

Kaplan-Meier and Cox Regression Are Preferable for the Analysis of Time to Revision of Joint Arthroplasty

Thirty-One Years of Follow-up for Cemented and Uncemented THAs Inserted From 1987 to 2000 in the Norwegian Arthroplasty Register

Stein Atle Lie, PhD, Anne Marie Fenstad, MSc, Stein Håkon L. Lygre, PhD, Gard Kroken, MSc, Eva Dybvik, PhD, Jan-Erik Gjertsen, PhD, Geir Hallan, PhD, Håvard Dale, PhD, and Ove Furnes, PhD

Investigation performed at the Norwegian Arthroplasty Register, Department of Orthopedic Surgery, Haukeland University Hospital, Bergen, Norway

Background: Previous studies have suggested that the probability function of 1 minus the Kaplan-Meier survivorship overestimates revision rates of implants and that patient death should be included in estimates as a competing risk factor. The present study aims to demonstrate that this line of thinking is incorrect and is a misunderstanding of both the Kaplan-Meier method and competing risks.

Methods: This study demonstrated the differences, misunderstandings, and interpretations of classical, competing-risk, and illness-death models with use of data from the Norwegian Arthroplasty Register for 15,734 cemented and 7,867 uncemented total hip arthroplasties (THAs) performed from 1987 to 2000, with fixation as the exposure variable.

Results: The mean age was higher for patients who underwent cemented (72 years) versus uncemented THA (53 years); as such, a greater proportion of patients who underwent cemented THA had died during the time of the study (47% compared with 29%). The risk of revision at 20 years was 18% for cemented and 42% for uncemented THAs. The cumulative incidence function at 20 years was 11% for cemented and 36% for uncemented THAs. The prevalence of revision at 20 years was 6% for cemented and 31% for uncemented THAs.

Conclusions: Adding death as a competing risk will always attenuate the probability of revision and does not correct for dependency between patient death and THA revision. Adjustment for age and sex almost eliminated differences in risk estimates between the different regression models. In the analysis of time until revision of joint replacements, classical survival analyses are appropriate and should be advocated.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Consider the situation that 1 surgeon performs total hip arthroplasties (THAs) at 2 different hospitals. Both hospitals utilize the same implant, the procedure is performed with the same operating team, and all other conditions are identical; the only difference between settings is that 1 hospital has a patient population with a high mortality rate and the other has patients with low mortality. The quality of the THAs performed is equal, which should be reflected in the statistical analysis. However, because patients at the high-mortality hospital may die before revision is needed, the low-mortality hospital will experience—and need to plan for—more revisions than the high-mortality hospital, even if the quality of the THAs is equal.

Because THAs are followed over time until the implant is revised or lost to follow-up, survival (time-to-event, event history) analyses are needed to analyze the risk of revision.

Competing-risk analyses have been increasingly popular for the assessment of joint-replacement data¹⁻⁴, and some studies have advocated the use of such analyses for follow-ups of >10 years⁵⁻⁷.

For time-to-revision data, some authors have claimed that the probability function of 1 minus the Kaplan-Meier survivorship overestimates the rate of revision in the presence of patient death^{2,5,6,8-11}.

Recently, there have been discussions regarding whether patient death is a competing risk relative to THA revision and

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (<http://links.lww.com/JBJSOA/A355>).

Copyright © 2022 The Authors. Published by The Journal of Bone and Joint Surgery, Incorporated. All rights reserved. This is an open access article distributed under the terms of the [Creative Commons Attribution-Non Commercial-No Derivatives License 4.0](https://creativecommons.org/licenses/by-nc-nd/4.0/) (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

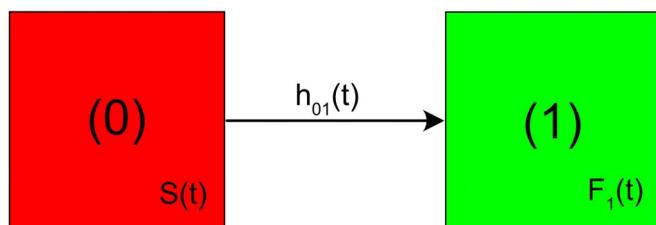


Fig. 1
Classical survival model. State 0 (red) is “primary THA” and state 1 (green) is “revised THA.” The probability of being in state 0 is $S(t)$ (survival probability) and the probability of being in state 1 is $F_1(t)$. The immediate risk (hazard) for shifting between states 0 and 1 is $h_{01}(t)$.

how results from competing-risk analyses should be interpreted¹²⁻¹⁴. These studies utilize either short-term follow-up or simulated data sets. With use of nearly complete, 30-year THA follow-up data from a national registry, the present study was performed to demonstrate and describe the inaccuracy of competing-risk analysis for revision THA. The differences between classical (i.e., Kaplan-Meier and Cox regression), competing-risk (i.e., cumulative incidence functions), and illness-death models are discussed. Additionally, we present flexible alternatives that utilize pseudo-data, analyzing restricted mean failure times. Finally, we aimed to explain the misunderstandings and interpretations of different methods, without the use of technical or mathematical terms.

