St. Michael's
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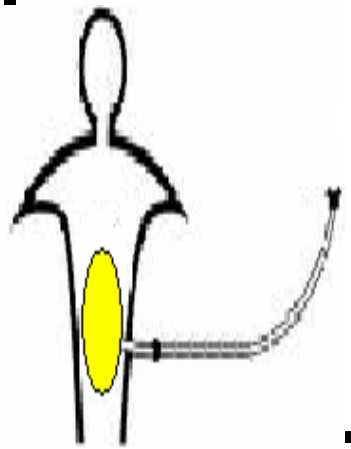
Inspiring Science.

UNIVERSITY OF TORONTO
FACULTY OF MEDICINE

Introduction To The Peritoneal Dialysis Outcomes and Practice Pattern Study

Western Canada PD Days
Friday February 8, 2013
Vancouver, British Columbia



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Disclosures

- Speaking Honoraria, Consultancy Fees:
  - Baxter Healthcare Canada
  - Amgen, Canada
  - Hemosphere USA
  - Shire Canada
- Unrestricted Educational Fellowship:
  - Baxter Healthcare Canada
- Salary Support:
  - Arbor Research Collaborative For Health

Remembering a Colleague, a Mentor and a Friend

Objectives

- Understand the reasons for discontinuation of PD therapy
- Understand Trends in PD Technique Failure in Canada
- Review patient, therapy and facility-specific risk factors for transfer to HD from PD
- Introduce The Peritoneal Dialysis Outcomes Practice Patterns Study (PDOPPS) as a Means to Recognize Modifiable Causes of Peritoneal Dialysis Technique Failure

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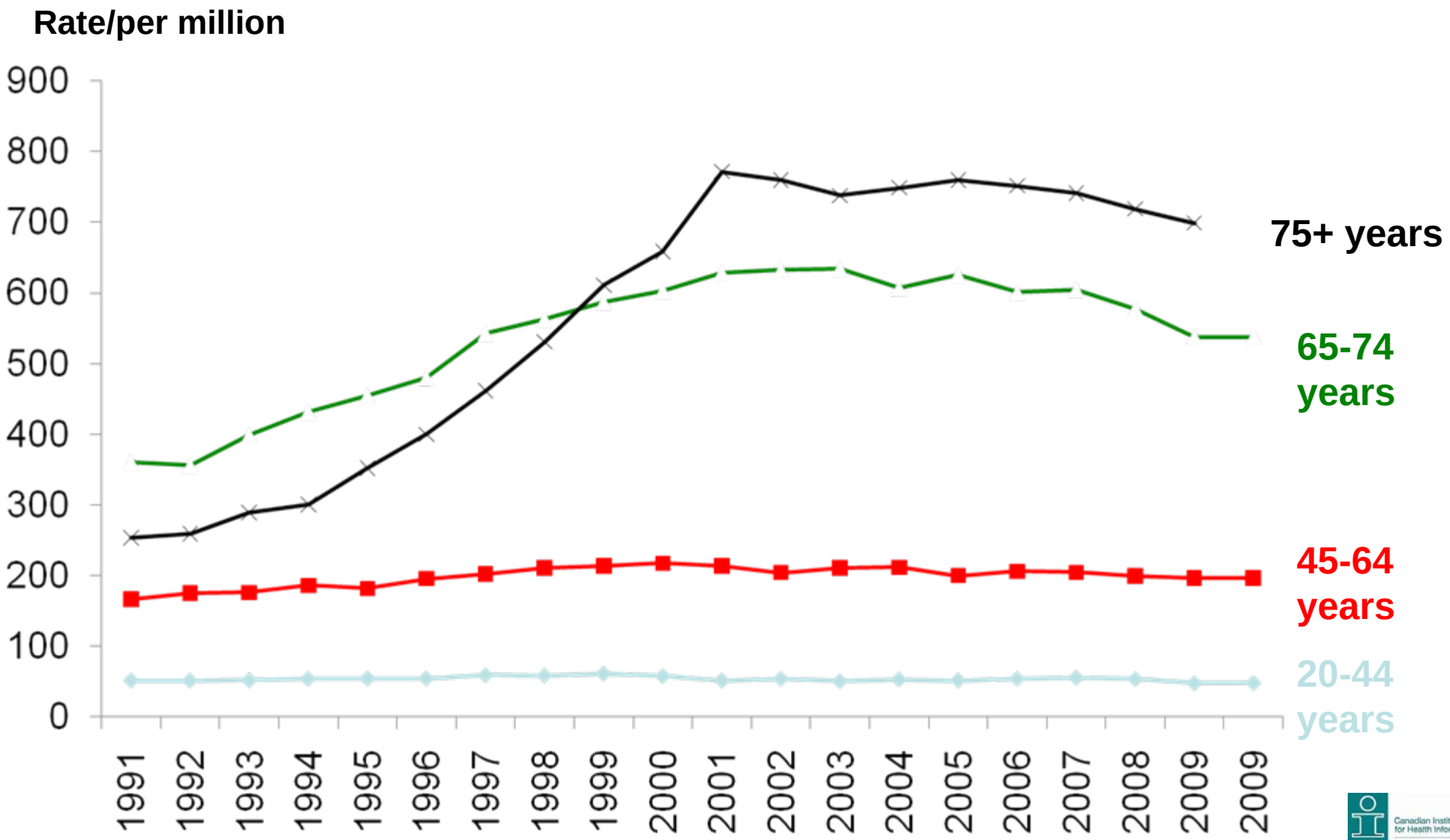
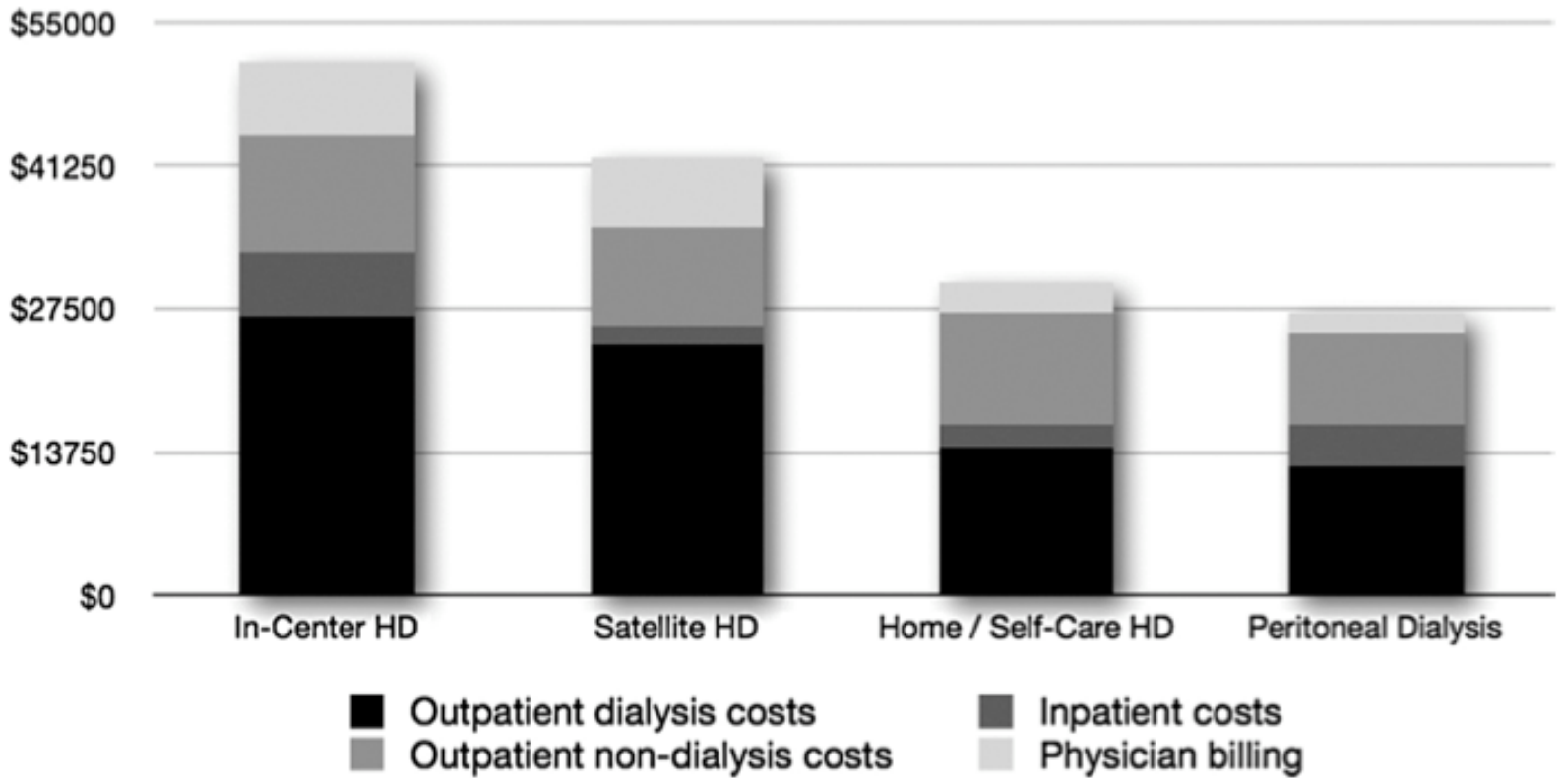
Incident ESRD By Age Group in Canada: Rate Per Million

