# Examining clinical outcomes in a cohort of incident *Clostridium difficile* patients using parametric survival methods

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## Introduction

*Clostridium difficile* infection (CDI) is the most commonly recognized cause of healthcare-associated diarrhea. An increase in the number of cases of CDI since 2000 in the U.S. and Europe has made it a growing infection control issue and a burden on the healthcare system.

In order to make well-informed infection control decisions, it is important to estimate both the outcomes of patients with CDI as well as their length of stay. Patients with longer lengths of stay may represent increased transmission risks, as they have greater opportunity to shed into the hospital environment. We explore here estimating death and discharge using two competing risk models – a cause-specific model, and a mixture model.

## Study Population

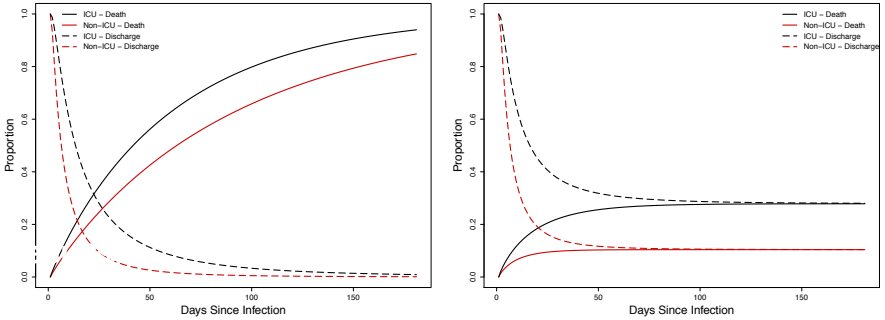
Patients in the Duke DICON network (28 hospitals in the Southeastern USA) over 18 years of age were drawn from incident cases between 7/1/2009 and 12/31/2010, for a total of 609. Patients were followed until death, discharge, or administrative censoring after 6 months. Patients with an unknown discharge date (~2% of the cohort) were interval censored from 12 hours after admission until the administrative cutoff.

## Results

Overall, there were 42 deaths and 118 discharges in the ICU patient population, compared with 43 deaths and 406 discharges in the non-ICU patient population.

| Model | $RT_D$ | 95% CI | $RT_N$ | 95% CI | $\pi_1$ | $\pi_0$ | $OR_\pi$ | 95% CI |
|---|---|---|---|---|---|---|---|---|
| Cause-Specific (Crude) | 0.72 | 0.39, 1.35 | 2.45 | 1.86, 3.25 | - | - | - | - |
| Cause-Specific (Adjusted)* | 0.65 | 0.37, 1.17 | 2.28 | 1.64, 3.17 | - | - | - | - |
| Mixture Model (Crude) | 2.24 | 1.25, 4.02 | 2.01 | 1.50, 2.69 | 0.26 | 0.10 | 3.36 | 1.85, 6.11 |
| Mixture Model (Adjusted)* | 1.94 | 0.94, 3.99 | 1.87 | 1.40, 2.50 | 0.28 | 0.10 | 3.33 | 1.83, 6.06 |

Abbreviations: $RT_D$, relative difference in mean time until death; $RT_N$, relative difference in mean time until discharge; $R_\pi$, odds ratio of mixing proportions in the ICU and non-ICU patient population; CI, confidence interval. *Adjusted for patient's age, gender and race, location prior to admission, whether or not patient was a surgical patient or on dialysis, and if this was a new CDI episode.




Figures 1 and 2. **Survival Curves for ICU and Non-ICU Patients**. These curves show the proportion of patients who have died or been discharged from the hospital for the cause-specific model (Figure 1) and the mixture model (Figure 2).

## Discussion

These results suggest that infection control efforts in the ICU may have a disproportionate impact both in reducing adverse clinical endpoints and in preventing environmental contamination by active CDI patients during their hospital stays.

Patients within the ICU had 3.33 times the odds of dying compared to non-ICU patients, and experience longer times until *both* death and discharge based on the mixture model. The conventional cause-specific competing risk model seriously underestimates the time until death by conflating the proportion of patients who die with their time until death.

## Analysis

Two different parametric survival models were used to estimate the ratio between the mean time until death ($RT_D$) and mean time until discharge ($RT_N$). The cause specific model estimates each separately, treating patients experiencing the other event are treated as censored. The mixture model, in contrast, estimates both outcomes simultaneously as a mixture of two survival models, estimating $RT_D$ and $RT_N$, as well as the proportion of patients in both the ICU and general hospital population who died ($\pi_1$ and $\pi_0$ respectively). From those, an estimate of a patient's relative odds of death ($OR_\pi$) may be obtained.

Control for confounding was achieved using inverse probability weights, including variables that were marginally associated (P value = 0.20) with either death or discharge (see table). This allows for the production of covariate-adjusted survival curves (see Figures 1 and 2). Missing data was handled using multiple imputation.

All analysis was done in SAS 9.2

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