Materials and Methods

To illustrate distinctions between statistical approaches, we used a data set from the Norwegian Arthroplasty Register, which started registration of THAs in September 1987, with a completeness of up to 97%¹⁵. Based on the Norwegian personal identification number, we linked primary and revision operations, with complete data on death or emigration¹⁵. Our primary exposure was 2 categories of fixation (i.e., cemented and uncemented for both components). We limited data to primary THAs implanted between 1987 and 2000. During that period, several poorly performing uncemented THAs^{16,17} and inferior cement types¹⁸ were utilized in Norway. Uncemented THAs were commonly utilized in younger patients and cemented THAs in elderly patients. Hence, patients with cemented THAs had higher mortality than those with uncemented THAs, which influences the results from the different statistical approaches. All 7,867 uncemented THAs were included, whereas a random subset of 15,734 of 112,873 cemented THAs, twice the number of uncemented procedures, were included.

The end of follow-up was December 31, 2018. Only 0.2% of patients emigrated, and these were considered censored for all models.

Statistical Methods

Classical Survival Analysis

In classical models of time to revision (Fig. 1), the hazard is defined as the immediate risk of revision just after time t , given that the implant is at risk at time t . In Figure 1, the hazard ($h_{01}[t]$) is indicated as an arrow between state 0 and state 1, specifying the

immediate risk of shifting states. For the classical survival model (Fig. 1), the Kaplan-Meier method¹⁹ estimates the cumulative probability of being in state 0. One minus the Kaplan-Meier will hence estimate the cumulative probability for state 1, and there is a 1-to-1 relationship between the hazard and the probabilities of being in each of the 2 states²⁰, assuming that time to revision and censoring are independent. Thus, analyses of hazards (e.g., Cox regression²¹) will be analyses of probabilities²². Importantly, the sum of the 2 probabilities will be 1 (100%). In the classical survival model (Fig. 1), loss of the patient to follow-up (including death or emigration) or end of follow-up in 2018 will lead to censoring of the follow-up time for the THA.

Competing Risks

In the competing-risk model (Fig. 2), patient death is included as a separate state. Hence, there are now 2 mutually exclusive hazards ($h_{01}[t]$ and $h_{02}[t]$) simultaneously influencing the probabilities for being in each of the 3 states (0, 1, or 2). The survival probability (i.e., the probability of state 0) can directly be calculated (applying the Kaplan-Meier method) based on the sum of the 2 mutually exclusive hazards ($h_{\text{sum}}[t] = h_{01}[t] + h_{02}[t]$). The cumulative probability of being in the 2 competing states (i.e., the cumulative incidence functions) is based on each of the hazards and the total survival²³. For the competing-risk model, analysis of each hazard (e.g., using Cox regression) is still valid, but does not reflect the probability of being in the states.

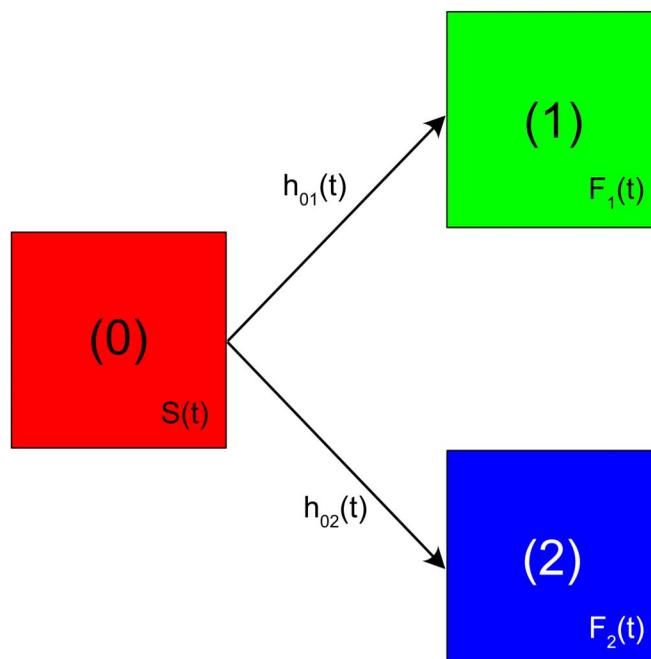


Fig. 2
Competing-risk model. State 0 (red) is “patient alive with primary THA,” state 1 (green) is “patient with revised THA,” and state 2 (blue) is “dead patient.” The probability of being in state 0 is $S(t)$ (survival probability), the probability of being in state 1 is $F_1(t)$, and the probability of being in state 2 is $F_2(t)$. The immediate risk (hazard) for shifting between states 0 and 1 is $h_{01}(t)$ and the hazard for shifting between states 0 and 2 is $h_{02}(t)$.

In the competing-risk model, calculation of cumulative incidence functions can be performed with use of the Aalen-Johansen estimator or via direct methods^{23,24}. The Aalen-Johansen method is based on the increments for the cumulative hazard (e.g., Nelson-Aalen method²⁵). Fine and Gray suggested a regression model for the cumulative incidence functions (i.e., the likelihood of being in the state of interest; e.g., state 1), expressed as sub-hazard ratios, with the possibility to adjust for covariates²⁶.

Illness-Deaths Models

Extending the competing risk model with a hazard ($h_{12}[t]$) for changing from revision THA (state 1) to patient death (state 2), we have an illness-death model (Fig. 3). Still, each hazard can be analyzed separately. Hence, Cox regression models will still be valid for the shifts between states but will not reflect probabilities for being in any of the states.

