

**St. Michael's**

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## **Hemodialysis vs. Peritoneal Dialysis: Does Modality Matter in the Patient with a Failed Kidney Transplant?"**

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**American Society of Nephrology  
Clinical Nephrology Conference  
Thursday November 18, 2010  
Denver, Colorado, USA**

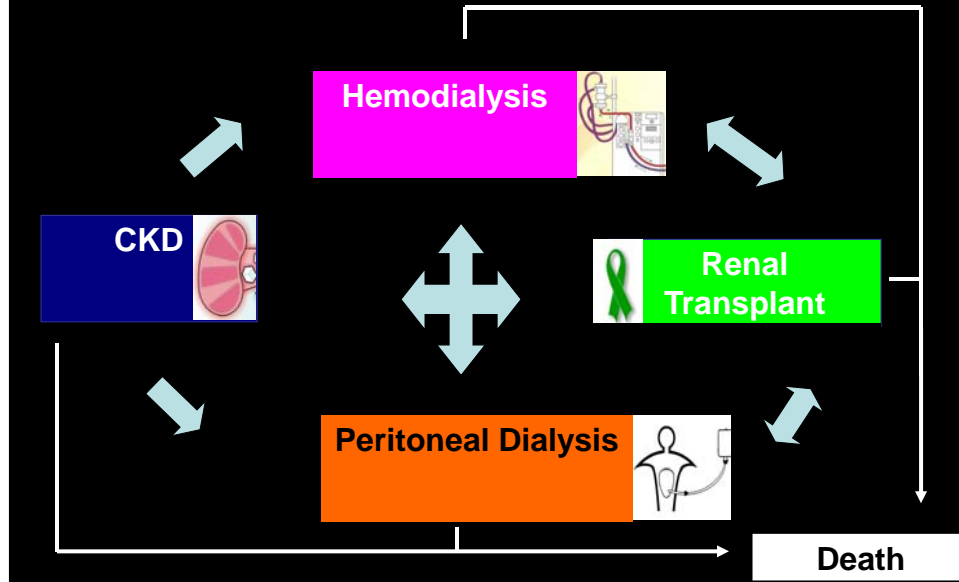


## **Disclosures**

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- Speaking honoraria:
  - Baxter Healthcare Canada
  - Amgen Canada
- Unrestricted educational fellowship:
  - Baxter Healthcare Canada

# The CKD Continuum



## Dialysis After Graft Loss: Unique Considerations

### Inflammatory Pseudotumor of the Kidney Allograft

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## **Objectives**

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- Epidemiology of dialysis after renal allograft loss
- Survival
- Impact of dialysis modality: PD vs. HD
- Outcomes on Peritoneal Dialysis
  - Patient survival
  - Technique survival
  - Infectious Complications
  - Peritoneal Membrane Function

## **Transplant Failure: Among the Top 5 Causes of Dialysis Initiation**

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- Increasing number of prevalent transplant recipients
- Relatively fixed duration of graft survival
- Limited opportunities for repeat transplantation

## Transplant Failure: Among the Top 5 Causes of Dialysis Initiation

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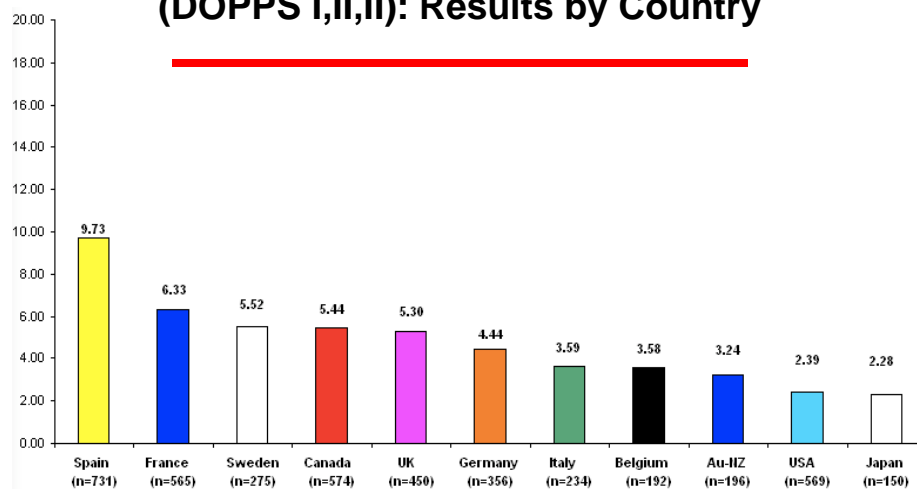
- ❑ US:
  - ❑ 2007-4.1% of new patients initiated dialysis after graft loss (DAGL)
  - ❑ 10% of these will be retransplanted
- ❑ Canada:
  - ❑ 2% to 3% of the annual incident dialysis patient population

