years, following the examples of Sweden [28], the United Kingdom [29], and the Netherlands [30]) in the long-term projections of the Spanish population (2012–2031) [17]. Finally, in "scenario 3: high primary KA utilization rate," the number of primary KAs was

Table 2 – Real data on age- and sex-specific primary KA rates, 2011.

Age group (y)	Number of primary KAs, 2011			Primary KA utilization rate (per 100,000 inhabitants)		
	Men	Women	Overall	Men	Women	Overall
0–44	122	81	203	0.9	0.6	0.8
45–64	2,330	4,653	6,983	40.6	78.5	59.9
65–74	4,635	11,365	16,000	259.7	551.3	416.0
≥75	3,872	9,811	13,683	246.5	398.7	339.4
Overall	10,959	25,910	36,869	48.2	110.6	79.9
Overall >64 y	8,507	21,176	29,683	253.5	468.3	376.8
Overall >44 y	10,837	25,829	36,666	119.1	247.2	187.5

KA, knee arthroplasty

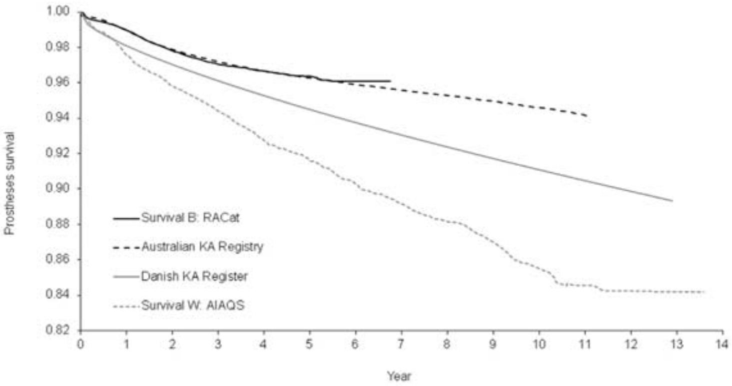

Fig. 2 – Prostheses survival curves according to different data sources. RACat, Catalan Arthroplasty Registry; KA, Knee Arthroplasty; AIAQS, Agency for Health Quality and Assessment of Catalonia.

predicted on the basis of an age-specific population group (aged ≥75 years), following the methodology described by Bashinskaya et al. [14]. See the Appendix in Supplemental Materials for details.

The preceding scenarios for primary KA utilization were combined with two scenarios for prosthesis survival time. The "scenario B: better survival (RACat)" function (5-year survival 96.5%) was based on the primary KAs and their first revision registered in RACat between 2005 and 2011 (n = 44,557), adjusted by age group (55–64 years, 65–74 years, and ≥75 years) and arthroplasty type (unicompartimental and patellofemoral, posterior cruciate ligament-retaining and posterior-stabilized, or others) through the Cox proportional hazards models for men and women separately. A distribution was adjusted for the survival time of the most frequent group (age ≥75 years and posterior cruciate ligament-retaining and posterior-stabilized [CR-PS], Table 1). This group was also used as the baseline group for the Cox model. The hazard ratios estimated for the other categories were applied to the parameters of the distribution according to each patient's characteristics. Table 1 includes the parameters and hazard ratios for age and type of prosthesis. The "scenario W: worse survival (AIAQS)" function (5-year survival 91.5%) considered the survival function estimated within a retrospective cohort study on KA in eight hospitals in Spain between 1995 and 2000 (n = 2,000) [31]. Survival time was modeled using the same distribution as in scenario B (Table 1). The survival functions were compared with the Australian [20] and Danish [21] KA registries, with 5-year survival rates of 96.5% and 95.0%, respectively (Fig. 2). See the Appendix in Supplemental Materials for details.

