Dependency issues in survival analyses of 55 782 primary hip replacements from 47 355 patients

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Summary

Artificial hip joints are used in only one hip for 85 % of the patients and in both hips (bilateral) for 15 %. The occurrence of bilateral prostheses and the influence they have in survival analyses of joint arthroplasties are seldom considered. In this study we therefore focus on issues related to bilateral hip prostheses and time to revision surgery.

We used information from 47 355 patients with 55 782 primary hip prostheses reported to the Norwegian Arthroplasty Register between 1987 and 2000. Due to the large number of diagnoses, fixation techniques for the prostheses, and combination of prostheses brands, we furthermore considered a "homogeneous" subset of 9 703 prostheses from 7 930 patients with primary osteoarthritis, and Charnley prosthesis fixed with antibiotic-containing Palacos cement.

Kaplan-Meier curves for all prostheses, ignoring that some patients have bilateral prostheses, were compared with Kaplan-Meier curves using only the first inserted prostheses, and with survival curves accounting for bilateral prostheses.

Cox regression analyses were used to assess explanatory variables and to adjust for confounding factors. The results from the ordinary Cox regression analyses were compared with results from a marginal model, a shared gamma frailty model, and a model using a time dependent covariate to condition on failures in the opposite hip.

We found no practical difference between the three calculated survival curves for the hip replacement data. The ordinary Cox-model and the marginal model gave equivalent results. In the shared gamma frailty model estimates for the risk factors were comparable with the former two approaches. The estimated frailty variance was high when all data were used, even after adjustment for confounding factors. For the "homogeneous" data the estimated frailty variance was negligible. Using a time dependent covariate to condition on previous revisions in the opposite hip, we found a high risk of revision for the remaining hip if the opposite hip had been revised (RR=3.51, $p<0.0001$).

There was no difference in risk for revision between right and left hip prostheses. If the time interval between the two primary operations was more than two years, for the full data, the first hip prosthesis had an increased risk of revision compared to prostheses in patients with only one prosthesis (RR=1.26, $p=0.0066$). While for the "homogeneous" data no statistically significant difference was found between unilateral and bilateral prostheses.

In analyses of survival and assessment of standard risk factors, dependence between two hip prostheses from one patient may be ignored. However, revision in the opposite hip is a risk factor itself and can be used as a predictor for the survival of the index hip.

1. Introduction

Survival analysis is a standard tool for analyzing time to failure for joint arthroplasties [1, 2]. The common approach is to use each hip as the unit of observation and ignore that more than 20 % of the hip prostheses are bilateral. However, to use hip as the unit in the analyses and ignore that some hip replacements are clustered within patients may be problematic [3].

In 1993 Havelin et al. [4] showed that Femora prosthesis inserted in the right hip had poorer results than Femora prostheses inserted in the left hip. This was due to the design of the prosthesis with right-handed threads, both for left and right hip prosthesis. A possible difference between time to failure of the right and left prosthesis is the first issue related to the topic of bilateral prostheses. Secondly, prostheses in bilaterally operated patients may have a different time to failure than prostheses in unilateral operated patients. This difference may also depend on the time interval between insertion of prostheses in the two hips. Third and most complicated, there may be dependencies in time to failure between two prostheses in the same patient. In this context dependency can be understood as a potential change in risk of revision (failure), for the index hip, conditioned on a revision in the opposite hip.

Some studies have discussed bilateral hip prostheses in analysis of time to failure for the prostheses [2, 3, 5, 6]. Ripatti and Palmgren [7] looked at more flexible multivariate frailty models using penalized partial likelihood and used data on total hip replacements to exemplify their results. Schwarzer et al. also used a shared gamma frailty model to model bilateral dependencies for primary hip prostheses data [8]. Dependencies between bilateral hip prostheses have also been discussed in the orthopaedic literature as a problem to consider when survival of hip prostheses is studied [3]. Some studies have selected one prosthesis from each patient to avoid possible problems with bilateral prostheses. This is a simple approach, which easily can be compared with results from the analyses using the complete data [9]. The reason why so few studies on bilateral hip prostheses have been undertaken, may be that statistical tools for dependent survival observations are somewhat complex and have not been implemented in standard statistical program packages.

In this paper we use several approaches to study the issue of bilateral hip prostheses. First ordinary Kaplan-Meier survival curves are used to visualize time between two primary operations for the two hips in the same patient.

Furthermore, analyses of time to failure (revision defined as removing or replacing of the primary prosthesis) for each of the primary prostheses was considered. Ordinary Kaplan-Meier survival curves, using all observations, was compared with Kaplan-Meier curves using only one prosthesis observation from each patient, and thereafter a survival curve for bivariate data accounting for possible heterogeneity among patients.

