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Modeling the Cost-Effectiveness for Cement-Less and Hybrid Prosthesis in Total Hip Replacement in Emilia Romagna, Italy

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Background. **The aim of the present study was to assess the cost-effectiveness of cement-less *versus* hybrid prostheses in total hip replacement (THR) in patients diagnosed with primary osteoarthritis.**

Methods. **Effectiveness data were obtained from the Emilia-Romagna Regional Registry on Orthopaedic Prosthesis (RIPO), which collects information on all orthopaedic intervention performed in Emilia-Romagna (41,199 total hip replacements performed from 2000 to 2007), and from which we obtained survival curves and transition probabilities for the cement-less and hybrid prostheses, respectively. Conversely, costs were derived from regional databases through a specific procedure, which allowed us to register individual component's costs for both primary and subsequent revision interventions. A specific Markov transition model was constructed in order to consider the 3 types of revisions that an implant could possibly undergo through its life-span: total, cup or stem, head insert or neck. The cost-effectiveness was expressed in terms of cost per "revision-free" life year.**

Results and conclusions. **Considering a 70-y old patient undergoing THR, the cementless strategy resulted more effective but more costly than the hybrid solution, with an incremental cost effectiveness ratio of 2401.63 € per revision-free life year. Following a deterministic sensitivity analysis, hybrid and cementless fixation showed, respectively, a dominance profile for patients older than 83 y and younger than 43 y, whereas for all ages in between, we report a progressive increase in the ICER of cementless prostheses. Our results proved to be robust, as underlined by the probabilistic sensitivity analysis performed using cost distributions.**

Key Words: **total hip replacement; cost effectiveness analysis; Markov model; sensitivity analysis; economic evaluation.**

INTRODUCTION

The successful history of total hip replacement (THR) has been well documented and recently described as "the operation of the century" [1]. Over the past decades, it has been established as a successful surgical intervention, with an excellent risk/benefit profile, delivering superb clinical results. Additionally, it has been proven to have a favorable cost-effectiveness profile, comparable to other commonly accepted procedures and, thus, providing "value for money" [2]. Nevertheless, despite its unquestionable positive impact on patient's clinical status, a number of factors keep total hip replacement surgery constantly under the spotlight.

On one hand, it has become one of the most frequent causes of hospital admission for elective surgery, and its demand is projected to increase in the future: driven by the progressive shift towards an older population, characterized by a higher prevalence for arthritic disease [3]. On the other hand, in recent years, the mean age for primary intervention has shifted towards much younger ages [4]. Finally, implants tend to wear

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TABLE 1

Hip Replacement: National and Regional Overview (2000–2005)

ICD9-CM code	Description	2000	2001	2002	2003	2004	2005
8151	Total substitution	44,001	45,431	48,531	51,448	54,668	55,868
		4,285	4,563	4,634	5,028	5,347	5,536
8152	Partial substitution	20,263	20,643	21,328	21,030	21,658	22,464
		1,756	2,124	1,936	2,021	2,233	2,280
8153	Revision	5,421	5,517	5,918	5,951	6,120	6,400
		720	852	866	855	851	822
Total		69,685	71,591	75,777	78,429	82,446	84,732
		6,761	7,539	7,436	7,904	8,431	8,638

(Source: Italian Ministry of Health and RIPO).

out with time and they need to be replaced through revision surgery.

Still, the evaluation of the clinical impact of THR has proven to be extremely hard to tackle, leaving unanswered questions about efficacy, safety, and durability. This places the technology among those less prone to be assessed through RCTs, since the effects of the innovative prostheses are measurable, if present at all, only after a long follow-up period. Despite a slight increase in the number of reports in the past few years, studies still remain poorly designed and offer limited information, mainly due to insufficient follow-up and the small population enrolled [5].

The scarcity of pharmaco-economic studies is a result of the paucity of efficacy data, even if, undoubtedly, the number of research publications devoted to economically related topics in THR has increased over the years [6]. However, some studies are not full economic evaluations, whereas others have adopted a cost-minimization template [7]. Meanwhile, the focus has progressively shifted to other aspects, such as alternative bearing surfaces, metal-on-metal resurfacing [8], antimicrobial prophylaxis [9], bone grafting [10], and minimal incision surgery [11]. However, the core issue of which fixation technique is the most suitable for a given patient is still much debated, leaving both clinicians and policy makers to deal with much uncertainty [7].

In order to fill this gap of knowledge, researchers have positively advocated an alternative source of information such as specialized patients registries [12].

