

Patient-Level Factors and Salvage Timing Associated with Progression to Above-Knee Amputation After Periprosthetic Knee Infection

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Introduction

- Above-knee amputation (AKA) is one of the most severe endpoints in the treatment course of periprosthetic joint infection (PJI) after a total knee arthroplasty (TKA), carrying significant patient consequences
- Although AKA is generally reserved for failed salvage or non-reconstructable infection, the clinical trajectory from PJI diagnosis to limb loss remains poorly defined, characterized by small sample size analyses and studies that relied on individual comorbidity indicators
- As a result, it remains unclear whether progression to AKA is driven primarily by baseline host frailty, delays or mismatches in salvage strategy, demographic differences in treatment response, or a combination of these factors

Primary Objective: Identify patient-level factors associated with progression to AKA after knee PJI, utilizing an amputation-weighted frailty framework on a large federated health research network (TriNetX) that captures cumulative physiologic vulnerability

Secondary Objectives:

- Determine whether demographic differences persists after accounting for frailty and treatment patterns
- Characterize the relationship between frailty burden and amputation risk
- Evaluate whether the timing to the first salvage procedure is associated with limb-loss risk

Methods

- Retrospective cohort study utilizing de-identified patient information from the TriNetX Research Network database
- Demographic:** Patients, ages 18 and older, who underwent primary or revision TKA between 1989 and 2025 and developed PJI within 3 years of surgery
- N = 10,160** (mean age 64.2 ± 9.9 years; 5,147 men (50.7%); 5,013 women (49.3%))
- Primary Outcome:** AKA occurring after PJI diagnosis
- Primary Exposure:** Biological sex, patient frailty via the Accumulated Frailty Index (AFI), timing to first salvage procedure, and self-reported race and ethnicity
- Multivariable logistic regression identified independent predictors of AKA

Results

- Among the 10,160 patients, 218 patients (2.15%) underwent AKA
- Female Sex was independently protective against AKA (adjusted OR 0.71, 95% CI 0.54–0.94, P = 0.017) despite higher baseline frailty, resulting in lower amputation rates than men (1.82% vs 2.47%, P = 0.028; **Figure 1**)
- Amputation risk increased with AFI burden across the cohort (**Figure 2**). Patients in the highest frailty quartile (AFI >0.156) experienced 4.2-fold higher amputation rates compared to the lowest quartile (3.74% vs 0.90%, P < 0.001 for trend)
- Among patients who underwent salvage procedures, timing demonstrated a non-linear relationship with amputation risk (**Figure 3**). Intermediate salvage timing (8-30 days) showed the highest amputation rates (5.64%) with significantly elevated risk versus early salvage ≤7 days (2.94%; adjusted OR=1.89, 95%-CI 1.17-3.04, P = 0.009), while delayed salvage >30 days (3.31%) had comparable outcomes to early intervention (OR=1.12, P = 0.597)
- Kaplan-Meier survival analysis confirmed no significant differences in 3-year limb salvage rates across racial groups (White: 97.8%; Black: 97.9%; Hispanic: 98.5%; log-rank P = 0.751; **Figure 4**)