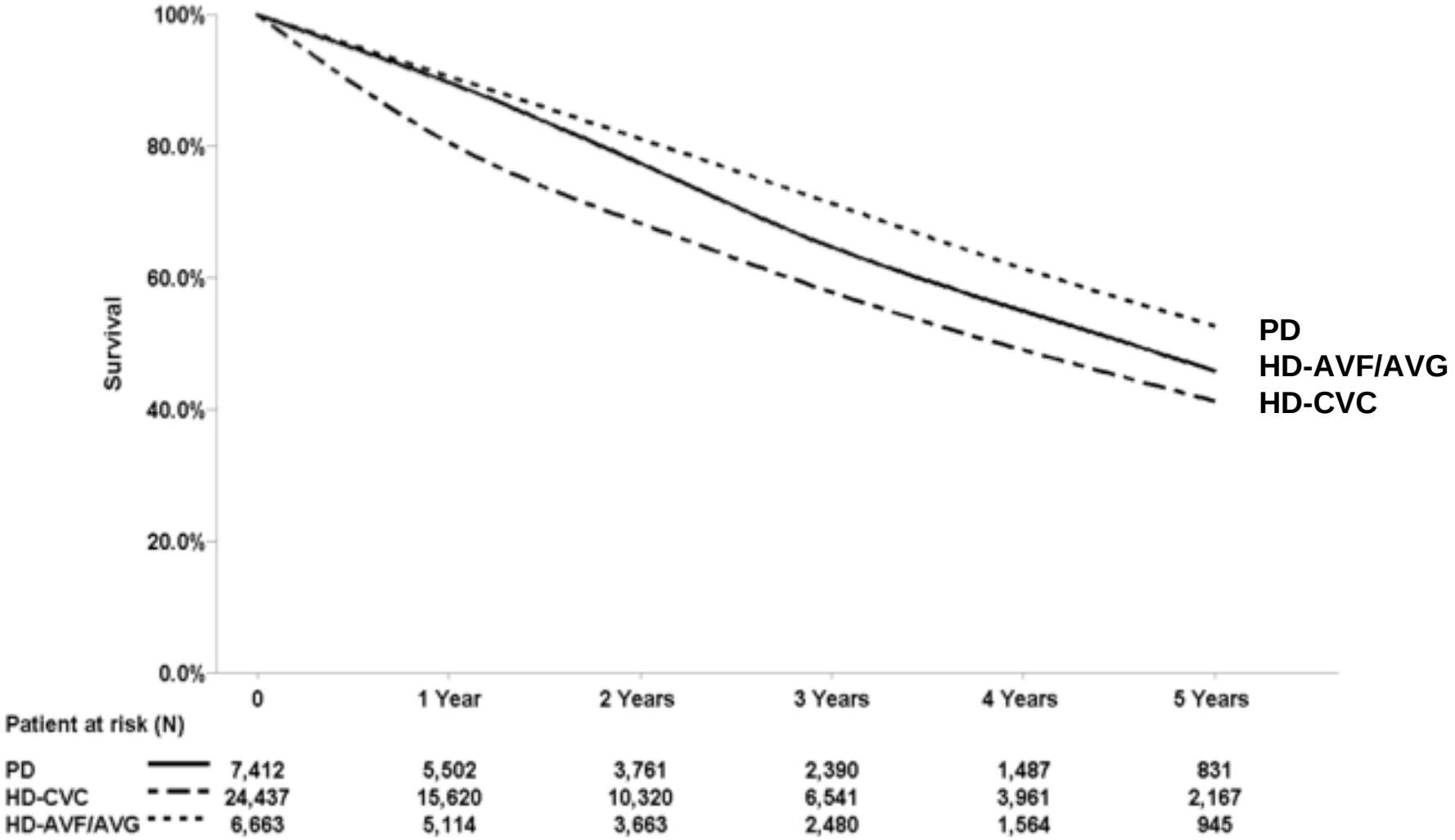


Cost Per Year: PD vs. HD



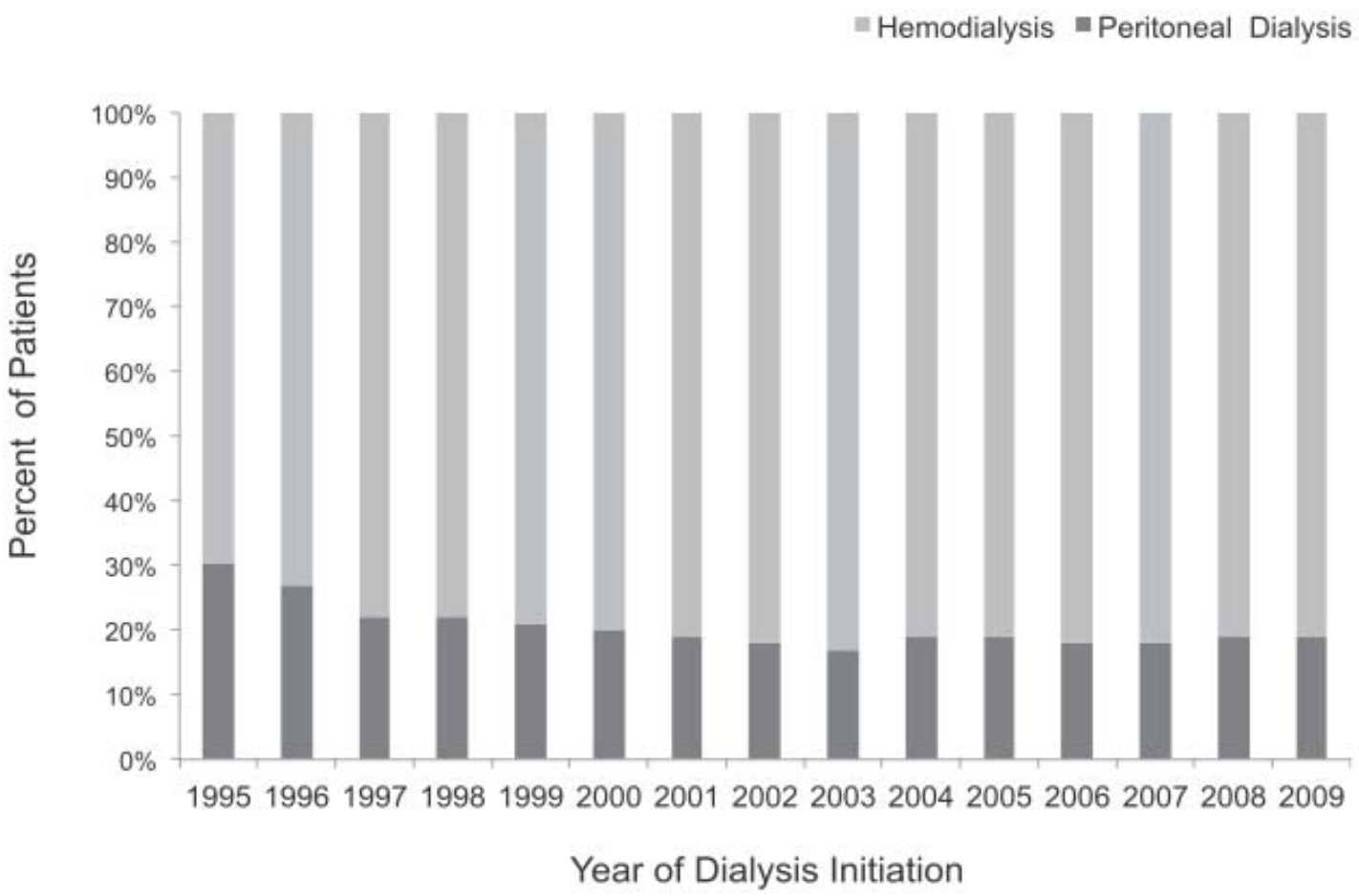
Klarenbach et al *Seminars in Nephrology,* Vol 29, No 5, 2009