In 1990, the Rizzoli institute, a mono-specialty research hospital, established its own registry with the specific aim of monitoring all hip and knee substitutions, as a tool for internal clinical audit [13]. This experience has been later extended to the whole Emilia Romagna region, including 47 public and 24 private orthopedics units, through the institution of the Register of Orthopedic Prosthetic Implants (RIPO): 46,709 interventions, equal to 10.1% of all cases treated in Italy, from 2000 to 2005 (Table 1). A recently published report highlighted the success of this initiative and the high quality of data generated [14].

In the present study, we developed a Markov model supported by empirical information drawn from RIPO in order to evaluate the cost-effectiveness of different fixation techniques (cementless *versus* hybrid, respectively, 69.2% and 17.8% of all prostheses fitted in patients with primary coxarthrosis) and to explore to what extent the results could be affected by factors such as patient age, implant cost, and revision rate.

MATERIAL AND METHODS

Model Structure

Health states, transition probabilities, and corresponding cost/outcomes associated with each state are the key components of a Markov model. The model tracks patients in their transitions among the different health states in which they spend a certain amount of time, defined by the cycle length [15]. Briefly, the model adopts a lifetime perspective and encompasses nine possible health states (Fig.1): the entry point of the model is the "THR implanted" state. Subsequently, patients might not experience any problem or might require a second surgical intervention, due to first implant failure. In case of revision, it was assumed that patients could transit through one of three possible states corresponding to the different types of revisions: total (all components), partial (cup or stem), or minor (head, insert and/or neck). Hence, compared with previous analyses, the present model

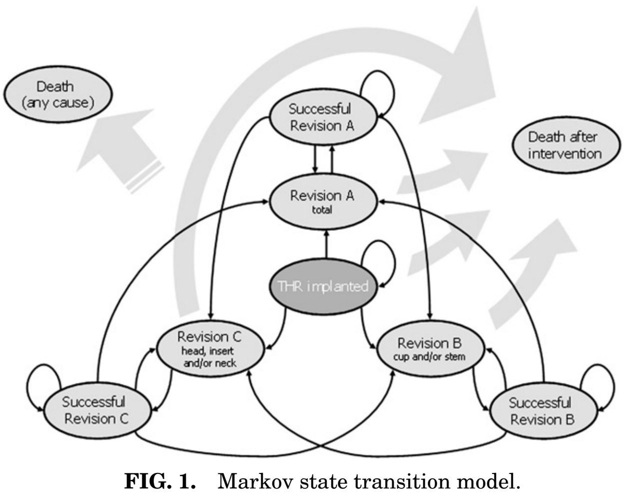

FIG. 1. Markov state transition model.

TABLE 2

Transition Probabilities Between the Markov States of the Model

Transition	Probability (*100)	
	Cementless	Hybrid
THR implanted -> revision A	From survival curves*	From survival curves*
THR implanted -> revision B		
THR implanted -> revision C		
revision A -> successful revision A	If not dead after intervention or dead for any other cause	If not dead after intervention or dead for any other cause
revision B -> successful revision B		
revision C -> successful revision C		
Successful revision A -> revision A	9.09091	
Successful revision A -> revision B	9.09091	
Successful revision A -> revision C	0.00000	
Successful revision B -> revision A	1.70940	
Successful revision B -> revision B	5.12821	
Successful revision B -> revision C	2.56410	
Successful revision C -> revision A	0.00000	
Successful revision C -> revision B	4.54545	
Successful revision C -> revision C	0.00000	
THR implanted -> death after intervention	0.07500	0.19743
Revision A -> death after intervention	0.71556	
Revision B -> death after intervention	0.35308	
Revision C -> death after intervention	0.58140	
all states -> death (any cause)	From Emilia-Romagna mortality tables	

All transition probabilities in the model are calculated from the tabulated ones conditioned on survival.

*$Pt = (S(t)-S(t+1))/S(t)$

distinguishes among the different kinds of revisions, which necessarily imply different costs. After the occurrence of revision, patients move into a state of successful revision, where they may remain until death or they potentially undergo a further revision event. In the former case, age-adjusted probabilities were extracted from available statistics on the Emilia-Romagna population, whereas in the latter case, they were directly derived from RIPO statistics [16, 17]. As a cycle length of 1 y was chosen, for consistency, transition probabilities between states were all expressed as 1-y probabilities, as shown in Table 2.

A yearly discount rate of 3.5% was applied in order to compute the present value of future costs and outcomes [18]. The model was developed using Treeage DataPro (TreeAge Software Inc, Williamstown, MA) whereas all statistical analysis were performed with Stata10 (StataCorp LP, College Station, TX).