Simulation and Analysis of Results

The discrete-event simulation model was built in ARENA version 14.0 (Rockwell Software, Inc., Milwaukee, WI). The results were analyzed as the mean of 100 replications in the short-term (results at year 2015) and in the long-term (results at year 2030). The survival analysis was performed using both the Kaplan-Meier method and the Cox proportional hazard model were performed using STATA version 11 (Stata Corporation, College Station, TX).

Future demand for resources for KA in the Spanish National Health System between 2012 and 2031 was estimated from the simulation outputs through operating room time. The latter was defined as the time, including anesthesia, surgery, and cleaning, that an operating room was occupied for to perform one intervention, with values of 2 and 3 hours for primary and revision surgery, respectively. The percentage of change in resource demand from 2011 was calculated.

The assumptions used in the model were developed by reviewing data from the National Joint Registers [32] and RACat, as well as from clinical expert opinion and the literature [33]. The research team, including orthopedic surgeons, epidemiologists, and statisticians, analyzed the results of the model and considered the model as valid, credible, and useful for the study objectives. Validation results on inputs and outputs are included in the Appendix in Supplemental Materials.

Results

From 1997 to 2011, a total of 473,460 KAs were registered, ranging from 12,819 to 43,602. Of these, 431,349 were primary KAs (ranging from 12,126 in 1997 to 38,756 in 2011) and 42,111 were revisions (ranging from 693 to 5,139 in 2011) (Fig. 3).

Simulation results confirmed that the number of primary KAs was similar throughout the simulation horizon for scenario 1 (low primary KA utilization rate) but increased for the other scenarios: 3.4% in the short-term and 32.9% in the long-term for scenario 2 (moderate primary KA utilization rate) and 21.0% in the short-term and 87.1% in the long-term for scenario 3 (high primary KA utilization rate). The variations in the number of revisions depended on both the primary utilization rate and the survival function applied, ranging from an increase of 8.3% to 31.6% in the short-term and from 38.3% to 176.9% in the long-term. These extreme values were obtained from the simulations combining scenario 1 (low primary utilization rate) and survival function B (better survival) versus scenario 3 (high primary utilization rate) and survival function W (worse survival), respectively. For the same scenarios, the predicted increase in overall surgeries ranged from 0.1% to 22.3% in the short-term and from 3.7% to 98.2% in the long-term (Table 3). Resource demand in terms of operating room time showed similar or slightly higher increases than those for the overall number of KAs.

Figure 4 shows the number of primary KAs: real data between 1997 and 2011 and simulation results from 2011 to 2031, according to the three scenarios on primary KA utilization (1, low; 2, moderate; and 3, high).

Figure 5 shows the number of revision KAs: real data between 1997 and 2011 and simulation results from 2011 to 2031,

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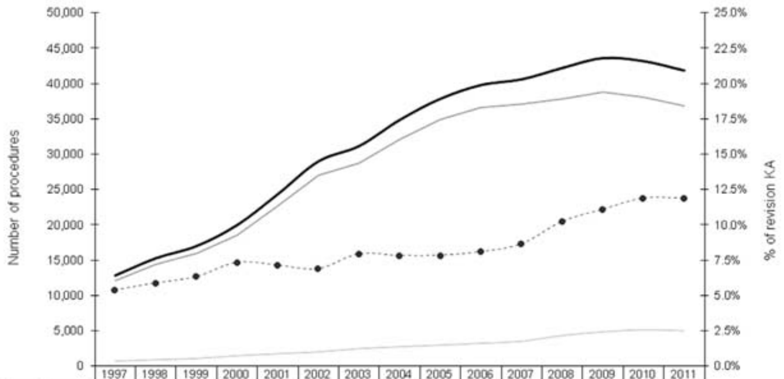