Survival: PD vs. HD



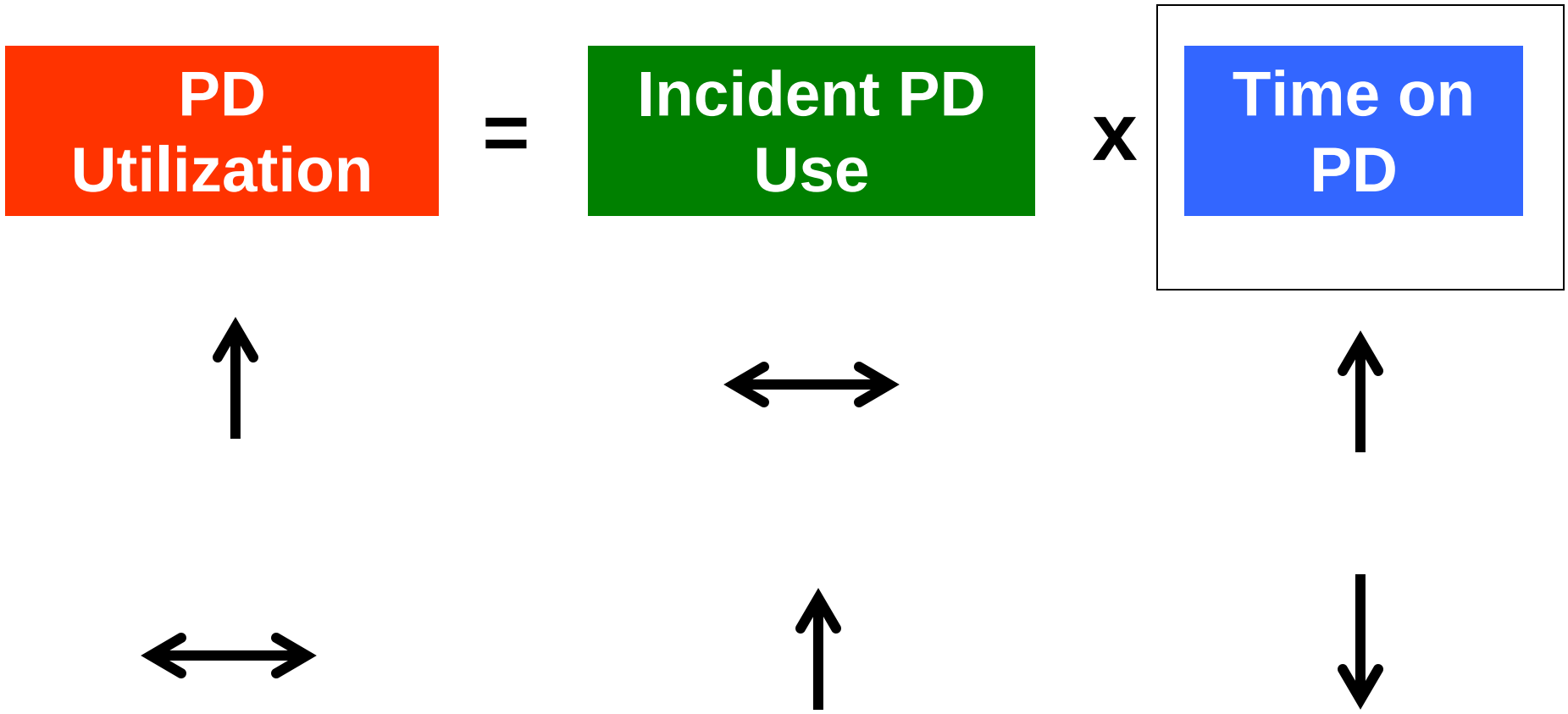
Perl et al JASN 2011

And Yet Incident PD Utilization has been decreasing in Canada

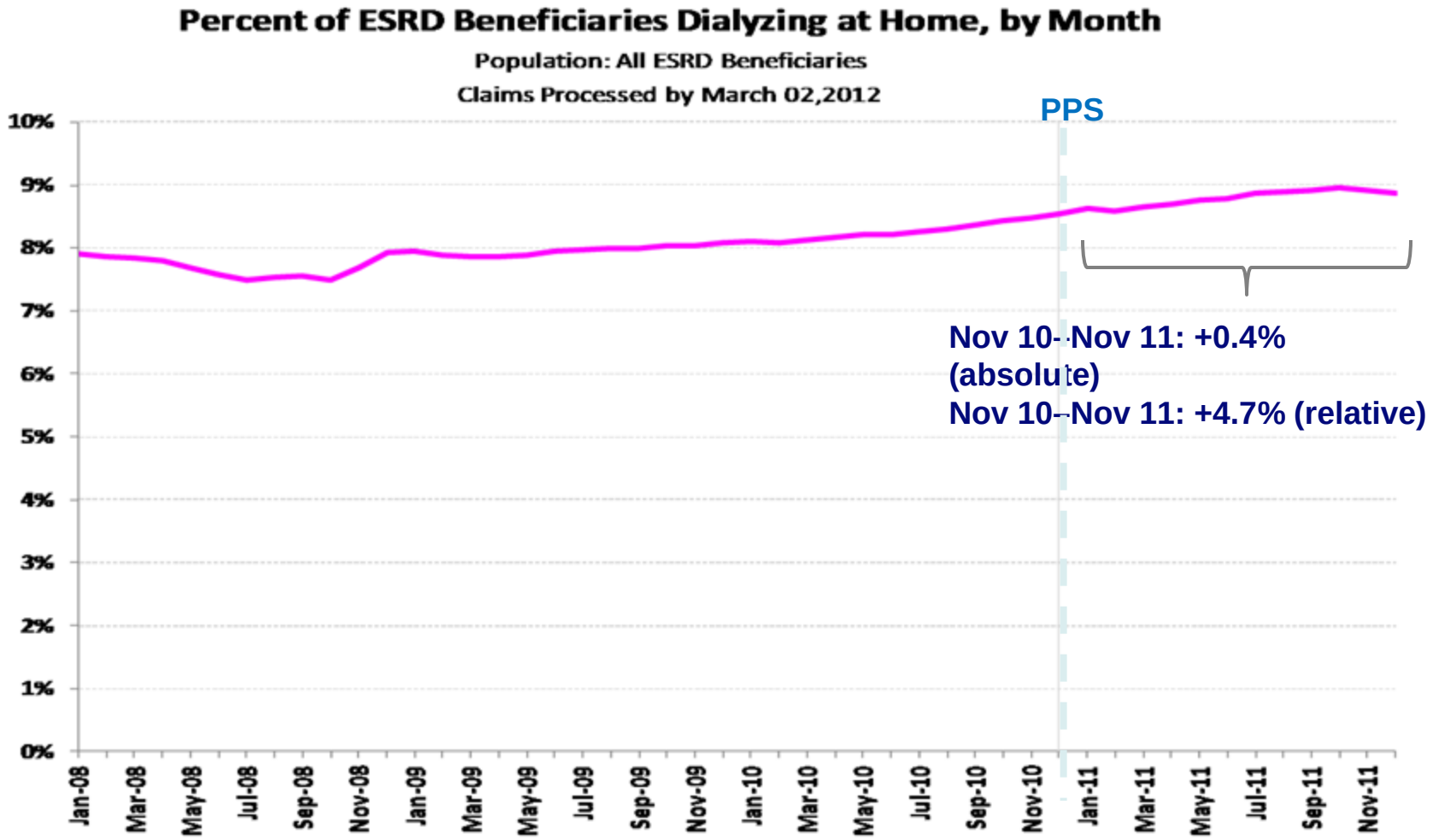


Perl…. Nessim CJASN 2012

Increasing PD Utilization



CMS ESRD Data: Overview of 2011 Claims-Based Monitoring

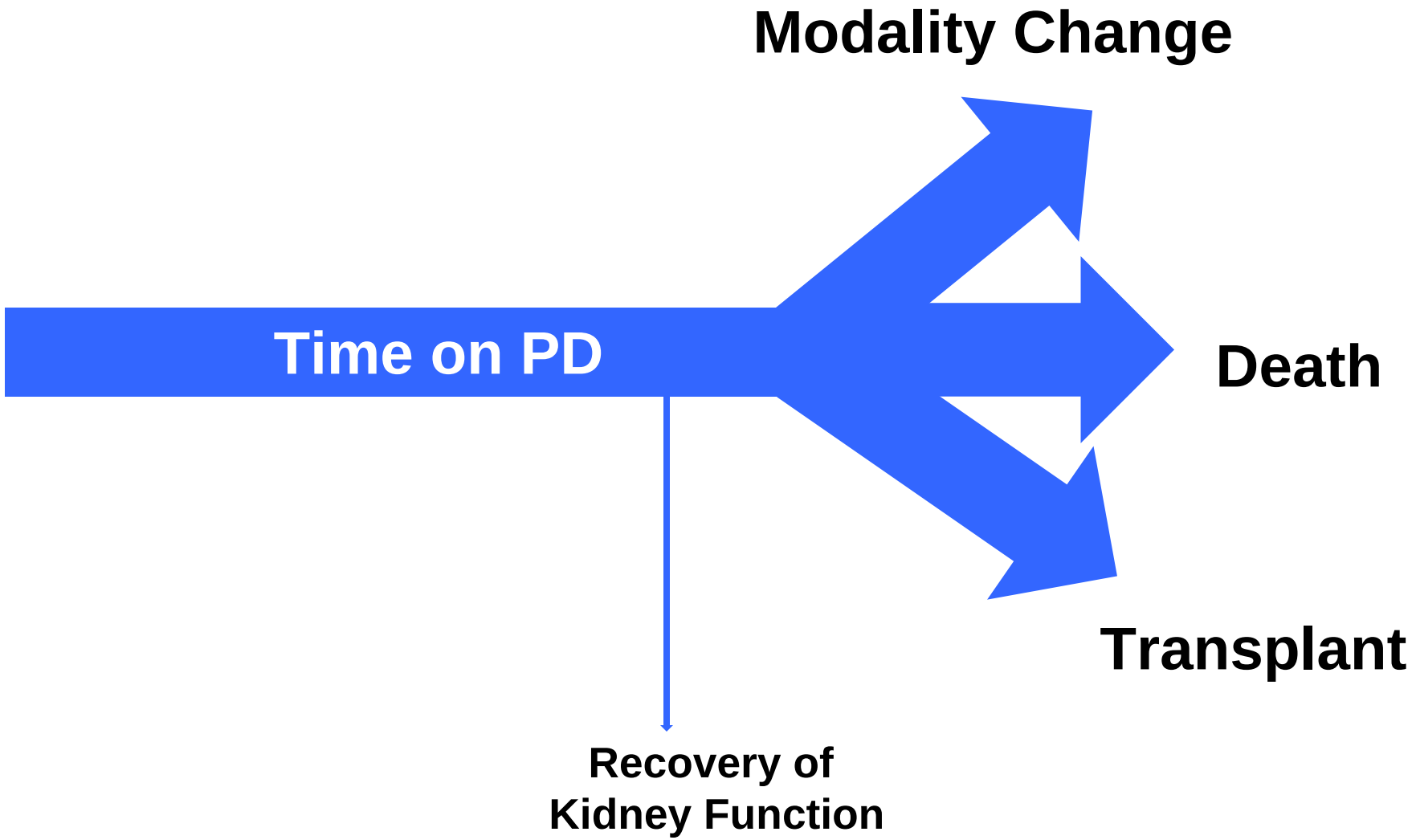


8% total in 2009 (7% PD, 1% HHD); PD in 6% of incident pts)

Greater PD Uptake in US: A New Frontier!

- Assuming projections hold, will greater PD use be due to:
  - Uptake by ‘novice facilities’
  - Uptake among under-represented patient groups?
  - Both?
- What will the effects be on PD technique survival?

Outcomes For Incident PD Patients



Definition of ‘’Technique Failure’’

- *any PD-related complication that leads to the permanent cessation of the therapy*
  - When does PD begin ?
  - Should it include death and change in modality ?
  - What is permanent?

When Does PD Begin ?

When Does PD Begin?

3886 patients who chose PD and
Underwent PD Catheter Insertion in Ontario
April 2002 – March 2010

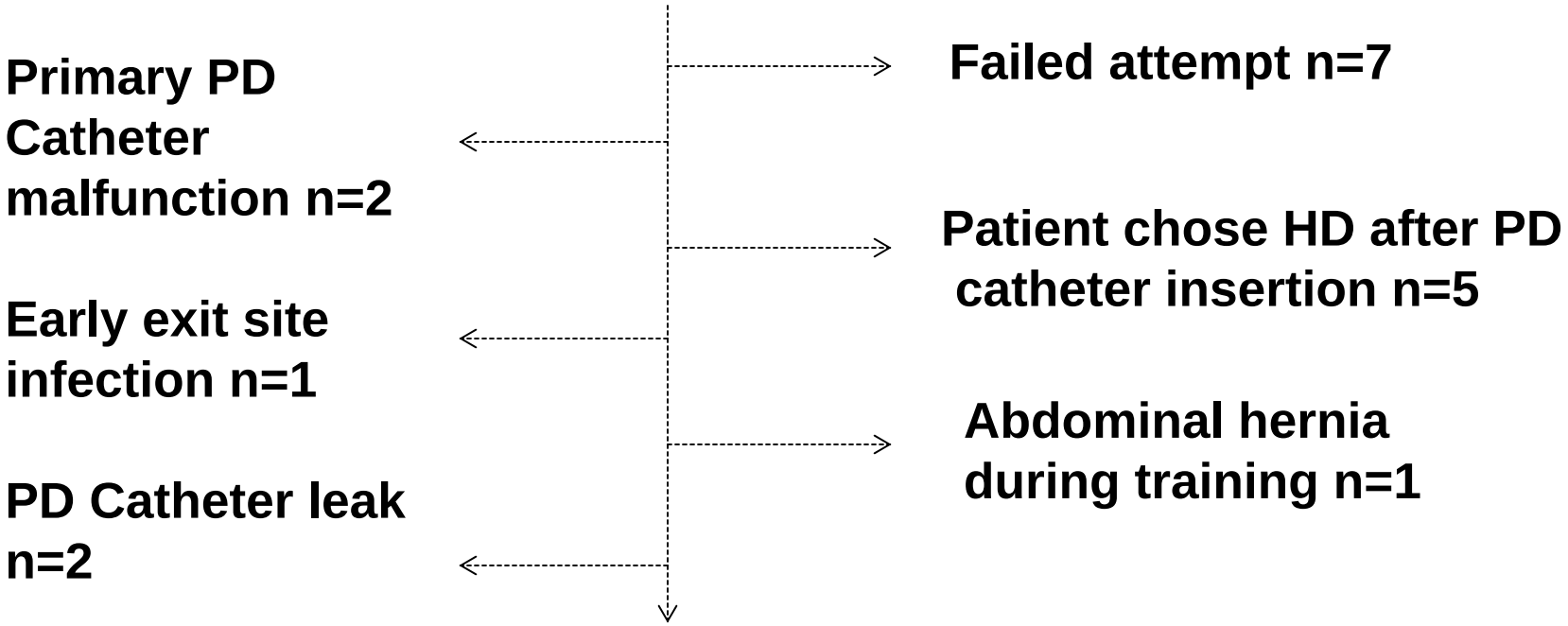
Death/Transplant/No Dialysis: n= 175 (5%)
Hemodialysis: n= 445 (12%)

3227(83%) patients had at least 4 weeks of PD use

Perl.. Oliver et al Unpublished

When does PD Begin ?

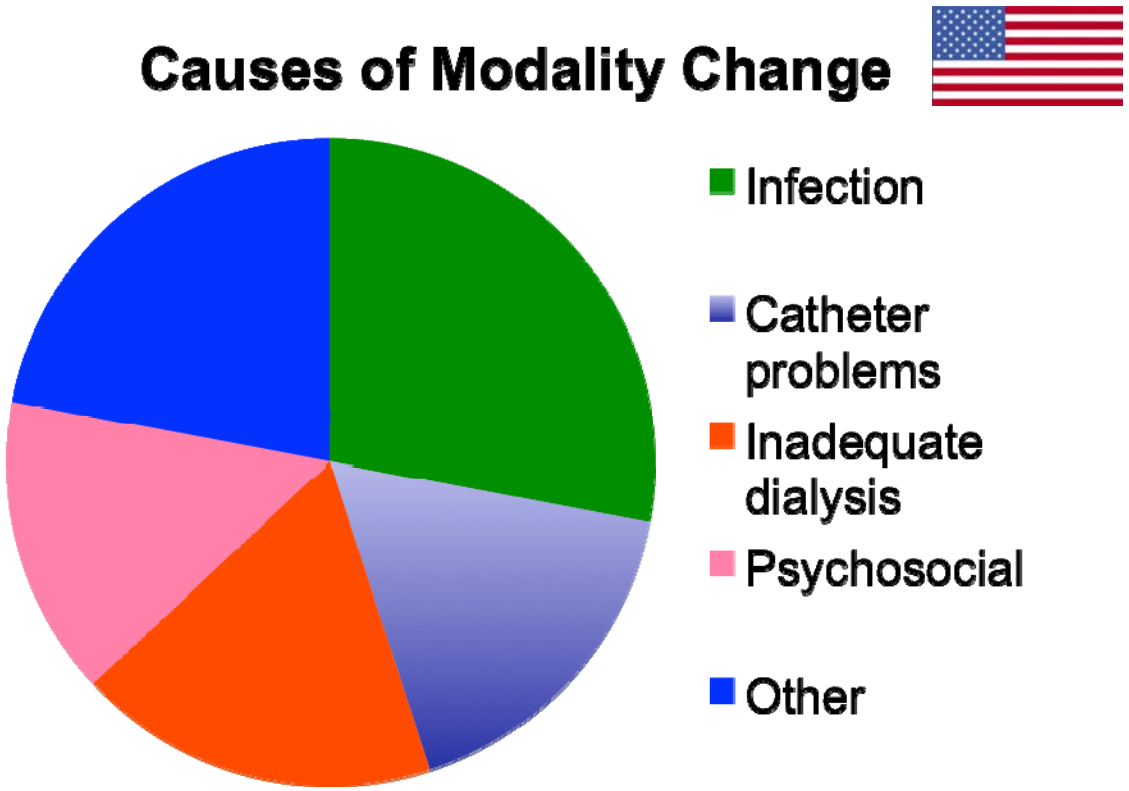
169 patients who chose PD and underwent a PD catheter attempt