Efficacy Data

The likelihood of primary implant failure and subsequent revision probabilities was estimated using data from the RIPO for all patients with a diagnosis of osteoarthritis (OA) and undergoing a THR during the period 2000–2004; this allowed to obtain specific survival curves (related to the three type of failure considered) based on a total of 10,667 cementless and 3039 hybrid prostheses implanted: in the 5 y of follow-up considered, the total numbers of failures observed were 161 (cementless) and 33 (hybrid) with an average age at first implant of 70.9 and 66.4 years, respectively (Log rank test for survival $P = 0.024$, Table 3).

However, since the model requires a time horizon longer than the 5 y, data have been integrated with the datasets of the Rizzoli Hospital (7120 cementless, 2811 hybrid first implants, with 316 and 113

TABLE 3

No. of Primary Interventions and Revisions by Type: Log Rank Tests (Mantel Cox)

	Primary interventions	No. of revisions			
		Any	Type A	Type B	Type C
RIPO (5y follow-up)					
Hybrid	3,039	33	3	17	13
Cementless	10,667	161	30	100	31
Chi-sq		5.094	4.11	5.832	0.959
"P"		0.024	0.043	0.016	0.328
Rizzoli Hospital (13y follow-up)					
Hybrid	2,811	113	26	68	19
Cementless	7,120	316	78	199	39
Chi-sq		0.364	0.329	0.576	0.546
"P"		0.546	0.566	0.448	0.46

failures, respectively, in the 13 y period of follow-up, see Table 3). In order to extrapolate the survival curves we fitted a range of parametric survival models:

$$S(t) = \left(1 + \frac{t^2}{\beta^2}\right)^{-\alpha}$$

estimating couples of values for α and β, which adapted better to the empirical data. For this purpose, weighted least squares were used, with weights equal to the inverse of the variance of the punctual estimates. It should be noted that we assumed failure and revision probabilities as age-independent.

Costs

The analysis adopts the provider perspective and is focused primarily on the acquisition cost of each modular components, with the exception of hybrid prostheses, for which the following supplementary cost have been considered: two bags of cement, vacuum-mixing system, wash and drying system, two caps, and the differential cost due to the longer utilization of the operating theatre. All other costs have been assumed identical and therefore were not computed.

The RIPO does not routinely collect any cost data, but nevertheless was very helpful in identifying key information, such as manufacturer, batch, model that provide an unique ID. The single component ID was then linked to the administrative database, in order to extract single component costs. The same approach has been adopted to quantify both the costs of primary and revision implants. The mean cost values obtained were the following: for primary hybrid € 3149.50 (estimated on 392 implants) and € 3449.01 (3459) for cementless prostheses, with a relatively higher degree of variation for the former (Table 4). As for revisions, mean costs values were € 3113.05 for total revision, € 1283.21 for a type B (cup and/or stem) and € 400.04 for type C (head, insert and/or neck) revision, respectively.

To take into account the asymmetric costs distribution (as shown by the statistically significant Shapiro Wilk test for normal distribution), we applied the bootstrap method and estimated the standard errors to evaluate the confidence intervals (95%) around the mean, under the assumptions of a normal distribution (through the central limit theorem). These have been then used for the probabilistic sensitivity analysis.

RESULTS

The base-case analysis considers a 70-y-old patient undergoing THR and reflects the mean age of the RIPO population (which is currently 68.9). Considering two cohorts of 1000 subjects, 243 revisions are expected to take place in the cementless cohort *versus* 300 in the hybrid one, equal to 19% difference and with a number needed to treat (NNT) of 18. In further detail, the cementless intervention appeared to be associated with more type A (+9%) and type C (+12%) revisions, whereas the opposite was observed for type B revisions, which were instead much more frequent for the hybrid-implanted cohort (+53%). Consequently, a cementless primary implant would be expected to survive 11.15 y, in the absence of any complication *versus* the 11.04 y provided by the hybrid primary intervention. Since more revisions translate to a higher risk to die due to complications, we also witnessed a different postoperative mortality among the two strategies: 1.9‰ for the

TABLE 4

Costs Associated with Interventions (Primary and Revisions)

Procedure	N	Mean	Min	Max	Median	St. Dev	Normality Shapiro-Wilk test		St. error (bootstrap)	95%CI (bias corrected)	
							z	P			
Primary intervention											
Hybrid	392	3,149.50	1,852.52	5,474.93	2,948.94	542.37	10.05	<0.00001	27.41	3,097.02	3,203.85
Cementless	3,459	3,449.01	1,587.76	7,571.78	3,468.09	494.77	12.70	<0.00001	8.38	3,432.84	3,465.45
Revision											
A	164	3,113.05	1,560.76	6,201.61	2,945.50	934.23	5.22	<0.00001	69.95	2,976.90	3,251.55
B	660	1,283.21	324.31	4,094.06	1,173.04	669.40	9.35	<0.00001	26.19	1,231.51	1,338.55
C	59	400.04	120.33	1,205.41	426.00	197.55	3.64	0.00014	25.09	356.29	457.17

cementless and 3.2‰ for the hybrid cohort, respectively.