The Use of Pseudo-Data

With use of pseudo-data, a variety of analyses of classical survival, competing-risk, illness-death, and elaborate multistate models can be performed. The calculation of pseudo-data is described elsewhere²⁷. Pseudo-data can be expressed as several quantities, such as probabilities of being in different states or restricted mean duration in a given state (e.g., restricted mean

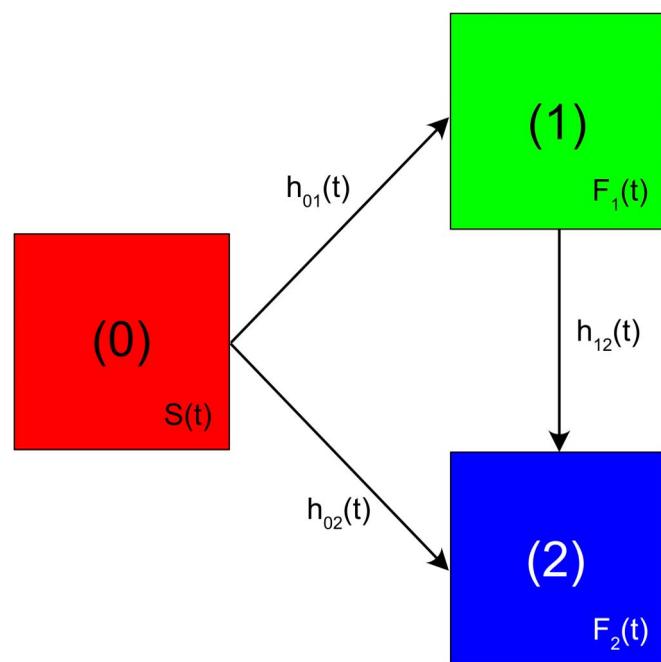


Fig. 3
Illness-death model. State 0 (red) is “patient alive with primary THA,” state 1 (green) is “patient alive with revised THA,” and state 2 (blue) is “dead patient.” The probability of being in state 0 is $S(t)$ (survival probability), the probability of being in state 1 is $F_1(t)$, and the probability of being in state 2 is $F_2(t)$. The immediate risk (hazard) for shifting between states 0 and 1 is $h_{01}(t)$, the hazard for shifting between states 0 and 2 is $h_{02}(t)$, and the hazard for shifting between states 1 and 2 is $h_{12}(t)$.

TABLE I Descriptive Data for the Cemented and Uncemented THAs*

	Cemented THAs	Uncemented THAs
No.	15,734 (100%)	7,867 (100%)
Age (yr)	72.4 ± 8.7	53.3 ± 11.8
Male sex	4,589 (29.2%)	3,104 (39.5%)
No. of revisions	1,167 (7.4%)	2,695 (34.3%)
No. of deaths	7,431 (47.2%)	2,320 (29.5%)

*Values are given as the count with the percentage in parentheses or as the mean ± standard deviation.

survival or restricted mean failure time). Pseudo-data are typically analyzed with use of generalized estimating equations with an appropriate link-function and distribution²⁸.

In the present study, pseudo-data were utilized to calculate differences in probabilities (hazard scale, using a complementary log-log link function) and restricted mean differences in time spent (using an identity link function) in state 1 (restricted mean failure times). Pseudo-data and probability curves were calculated with use of the R statistical framework (R Foundation for Statistical Computing). Regression models were analyzed with use of Stata (version 16; StataCorp). Significance was set at 0.05.

Source of Funding

There was no external funding for this study.

Results

The mean age at the time of the primary procedure was higher for cemented THAs than for uncemented THAs, and the frequency of males was higher for uncemented THAs (Table I). The numbers of revisions and patient deaths for cemented and uncemented THAs are presented in Table II. For the classical survival model, follow-up was censored at the time of patient death.

The estimated probabilities, calculated with use of the Kaplan-Meier method, show that the cumulative risk of revision was less for cemented (18.1%; 95% confidence interval [CI], 15.2% to 21.0%) than for uncemented THAs (42.2%; 95% CI, 39.5% to 44.9%) at 20 years (Figs. 4-A and 4-B).

Including patient death as a competing risk, we observed that the probability (cumulative incidence function) of observing a patient with a revised THAs (10.9%; 95% CI, 8.5% to 13.2%) was more influenced by mortality among patients with cemented THAs than uncemented THAs (36.4%; 95% CI, 33.7% to 39.0%) at 20 years (Figs. 4-C and 4-D).

In the illness-death model, with a transition from revision THAs to patient death, the probability of being alive at 20 years with a revised cemented THA (5.6%; 95% CI, 3.9% to 7.3%) was substantially lower than that of patients with a revised uncemented THA (31.2%; 95% CI, 28.7% to 33.8%) (Figs. 4-E and 4-F).

Risk estimates comparing cemented THA with uncemented THA with use of the unadjusted Fine and Gray model were larger

TABLE II Transitions Between Primary THA, Revision THA, and Death for the Cemented and Uncemented THAs*

	From	To	
		Revision THA (State 1)	Patient Death (State 2)
Cemented			
Primary THA (state 0)	15,734	1,167 (7.4%)	6,965 (44.3%)
Revision THA (state 1)	1,167		466 (39.9%)
Total		1,167 (6.9%)	7,431 (44.0%)
Uncemented			
Primary THA (state 0)	7,867	2,695 (34.3%)	1,824 (23.2%)
Revision THA (state 1)	2,695		496 (18.4%)
Total		2,695 (25.5%)	2,320 (22.0%)

*Values are given as the count with the percentage in parentheses.

than estimates from the unadjusted Cox model because of the high mortality for patients with cemented THAs. These 2 estimates were more similar following adjustment for age and sex (Table III).