147 (87%) patients who received PD therapy

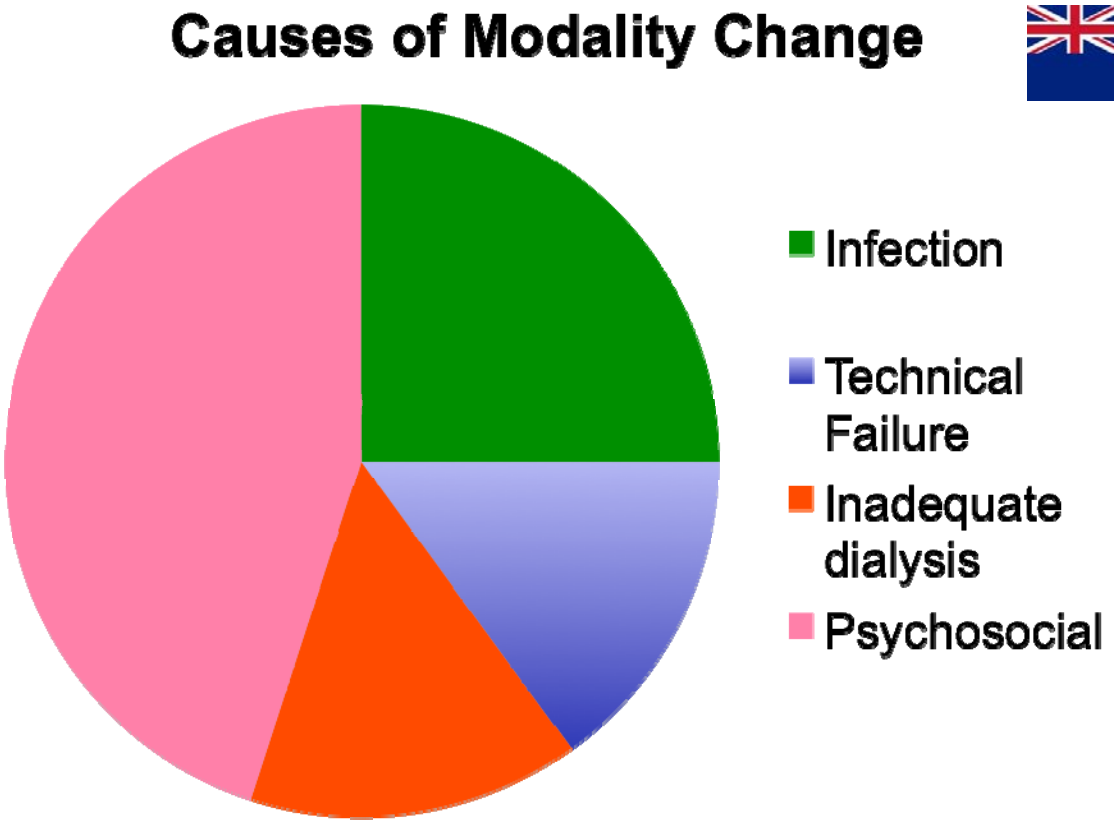
Oliver et al NDT 2011

Causes of Modality Change Among PD patients



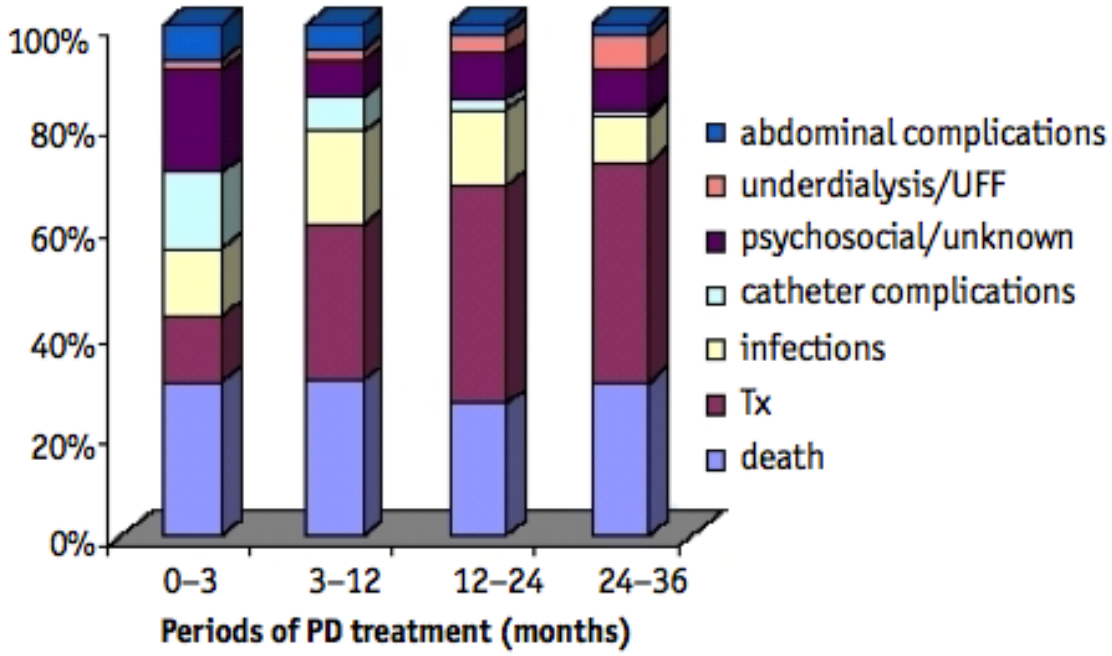
Mujais et al *Kidney International* (2006) 70, S21–S26

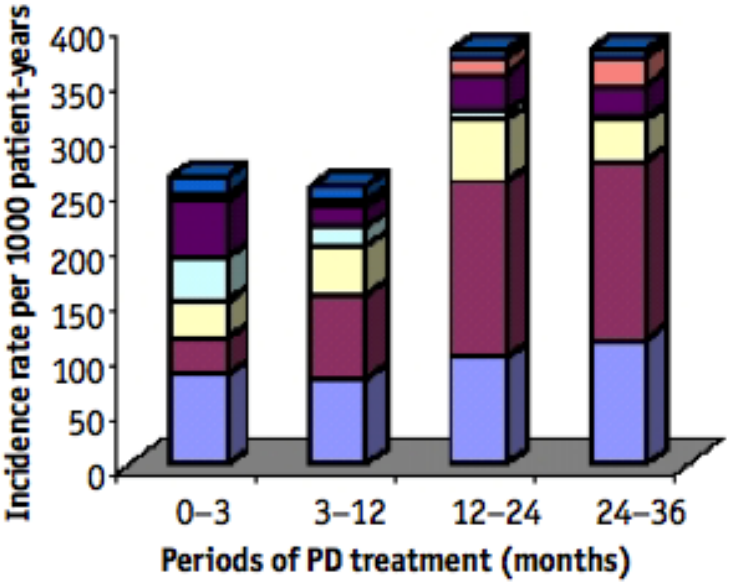
Causes of Modality Change Among PD patients



Jose et al *Nephrology* **16** (2011) 19–29

Causes of Modality Change Vary By Time on Therapy





Kolesnyk et al PDI MARCH 2010 – VOL. 30, NO. 2

Why Do Modality Changes Occur After Peritonitis

- A marker of non-adherence to therapy
- A marker of functional decline and/or increased comorbidity
- Severe intraperitoneal inflammation
  - loss of ultrafiltration capacity
  - Loss of small solute clearance
- Fear of second episode from patient
- Medical need to remove the catheter for resolution
  - Concomitant exit site infection
  - Fungal
  - Recurrent or repeat episode
  - Not responding to medical therapy
  - Temporary vs. Permanent HD
    - Patient-driven
    - Physician-driven
    - System-driven

Psychosocial Causes of Modality Change From PD

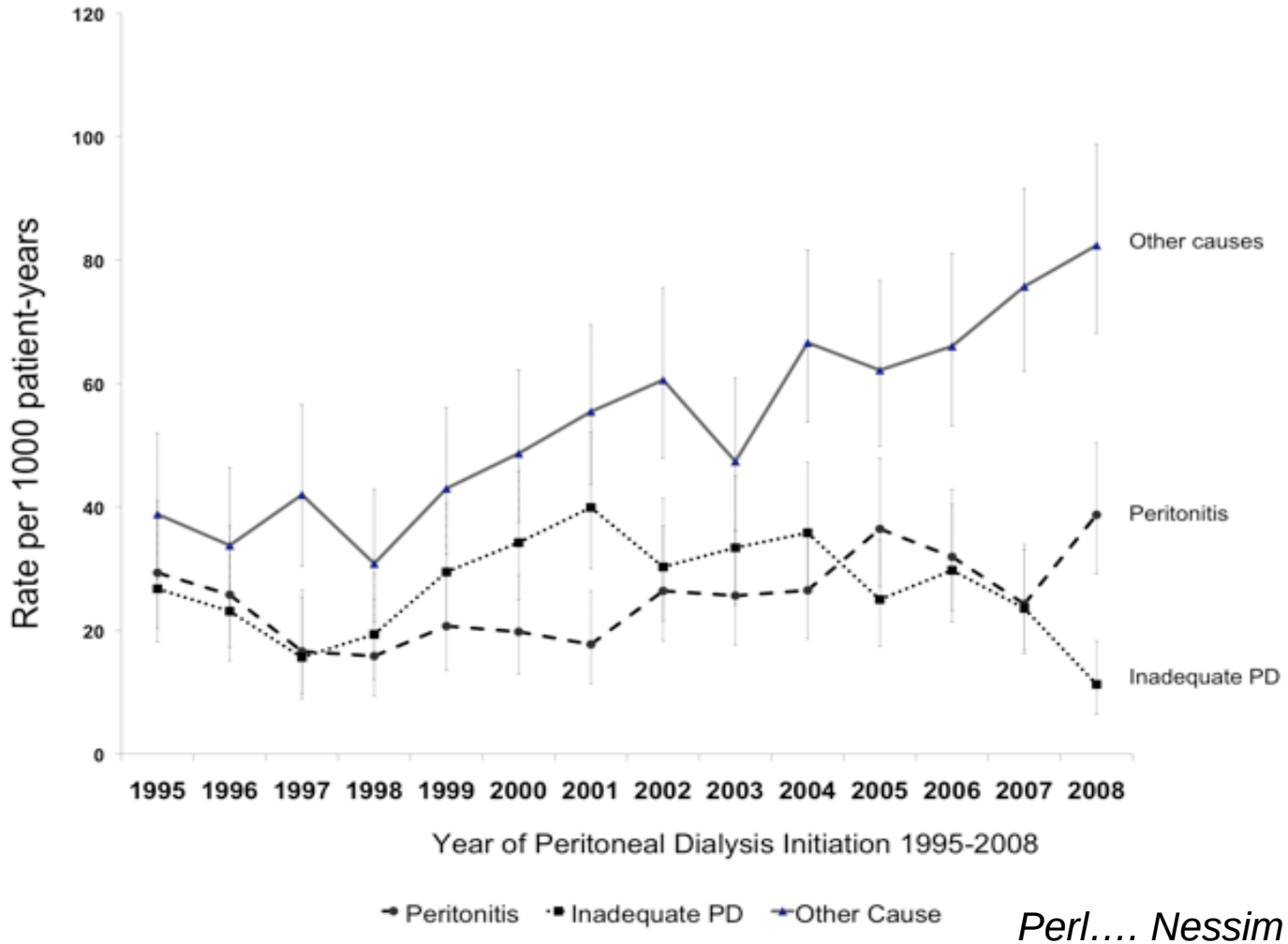
Inability to perform self-care dialysis

- **Acquired comorbidities**
- **Loss of caregiver/caregiver burnout**
- **Change in living conditions**
- **Deteriorating functional and cognitive status**

Patient preference

- **Play a role in other causes of modality switch**
- **Patient burnout**
- **Poorly understood**

Cause of Modality Change Among PD Patients: Canadian Data



Perl…. Nessim CJASN 2012

The 160th PD Patient at UHN

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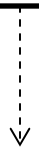
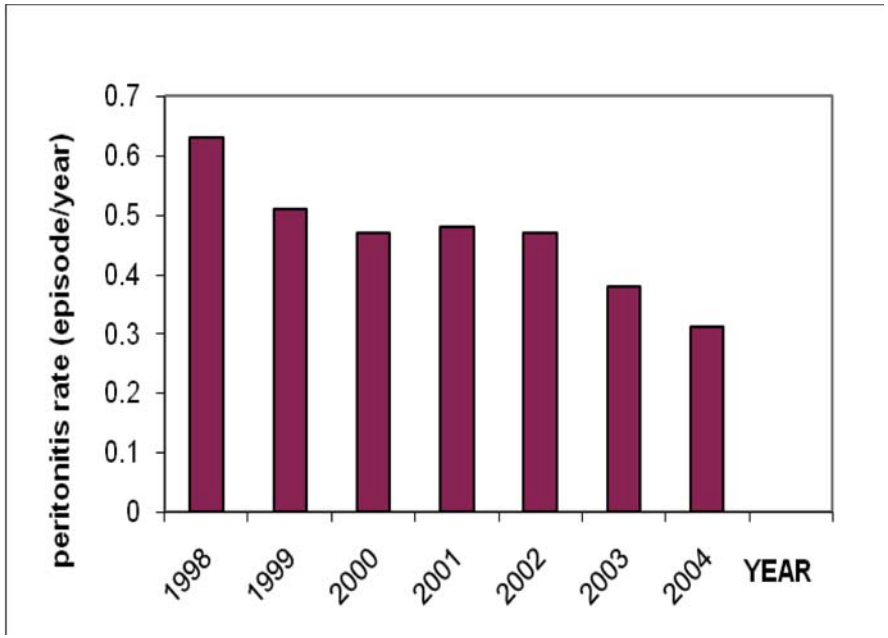
The Last 15 years of PD in Canada