However, the better efficacy of the cementless in comparison with the hybrid prosthesis comes with a higher cost: the average lifetime costs of the former strategy would be € 3732.60 *versus* € 3457.81. When the difference in effectiveness is put in relation to the difference in lifetime costs, the resulting incremental cost effectiveness ratio is equal to € 2402 per revision-free life year.

Sensitivity analysis is a powerful tool to handle the intrinsic uncertainty related to the model adopted and the data used, to identify driving variables and to show to which extent initial assumptions might influence the results obtained in the base-case scenario [19].

Patient's age at first implant was challenged by performing cohort simulations at various THR ages and, consequently, by recalculating mean costs, outcomes, and ICERs (Table 5). The cementless strategy proved as dominant (i.e., less costly and, at the same time, more beneficial compared with the hybrid solution) for patients up to 42-y-old. From 43-y-old onwards, it still remains more effective but with an additional cost: the resulting incremental cost-effectiveness ratios show a direct proportionality to age increase (at 77-y-old the ICER is € 15,658, at 78-y-old € 23,855, and finally at 79-y-old i€ 40,604). From 80-y-old onwards, the value of ICER would be so high that cementless prosthesis is not worth the major initial costs. Finally, from 83 y the cementless strategy is dominated, since the hybrid fixation strategy is now able to deliver a major number of revision-free years at minor costs.

We assessed as well the impact of uncertainty over costs: we ran 10,000 trials estimating the costs from the empirical distributions of primary and revision interventions. The cost effectiveness acceptability curve (Fig. 2) substantiates the cementless intervention as a strategy with a high probability of being cost effective at 70 y from values of willingness to pay above € 2400: for instance, adopting an arbitrary ceiling value of € 2700, the probability of cementless being cost effective is 0.88. Conversely, in case of a 75-y-old patient and a value of WTP of € 9000, a cementless approach results cost effective with a probability of 0.89.

DISCUSSION

In 1998 Fitzpatrick conducted a systematic review, which highlighted the "*striking paucity of clear and relevant evidence on which to make well-informed choices about prostheses for primary THR*" [5]. Nowadays, there is the desperate need to constantly update or eventually to set more rigorous standards. The potential risk is to witness to an increase in costs not proportionate to the additional benefits [20].

RIPO provided solid effectiveness data and despite not being part of its core mission, has allowed us to obtain the acquisition cost of individual components. In the base case scenario, cementless prosthesis had an incremental cost effectiveness ratio of 2401.63 €/revision-free life year.

Compared with a recent study, our model was able to distinguish different kinds of revisions, which might have a totally different impact on costs (minimum € 400.04; maximum € 3113.05) and allowed multiple revision events for each patient [21]. For this latter reason, our analysis might eventually overestimate the total number of revisions, due to the fact that, regardless of the patient's age, the model does not discriminate between a "wait and see" strategy

TABLE 5

Cost Effectiveness Results from the Model

Age at THR	Cementless			Hybrid			ICER (€)
	Costs (€)	Revision free life years	Costs (€) per life year gained	Costs (€)	Revision free life years	Costs (€) per life year gained	
30	4,422	20.1907	219	4,548	17.9767	253	Cementless dominates
35	4,357	19.5934	222	4,436	17.678	251	Cementless dominates
40	4,285	18.8757	227	4,312	17.2743	250	Cementless dominates
45	4,203	18.0053	233	4,175	16.7234	250	22
50	4,116	16.9847	242	4,029	16.0126	252	89
55	4,022	15.7997	255	3,879	15.1128	257	208
60	3,925	14.4528	272	3,730	14.0109	266	442
65	3,827	12.8877	297	3,586	12.6394	284	968
70	3,733	11.1579	335	3,458	11.0435	313	2,402
75	3,648	9.3119	392	3,351	9.275	361	8,028
80	3,579	7.5139	476	3,271	7.5104	436	87,839
85	3,526	5.7072	618	3,216	5.712	563	Hybrid dominates
90	3,494	4.4073	793	3,185	4.4106	722	Hybrid dominates

Mean costs for strategy and revision free life years gained, cost effectiveness ratio and ICER for age at first implant.