Classical and competing-risk models for the probability of revision THA based on pseudo-data corresponded to the results from the Cox and Fine and Gray methods, respectively (Table IV). Additionally, in the illness-death model, the difference in probability of a patient being alive with a revision (state 1) was even larger between patients with uncemented and cemented THAs than for the 2 former approaches (Table IV).

Using pseudo-data to analyze the restricted mean failure time based on 25 years of observation, we observed that uncemented THAs were revised at an average of 4.13 years earlier than cemented THAs (Table V). Including patient mortality, we observed that patients with uncemented THAs underwent revision at a mean of 4.31 years earlier than patients with cemented THAs. Furthermore, patients with uncemented THAs lived an average of 4.23 years longer following revision. Adjusting for age and sex, the different regressions performed with use of pseudo-data had similar results to each other (Tables IV and V).

Discussion

There is an important difference between the classical, competing-risk, and illness-death models. For the classical analyses, we emphasize that revision of the implant is analyzed. This is also highlighted in the naming of the 2 states in the Figure 1 legend: “Primary THA” and “Revised THA.” For the competing-risk and illness-death models, which include patient death as a separate state, the definition of the initial state changes to “Patient alive with primary THA.” This change is of crucial importance because it demonstrates that the analysis is focused on the patient rather than singularly on the THA, as is the case with classical analysis.

Several authors have claimed that competing-risk analyses of joint replacements, utilizing patient death as a competing risk, should replace the classical statistical approaches, particularly for cohorts with >10 years of follow-up and a high rate of mortality⁵⁻⁷. These recommendations represent a misunderstanding of the concepts of competing-risk analysis and

of the assumptions for the classical survival analysis. Some studies have acknowledged that competing-risk analysis is not directly comparable with the classical survival analysis^{1,12,13}, and in a recent article, Sayers et al. demonstrated the appropriateness of Kaplan-Meier estimation for the risk of revision THA¹². Furthermore, Buzkova et al. showed that death as a competing risk can yield misleading results²⁹.

Independency between the time to censoring and time to revision or failure is a crucial assumption in the calculation of Kaplan-Meier estimates. This assumption implies that implants lost to follow-up (i.e., censored) have the same probability of revision as implants still at risk. If there is dependency between time to THA revision and patient death, the Kaplan-Meier estimate will be biased. In the example, if the implants in patients who died were more likely to be loose, they would have had a higher risk of THA revision at the time of death; thus, as shown by Murray et al., 1 minus the Kaplan-Meier estimate will falsely underestimate the true revision risk³⁰. Conversely, if the THA in a dead patient had a lower risk of revision, 1 minus the Kaplan-Meier estimate will falsely overestimate the true revision risk. Adding death as a competing risk relative to THA revision will always attenuate the probability of THA revision and consequently does not correct for dependency between time to death and time to revision. This was clearly illustrated by Sayers et al.¹². The sum of probabilities for the different states will always equal 1 (100%); therefore, adding a new state will always attenuate the probabilities for the other states. The assumption of independency between the times to revision, death, and censoring is still present in competing-risk analysis. Methods to adjust the Kaplan-Meier estimate for dependency exist, such as utilizing inverse probability weights to adjust for the censoring process (e.g., see page 175 in the book by Aalen et al.³¹).

For analysis of patient mortality after joint replacement surgery, survival analysis is needed^{32,33}. Overall mortality is often of primary interest. If multiple causes of death are studied³⁴, competing-risk analysis is appropriate, and each cause of death (respiratory disorders, circulatory disorders, etc.) represents competing causes/risks³⁵. Hence, for analysis of 1 cause, considering the other causes as competing risks, using cumulative