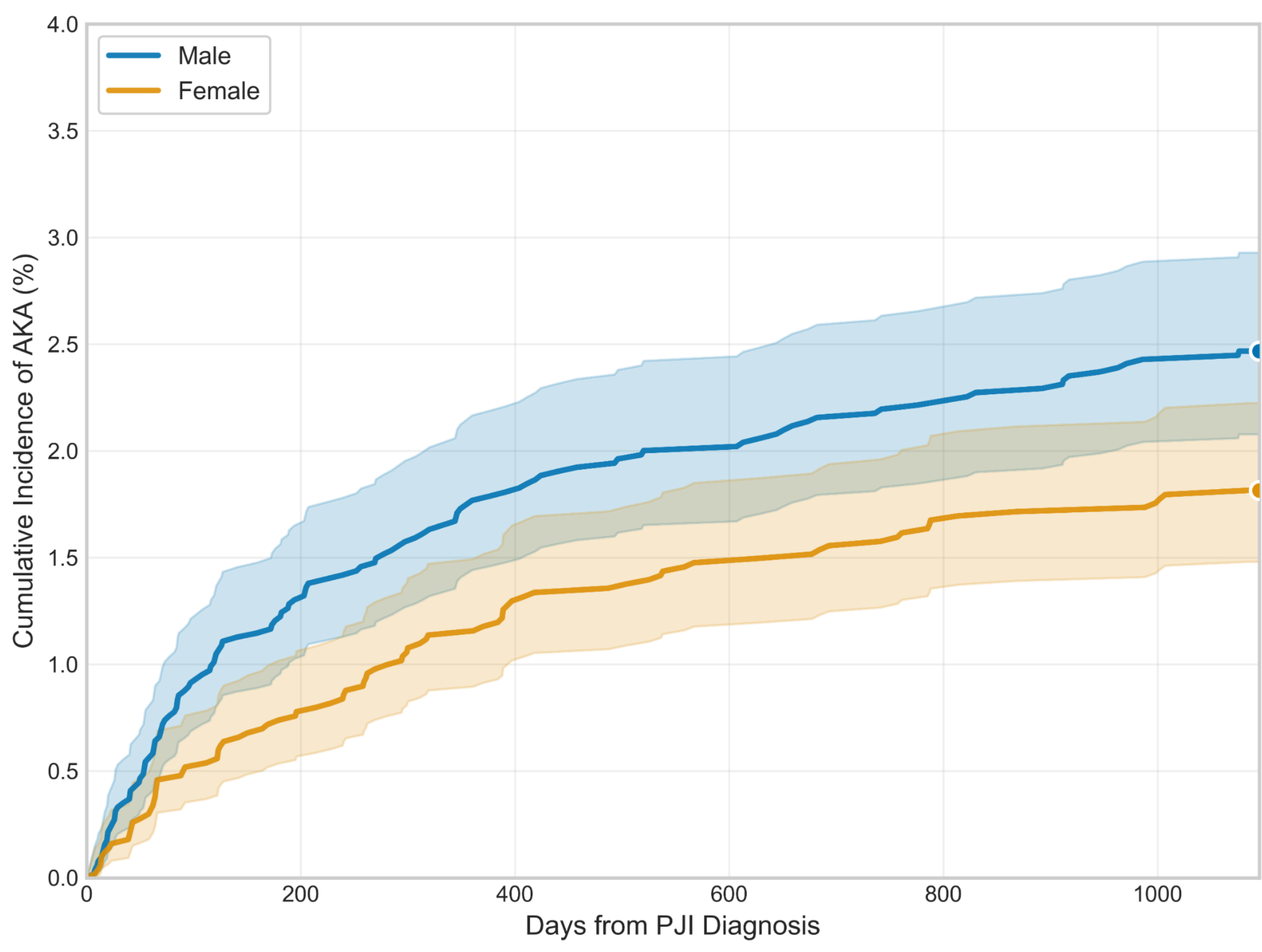


Figure 1. Cumulative Incidence of Above-Knee Amputation by Sex

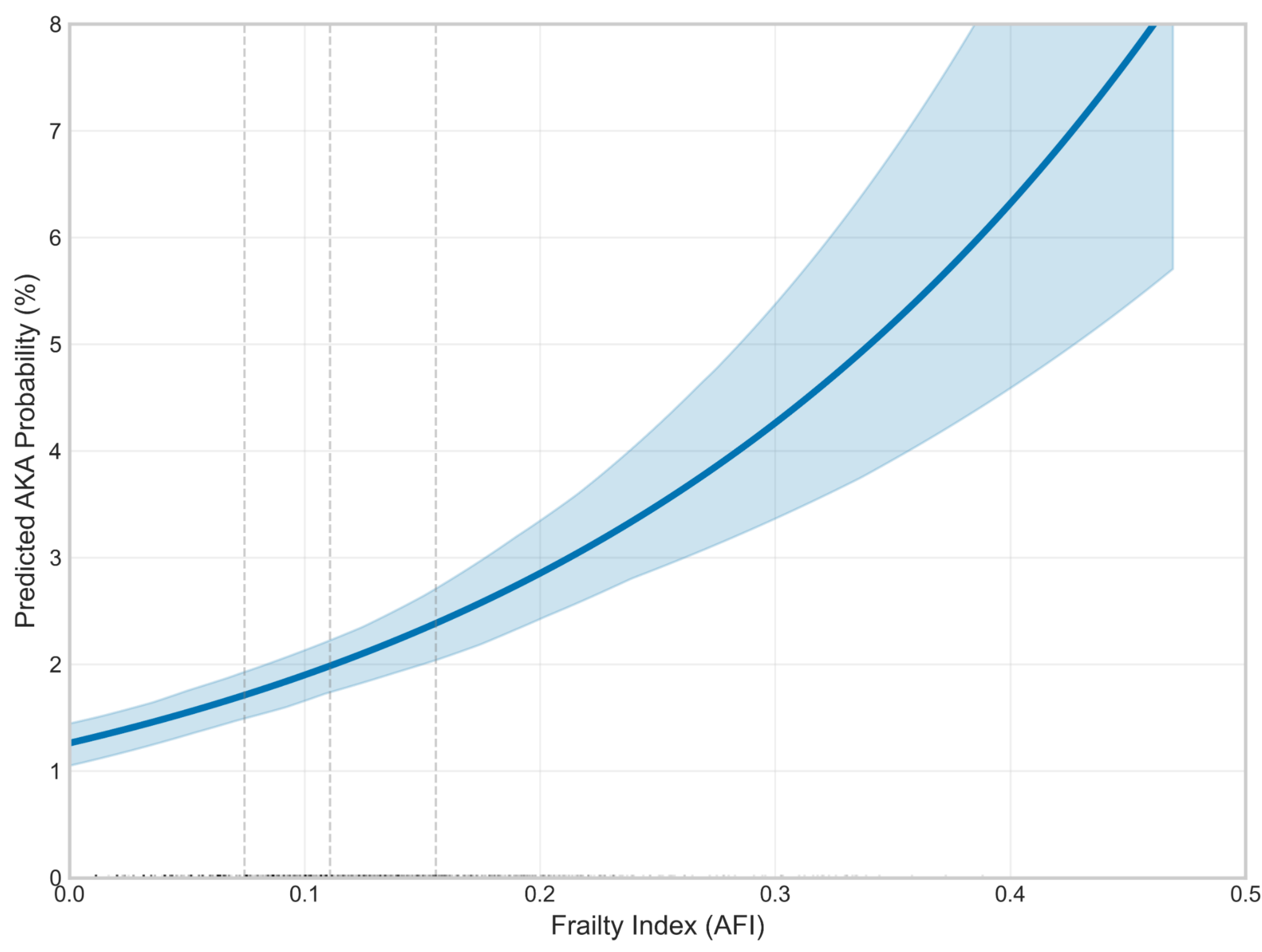


Figure 2. Relationship Between Frailty Index and Predicted Amputation Risk

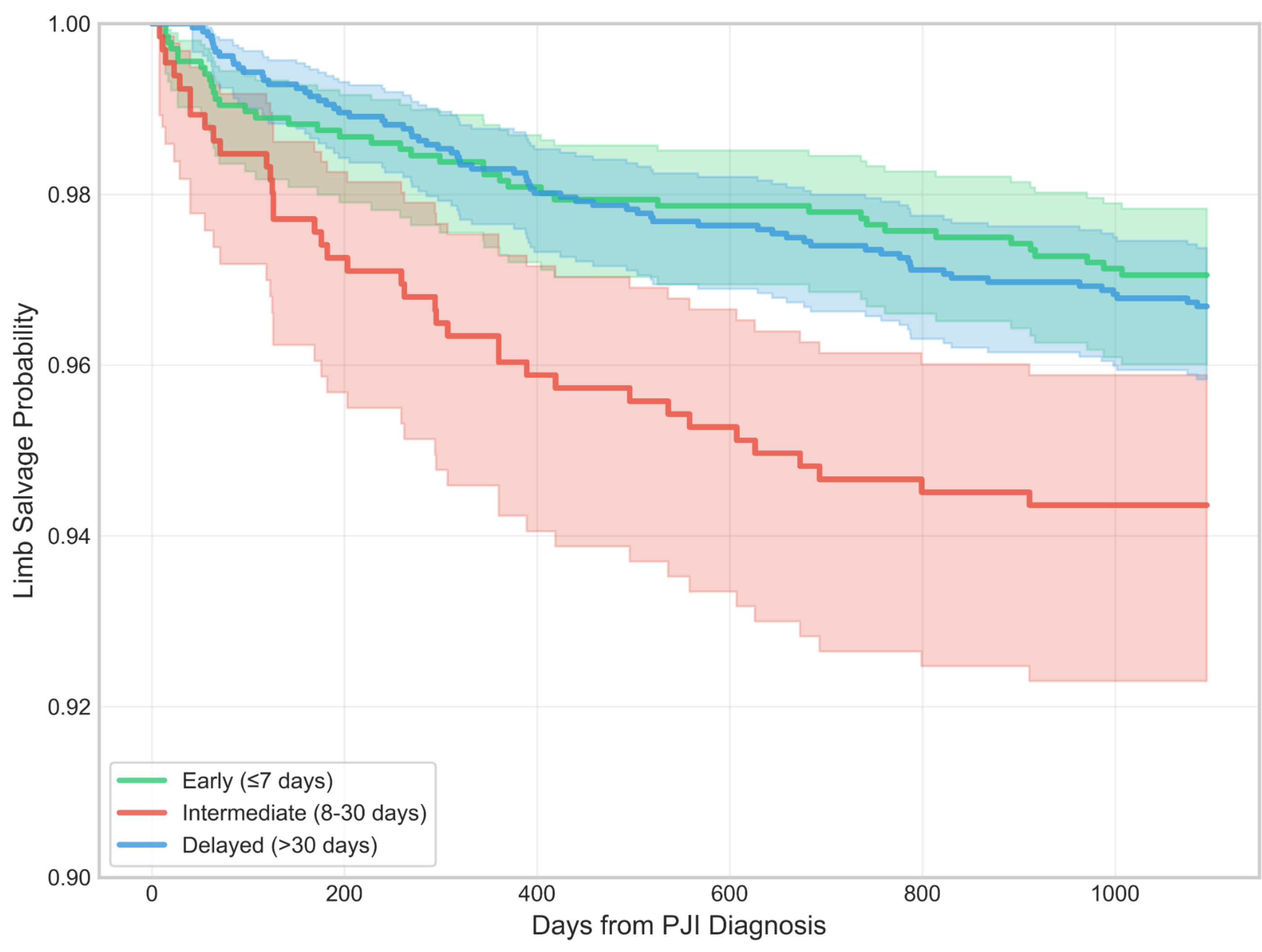


Figure 3. Limb Salvage by Time to First Salvage Procedure