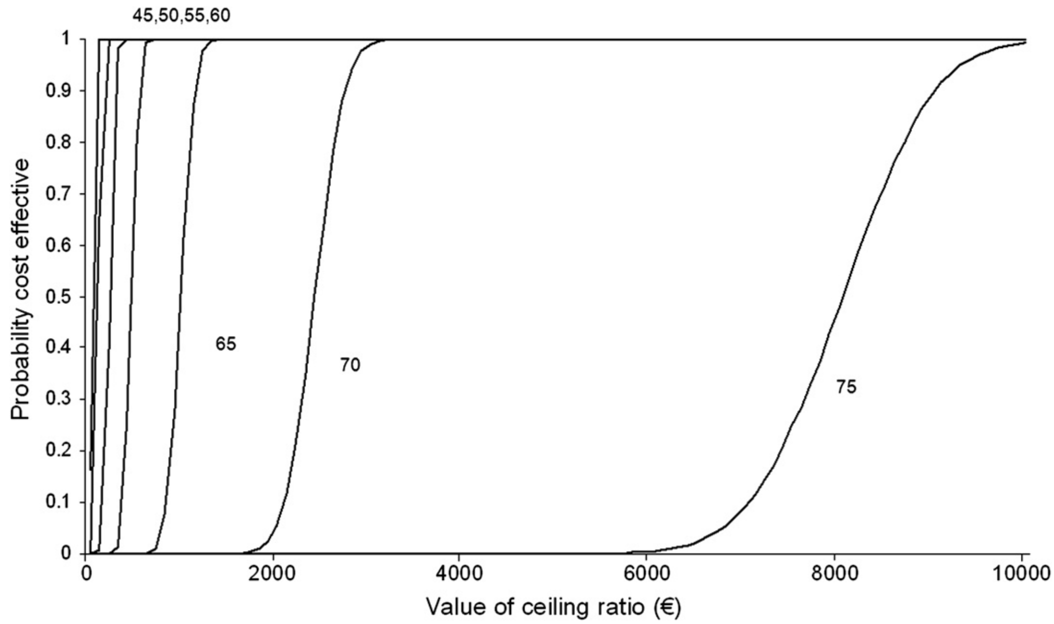

FIG. 2. Cost effectiveness acceptability curves for different ages at THR.

and a surgical intervention, but is always opting for the latter.

Likewise, we should acknowledge that the present analysis is not free from limitations. First of all, instead of OA-specific mortality rates, we used standard age-adjusted population statistics, which might result in a prolonged exposure to the risk to undergo revision surgery.

Secondly, the outcome chosen for the analysis is a reasonable end-point, in line with the survival analysis performed by other registries, and a measure that includes both the chance to undergo revision and to die due to surgical or natural causes. Nevertheless, it does not fully capture patients' preferences and is not easily comparable with other healthcare interventions. Both shortcomings could be overcome by adopting the cost per quality adjusted life year (QALY), which remains the gold standard in health economics. Thirdly, we have restricted the scope of our analysis to the cost of the prosthesis, which is one of the main drivers of total costs [22]. Future analysis must include other costs, such as hospitalization and rehabilitation, in order to estimate the full production cost. Cost analysis should include indirect costs as well, thus shifting the study's perspective from the provider to the whole society. In fact, younger patients are more likely to experience productivity loss, whereas elderly patients might need the assistance of family members or professional caregivers.

Revision not only implies the removal of the old implant and the fitting of a new one but could be more resource consuming and might not guarantee a good functional result. Unfortunately, at present, our simulation was not able to catch either of these aspects and, consequently, our results might be interpreted as conservative: cementless implants might be dominant and cost effective for patients older than 40 and 79 y, respectively.

Our results are in line with the current practice of using cementless prostheses; in fact there is an increasing trend in implant cementless types, i.e., the cementless/hybrid proportion, which was 0.72 in 2000, has increased to 0.91 in 2007 in Emilia Romagna. Moreover, cementless prostheses are preferred in younger patients since they are more likely to outlive their implant and undergo at least one revision procedure during their lifetime; from the RIPO database the proportion of cementless prostheses decreases from 96% in 45–55 y-old patients to 69% in the 75–85 age group. This trend seems to be in agreement with the cost effectiveness profiles suggested by our analysis.

Finally, our study might provide some valuable insights for budget holders in order to quantify, through a budget impact analysis, the additional costs required to guarantee the most cost-effective strategy to the population.

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