

The Incidence, Cost, and Outcome Effects of Infections Two Years Before and After Kidney Transplantation

Kutinova A, MA; Woodward RS, PhD; Ricci JF, PhD;
and Brennan DC, MD

University of New Hampshire, Durham, NH; Washington University, St Louis,
MO; Novartis Pharma, AG, Basle, Switzerland



Background

- Pediatric patients: post-transplant infections lead to more hospitalizations than acute rejections.

[Dharnidharka et al, *Am J Transplant* 2004]

- Sepsis and pneumonia: most commonly diagnosed infections in dialysis patients and kidney transplant recipients.

[Abbott et al, *Am J Nephrol* 2001; Abbott et al, *J Nephrol* 2002; Tveit et al, *J Nephrol* 2002; Sileri et al, *Clin Transplant* 2002; Chang et al, *Chest* 2004; Sarnak et al, *Chest* 2001]

- Negative impact of infections on patient and graft survival.

[Witzke et al, *J Urol* 2001; Brayman et al, *Arch Surg* 1992]

Aim

- Estimate the incidence, financial costs, and graft survival consequences of infections in the two years before and after renal transplantation.

Data

- United States Renal Data System (USRDS)
- Inclusion criteria:
 - First kidney transplants,
 - January 1, 1995 to December 31, 2001,
 - Medicare as the primary payer,
 - Complete information,
→ 44,916 observations.
- Start of follow-up: first physician/supplier or institutional claim.
- End of follow-up: last claim, last follow-up, death, or December 31, 2001.

Methods: Incidence

- Incidences of diagnoses calculated daily among followed individuals.
- Reported as the number of individuals with sepsis/pneumonia claims per 100 patient years.
- Claims: USRDS institutional and physician/supplier files with ICD-9-CM diagnoses.
 - Sepsis: 038
 - Pneumonia: 480-487

Methods: Cohort Analysis (Costs and Graft Survival)

- Infection “onset”: date of first inpatient and/or second outpatient claim with a relevant ICD-9-CM code.
- 5 cohorts:
 - 1) Infection onset 2nd year pre-transplant,
 - 2) Infection onset 1st year pre-transplant,
 - 3) Infection onset 1st year post-transplant,
 - 4) Infection onset 2nd year post-transplant,
 - 5) Patients with no infection claim in the 2 years pre- or post-transplant.

Methods: Costs

- Average Accumulated Medicare Payments (AAMPs): Medicare payments for treating an average patient in our 5 cohorts accumulated over 2 years before and after transplantation.

$$\text{AAMP}(t) = \text{AAMP}(t-1) + [\text{total Medicare payments } (t) / \text{number of individuals followed } (t)]$$

- Confirmatory analyses:
 - 1. Bootstrap techniques used to identify significant differences.
 - 2. Multiple regression analyses of Medicare payments at one year post transplant (for individuals followed at least one year post transplant) controlling for significant recipient, donor, and transplant characteristics (age, gender, race/ethnicity, CMV status, HLA mismatches, warm ischemia time, cold ischemia time, immunosuppression regimen).

Methods: Graft Survival

- Graft survival rates calculated over 2 years post transplantation separately for our 5 patient cohorts.
- Kaplan-Meier graft survival curves.
- Pairwise log-rank statistics used to test the equality of graft survival across patient cohorts.