US Renal Data System:USRDS 2007 Annual Data Report. In, Bethesda, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2007

2002 CORR Preliminary Report: Preliminary Statistics for Renal Failure and Solid Organ Transplantation in Canada. . In, Ottawa, ON: , Canadian Organ Replacement Register 2002, 2002

## Percentage of Hemodialysis Patients Admitted to a DOPPS Facility After Transplant Failure (DOPPS I,II,II): Results by Country

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Perl et al, in press

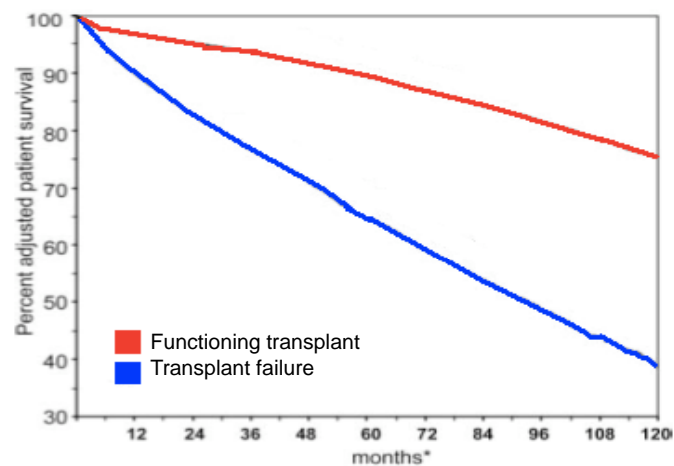
## What is the mortality of these patients?

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- Relative to patients with ongoing graft function
- Relative to incident dialysis patients

## Survival After Graft Loss vs. Patients with Ongoing Graft Function

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Kaplan et al AJT 2002: 970-974

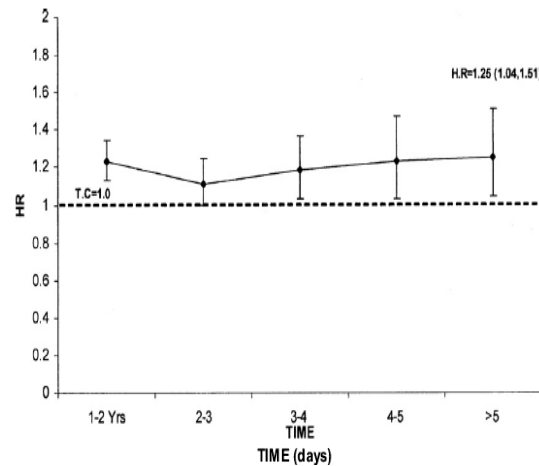
## Patient Survival: Dialysis After Graft Loss

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- ❑ Patients who return to dialysis after transplantation experience a rapid decline in quality of life and reduced survival.
- ❑ Is their mortality worse than incident (transplant-naive) dialysis patients?