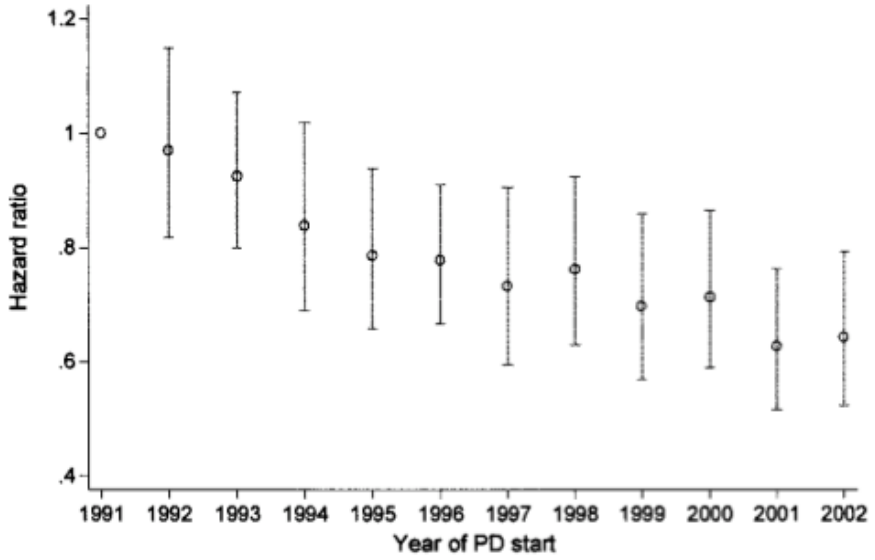
- Increasing availability and use of novel PD solutions
- Less stringent guidelines for small solute removal
- Improvement peritonitis prevention strategies i.e.
  - Improvements in PD connectology
  - Use of exit site prophylaxis



? Impact on Time on PD Therapy

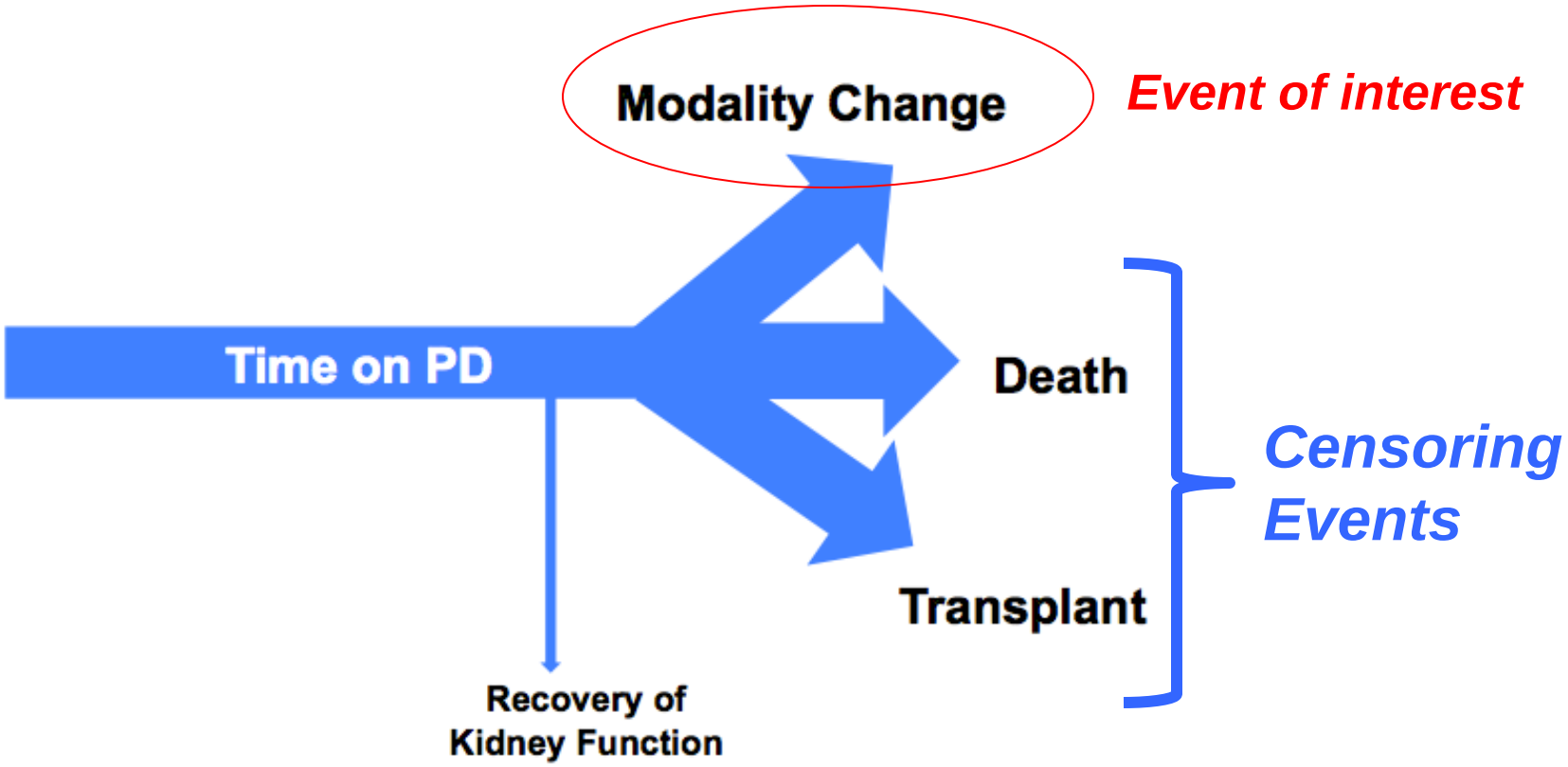
Rates of PD Peritonitis Have Been Decreasing





1. *Baxter POET Database: Courtesy Dr. Sharon Nessim*
2. *McDonald et al PDI, 2004 VOL. 24, NO. 4*

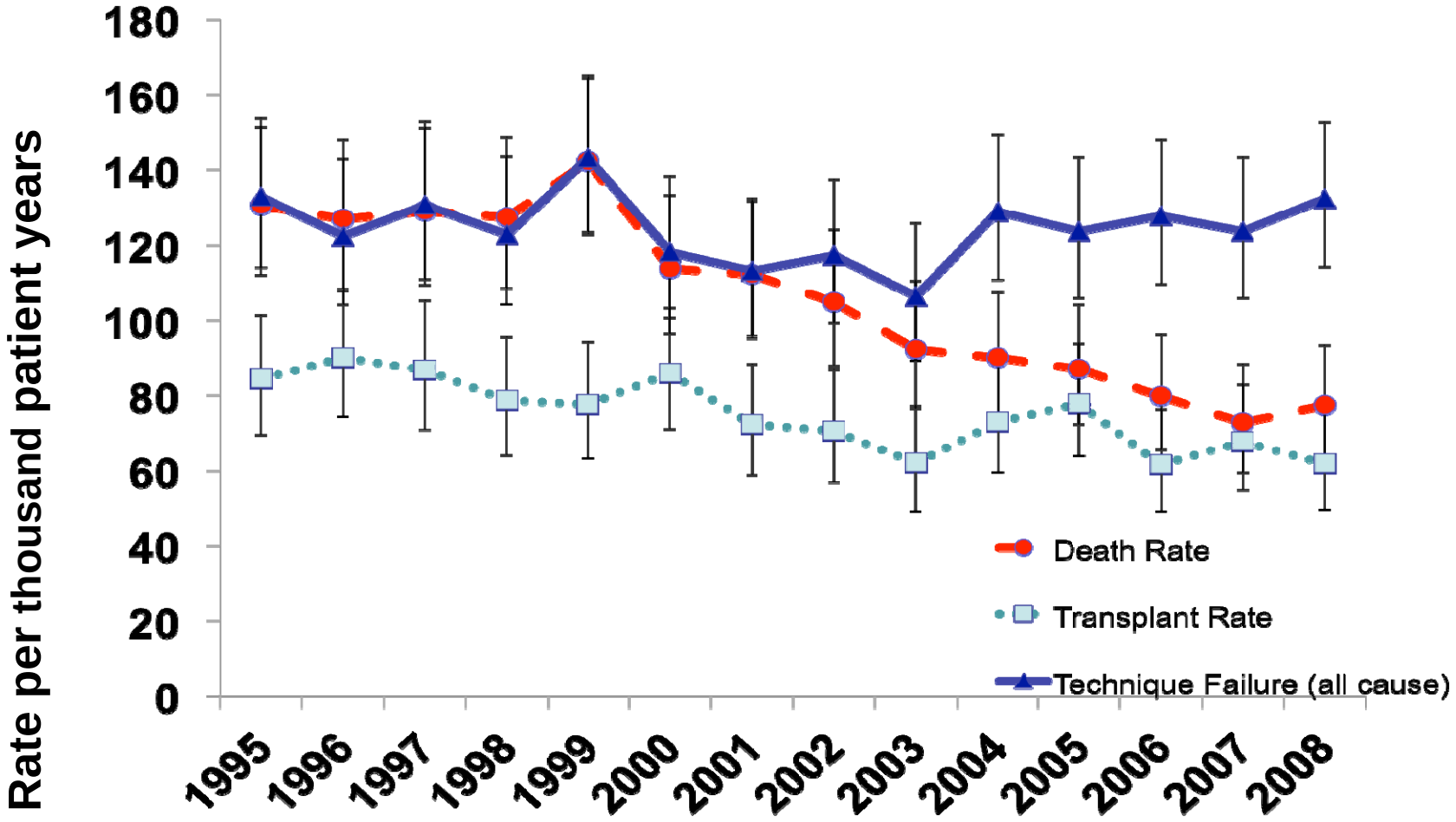
Time on PD: A Tale of Competing Risks



Time on PD: A Tale of Competing Risks

- Traditional analyses of time to PD modality switch have censored patients at death and transplantation
- Requires that individuals who are censored have the same risk of modality switch as individuals who are not (non-informative)
- Patients that received a transplant might have been at lower risk of TF had they remained on PD
- Individuals that died might have been at higher risk of TF had they survived.