Ordinary Cox proportional hazards models, ignoring bilateral prostheses, were compared with a marginal model adjusting the parameter variance estimates (and p-values) to account for possible dependencies between two hips from one patient. The analyses were also performed using a shared gamma frailty model. Finally a model using a time dependent covariate to condition on possible events in the opposite hip was considered.

2. Hip replacement patients

All hospitals where total hip replacement surgery is performed in Norway report their operations to the Norwegian Arthroplasty Register [10]. In this study we have included 55 782 primary (first time) total hip replacement operations from 47 355 patients reported to the register between September 1987 and May 2000. Patients who had had their first hip replacement operation before September 1987 and the second primary operation in the opposite hip within the period were excluded (2378 patients). Information regarding the prosthesis operation was collected using a standard questionnaire filled in by the surgeon immediately after the surgery.

Risk factors of main interest for revision surgery were right or left hip and sequence for the prostheses. Sequence for the prostheses were used to distinguish between patients with one and two prostheses and is further explained in section 4 on regression analyses.

Age, gender, diagnosis (reason for hip surgery), year of operation, and quality of the hip prosthesis were considered as potential confounders and used as adjustment variables. Age and year of operation were handled as continuous linear variables, due to the linear relationship with the outcome for these variables. Diagnosis at hip surgery was categorized as primary osteoarthritis, rheumatoid arthritis, fracture of the femoral neck, pediatric hip diseases (dysplastic hips with and without dislocation, Perthes' disease, and patients with slipped capital femoral epiphysis), and the remaining as "other diagnoses" (encompassing 70 different

diagnoses). Hip prostheses were categorized as cemented prostheses with antibiotics in the cement, cemented prostheses without antibiotics, inferior uncemented prostheses, good performing uncemented prostheses, uncemented acetabulum prosthesis and cemented femur prosthesis with antibiotics, and finally uncemented acetabulum prosthesis and cemented femur prosthesis without antibiotics. See Furnes et al. (2001) for a further description.

Revision surgery (defined as removing or replacing of the primary prosthesis) was considered as failure (event) in the analyses. Prostheses with no failure until date of death for the patients, obtained from Statistics Norway, or still intact at the end of study (May 1st 2000) were handled as censored observations. Observation time was measured from the primary (first) operation for each hip. Primary operations in both hips at the same time were reported for 106 patients.

Analyses were first done using data from all patients. Additionally, due to the large number of different diagnoses, fixation techniques for the prostheses, and combinations of prosthesis brands, we analyzed a more homogeneous subset. The large "homogeneous" subset, with well-documented results, includes 7 930 patients (9 703 prostheses) with primary osteoarthritis, Charnely prosthesis, and Palacos cement with antibiotics (gentamycin) in both acetabulum and femur.

3. Survival curves

Time between two primary prostheses operations for the same patient was visualized using ordinary Kaplan-Meier curves. No further analyses are presented for the time between two primary prostheses.

Let T_{ij} be time from the primary operation to revision surgery or till end of follow up for prosthesis j (j = 1 or 2) in patient i (i=1, …, n). Hence $T_{ij}=\min(V_{ij},W_{ij})$ where V_{ij} is time to revision and W_{ij} is time till end of follow-up, or loss to follow-up for other reasons, for prosthesis j in patient i. A revision of prosthesis j in patient i is identified by $D_{ij}=I(V_{ij}\leq W_{ij})$, which is 1 if a revision is observed and 0 otherwise. We observe T_{ij} and D_{ij}.

First, the ordinary Kaplan-Meier method was used to calculate time to revision for all hip prostheses ignoring possible dependence between two prostheses for approximately 15 % of the patients. Secondly ordinary Kaplan-Meier curves based on the first hip prosthesis from

each patient were calculated. Alternatively one hip could be drawn from each patient at random. This approach removes possible dependence between bilateral prostheses, but also reduces the size of the data considerably. Third, an alternative approach using the ideas of Aalen et al. [11] to calculate mean survival accounting for possible heterogeneity was therefore considered.

Let $Y_i(t)$ be the number of prostheses (1 or 2), for patient *i*, with life time greater than, or equal to, *t*. Let $Y_{ij}(t) = 1$ define if prosthesis *j* from patient *i* is at risk at time *t* and 0 otherwise, $Y_{ij}(t) = \mathrm{I}(t \le T_{ij})$. Hence $Y_i(t) = \sum_j Y_{ij}(t)$.