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Primary KA	12,126	14,370	15,915	18,498	22,595	26,989	28,673	32,129	34,871	36,563	37,080	37,877	38,756	38,038	36,869
Revision KA	693	900	1,079	1,468	1,742	2,003	2,480	2,729	2,974	3,228	3,520	4,330	4,846	5,139	4,980
Total KA	12,819	15,270	16,994	19,966	24,337	28,992	31,153	34,858	37,845	39,791	40,600	42,207	43,602	43,177	41,849
% of Revision KA	5.4%	5.9%	6.3%	7.4%	7.2%	6.9%	8.0%	7.8%	7.9%	8.1%	8.7%	10.3%	11.1%	11.9%	11.9%

Fig. 3 – Number of knee arthroplasties in Spain, real data from 1997 to 2011. KA, Knee Arthroplasty.

according to the six scenarios simulated. Simulations applying the worse survival function (W) showed both the highest number of revisions and the steepest increase in this number in both the short-term and the long-term. Assumptions of a moderate growth or no change in primary KA utilization showed similar results in the short-term, independent of the survival profile.

Discussion

The results of the discrete-event simulation model used in this study show that an increase in the need for revision is expected both in the short-term and in the long-term. Variations in these increases were found according to prosthesis survival and projections for primary KA utilization. Our scenarios showed increases in the number of revisions between 8.3% and 31.6% in the short-term and between 38.3% and 176.9% in the long-term. When translating the number of surgeries to operating room time, we found that the necessary increases varied between 0.6% and 22.9% in the short-term and between 5.6% and 102.8% in the long-term.

The simulation results demonstrated that prosthesis survival had a greater effect on demand for revision KA than the proposed scenarios for future increases in primary KA utilization. Consequently, our recommendation is that public health care policies should focus on improving prosthesis survival. In this regard, arthroplasty registries play a critical role in improving the outcomes of joint replacement surgery, by comparing the effect of multiple factors on these outcomes. Through continuous monitoring, they are also sensitive to the impact of changing practice. The Spanish health system does not have a national arthroplasty registry and few data are available on the survival of knee prostheses. Some registries, however, have been created by the regional scientific societies with the support of local health systems [26]. The first example (started in 2005) is the RACat [27], the data of which were used in this study to estimate prosthesis survival.

The impact of future demand for revision KA on demand for operating room time requires a relatively manageable increase in resources in the short-term (a maximum of 23% in operating room occupancy time). The long-term impact, however, is much greater (98.2% increase). In a context of economic constraints and limited availability of resources, meeting the increased demand for revision surgery without a corresponding increase in resources implies a decrease in the number of primary KA surgeries or enhanced operating room productivity. Nevertheless, it should be noted that rates of primary (and revision) KA in Spain are much lower than in other European and developed countries [34]. The projections presented in this study are similar to those estimated for primary KA in Sweden [15] using a model with upper asymptote [16]. The studies in the United States present substantially higher increases in the number of primary arthroplasties [3,14] and revisions [3], the latter using a Poisson model for projection of historical data. None of the published studies used prosthesis survival for prediction of future revisions.

This study makes a number of assumptions and has some limitations. First, age, sex, and type of arthroplasty were used to predict the risk of revision KA, although other studies have revealed that the risk of revision is also associated with other variables, including race, body mass index, diabetic status, bilateral procedures, and high-flex implants. A systematic review of epidemiological studies of total KA and total hip arthroplasty noted disparities in the KA utilization rates on the basis of ethnicity, sex, and region [35]. At present, RACat is being used to explore other predictors such as surgical risk or specific medication use. Moreover, geographical variations in the rates of KA surgery have been observed that cannot be explained by epidemiological differences. This finding was not taken into account in our study because we were interested in forecasting the overall demand for KA.

Second, this study did not include private sector activity. Our study was focused on demand in the Spanish National Health System, which provides universal coverage and access to KA without co-payment. Around 13.3% of the inhabitants of Spain have double health care coverage (public and private) [17].

A third limitation is that our model did not include regional variability, although moderate regional variability has been reported in the rate of both primary and revision KAs in Spain [6,7,36,37]. Moreover, the model assumes no changes in the indication threshold for surgery.