Event Rates over Time Among Incident PD patients

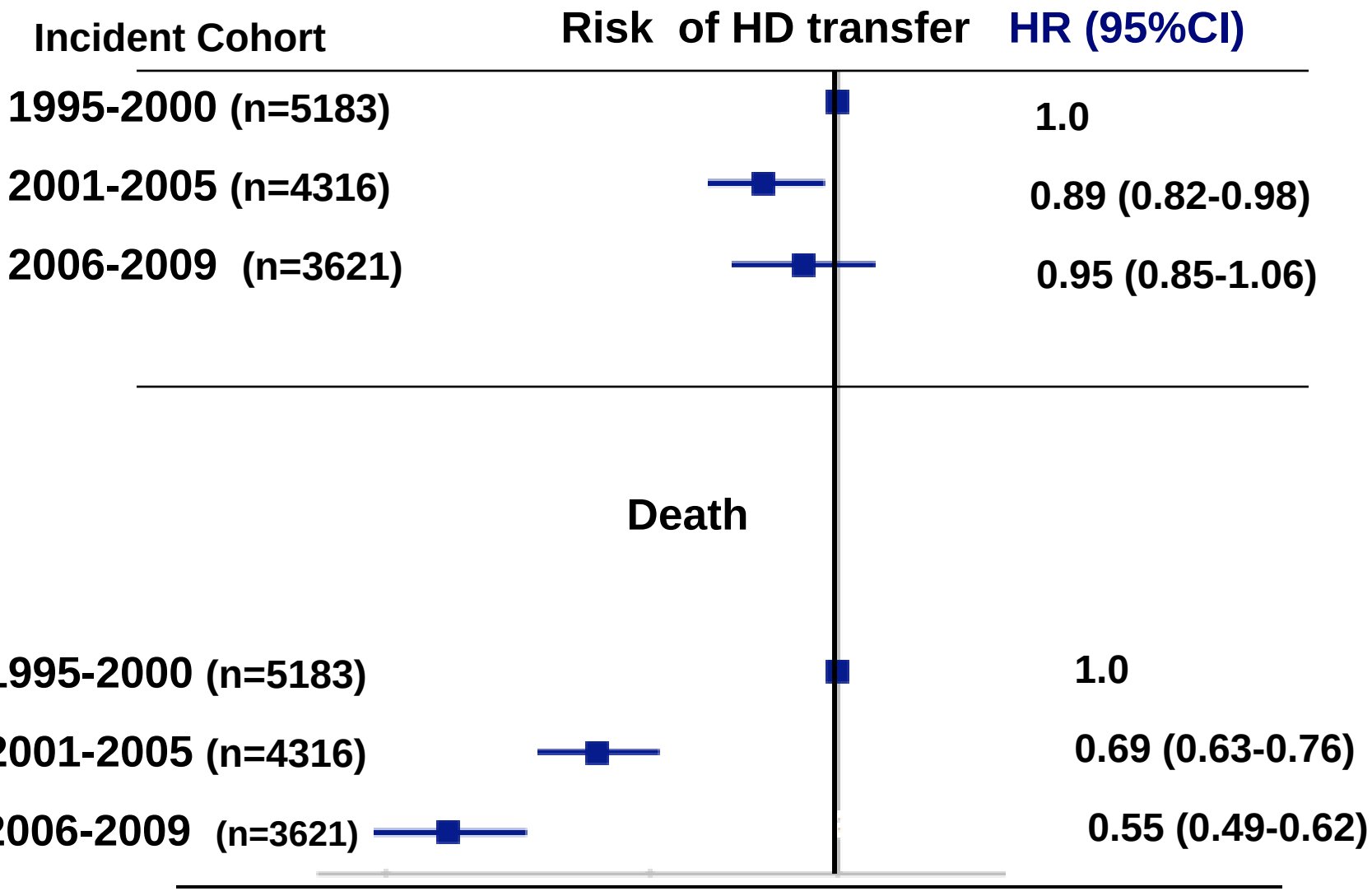


Perl…. Nessim CJASN 2012

Patient Characteristics At PD Initiation

	Year of Dialysis Initiation			*P* Value
	1995–2000 (*n*=5183)	2001–2005 (*n*=4316)	2006–2009 (*n*=3621)	
Age group (yr)				
18–44	20.6	15.9	14.7	<0.001
45–54	16.6	17	16.7	
55–64	20.9	22.5	24.4	
65–74	26.5	25.3	24.9	
≥ 75	15.5	19.3	19.2	
Race				
Caucasian	71.3	70.9	67.9	<0.001
Asian	7.7	8.7	9	
black	3.5	3.4	3.9	
other	10	12.8	13.6	
unknown	7.5	4.2	5.7	
Female	43.1	42.5	42.5	0.77
Primary diagnosis				
GN	18.8	17.4	16.2	<0.001
diabetes	34.2	36.6	35.4	
renal vascular disease	18.3	17.3	17.5	
polycystic kidney disease	5.1	6.9	6.8	
other	10.6	9.6	12.9	
unknown	13	12.2	11.1	
Comorbid conditions				
diabetes[a]	5.7	5.7	8.3	<0.001
coronary artery disease[b]	29.8	26.1	21	<0.001
peripheral vascular disease	13.7	13.9	11.1	<0.001
malignancy	6.6	6.8	7.6	0.18
lung disease	7.2	6.7	5.4	0.003
pulmonary edema	22.8	13.8	9.6	<0.001
hypertension	81.5	87.8	82.7	<0.001
current smoker	12.2	12.4	11.8	0.69
Automated PD (%)	29.1	28.4	26.5	0.03
Body mass index (kg/m^2)	24.6 (6.0)	25.7 (6.4)	26.6 (7.3)	<0.001
Late referral (%)[c]	—	17.7	11.1	<0.001
Hemoglobin (g/L)[c]	—	111 (21)	111 (18)	0.42
Estimated GFR (ml/min/1.73 m^2)[c,d]	—	8.9 (4.7)	9.6 (5.0)	<0.001
Albumin (g/L)[c]		36 (7)	37 (8)	<0.001
Prevalent PD center size[e]	25 (52)	26 (37)	27 (49)	—

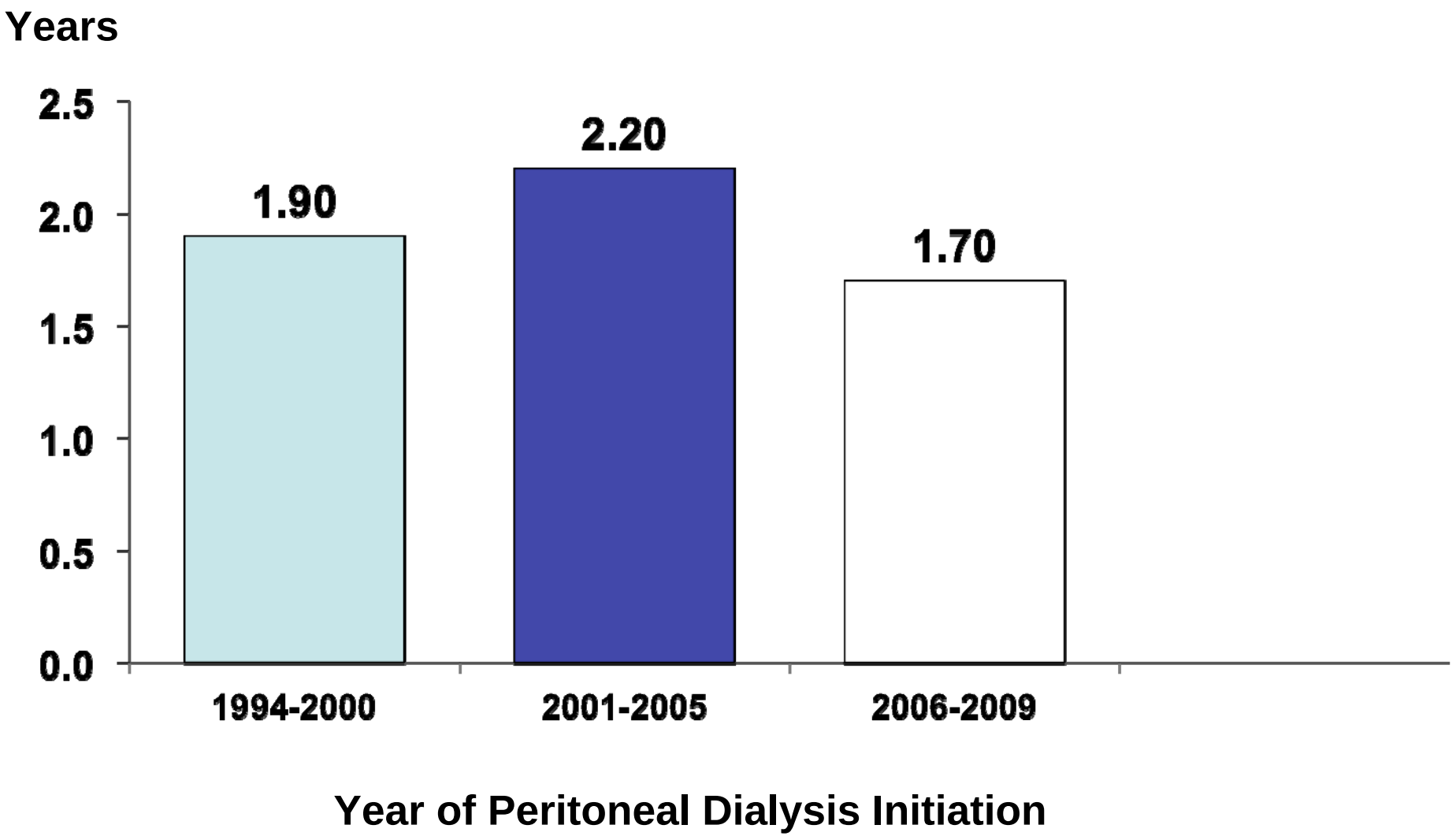
Adjusted Risk of Death and modality switch By Incident PD Cohort Period



Adjusted for age, race, sex, body mass index, ESRD comorbidity index, primary diagnosis, PD modality (automated PD versus continuous ambulatory PD), province, and PD center size