Further, we let $N_i(t)$ be a counting process counting the number of revised prostheses (1 or 2) up till (before) time *t*, for patient *i*. Let *R*(*t*) be the set of patients with at least one prosthesis lasting longer than *t*, and *Y*(*t*) the number of such patients. Then

$$Y(t) = \sum_{\forall i} \mathrm{I}(Y_i(t) > 0). \tag{1}$$

The Kaplan-Meier-like survival curve accounting for possibly heterogeneity of bilateral observations can be written as

$$\hat{S}(t) = \prod_{i \in R(t)} (1 - d\hat{\Lambda}_i(t)). \tag{2}$$

Here $\hat{\Lambda}_i(t)$ is the integrated hazard for individual *i* and is defined as

$$\hat{\Lambda}_i(t) = \int_0^t \frac{1}{Y_i(s)} dN_i(s). \tag{3}$$

If there is only one observation for each individual $\hat{S}(t)$ equals the ordinary Kaplan-Meier estimator.

Pointwise 95 % log transformed confidence limits [11] with a lower limit adjustment for the number of observations at risk [12] are calculated for the survival curves.

4. Regression analyses

To study the effect of explanatory variables on the time to prosthesis revision and to model possible dependence between two prostheses in the same patient, simple proportional hazard models and extensions were considered [13]. The effect of having two prostheses was

represented using a time dependent covariate defining the order for the prosthesis. Let j=1 be the first inserted prosthesis and j=2 the second inserted prosthesis. Let B_i be the time between insertion of the two prostheses (j=1 and 2) for patient i. We observe B_i only if $B_i \leq W_{i1}$. If primary operations on both sides is carried out at the same time then $B_i = 0$. Let $X_{ij}(t)$ be a time dependent covariate defining the sequence for the prosthesis operations for prosthesis j in patient i. We let

$$X_{ij}(t) = \begin{cases} 0 - \text{The patient has only one prosthesis } (j=1),\ t \leq B_i \\ 1 - \text{1st prosthesis } (j=1), \text{ the patient obtained two prostheses within two years, } B_i \leq 2,\ B_i \leq t \\ 2 - \text{1st prosthesis } (j=1), \text{ the patient obtained two prostheses beyond two years, } 2 < B_i \leq t \\ 3 - \text{2nd prosthesis } (j=2), \text{ the patient obtained two prostheses within two years, } B_i \leq 2 \\ 4 - \text{2nd prosthesis } (j=2), \text{ the patient obtained two prostheses beyond two years, } 2 < B_i \end{cases} \quad (4)$$

A patient is hence considered to have only one prosthesis until a second prosthesis is inserted in the opposite hip. We distinguish between prostheses where the time interval between two primary operations (for patient i) is more or less than two years.

First an ordinary Cox proportional hazard model with only the time dependent variable, ignoring other known explanatory variables was considered.

$$\lambda_{ij}(t) = \lambda_0(t) \cdot e^{\beta \cdot x_{ij}(t)}. \quad (5)$$

Were $\lambda_{ij}(t)$ is the hazard for prosthesis j in patient i and $\lambda_0(t)$ is the common baseline hazard function for all observations. A simple model including only side of the body as the explanatory variable was also considered. Furthermore a model including adjustment for known important risk factors, described in section 2, was applied.

To adjust the variance estimates for possible correlation between two hip prostheses from the same patient, the same set of analyses was considered using a marginal model. The marginal model first calculates the parameters in the standard proportional model ignoring possible dependence and thereafter calculates robust variance estimates to account for possible dependence [13-15].

A proportional hazard frailty model (shared gamma frailty) to estimate and adjust for possible dependence between bilateral prostheses was thereafter considered. The proportional hazard frailty model including only the time dependent covariate is

$$\lambda_{ij}(t) = \lambda_0(t) \cdot \nu_i \cdot e^{\beta x_{ij}(t)}. \quad (6)$$

In this model v is the frailty variable, which follows a gamma distribution, with mean equal to 1. This model assumes that each patient, *i*, has its own frailty influencing the risk for revision for all observations from the patient. Two hips in one patient share therefore the same frailty, hence the term "shared frailty". The frailty model can be rewritten in terms of a random effect model,

$$l_{ij}(t) = l_0(t) \cdot e^{ßx_{ij}(t) + wZ_i} . \quad (7)$$

Where *w* are distributed as log of a gamma distribution, with mean equal to 0 and variance equal to *q* and Z_i identifies patient *i*. Estimation and testing of the frailty variance was performed using penalized partial likelihood estimation methods, as described by Therneau and Grambsch [13] and by Ripatti and Palmgren [7]. Testing of the frailty term was performed using a likelihood ratio test [13].

The last alternative we considered was to condition on the failure status of the prosthesis in the opposite hip. If we extend the time dependent covariate (4) it can be used to condition on the status of the opposite hip. The result of the relation between revisions in two hips from the same patient can thus be expressed as a hazard rate ratio.