Another limitation is that using a linear model for both prediction of the number of primary KAs in the scenario of high utilization and the proportion of women may lead to unfeasible

Table 3 – Results of the prediction of future KA utilization for each simulation scenario combining future primary KA utilization and prosthesis survival.

Outcome	Scenario 1 and survival B			Scenario 1 and survival W		
	2011	2015	2030	2011	2015	2030
Number of procedures						
Primary KA	38,038	37,654	37,655	37,252	36,868	36,869
Revision KA	5,139	5,567	7,108	5,266	6,552	10,572
95% CI	5,132–5,146	5,560–5,574	7,100–7,116	5,258–5,274	6,545–6,559	10,563– 10,581
Total procedures	43,177	43,221	44,763	42,518	43,420	47,441
% Revision KA	11.9	12.9	15.9	12.4	15.1	22.3
Percentage change from 2011						
Primary KA	0.0	−1.0	−1.0	0.0	−1.0	−1.0
Revision KA	0.0	8.3	38.3	0.0	24.4	100.8
Total procedures	0.0	0.1	3.7	0.0	2.1	11.6
Operating room time demand						
Total time (h/y)*	91,493	92,009	96,634	90,302	93,392	105,454
Percentage change from 2011	0.0	0.6	5.6	0.0	3.4	16.8
	Scenario 2 and survival B			Scenario 2 and survival W		
	2011	2015	2030	2011	2015	2030
Number of procedures/y						
Primary KA	37,252	38,520	49,514	37,252	38,520	49,514
Revision KA	5,139	5,721	7,764	5,232	6,585	12,028
95% CI	5,132–5,146	5,714–5,728	7,756–7,772	5,224–5,240	6,578–6,592	12,019– 12,037
Total procedures	42,391	44,241	57,278	42,484	45,105	61,542
% Revision KA	12.1	12.9	13.6	12.3	14.6	19.5
Percentage change from 2011						
Primary KA	0.0	3.4	32.9	0.0	3.4	32.9
Revision KA	0.0	11.3	51.1	0.0	25.9	129.9
Total procedures	0.0	4.4	35.1	0.0	6.2	44.9
Operating room time demand						
Total time (h/y)*	89,921	94,203	122,320	90,200	96,795	135,112
Percentage change from 2011	0.0	4.8	36.0	0.0	7.3	49.8
	Scenario 3 and survival B			Scenario 3 and survival W		
	2011	2015	2030	2011	2015	2030
Number of procedures/y						
Primary KA	37,252	45,084	69,710	37,252	45,084	69,710
Revision KA	5,139	5,852	8,923	5,232	6,884	14,488
95% CI	5,132–5,146	5,845–5,859	8,915–8,931	5,224–5,240	6,877–6,891	14,479– 14,497
Total procedures	42,391	50,936	78,633	42,484	51,968	84,198
% Revision KA	12.1	11.5	11.3	12.3	13.2	17.2
Percentage change from 2011						
Primary KA	0.0	21.0	87.1	0.0	21.0	87.1
Revision KA	0.0	13.9	73.6	0.0	31.6	176.9
Total procedures	0.0	20.2	85.5	0.0	22.3	98.2
Operating room time demand						
Total time (h/y)*	89,921	107,724	166,189	90,200	110,820	182,884
Percentage change from 2011	0.0	19.8	84.8	0.0	22.9	102.8

CI, confidence interval; KA, knee arthroplasty.

* Time demand calculated considering 2 h per primary KA and 3 h per revision KA. Scenarios of primary KA utilization: 1, low; 2, moderate; 3, high. Scenarios of prosthesis survival: W, worse, B, better.

inputs beyond our simulation horizon. Nevertheless, within our 20-year simulation horizon, the numbers used are comparable to real data from other countries and, thus, were considered as valid.