## Patient Survival: Dialysis After Graft Loss

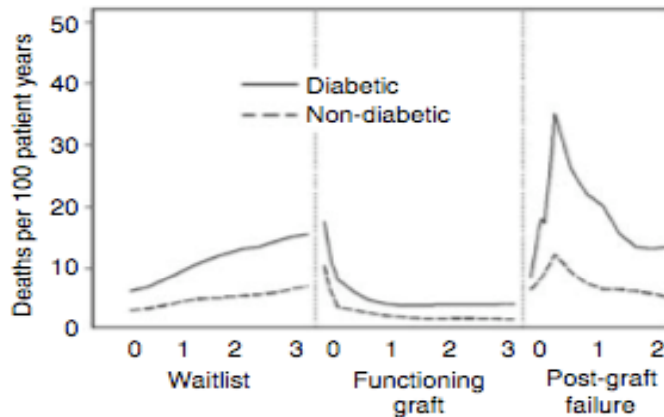
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Rao et al Am J Kidney Dis. 2007 Feb;49(2):294-300.

## Death After Graft Loss

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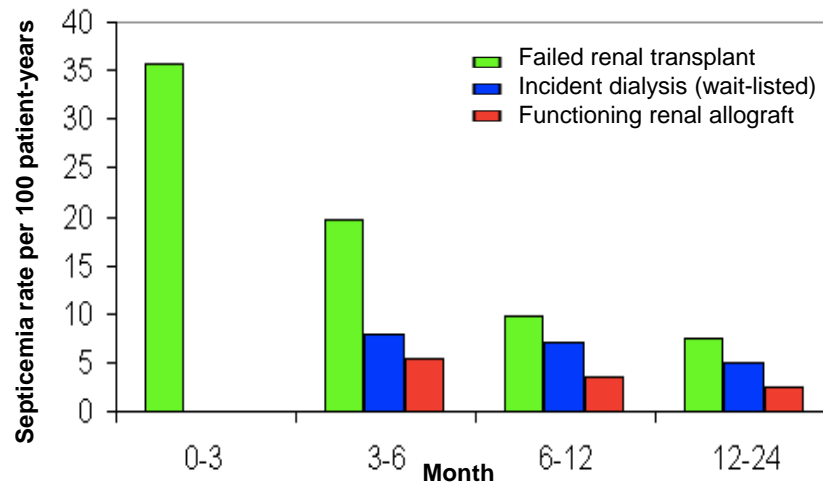
Gill et al, Kidney International (2007) 71, 442–447

## Patient Survival: Dialysis After Graft Loss

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- Why is mortality worse?
  - Effects of concomitant and prior immunosuppressive therapy?
  - Long “uraemic history”
    - pretransplant dialysis
    - graft CKD
  - Transplant Graft: chronic inflammatory state
    - Epo resistance
    - Hypoalbuminemia
    - Elevated CRP

## Rates of Septicemia: Transplant Failure vs. Functioning Renal Allograft vs. Incident Dialysis



Johnston et al J Am Soc Nephrol 18: 1331-1337, 2007

## Death after graft loss due to infection

Outcome	Mortality Risk for Transplant Failure Patients (Compared to Transplant Naive Patients)					
	Unadjusted			Adjusted*		
	HR	CI	P-value	HR	CI	P-value
All-Cause Death	1.37	(1.11-1.69)	0.003	1.32	(1.05-1.66)	0.02
Cardiovascular Death	1.56	(1.15-2.12)	0.004	1.52	(1.07-2.16)	0.02
Infection-Related Death	3.01	(1.82-4.99)	<.0001	2.45	(1.36-4.41)	0.003



Perl et al, in press



## **Survival After Graft Loss: Potentially Modifiable Risk Factors**

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- Improved predialysis care
- Method of immunosuppression tapering
- Better access to kidney retransplantation
- Graft Nephrectomy vs. Preservation of Transplant residual kidney function
- Mode of Dialysis: Peritoneal Dialysis vs. Hemodialysis