Let T_{ij}, D_{ij}, and B_i be defined as previous. Let Q_{ij} be the time from the primary operation in hip *j* (the current hip) to a revision in the opposite hip for patient *i*. The extended time dependent covariate can be defined as

$$X_{ij}(t) = \begin{cases} 0 - \text{The patient has only one prosthesis } (j=1), \ t < B_i \\ 1 - \text{1st prosthesis } (j=1), \text{ the patient obtained two prostheses within two years, } B_i \le 2, \ \text{P} \le t \le Q_{ij} \\ 2 - \text{1ste prosthesis } (j=1), \text{ the patient obtained two prostheses beyond two years, } 2 < B_i \le t \le Q_{ij} \\ 3 - \text{2nd prosthesis } (j=2), \text{ the patient obtained two prostheses within two years, } B_i \le 2, \ t \le Q_{ij} \\ 4 - \text{2nd prosthesis } (j=1), \text{ the patient obtained two prostheses beyond two years, } 2 < B_i, \ t \le Q_{ij} \\ 5 - \text{The prosthesis in the opposite hip } (j=1 \text{ or } 2) \text{ has been revised, } Q_{ij} < t \end{cases} . \quad (8)$$

This time-dependent covariate replaces the previous in an ordinary proportional hazards model and hence enables us to condition the result for hip *j* in patient *i* on the status for the opposite hip in the same patient.

Results for the explanatory variables are stated in terms of the relative risk (RR= e^{β}, hazard rate ratio) and p-values less than 0.05 were considered significant.

All analyses were performed using the statistical software package S-Plus (S-Plus 2000 for Windows, MathSoft, Inc., Seattle, Washington, USA) [13].

5. Results

Seventy percent of the prostheses patients were females. Mean age at primary operation was 67 years (SD=11) for females and 70 years (SD=10) for males. Fifty five percent of the primary prostheses operations were in the right hip.

Of the 47 355 patients 6 088 (12.9. %) patients had bilateral hip prostheses (Table 1). Thus 12 176 (21.8 %) prostheses out of 55 782 were bilateral. The Kaplan-Meier curves for time between two primary hip prostheses estimates that within 10 years 23.6 % (95 % CI: 23.1, 24.1) of the patients have bilateral prostheses (Figure 1). Within the first 2 years 11.3 % (95 % CI: 11.0, 11.6) of the patients had the second hip prosthesis, while only 0.8 % had a second prosthesis within the first 120 days. The "homogeneous" subset showed equal patterns for time between two primary prostheses operation.

There was virtual no difference between the three estimated survival curves for time to revision for all patients (Figure 2). The ordinary Kaplan-Meier curve gave a slightly lower revision rate (higher survival) (9.0 % (95 % CI: 8.6, 9.3) revised before 10 years) than the Kaplan-Meier curve for the first inserted prostheses (9.4 % (95 % CI: 9.0, 9.8) revised before 10 years) and the bivariate survival curve (9.3 % (95 % CI: 9.0, 9.7) revised before 10 years) (Figure 2). For the "homogeneous" subset the three survival curves were practically identical (Figure 3).

Regression analyses for the full dataset:

The standard Cox regression analysis showed no statistically significant difference between left or right side prostheses, but there was a slight tendency for lower risk of revision in the left hip (RR=0.94, p=0.074, Table 1). The first prostheses, when two prostheses was present in the patient and the time interval between the two primary operations were more than two years, had a statistically significant higher risk for revision than prostheses in patients with only one prosthesis (RR=1.26, p=0.0066, Table 1).

Adjustment of the variance of $\hat{b}$, for possible dependence between two prostheses from the same patient using the marginal approach gave nearly identical results as the ordinary Cox-model both for side of the body and sequence for the prosthesis.

For the frailty model including only the time dependent variable and no confounders, the frailty variance was estimated to be 3.08 ($p<0.0001$) and for a model including side of the body only, the frailty variance was estimated to be 3.20 ($p<0.0001$). Including the

confounding factors reduced the frailty variance to 1.42 ($p<0.0001$, Table 2), risk estimates and p-values for the explanatory variables changed just slightly compared to the former approaches.

Using the time dependent covariate to condition on possible failures in the opposite hip gave equal risk estimates and p-values for side of the body as previously. In patients with bilateral THR inserted more than 2 years apart, the first prostheses still had a statistically significant increased risk of revision compared to prostheses from unilateral patients (RR=1.25, p=0.010). Additionally the second prostheses had a statistically significant reduced risk for revision compared to prostheses from unilateral patients (RR=0.80, p=0.0027). We found a high risk for revision in the index hip if the opposite hip had been revised (RR=3.51, $p<0.0001$).