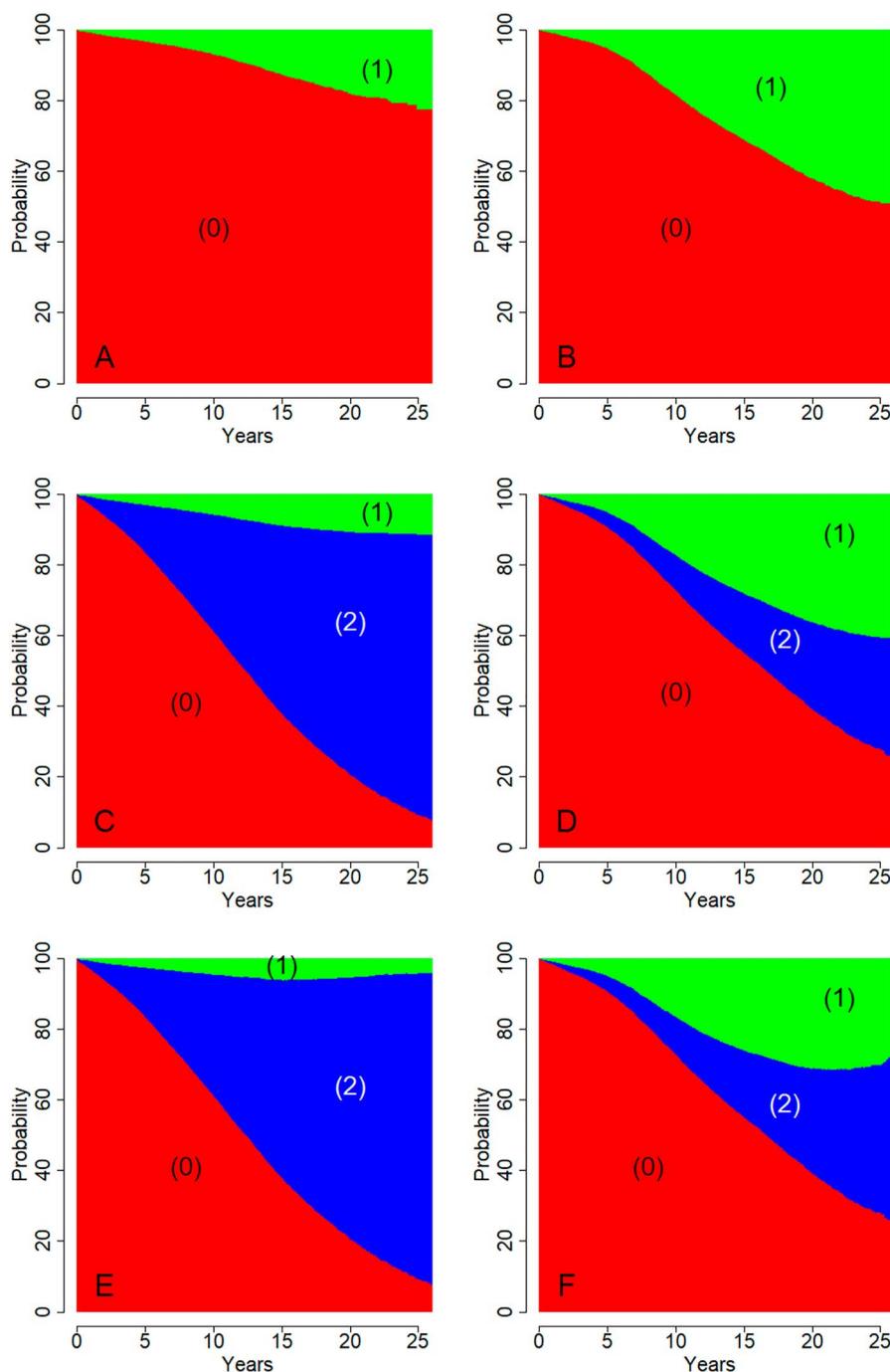


Fig. 4
Estimated probabilities: for a classical survival model for cemented (A) and uncemented (B) THAs, for the states described in Figure 1; for a competing risk model for cemented (C) and uncemented (D) THAs, for the states described in Figure 2; and for an illness-death model for cemented (E) and uncemented (F) THAs, for the states described in Figure 3. Red = state 0 (primary THA or patient alive with primary THA), green = state 1 (revised THA or patient with revised THA), and blue = state 2 (dead patient).

incidence functions, will cause the mortality estimates to properly sum to the total patient mortality.

In contrast, utilizing patient death as a competing risk relative to revision of a primary THA, the sum of probabilities for the 2 competing risks (i.e., revision THA and patient

mortality) is meaningless. Considering revision as a competing risk relative to patient death is also meaningless. This is not an argument against patient death as a competing risk relative to THA revision, but demonstrates that this analysis deviates from the original intention of competing-risk analysis.

TABLE III Cox and Fine and Gray Regression Models for Risk of Revision*

	Cox Model for $h_{01}(t)^\dagger$		Fine and Gray Model for State 1	
	Unadjusted	Adjusted [‡]	Unadjusted	Adjusted [‡]
Uncemented [§]	2.69 (2.57 to 2.81); <0.001	1.56 (1.47 to 1.65); <0.001	3.71 (3.56 to 3.87); <0.001	1.60 (1.51 to 1.70); <0.001
Age, per 5 yr		0.87 (0.87 to 0.88); <0.001		0.82 (0.81 to 0.83); <0.001
Male sex [#]		1.46 (1.41 to 1.52); <0.001		1.31 (1.26, to 1.36); <0.001

*Values are given as the hazard ratio with the 95% CI in parentheses, followed by the p value. [†] $h_{01}(t)$ is the hazard for shifting to State 1. [‡]Adjusted for age and sex. [§]Compared with cemented. [#]Compared with female sex.

Bilateral THA is another complicating issue. In the classical approach, Kaplan-Meier estimates can be adjusted to account for multiple implants per patient³⁶. Furthermore, multilevel approaches can be utilized to analyze multiple implants within a single patient (e.g., finger arthroplasties, dental implants, or dental fillings)³⁷.

For the competing-risk approach, considering multiple or bilateral implants becomes problematic. Simple cumulative incidence functions or regression models, ignoring bilateral implants, are inappropriate because the risks of revision for the 2 THAs are related³⁷.

Including random effects in the analysis will lead to a wrong dependency between the competing risks (e.g., see page 260 in the book by Aalen et al.³¹). The appropriateness of utilizing robust variance estimates in regression models or calculating cumulative incidence functions based on patient-averaged hazards is also debatable.