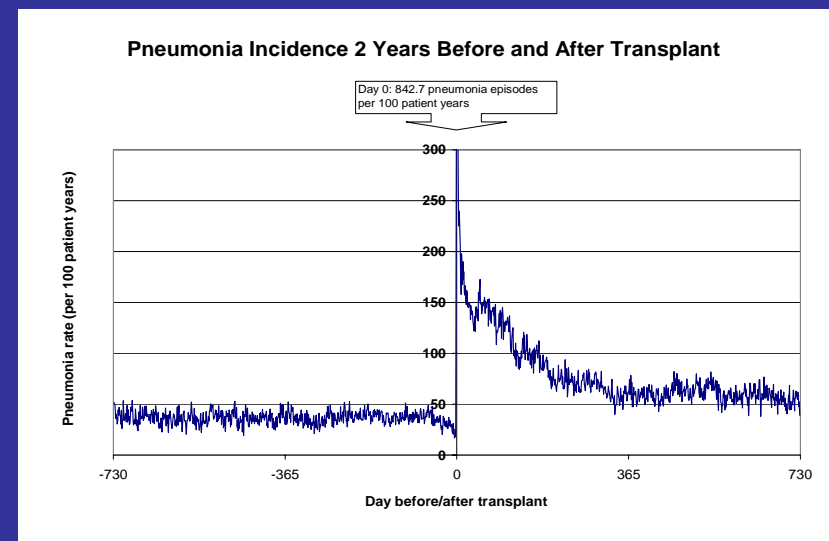
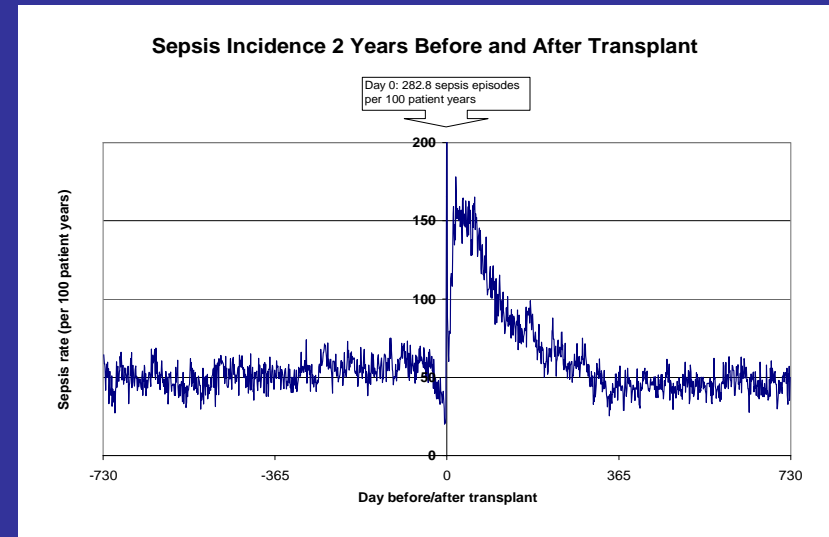
Results: Incidence

Sepsis:

- Pre-transplant:
52 episodes/100 patient years.
- 1st month post-transplant:
133 episodes/100 patient years.
- Post-transplant steady state:
46 episodes/100 patient years
($p < 0.001$).

Pneumonia:

- Pre-transplant:
37 episodes/100 patient years.
- 1st month post-transplant:
216 episodes/100 patient years.
- Post-transplant steady state:
60 episodes/100 patient years
($p < 0.001$).



Results: Costs

Sepsis:

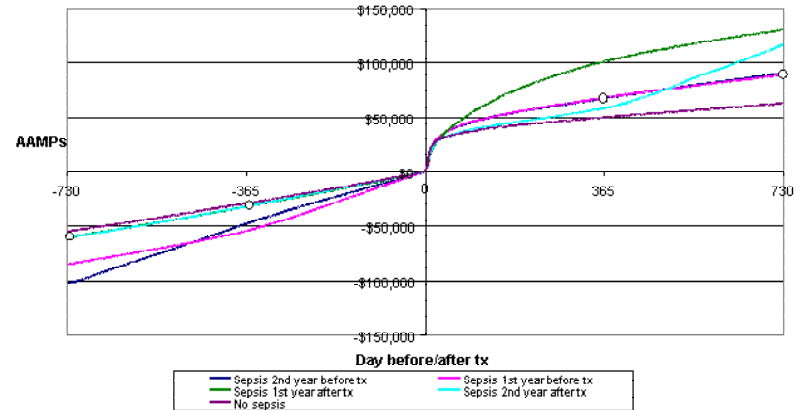
- No sepsis claims:
 - Pre-tx: \$27,400 annually,
 - 1st year post-tx: \$50,000,
 - 2nd year post-tx: \$13,000.
- Sepsis pre-transplant:
 - **\$27,400 extra** during the year of sepsis onset.
- Sepsis post-transplant:
 - **\$48,400 extra** during the year of sepsis onset.

Pneumonia:

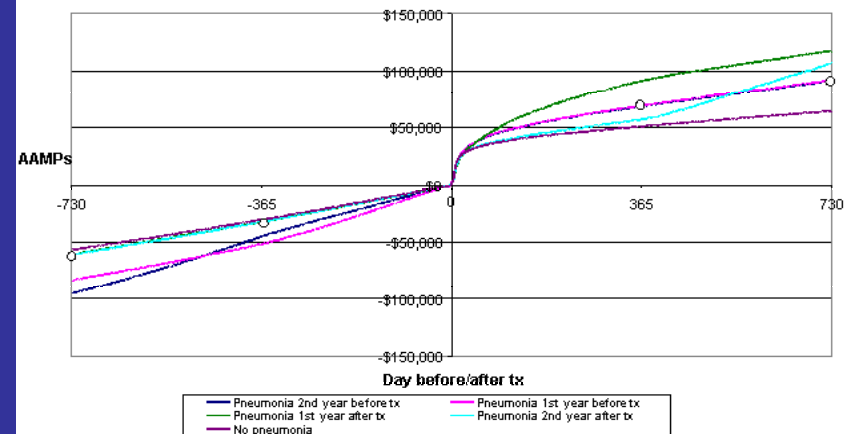
- No pneumonia claims:
 - Pre-tx: \$28,400 annually,
 - 1st year post-tx: \$51,100,
 - 2nd year post-tx: \$13,500.
- Pneumonia pre-transplant:
 - **\$22,800 extra** during the year of pneumonia onset.
- Pneumonia post-transplant:
 - **\$38,400 extra** during the year of pneumonia onset.