Finally, as we were interested in estimating the burden of revision KA for planning purposes, an analysis of waiting list times or incidence of KA was out of the scope of our study. An analysis of a waiting list at the level of the Spanish National Health System would not be applicable not only because health competences are transferred to the autonomous communities but also because a warranty time of 6 months applies to all KAs. Moreover, because re-revisions were not considered, our results on the number of revision KAs may be underestimated.

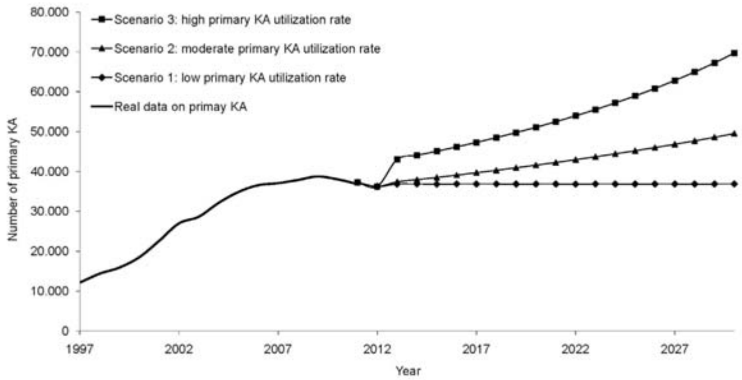

Fig. 4 – Real data on the number of primary knee arthroplasties and simulation results according to simulation scenarios, periods 1997–2011 and 2011–2030, respectively. KA, Knee Arthroplasty.

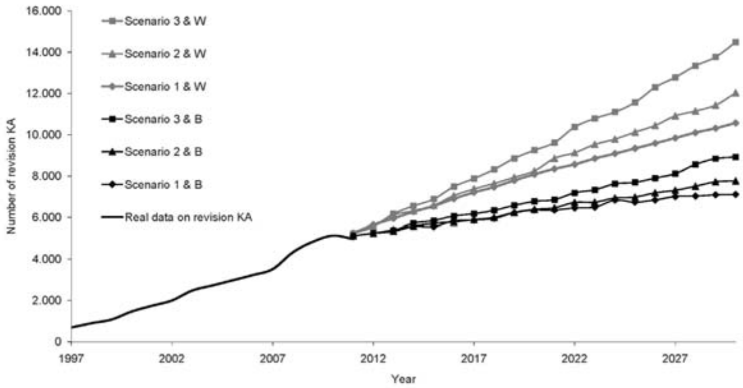

Fig. 5 – Real data on number of revision knee arthroplasties and simulation results according to simulation scenarios, periods 1997–2011 and 2011–2031, respectively. KA, Knee Arthroplasty. Scenarios of primary KA utilization: 1) low, 2) moderate, 3) high. Scenarios of prosthesis survival: W) Worse, B) Better.

To our knowledge, our study is the first to use simulation to predict the future burden of KA according to prosthesis survival and its impact on the demand for revision KA.

Conclusions

The simulation results demonstrated that the most important factor in the analysis is the effect of the prosthesis survival function. The required increase in resources will be relatively manageable in the short-term (a maximum of 23% in operating room occupancy time), but will be much greater in the long-term. Given the present economic constraints with no prospects for resource expansion, meeting the greater revision rate will entail reducing short- and long-term primary arthroplasties by about 1%. This trend has been observed since 2010.

Projections of the burden of revision KA require a quantitative basis for future policy decisions relating to the concentration of high-complexity procedures, the number of orthopedic surgeons required to perform these procedures, and the number of resources needed. This is important in Spain, given that the Spanish health system is publicly funded and that demand for KA is managed through waiting lists. Moreover, the methodology used in the present study will allow systematic evaluation and revision of projections for orthopedic surgery through regular updates in the coming years.

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Supplementary Materials

Supplemental material accompanying this article can be found in the online version as a hyperlink at http://dx.doi.org/10.1016/j.jval.2016.02.018 or, if a hard copy of article, at www.valueinhealthjournal.com/issues (select volume, issue, and article).

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