For bilateral THAs, each THA may experience patient death, resulting in the patient counted as dying twice on the same date. Such “double counting” results in a strong dependency between the bilateral THAs for the time to patient death. van der Pas et al. discovered that this problem can be exacerbated by consecutive implants, as these will always have a shorter time to patient death, resulting in unnecessary bias³⁸. This problem also increases when a patient has >2 implants (e.g., in the fingers). These examples represent multiple unnecessary

problems related to competing-risk models that are not present in the classical methods.

The same problems as in competing-risk models are present for illness-death models. Additionally, if a patient dies with 1 revised and 1 intact primary THA, a problematic dependency occurs between the 2 hazards (shifts) to patient death.

To give an example: for patients with pacemakers, failure of the pacemaker may be 1 of several causes of death. Therefore, adding the time of pacemaker failure as a competing risk for patient death is sensible. However, for an analysis of the longevity of pacemakers, death of the patient (as a result of causes other than pacemaker failure) leads to a loss of follow-up (censoring) of the pacemaker (i.e., the pacemaker was still working at the time of patient death). For the pacemaker itself, an empty battery, loose cables, etc., may be competing risks of failure.

For some situations, competing-risk analyses may at first glance seem odd, but they may also hold additional value. Consider the lifetimes of infants with special needs³⁹. Death of the mother as a competing risk can be a sensible inclusion from a resource-planning perspective because extra resources may be required to care for the infant following the death of the parent.

Thus, analysis of revision THA with patient death as a competing risk can be useful from a resource-planning perspective because it helps to predict the future burden of

TABLE IV Probability Models for Revision THA (State 1), Based on Pseudo-Data*

	Classical Survival Model		Competing-Risk Model		Illness-Death Model	
	Unadjusted	Adjusted [‡]	Unadjusted	Adjusted [‡]	Unadjusted	Adjusted [‡]
Uncemented [‡]	2.60 (2.42 to 2.78); <0.001	1.67 (1.5 to 1.83); <0.001	3.53 (3.31 to 3.76); <0.001	1.95 (1.79 to 2.13); <0.001	4.60 (4.30 to 4.93); <0.001	2.26 (2.06 to 2.49); <0.001
Age, per 5 yr		0.88 (0.87 to 0.90); <0.001		0.86 (0.85 to 0.87); <0.001		0.83 (0.82 to 0.85); <0.001
Male sex [§]		1.08 (0.99 to 1.17); 0.080		0.95 (0.88 to 1.03); 0.202		0.85 (0.78 to 0.93); <0.001

*Values are given as the hazard ratio with the 95% CI in parentheses, followed by the p value. [‡]Adjusted for age and sex. [‡]Compared with cemented. [§]Compared with female sex.

TABLE V Models for Differences in Restricted Mean Failure Time for Years Spent in the Revision THA State (State 1), Based on Pseudo-Data*

	Classical Survival Model		Competing-Risk Model		Illness-Death Model	
	Unadjusted	Adjusted†	Unadjusted	Adjusted†	Unadjusted	Adjusted†
Uncemented‡	4.13 (3.84 to 4.42); <0.001	2.32 (1.93 to 2.71); <0.001	4.31 (4.10 to 4.52); <0.001	1.86 (1.58 to 2.14); <0.001	4.23 (4.05 to 4.41); <0.001	1.54 (1.30 to 1.78); <0.001
Age, per 5 yr		-0.45 (-0.52 to -0.39); <0.001		-0.63 (-0.68 to -0.58); <0.001		-0.71 (-0.75 to -0.67); <0.001
Male sex§		0.71 (0.42 to 1.00); <0.001		0.17 (-0.04 to 0.38); 0.110		-0.26 (-0.44 to -0.08); 0.004

*Values are given as the beta coefficient (indicating the difference in time, in years) with the 95% CI in parentheses, followed by the p value. †Adjusted for age and sex. ‡Compared with cemented. §Compared with female sex.

revisions. However, when assessing implant survival and the quality of the THA procedure, competing-risk analysis cannot be compared with and interpreted as being equal to classical survival analysis. Presenting 1 minus the Kaplan-Meier estimate with cumulative incidence functions from such analyses is misleading and should be avoided. Patients alive with a THA revision may need special care, and the illness-death model will indicate the prevalence of such patients.

For the analyses in the present article, we showed that competing-risk and illness-death models sometimes have added value. However, these approaches do not circumvent assumptions from the classical approaches, but introduce additional problems not easily accounted for. Competing-risk and illness-death models are special cases of the multistate models described by Gillam et al.^{40,41}, ignoring that bilateral THAs are not independent for both time to revision and patient death.

Statistical consultants guiding the analysis of implant survival should be aware of the important differences between models and of the pitfalls when patient death is added as a competing risk. In the case of THA survival, the Kaplan-Meier method is designed to account for loss to follow-up for any reason. If the patient dies, emigrates, withdraws from the study, is excluded because of a change in health condition, or otherwise is lost from the study, the follow-up time of the THA will be censored. However, for the analysis of patient death and different causes of death, 1 minus the Kaplan-Meier estimate is incorrect for the probability of dying from a single cause. Likewise, if different causes of revision are analyzed, 1 minus the Kaplan-Meier estimate gives incorrect esti-

mates for revision for each cause. Hence, for both these situations, the competing causes—of patient death or THA revision—must be considered. When analyzing the overall risk of revision following THA, the Kaplan-Meier method and Cox regression are appropriate and correct, and should therefore be advocated. ■

NOTE: The authors thank the orthopaedic surgeons of Norway for their excellent reporting of joint-replacement surgeries to the national register.