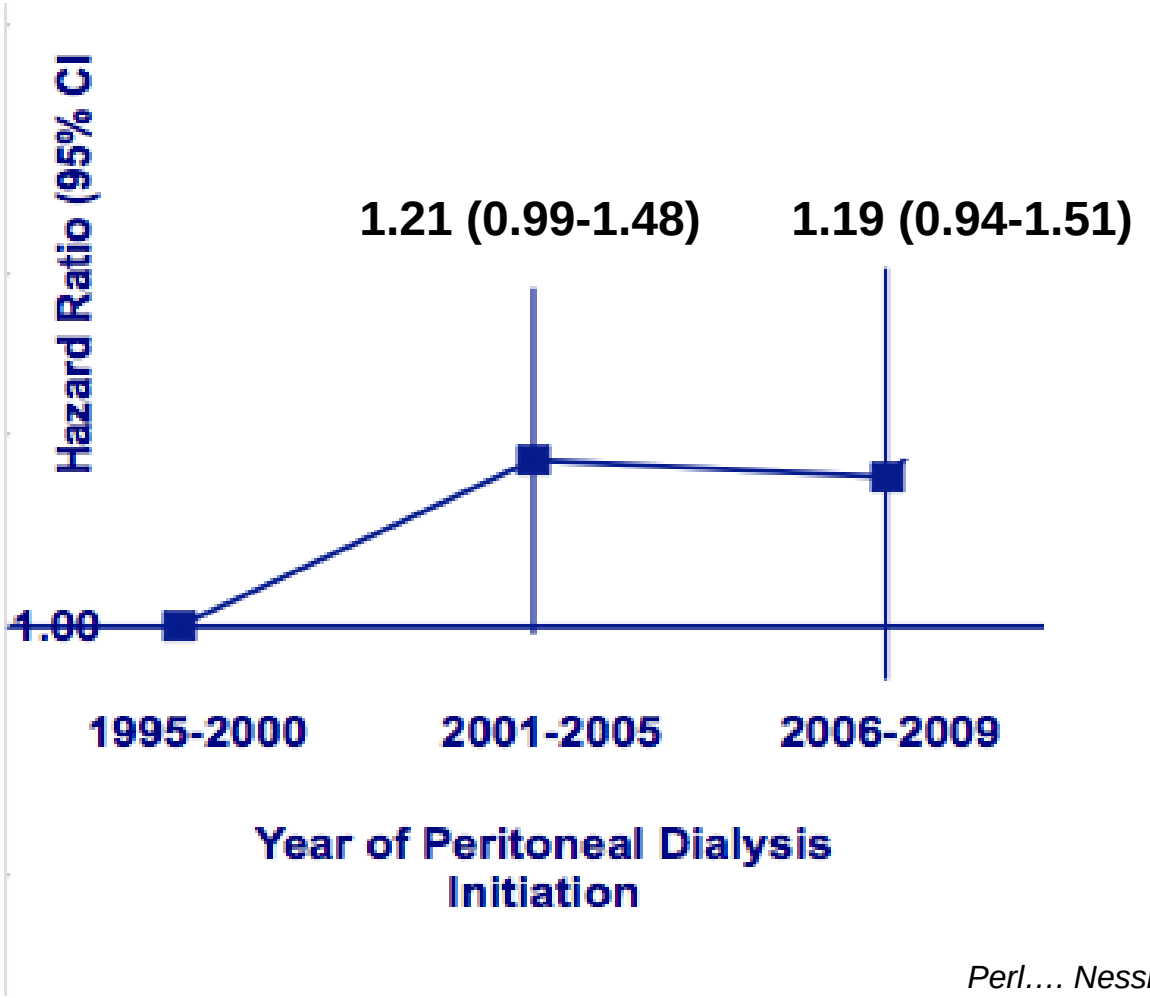
Perl…. Nessim CJASN 2012

Median Time To Modality Change



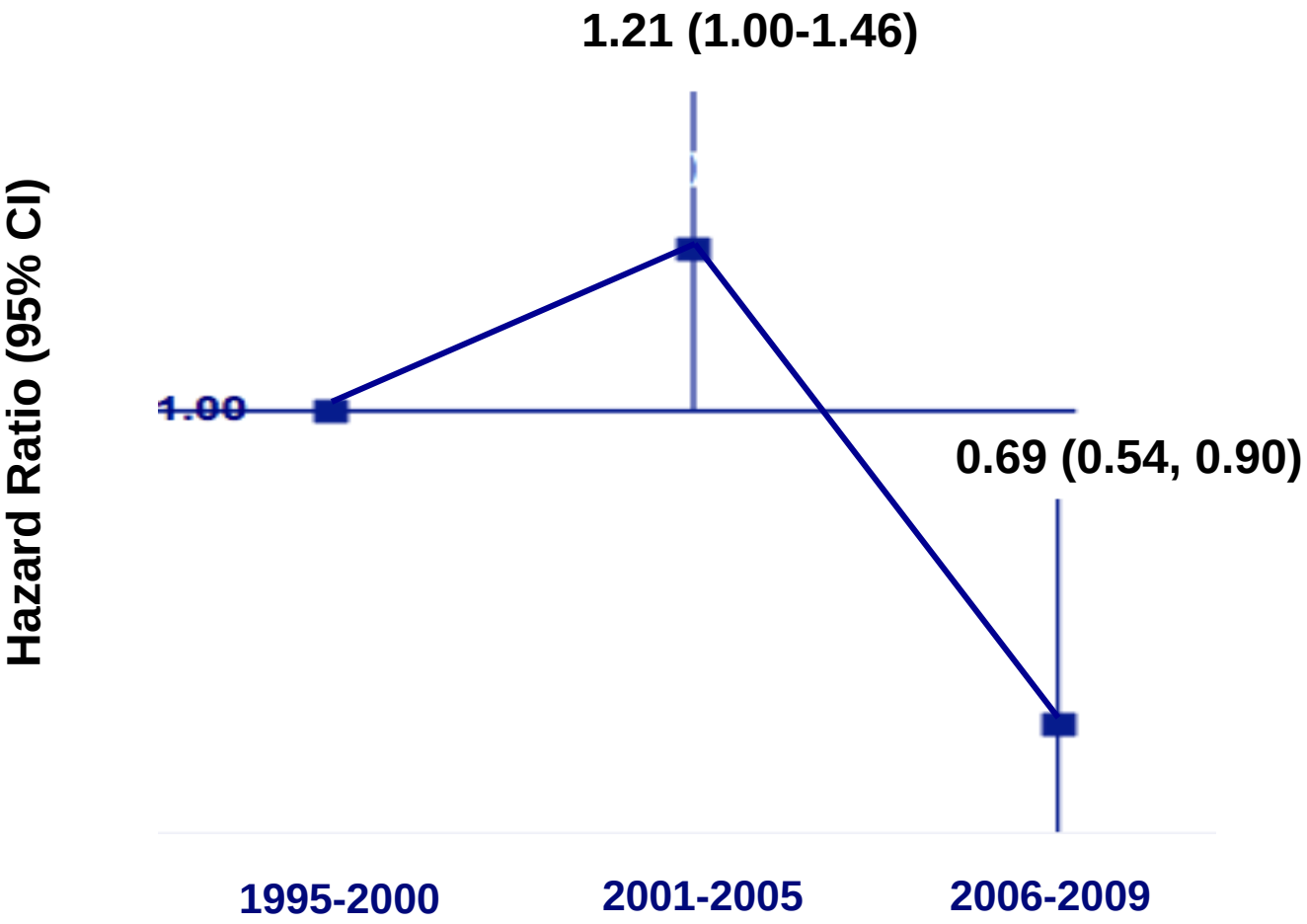
Perl…. Nessim CJASN 2012

Peritonitis-Related modality switch



Perl…. Nessim CJASN 2012

Modality Switch Related to Inadequate Dialysis



Perl…. Nessim CJASN 2012

Impact of Age and Era on The risk of All Cause PD Technique Survival

	1995-2000	2001-2005	2006-2009
Age ≤ 65	1.0	0.95 (0.85-1.06)	1.02 (0.90-1.15)
Age > 65	1.0	0.86 (0.75 ,0.97)	0.80 (0.69 ,0.93)

Perl…. Nessim CJASN 2012

Impact of Era on PD Technique Survival: Summary

- Little improvement in rates of modality change from PD over time
  - With the exception of patients over age of 65
- Significant improvement in patient survival

Impact of Era on PD Technique Survival: Summary

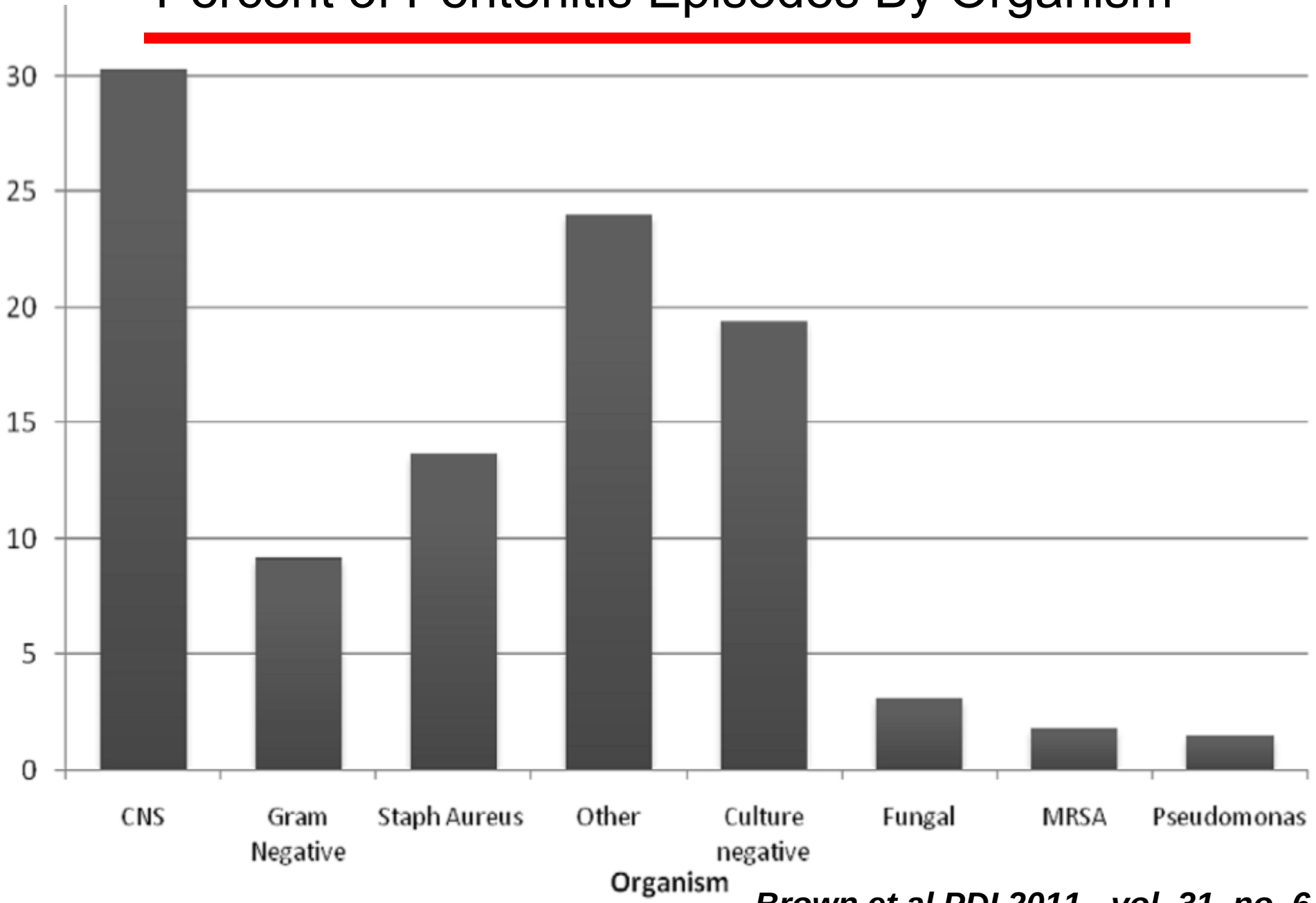
- No change in rates of peritonitis-related transfer to HD

- Initial increase in rates of transfer to HD due to inadequate dialysis and recent decrease
  - Less stringent guidelines for small solute removal

Why No Improvement in Peritonitis-Related Transfers To Hemodialysis ?

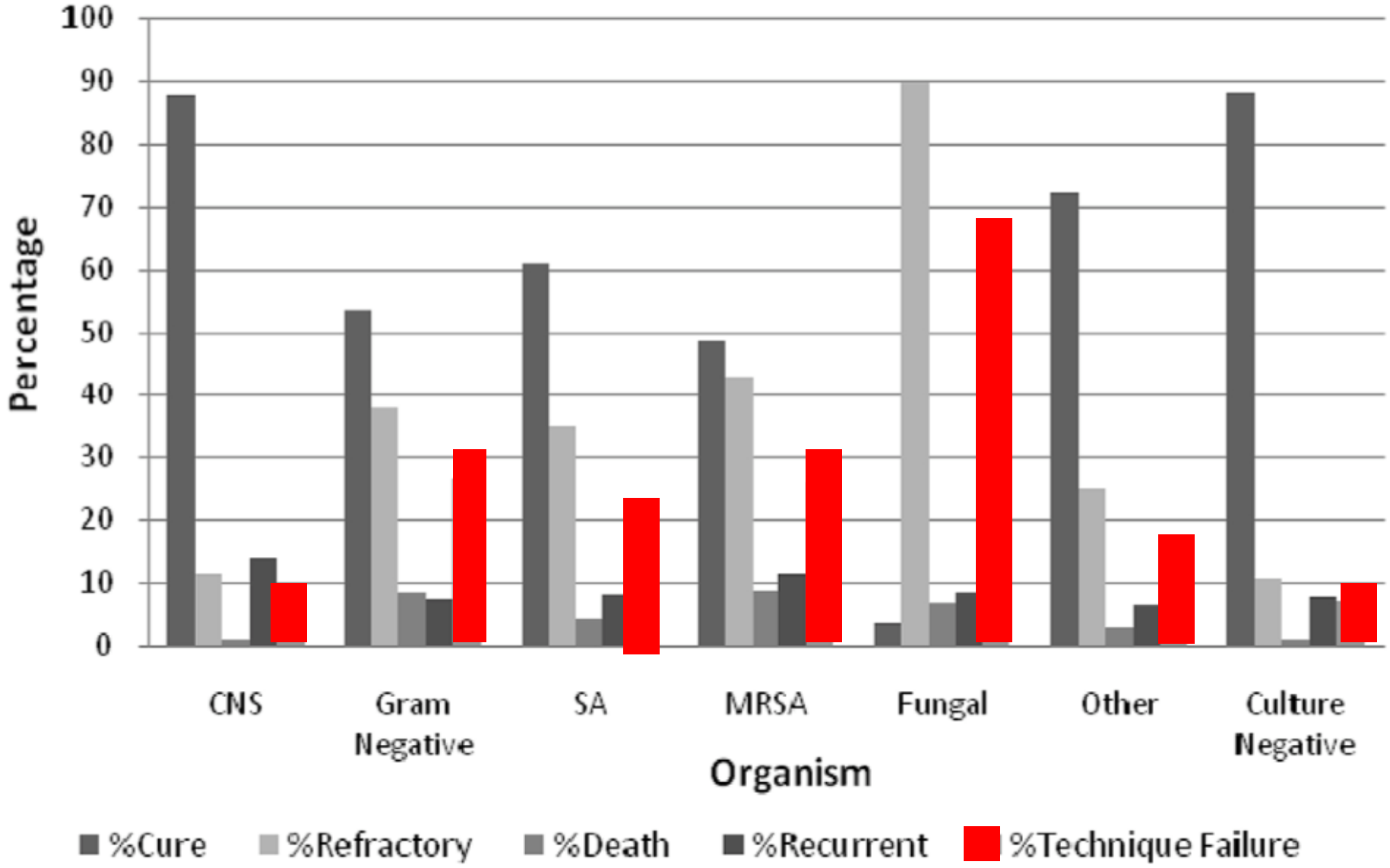
- Globally improving peritonitis rates but no change in peritonitis related technique failure
- More aggressive at catheter removal after peritonitis episode
- Greater reduction in peritonitis episodes of more indolent organisms (i.e. CNST) less likely to lead to catheter removal

Percent of Peritonitis Episodes By Organism



Brown et al PDI 2011 - vol. 31, no. 6

Outcomes of Peritonitis By Organism



Brown et al PDI 2011 - vol. 31, no. 6

Improving Outcomes for Elderly PD Patients

- Not mediated by reduction in peritonitis-related TF, or technique failure due to inadequate PD
- Largest growing segment of The ESRD population
- Increasing use of home-assisted PD for elderly patients across several regions in Canada

Impact of Assisted PD on Technique Survival

Is Assisted Peritoneal Dialysis Associated with Technique Survival When Competing Events Are Considered?