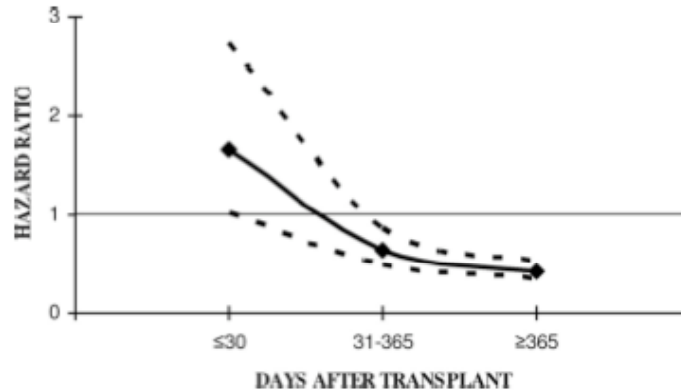
## **Survival After Graft Loss: Potentially Modifiable Risk Factors**

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## Retransplantation is associated with improved survival

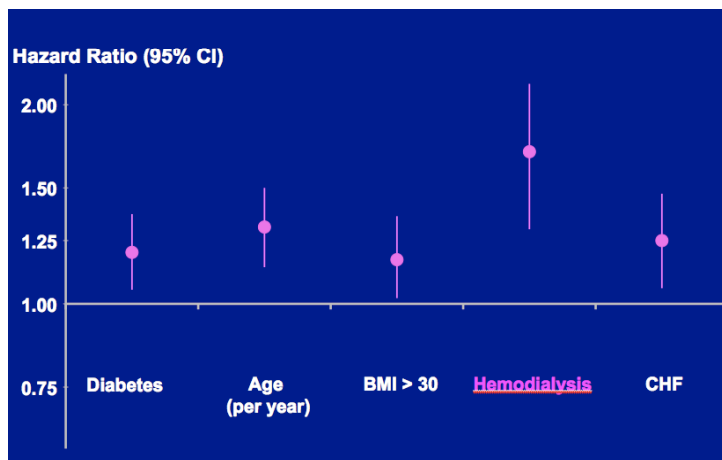
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Rao et al *Transplantation* 82:669-674, 2006

## Hemodialysis is associated with a greater risk of sepsis after transplant failure

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Johnston et al *J Am Soc Nephrol* 18: 1331-1337, 2007

## High Rates of catheter use after return to dialysis after transplant failure



Odds of an AVF or AVG:

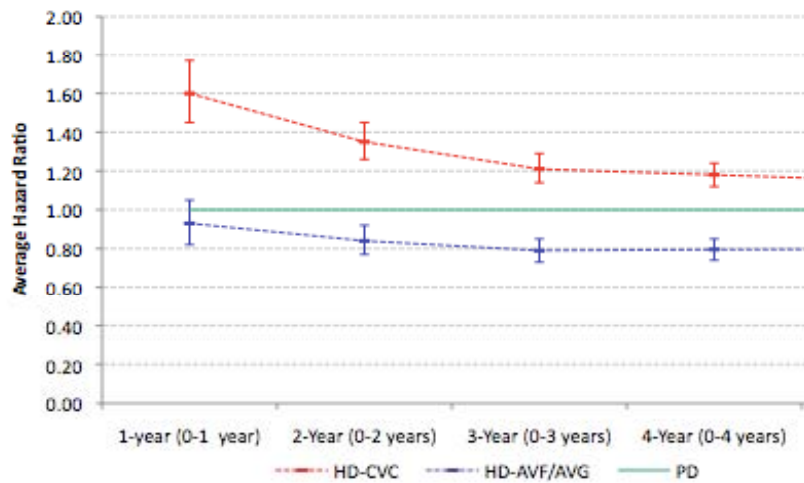
3 months: 0.45 (0.32-0.62)

Overall: 0.85 (0.70-1.03)

Perl et al , unpublished



## Impact of Catheter use on survival in incident dialysis patients



Perl et al submitted in press

## PD technique and Patient Survival after transplant failure

Author	Period	Failed Transplant	control	Patient survival	Technique success
Davies et al	1989-2001	28	469	Similar	Similar
Sasal et al	1989-1996	42	43	Lower	Lower
Duman et al	NA	34	82	Similar	Similar
De Jonge et al	NA	21	136	Similar	Similar
Mujais et al	2000-2003	494	491 (new RRT) 479 (HD->PD)	Similar	Similar
Badve et al	1991-2004	309	13 947	Similar	Similar