Regression analyses for the "homogeneous" dataset:

The ordinary Cox model showed no statistically significant differences for sequence for the prostheses or for side of the body (Table 2). The marginal approach gave similar results. Further, in the frailty model including only the time dependent variable, and not any confounders, the frailty variance was estimated to be 0.342 (p=0.62) and for a model only including side of the body the frailty variance was estimated to be 0.376 (p=0.72). Including the confounding factors the frailty variance reduced to 0.002 (p=0.78, Table 2). Furthermore, the risk estimates and p-values for the explanatory variables did not change compared to the former approaches. Conditioning on failures in the opposite hip had a slight influence on the risk estimates and p-values, yet none were statistically significant. Furthermore, there was an high risk of revision in the index hip if the opposite hip had been revised (RR=2.30, p=0.045, Table 2)

6. Discussion

In this study we have considered several approaches for analyses of event history data with partly paired data from total hip replacement patients. We found that analyses treating all operations as independent observations, ignoring that some patients may have two primary prosthesis operations, generally is an acceptable approach for analyses of these data. If a

patient had a revision in one of the hips this would however influence the risk for a revision in the opposite hip.

There are about 1 million individuals receiving prostheses worldwide per year [16] and a large number of these patients have bilateral prostheses. The aim for collecting data on prosthesis operations is quality control of prosthesis brands and operation methods.

There has been some clinical focus related to patients with two hip prostheses, how these observations may cause bias for the results for the prostheses, how these clustered observations should be handled, and which results these prostheses may have [3, 5, 6]. Some methodological studies have also used data on total hip replacements, either to model more complicated frailty structures for repeated hip replacement operations [7], or to look at the influence of bilateral hip prostheses including consideration of death and reoperation as competing risks [8].

The simplest approach to avoid possible dependency problems with bilateral observations is to select one observation from each patient (either systematic or randomly). This approach may be satisfactory for some situations, but it is not ideal as it may reduce the data substantially. Comparing results from this simple approach with results from the complete data may be a simple way to inspect possible effects of bilateral observations. In this paper we compare Kaplan-Meier curves using these two approaches with survival curves calculated using a simple nonparametric method accounting for multiple observations for each individual. There was practically no difference between the three survival curves for the hip replacement data, neither for all data, nor for the "homogeneous" subset. Other studies have discussed further methods for handling bivariate or multivariate data when nonparametric survival curves are calculated [11, 17, 18].

A standard proportional hazard model including a time dependent covariate for the number of prostheses in each patient and side of the body as explanatory variables was considered. This approach may be appropriate under ordinary circumstances when analysis of primary hip prostheses are done. The argument is based on our findings of no difference between the standard model and a marginal model correcting the variance estimates for correlation between observations from the same individual. Furthermore, the shared gamma frailty model had similar results for the effect estimates for the explanatory variables and their variances, even though the frailty variance was large for the full data set. This indicates

heterogeneity between individuals for the complete data while for the “homogeneous” data including known confounding factors the frailty variance was close to zero. It should be noted that the interpretation of frailties and frailty models is not straightforward [19], particularly not for the proportional hazard model [20]. A parametric model (e.g. a Weibull model) can be an alternative, with an easier interpretation of frailty effects, but the model assumption may be stricter in terms of a parametric baseline hazard.

We claim that for the present situation, the most appealing presentation of the relation of risk for revision between two hip prostheses in the same patient, is modeled using the time dependent covariate, conditioning on possible events in the opposite hip. A further adjustment of the variance estimates in this model can be argued for. We did these analyses for our data with no change in the results.

In this study we found no indication for any large influence on the results, for the explanatory variables, if bilateral hip prostheses were accounted for. One may, on the other hand, not conclude that this is the case for any material on joint arthroplasties.

Using a model including a time dependent covariate to condition on failures in the opposite hip, we found that patients with a revised (failed) prostheses in one hip had an increased risk for revision in the opposite hip. If two hip replacements is present in the patient and the time interval between the two primary operations is larger than two years, it is more likely that the first primary prosthesis is a prosthesis with inferior quality, which has been abandoned the later years. For the “homogeneous” subset, with the same prosthesis type for the whole time period, this effect was not present.

In analyses of standard risk factors, dependence between two hip prostheses from one patient may be ignored. However, revision in the opposite hip is a risk factor itself and can be used as a predictor for the survival of the index hip.

Legends to figures

Figure 1: Percentage of unilateral hip prostheses by years after first hip prosthesis for 47 355 patients. (With 95 % confidence limits).

Figure 2: Kaplan-Meier curve for time to revision surgery (B), Kaplan-Meier curve for the first inserted prosthesis (C), and a survival curve accounting for bilateral prostheses (A) for 47 355 patients (55 782 prostheses).

Figure 3: Kaplan-Meier curve for time to revision surgery (B), Kaplan-Meier curve for the first inserted prosthesis (C), and a survival curve adjusted for bilateral prostheses (A) for a "homogeneous" subset of 7 930 patients (9 703 prostheses) with primary osteoarthritis, Charnley prosthesis, and Palacos cement with antibiotics.

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Table 1: Full data set:
Proportional hazard models for 55 782 primary hip prostheses operations in 47 355 patients with 3 105 revision operations. Standard Cox proportional hazard model is compared with a marginal model (Marginal), a shared gamma frailty model (Frailty), and a conditional model using a time dependent covariate to condition on failures in the opposite hip (Conditional).