Stein Atle Lie, PhD^{1,2}
 Anne Marie Fenstad, MSc¹
 Stein Håkon L. Lygre, PhD^{1,3}
 Gard Kroken, MSc¹
 Eva Dybvik, PhD¹
 Jan-Erik Gjertsen, PhD^{1,4}
 Geir Hallan, PhD^{1,4}
 Håvard Dale, PhD^{1,4}
 Ove Furnes, PhD^{1,4}

¹The Norwegian Arthroplasty Register, Department of Orthopedic Surgery, Haukeland University Hospital, Bergen, Norway

²Department of Clinical Dentistry, University of Bergen, Bergen, Norway

³Department of Occupational Medicine, Haukeland University Hospital, Bergen, Norway

⁴Department of Clinical Medicine, University of Bergen, Bergen, Norway

Email for corresponding author: stein.lie@uib.no

References

- Ranstam J, Kärrholm J, Pulkkinen P, Mäkelä K, Espehaug B, Pedersen AB, Mehnert F, Furnes O; NARA study group. Statistical analysis of arthroplasty data. II. Guidelines. *Acta Orthop*. 2011 Jun;82(3):258-67.
- Maradit Kremers H, Kremers WK, Sierra RJ, Lewallen DG, Berry DJ. Competing Risk of Death When Comparing Tibial Implant Types in Total Knee Arthroplasty. *J Bone Joint Surg Am*. 2016 Apr 6;98(7):591-6.
- Cuthbert AR, Graves SE, Giles LC, Glonek G, Pratt N. What Is the Effect of Using a Competing-risks Estimator when Predicting Survivorship After Joint Arthroplasty: A Comparison of Approaches to Survivorship Estimation in a Large Registry. *Clin Orthop Relat Res*. 2021 Feb 1;479(2):392-403.
- Gillam MH, Ryan P, Graves SE, Miller LN, de Steiger RN, Salter A. Competing risks survival analysis applied to data from the Australian Orthopaedic Association National Joint Replacement Registry. *Acta Orthop*. 2010 Oct;81(5):548-55.
- Wongworawat MD, Dobbs MB, Gebhardt MC, Gioe TJ, Leopold SS, Manner PA, Rinnac CM, Porcher R. Editorial: Estimating survivorship in the face of competing risks. *Clin Orthop Relat Res*. 2015 Apr;473(4):1173-6.
- Biau DJ, Latouche A, Porcher R. Competing events influence estimated survival probability: when is Kaplan-Meier analysis appropriate? *Clin Orthop Relat Res*. 2007 Sep;462(462):229-33.