*Perl et al, Semin Dial. 2008 May-Jun;21(3):239-44*

## Transplant Residual Renal Function and PD

- CANUSA data: PD patients have an estimated 12% decrease in the relative risk of death with each additional 5L/wk/1.73m<sup>2</sup> increase in GFR
- In the patient with DAGL this must be balanced with the risks of ongoing immunotherapy to preserve GFR
- Jassal *et al* performed a decision analysis to assess the risks vs. benefits of continued transplant immunosuppression

Jassal *et al*, Continued transplant immunosuppression may prolong survival after return to peritoneal dialysis: results of a decision analysis. Am J Kidney Dis. 2002 Jul;40(1):178-83.

## Results

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- Life expectancy for a patient not on immunotherapy was 5.3 years vs. 5.8 years with continued immunotherapy
- Survival benefit higher at higher levels of additional GFRtx
- At all levels of GFRtx

## Impact on Peritonitis

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- ❑ Post transplant failure: higher rates of infection and infectious mortality
- ❑ Andrews et al: increased peritonitis rates in immunosuppressed patients
- ❑ No difference in peritonitis rates between transplant failure and transplant naive patients:
  - ❑ Badve et al HR: 0.92 (0.72-1.16)
- ❑ No difference in technique failure due to peritonitis
  - ❑ Mujais et al: 27.2% vs. 25%

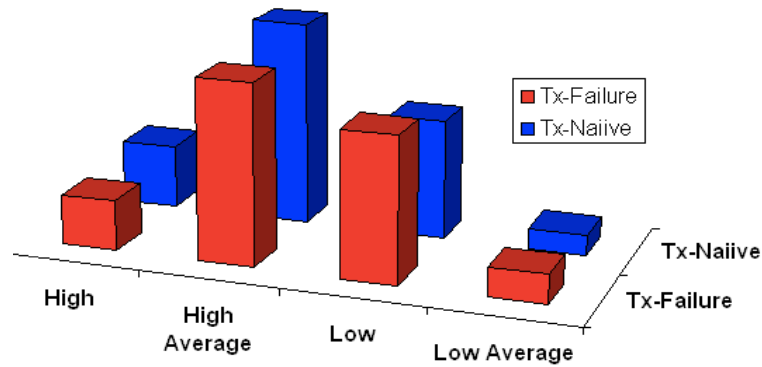
Johnston O et al *J Am Soc Nephrol* 2007

Andrews PA et al *Nephrol Dial Transplant* 11:1104-1108, 1996

Badve SV et al *Nephrol Dial Transplant* 21:776-783, 2006

Mujais S et al *Kidney Int Suppl*:S133-137, 2006

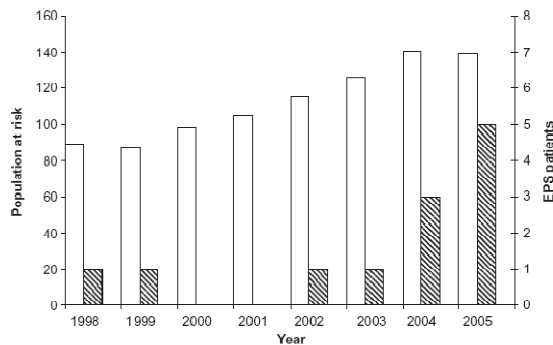
## Impact on Peritoneal Membrane Transport Status



N=5746

Badve et al NDT 2006

## EPS and Renal Transplantation



18 patients in total:

- 13 patients either on HD or transplanted at time of diagnosis

- Increasing incidence of EPS exceeded the increase in patients at risk

- 83% of patients had a history of kidney transplantation

- Mortality 50%

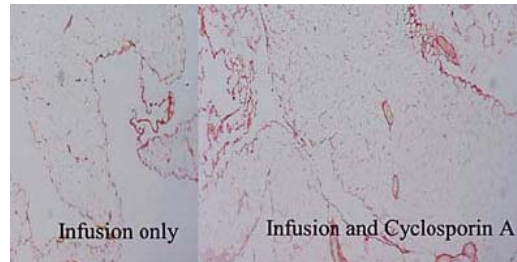
- Shorter period to development of EPS than previous reports

Fig. 1. EPS cases and the population at risk for EPS in Rotterdam centre in 1998–2005. Population at risk is defined by patients with a kidney transplant and a history of PD (open boxes). EPS cases are shown (lined boxes) in Rotterdam. Significant trend of increase of EPS independent of the increase in the defined population at risk ( $P=0.038$ , chi-square trend analysis).

Korte et al NDT 2007

# EPS and Calcineurin Inhibition

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Increased areas of fibrosis in intersegmental and perivascular areas of Cys A exposed rats

*Westrhenen et al Blood Purif 2007*

## How might dialysis modality affect survival after transplant failure?

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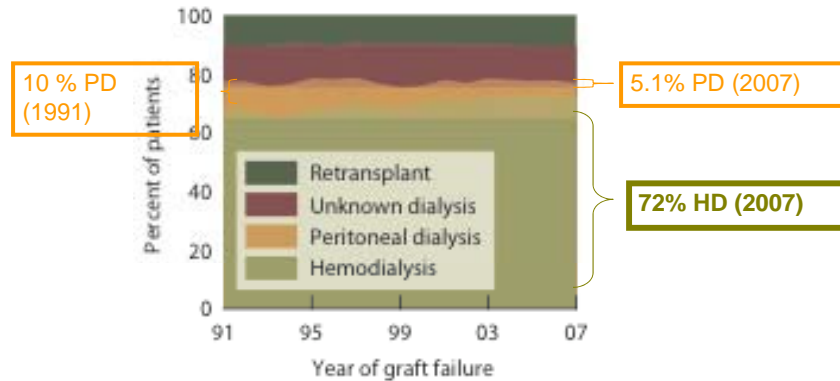
- Limited generalizability from current observational studies of incident patients
- PD vs. HD: time varying survival
- Little is known regarding RKF preservation and its importance after transplant
- Rates of infection high early post transplant failure
- PD associated with lower infectious related mortality

Vonesh EF et al Mortality studies comparing peritoneal dialysis and hemodialysis: what do they tell us? *Kidney Int Suppl* 2006; S3-11

Johnston O, Zalunardo N, Rose C, Gill JS. Prevention of sepsis during the transition to dialysis may improve the survival of transplant failure patients. *J Am Soc Nephrol* 2007

Aslam N, Bernardini J, Fried L, Burr R, et al. Comparison of infectious complications between incident hemodialysis and peritoneal dialysis patients. *Clin J Am Soc Nephrol* 2006; 1: 1226-1233

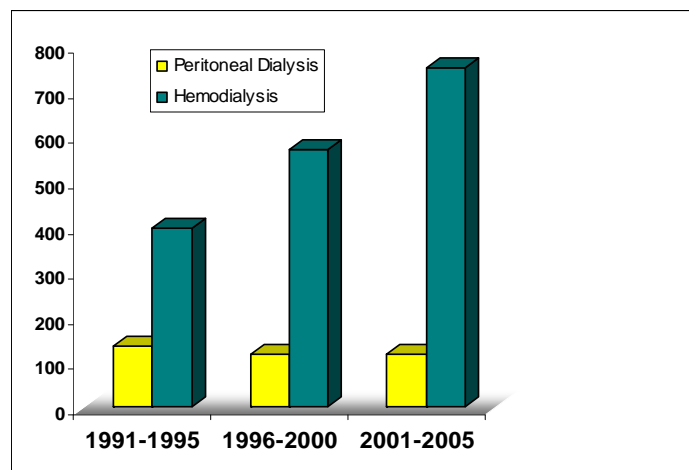
## Use of Peritoneal Dialysis After Allograft Failure