			Standard		**Marginal**		**Frailty**		**Conditional**			
	N[a]	E[b]	RR[c]	p	RR[c]	p	RR[c]	p	N[a]	E[b]	RR[c]	p
Only 1 prosthesis	47 964	2 342	1	-	1	-	1	-	47 207	2 232	1	-
1st of 2 within 2 years	5 483	327	1.03	0.63	1.03	0.62	0.99	0.98	5 289	267	0.89	0.091
1st of 2 beyond 2 years	3 091	169	**1.26**	0.0066	**1.26**	0.0069	**1.27**	0.0067	3 091	161	**1.25**	0.010
2nd of 2 within 2 years	5 002	269	0.96	0.48	0.96	0.48	0.96	0.57	5 002	218	**0.80**	0.0027
2nd of 2 beyond 2 years	3 091	105	1.11	0.32	1.11	0.32	1.19	0.11	3 091	98	1.08	0.47
Opposite side is revised									951	129	**3.51**	<0.0001
Right	30 947	1 738	1	-	1	-	1	-	30 947	1 738	1	-
Left	24 835	1 367	0.94	0.074	0.94	0.075	0.93	0.066	24 835	1 367	0.93	0.064
Frailty variance ($\hat{q}$)							**1.42**	<0.0001				

a Number of primary prosthesis operations for each category.
b Number of revisions (events)
c Relative risk (hazard rate ratio)

The analyses were adjusted for age, gender, diagnosis at hip surgery, year of operation, and quality of the hip prosthesis.

Table 2: Homogenous data set:
Proportional hazard models for 8 703 primary hip prostheses operations in 7 930 patients with 253 revision operations. Standard Cox proportional hazard model is compared with a marginal model (Marginal), a shared gamma frailty model (Frailty), and a conditional model using a time dependent covariate to condition in failures on the opposite hip (Conditional).

			Standard		**Marginal**		**Frailty**		**Conditional**			
	N[a]	E[b]	RR[c]	p	RR[c]	p	RR[c]	p	N[a]	E[b]	RR[c]	p
Only 1 prosthesis	7 377	189	1	-	1	-	1	-	7 298	189	1	-
1st of 2 within 2 years	755	19	0.92	0.74	0.92	0.74	0.92	0.74	721	15	0.78	0.36
1st of 2 beyond 2 years	434	10	1.25	0.51	1.25	0.50	1.25	0.51	434	10	1.30	0.43
2nd of 2 within 2 years	738	21	1.00	0.99	1.00	0.99	1.00	0.99	738	19	0.93	0.78
2nd of 2 beyond 2 years	617	14	1.14	0.65	1.14	0.66	1.14	0.65	617	14	1.18	0.57
Opposite side is revised									113	6	**2.30**	0.045
Right	5 097	158	1	-	1	-	1	-	5 097	158	1	-
Left	3 606	95	0.79	0.078	0.79	0.083	0.79	0.078	3 606	95	0.79	0.075
Frailty variance ($\hat{q}$)							0.002	0.78				

a Number of primary prosthesis operations for each category.
b Number of revisions (events)
c Relative risk (hazard rate ratio)

The analyses were adjusted for age, gender, diagnosis at hip surgery, and year of operation.