7. Martin BI. CORR Insights®: What Is the Effect of Using a Competing-risks Estimator when Predicting Survivorship After Joint Arthroplasty: A Comparison of Approaches to Survivorship Estimation in a Large Registry. *Clin Orthop Relat Res.* 2021 Feb 1;479(2):404-5.
8. Fennema P, Lubsen J. Survival analysis in total joint replacement: an alternative method of accounting for the presence of competing risk. *J Bone Joint Surg Br.* 2010 May;92(5):701-6.
9. Lacy S, Wilson T, Clement F, Roberts DJ, Faris PD, Ghali WA, Marshall DA. Kaplan-Meier Survival Analysis Overestimates the Risk of Revision Arthroplasty: A Meta-analysis. *Clin Orthop Relat Res.* 2015 Nov;473(11):3431-42.
10. Keurentjes JC, Fiocco M, Schreurs BW, Pijls BG, Nouta KA, Nelissen RGHH. Revision surgery is overestimated in hip replacement. *Bone Joint Res.* 2012 Oct 1; 1(10):258-62.
11. Porcher R. CORR Insights®: Kaplan-Meier Survival Analysis Overestimates the Risk of Revision Arthroplasty: A Meta-analysis. *Clin Orthop Relat Res.* 2015 Nov; 473(11):3443-5.
12. Sayers A, Evans JT, Whitehouse MR, Blom AW. Are competing risks models appropriate to describe implant failure? *Acta Orthop.* 2018 Jun;89(3):256-8.
13. Van Der Pas S, Nelissen R, Fiocco M. Different competing risks models for different questions may give similar results in arthroplasty registers in the presence of few events. *Acta Orthop.* 2018 Apr;89(2):145-51.
14. Ranstam J, Robertsson O. The Cox model is better than the Fine and Gray model when estimating relative revision risks from arthroplasty register data. *Acta Orthop.* 2017 Dec;88(6):578-80.
15. Havelin LI, Engesaeter LB, Espehaug B, Furnes O, Lie SA, Vollset SE. The Norwegian Arthroplasty Register: 11 years and 73,000 arthroplasties. *Acta Orthop Scand.* 2000 Aug;71(4):337-53.
16. Havelin LI, Espehaug B, Vollset SE, Engesaeter LB. Early aseptic loosening of uncemented femoral components in primary total hip replacement. A review based on the Norwegian Arthroplasty Register. *J Bone Joint Surg Br.* 1995 Jan;77(1):11-7.
17. Havelin LI, Vollset SE, Engesaeter LB. Revision for aseptic loosening of uncemented cups in 4,352 primary total hip prostheses. A report from the Norwegian Arthroplasty Register. *Acta Orthop Scand.* 1995 Dec;66(6):494-500.
18. Havelin LI, Espehaug B, Vollset SE, Engesaeter LB. The effect of the type of cement on early revision of Charnley total hip prostheses. A review of eight thousand five hundred and seventy-nine primary arthroplasties from the Norwegian Arthroplasty Register. *J Bone Joint Surg Am.* 1995 Oct;77(10):1543-50.
19. Kaplan EL, Meier P. Nonparametric-Estimation from Incomplete Observations. *J Am Stat Assoc.* 1958;53(282):457-81.
20. Andersen PK, Keiding N. Multi-state models for event history analysis. *Stat Methods Med Res.* 2002 Apr;11(2):91-115.
21. Cox DR. Regression Models and Life-Tables. *J Royal Stat Soc B.* 1972;34(2): 187-220.
22. Andersen PK, Geskus RB, de Witte T, Putter H. Competing risks in epidemiology: possibilities and pitfalls. *Int J Epidemiol.* 2012 Jun;41(3):861-70.
23. Andersen PK, Abildstrom SZ, Rosthøj S. Competing risks as a multi-state model. *Stat Methods Med Res.* 2002 Apr;11(2):203-15.
24. Aalen OO, Johansen S. Empirical Transition Matrix for Nonhomogeneous Markov-Chains Based on Censored Observations. *Scand J Stat.* 1978;5(3):141-50.
25. Aalen O. Nonparametric Estimation of Partial Transition-Probabilities in Multiple Decrement Models. *Ann Stat.* 1978;6(3):534-45.
26. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc.* 1999 Jun;94(446):496-509.
27. Andersen PK, Perme MP. Pseudo-observations in survival analysis. *Stat Methods Med Res.* 2010 Feb;19(1):71-99.
28. Klein JP, Gerster M, Andersen PK, Tarima S, Perme MP. SAS and R functions to compute pseudo-values for censored data regression. *Comput Methods Programs Biomed.* 2008 Mar;89(3):289-300.
29. Buzkova P, Barzilay JI, Mukamal KJ. Assessing risk factors of non-fatal outcomes amid a competing risk of mortality: the example of hip fracture. *Osteoporos Int.* 2019 Oct;30(10):2073-8.
30. Murray DW, Britton AR, Bulstrode CJ. Loss to follow-up matters. *J Bone Joint Surg Br.* 1997 Mar;79(2):254-7.
31. Aalen O, Borgun O, Gjessing H. *Survival and Event History Analysis: A Process Point of View.* Springer New York; 2008.
32. Lie SA, Engesaeter LB, Havelin LI, Gjessing HK, Vollset SE. Mortality after total hip replacement: 0-10-year follow-up of 39,543 patients in the Norwegian Arthroplasty Register. *Acta Orthop Scand.* 2000 Feb;71(1):19-27.
33. Lie SA, Pratt N, Ryan P, Engesaeter LB, Havelin LI, Furnes O, Graves S. Duration of the increase in early postoperative mortality after elective hip and knee replacement. *J Bone Joint Surg Am.* 2010 Jan;92(1):58-63.
34. Lie SA, Engesaeter LB, Havelin LI, Furnes O, Vollset SE. Early postoperative mortality after 67,548 total hip replacements: causes of death and thromboprophylaxis in 68 hospitals in Norway from 1987 to 1999. *Acta Orthop Scand.* 2002 Aug;73(4):392-9.
35. Hunt LP, Ben-Shlomo Y, Whitehouse MR, Porter ML, Blom AW. The Main Cause of Death Following Primary Total Hip and Knee Replacement for Osteoarthritis: A Cohort Study of 26,766 Deaths Following 332,734 Hip Replacements and 29,802 Deaths Following 384,291 Knee Replacements. *J Bone Joint Surg Am.* 2017 Apr 5; 99(7):565-75.
36. Aalen OO, Bjertness E, Sørnju T. Analysis of dependent survival data applied to lifetimes of amalgam fillings. *Stat Med.* 1995 Aug 30;14(16):1819-29.
37. Lie SA, Engesaeter LB, Havelin LI, Gjessing HK, Vollset SE. Dependency issues in survival analyses of 55,782 primary hip replacements from 47,355 patients. *Stat Med.* 2004 Oct 30;23(20):3227-40.
38. van der Pas SL, Nelissen RGHH, Fiocco M. Patients with Staged Bilateral Total Joint Arthroplasty in Registries: Immortal Time Bias and Methodological Options. *J Bone Joint Surg Am.* 2017 Aug 2;99(15):e82.
39. Moucheraud C, Worku A, Molla M, Finlay JE, Leaning J, Yamin A. Consequences of maternal mortality on infant and child survival: a 25-year longitudinal analysis in Butajira Ethiopia (1987-2011). *Reprod Health.* 2015 May 6;12(Suppl 1):S4.
40. Gillam MH, Lie SA, Salter A, Furnes O, Graves SE, Havelin LI, Ryan P. The progression of end-stage osteoarthritis: analysis of data from the Australian and Norwegian joint replacement registries using a multi-state model. *Osteoarthritis Cartilage.* 2013 Mar;21(3):405-12.
41. Gillam MH, Ryan P, Salter A, Graves SE. Multi-state models and arthroplasty histories after unilateral total hip arthroplasties: introducing the Summary Notation for Arthroplasty Histories. *Acta Orthop.* 2012 Jun;83(3):220-6.