Source: 2009 USRDS Annual Data Report <http://www.usrds.org/>



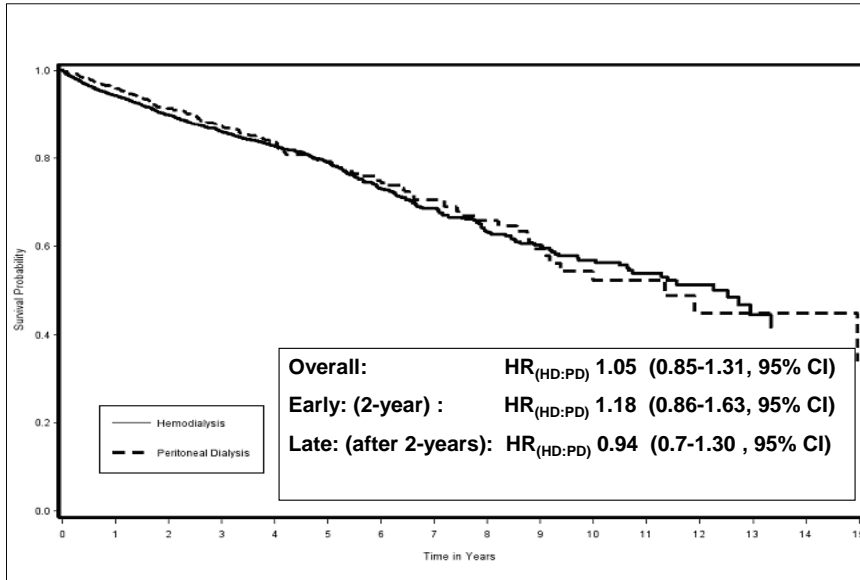
## Use of PD After Allograft Failure



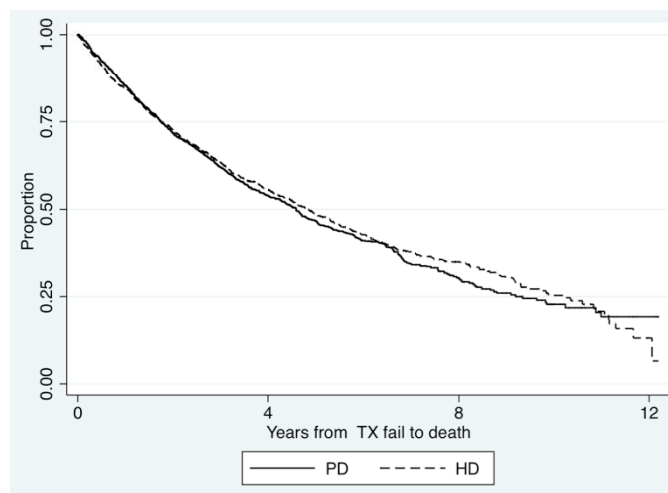
Source: Canadian Organ Replacement Register



## Adjusted Survival PD vs. HD



## Propensity Score Matched survival PD vs. HD



Perl et al, unpublished.

## **Propensity Score Matched survival PD vs. HD**

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Table: Hazard ratio over time frame after adjusting other variables

	0- 1yr	1-2 yr	>2 yr
HD	1	1	1
PD	0.83(0.69-0.99)	0.93 (0.74- 1.16)	1.11 (0.95- 1.30)

Perl et al, unpublished.

## **Conclusions (1):**

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- Reduced survival following return to dialysis after renal allograft loss
  - Compared to patients with ongoing graft function
  - Compared to wait listed incident patients
- Higher rates of sepsis and death due to infection
- Higher rates of catheter use at dialysis initiation

## Conclusions (2):

- PD No increased risk:
  - technique failure
  - death
  - peritonitis
  - Peritoneal membrane function?
- Mortality similar to hemodialysis patients
- ?Early survival benefit - avoidance of use of a catheter
  - transplant residual kidney function

## Questions Comments



**The Home Dialysis Team**  
**St. Michael's Hospital**

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