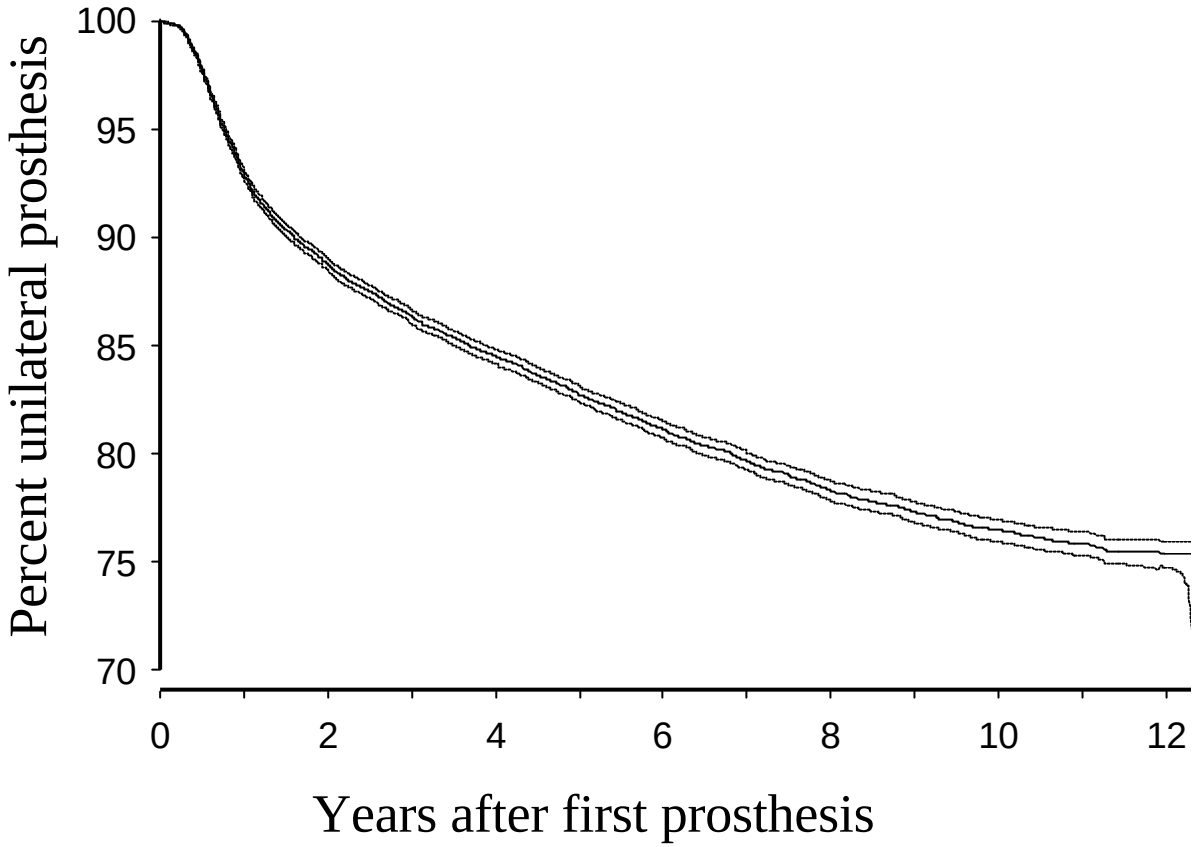
Percent unilateral prosthesis
100
95
90
85
80
75
70
0
2
4
6
8
10
12
Years after first prosthesis

Figure 1

TOP ↑

Figure 1

Title: “Dependency issues in survival analyses of 55 782 primary hip replacements from 47 355 patients”

Author: Stein Atle Lie

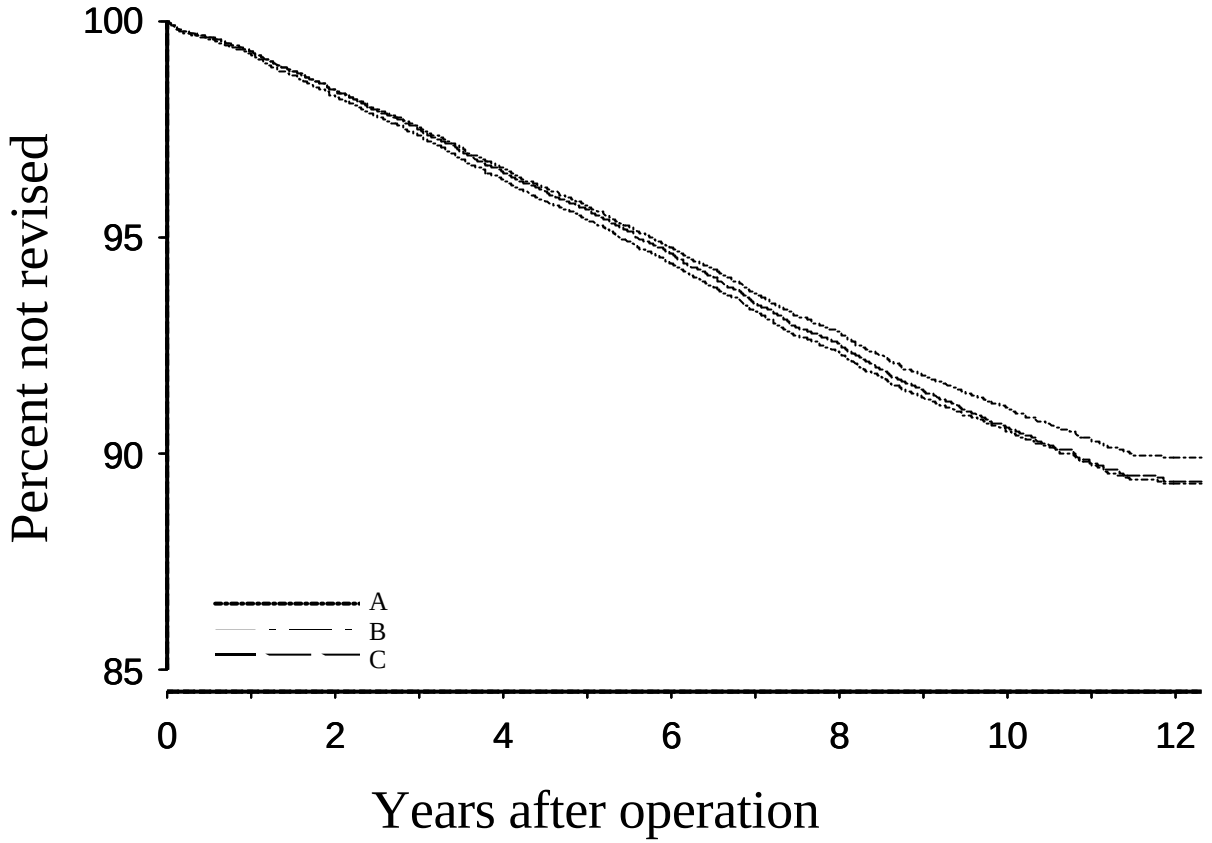
100
95
90
85
Percent not revised
A
B
C
0
2
4
6
8
10
12
Years after operation