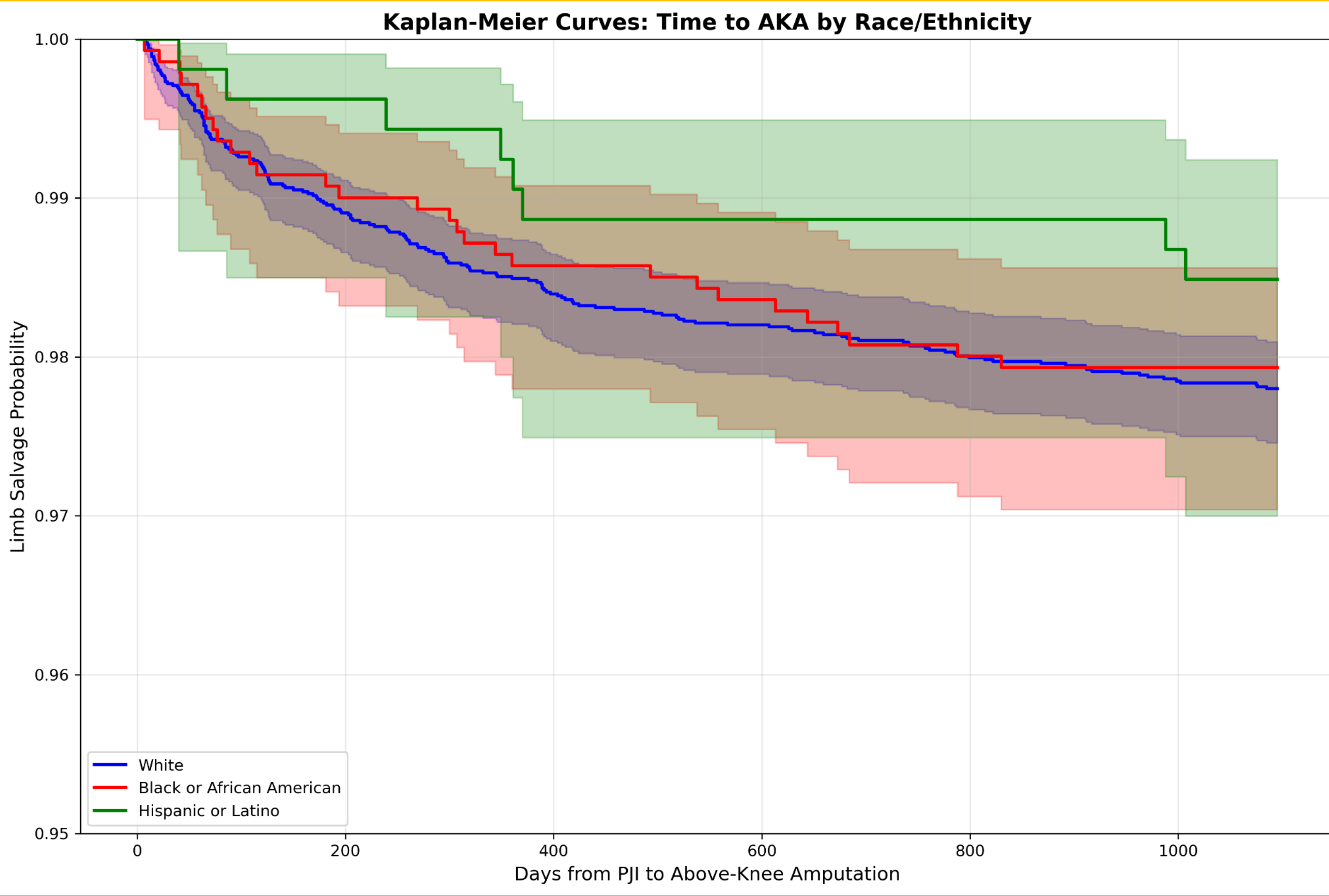


Figure 4. Limb Salvage Probability by Race and Ethnicity

Discussion/Conclusion

- Progression to AKA after knee PJI was independently associated with male sex, increasing accumulated frailty burden, and intermediate delay of 8-30 days to initial salvage intervention
- Female patients demonstrated a protective effect against amputation despite higher baseline frailty, demonstrating the importance of accounting for cumulative physiologic reserve rather than isolated comorbidities when assessing risk
- Differences in amputation rates across frailty groups provide a practical context for patient counseling while reinforcing that limb salvage remains achievable for most patients
- The relationship between salvage timing and amputation suggests a vulnerable interval during which implant-retaining strategies may be less effective