Size and significance of cost differences confirmed by bootstrapping and by multivariate regression techniques.

Sepsis: Average Accumulated Medicare Payments



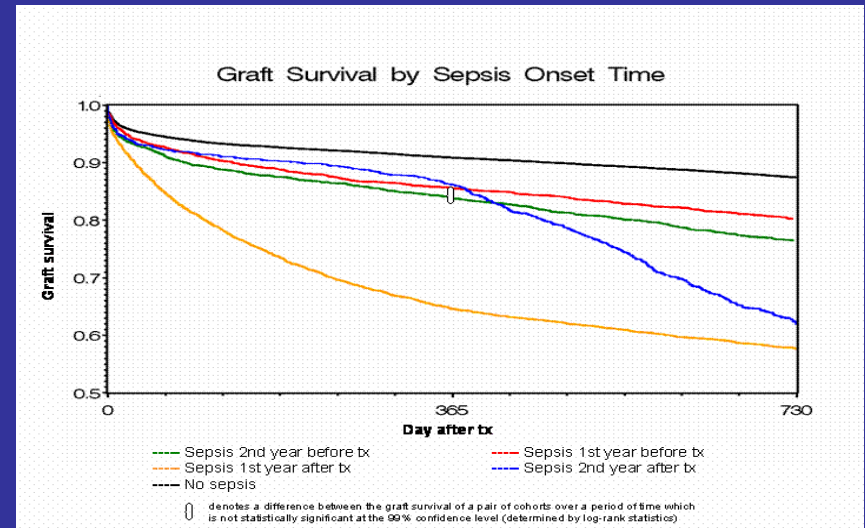
Pneumonia: Average Accumulated Medicare Payments



Results: Graft Survival

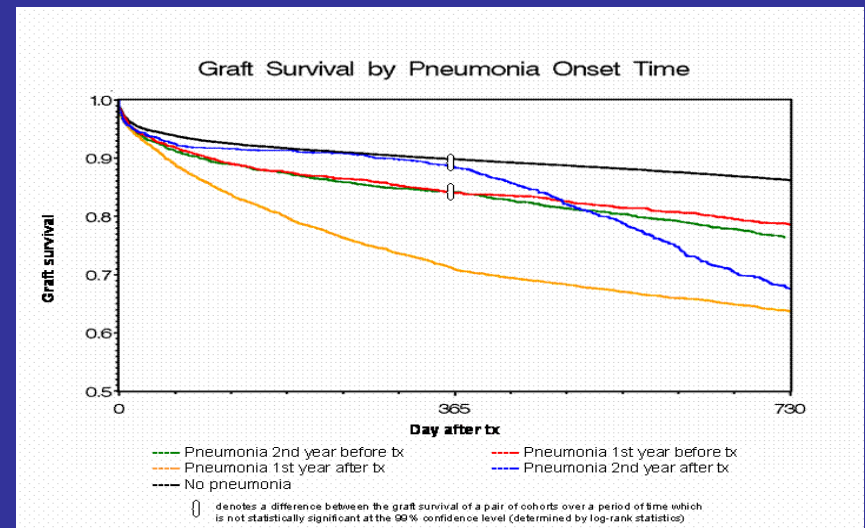
Sepsis:

- No sepsis claims:
 - 1-year graft survival: 91%.
- Sepsis pre-transplant:
 - 1-year graft survival: **86%** ($P < 0.01$).
- Sepsis 1st year post-transplant:
 - 1-year graft survival: **65%** ($P < 0.01$).



Pneumonia:

- No pneumonia claims:
 - 1-year graft survival: 90%.
- Pneumonia pre-transplant:
 - 1-year graft survival: **84%** ($P < 0.01$).
- Pneumonia 1st year post-transplant:
 - 1-year graft survival: **71%** ($P < 0.01$).



Conclusions

- Substantial, but temporary, increases in the incidences of sepsis and pneumonia immediately following kidney transplantation.
 - Incidence of sepsis in the 2nd year post-transplant slightly lower than in the 2 years before transplantation BUT incidence of pneumonia significantly above the pre-transplant value.
 - Onsets of sepsis and pneumonia a strong and immediate impact on Medicare payments.
 - Sepsis and pneumonia a significant detrimental effect on graft survival.
- Strategies to reduce the incidences of sepsis and pneumonia infections needed to improve the graft outcomes and the cost-effectiveness of renal transplantation.