Figure 2

TOP ↑

Figure 2

Title: “Dependency issues in survival analyses of 55 782 primary hip replacements from 47 355 patients”

Author: Stein Atle Lie

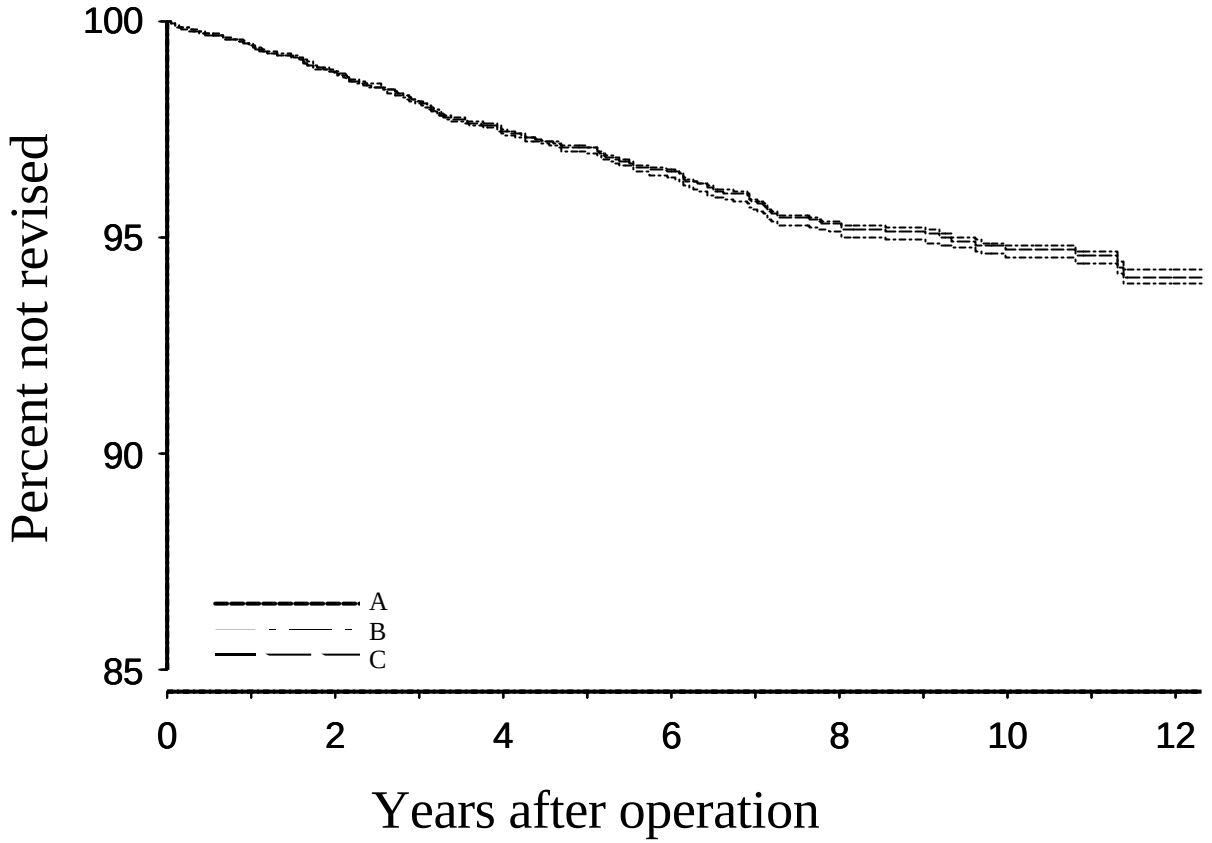
100
95
90
85
Percent not revised
A
B
C
0
2
4
6
8
10
12
Years after operation

Figure 3

TOP ↑

Figure 3

Title: “Dependency issues in survival analyses of 55 782 primary hip replacements from 47 355 patients”

Author: Stein Atle Lie