**Title:** A web based risk calculator incorporating preoperative opioid use to predict revision of total-knee arthroplasty

**Background:** Over 700,000 total-knee arthroplasties (TKAs) are performed in the United States each year1 with 6% requiring revision after 5 years due to wear, osteolysis, instability, infection, or other causes2-4. Some risk factors for knee revision have been previously identified5-8. However, given the high prevalence of prescription opioid use in the United States9, we sought to specifically investigate the role of opioids in TKA revision. Additionally, due to the increased complexity, expense, morbidity, and mortality associated with TKA revision1,10, we aimed to create a freely available online calculator to assist providers in estimating the risk of TKA revision.

**Methods:** We retrospectively analyzed the medical records of all Veterans Administration patients who underwent unilateral TKA from Jan. 1, 2006 to Dec. 31, 2011. Exclusion criteria included bilateral knee replacement in a single procedure, undetermined surgical laterality, or irreconcilable surgical dates. Preoperative daily morphine equivalent doses were calculated for each patient based on prescription records from Jan. 1, 2005 to their initial TKA date. All patients were followed from their initial TKA date until Dec. 31, 2012. Time to knee revision, grouped by non-opioid users versus tertiles of opioid users, was plotted using Kaplan-Meier curves11. A multivariate Cox proportional hazard model was then fit to predict TKA revision with daily morphine equivalent dose as a continuous variable. Backwards stepwise selection with the Akaike information criterion (AIC), employing 10-fold cross validation, was used for variable selection12. P-values less than 0.05 were considered significant. Model performance was evaluated by the accuracy of the survival function on a 40-sample bootstrapped calibration plot for predicting TKA revision at 1 year12. The model was used for a decision support application13 to quantify the risk of knee revision following TKA. R (version 3.1.2; http://www.r-project.org) was utilized for data analysis and application development14.

**Results:**  A total of 34,461 VA patients who underwent TKA between 2006-2011 were identified, and 33,642 patients met inclusion criteria. The cohort was 94% male with a mean age of 64.4 (sd = 9.5). Follow-up time ranged from 1 to 7 years (median = 3.70). A total of 1,715 (5.10%) patients required revision. Figure 1 displays the distribution of morphine equivalent dose use in our cohort. Figure 2 displays Kaplan-Meier curves comparing TKA revision by opiate use group. Patients not using opiates were less likely to need a revision than patients in the first tertile using up to 3.7 morphine equivalents daily (p = 0.016). Furthermore, patients in the first tertile were less likely to be revised than patients in the second tertile (3.7 – 14.1 morphine equivalents) or third tertile (>14.1 morphine equivalents) (p = 0.002). For the Cox model, hazard ratios and associated p-values for all variables included are listed in Table 1. Daily morphine equivalents were independently associated with TKA revision (HR 1.0008, p = 0.0013). Accuracy of the model at 1 year is displayed in the calibration plot shown in Figure 3. The bias corrected mean absolute error was 0.0027. Using the model, we generated a web based risk calculator for TKA revision ([bit.do/tka](http://bit.do/tka)). A screen shot of the application is shown in Figure 4.

**Conclusions:** Preoperative opioid use is an independent predictor of TKA revision in a dose-dependent manner.In an effort to quantify the preoperative risk of TKA revision for patients undergoing TKA, a risk calculator was created and published online.

Figure 1: Histogram showing the distribution of daily morphine equivalent dose usage among patients in our study cohort.

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Figure 2: Kaplan-Mayer curves showing earlier TKA revision for patients with higher daily opioid consumption. MED = morphine equivalent dose.

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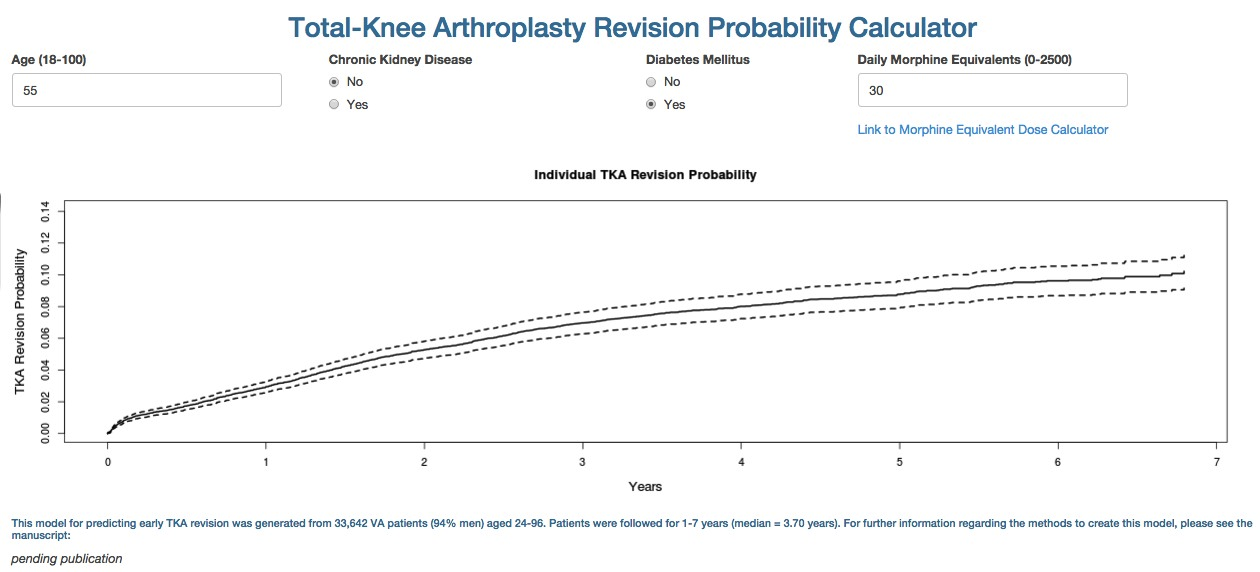
Table 1: Variables included in the Cox proportional hazard model predicting TKA revision.

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| --- | --- | --- | --- |
| **Variable** | **Hazard Ratio** | **95% CI** | **P-Value** |
| Age | 0.9518 | 0.9489 - 0.9547 | < 0.0001 |
| CKD | 1.5106 | 1.3820 - 1.6512 | < 0.0001 |
| Daily Oral Morphine Equivalents (mg) | 1.0008 | 1.0005 - 1.0009 | 0.0013 |
| Diabetes | 1.1616 | 1.0979 - 1.2290 | 0.0079 |

Figure 3: Calibration plot of the TKA Revision model at 1 year showing predicted versus observed revision rates. A histogram plotting frequencies of each predicted revision rate is inlaid on the x-axis.

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Figure 4: Screen shot of the decision support application at [bit.do/tka](http://bit.do/tka) for predicting knee revision following TKA. The user is prompted to enter the patient’s age, daily morphine equivalent dose, and diabetes and chronic kidney disease status. The application displays the patient’s time dependent risk for knee revision.



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