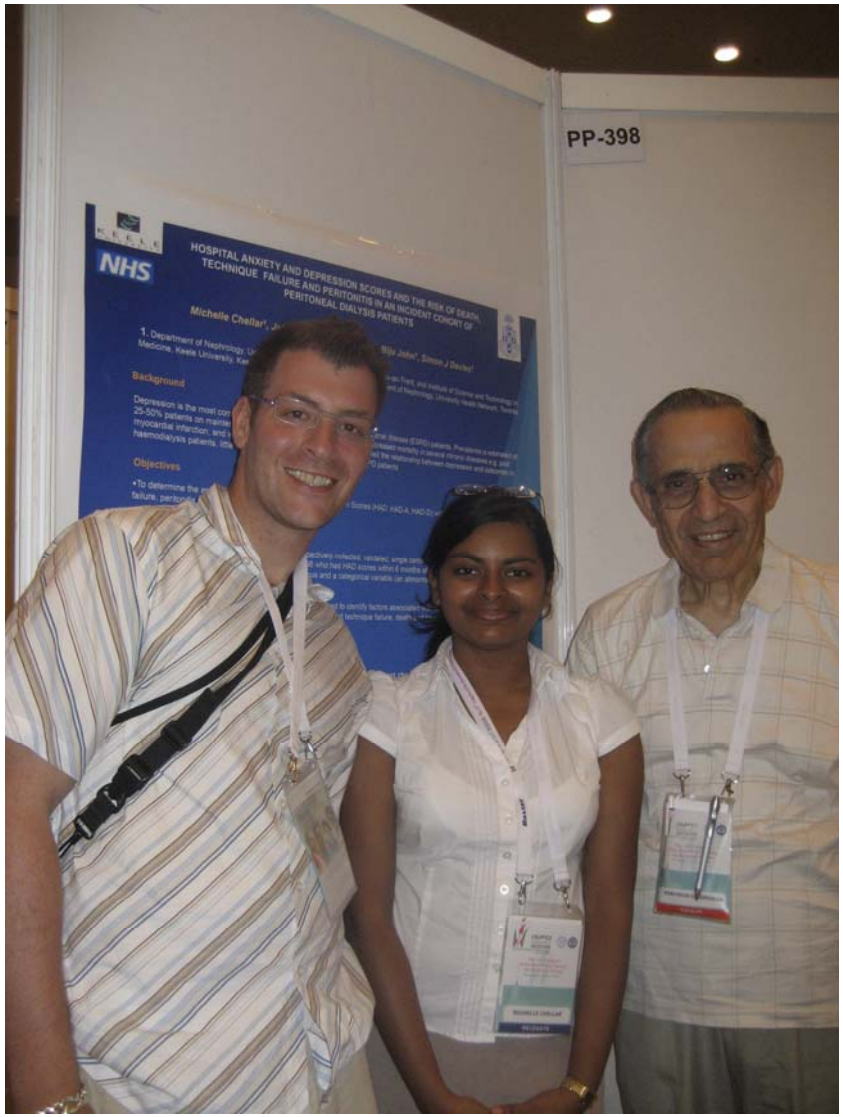
Thierry Lobbedez, Christian Verger,† Jean-Philippe Ryckelynck,* Emmanuel Fabre,† and David Evans†‡§*

	Fine and Gray Model: Sub distribution Relative Hazard (95% CI)
Nurse-Assisted PD	0.81 (0.70–0.94)
Family-Assisted PD	0.72 (0.63–0.81)

Adjusted for age, sex, modified Charlson comorbidity index, and underlying nephropathy

Lobbedez et al CJASN: 612–618, 2012

ISPD: Istanbul



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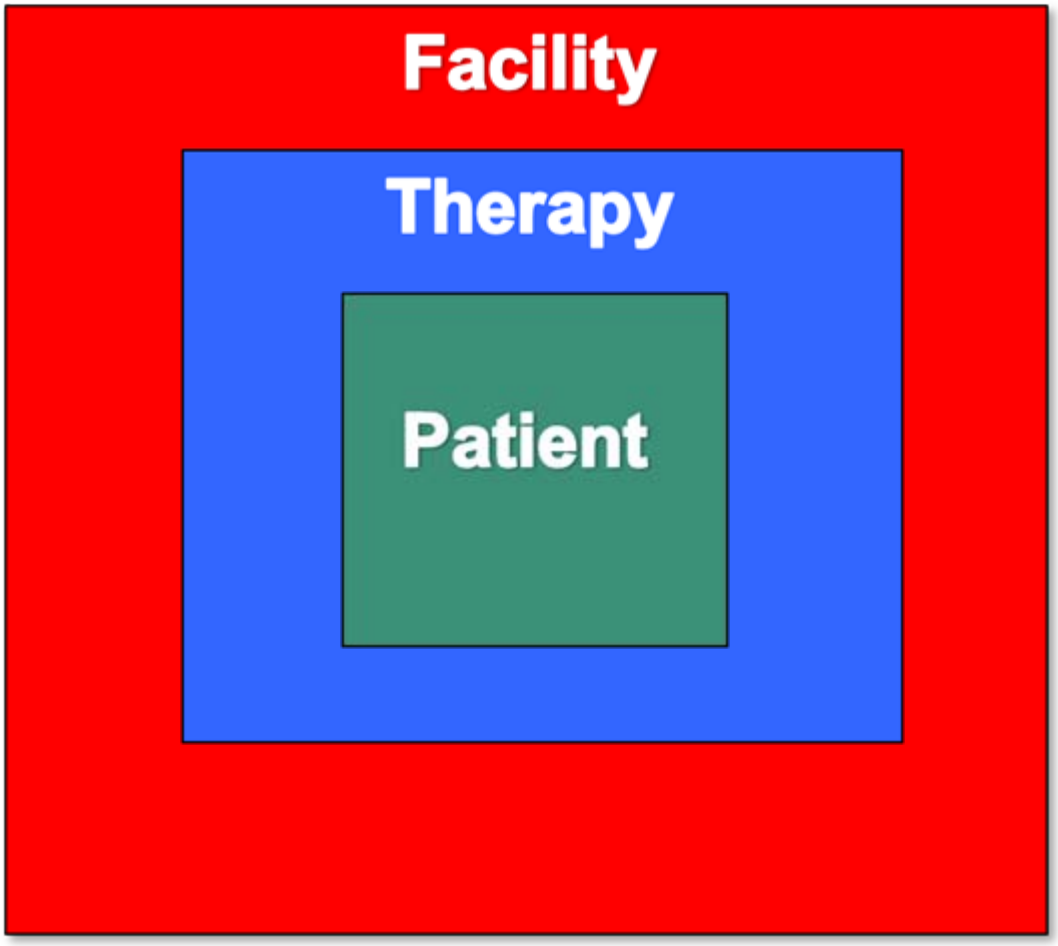
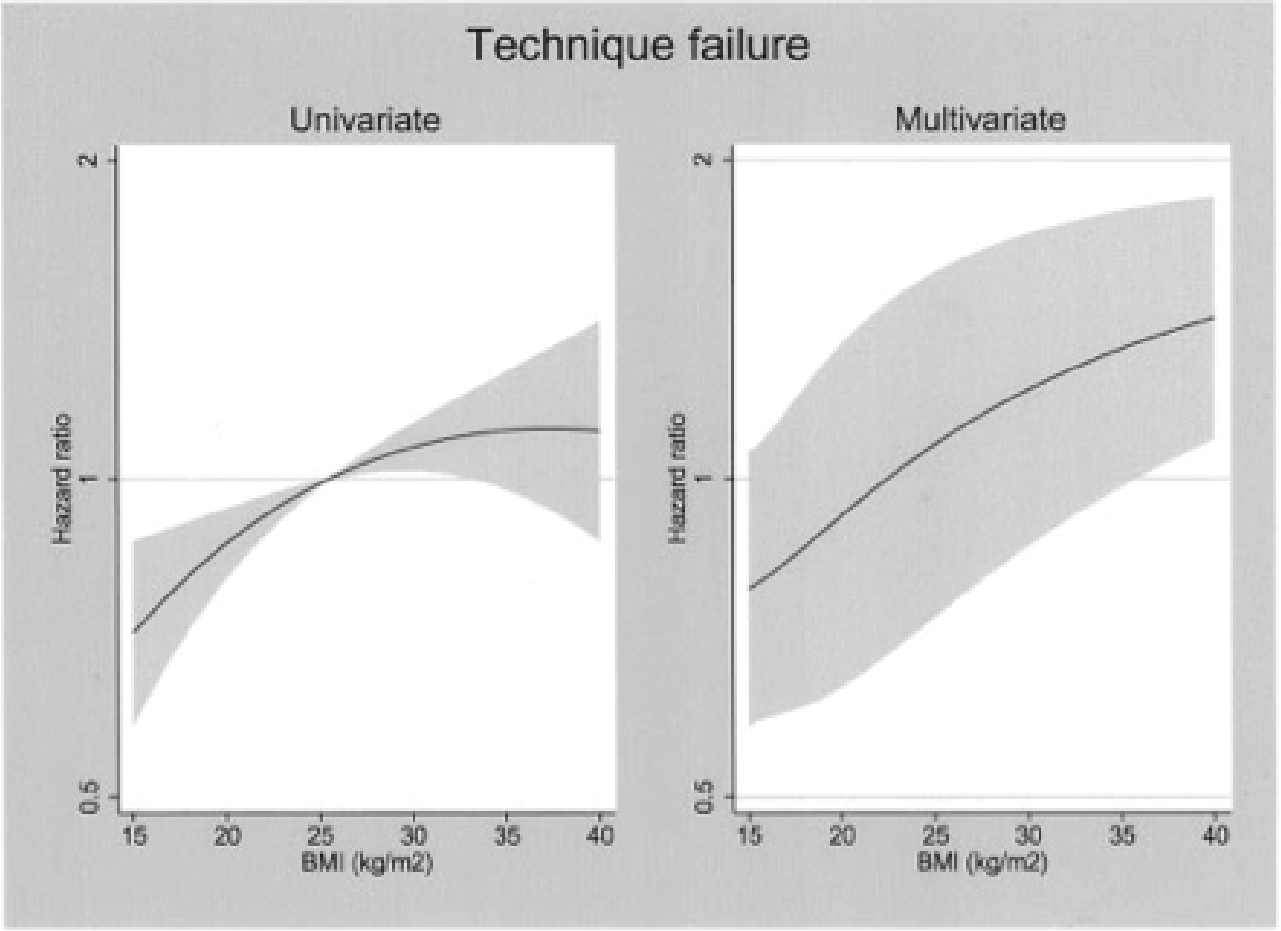
Risk Factors For Transfer to HD From PD



Patient Factors

- **Age:**
  - CORR: 0.95 [0.91, 0.98] per year
  - French Registry: 0.98 [0.98–0.99] per year
  - USRDS: 1.0007 ($p<0.0001$)
- **Gender**
  - CORR: 0.9 [0.82-0.99] Females: Males
  - Consistent Across US, Canadian, French Registries
- **Diabetes**
  - CORR: 1.16 [1.00, 1.34]
- **Ethnicity**
  - Aboriginals 1.48 [1.07-2.03]
  - Blacks 1.27 [1.01-1.61]

Relationship Between BMI and Risk of Transfer to HD



McDonald et al PDI, 2004 VOL. 24, NO. 4

Socioeconomic Factors

Variable (n= 5162) (1999-2005)	AHR (95% CI)
Neighborhood education level ≤high school	2.9 [1.755–4.877]
Rural residence	0.9 [0.740–1.129]
Distanc	

Rurality	
Urban	1.00
Large rural	1.00 (0.93 to 1.06)
Small rural	1.01 (0.86 to 1.19)
Remote rural	1.33 (1.05 to 1.69)

1. Chidambaram et al PDI 2011
2. Mehrotra et al PDI 2012

Distance From The Nephrologist

Distance From Nephrologist	Technique Failure Hazard	Mortality Hazard
Within 50 Km (ref)	1.0	1.0
50.1-100 Km	0.86 (0.75, 0.97)	1.17 (1.07, 1.27)
150.1-300 Km	0.78 (0.65, 0.94)	1.07 (0.95, 1.21)
> 300 Km	0.63 (0.50, 0.79)	1.15 (1.00, 1.32)

Toneli et al Kidney International (2007) 72, 1023–1028

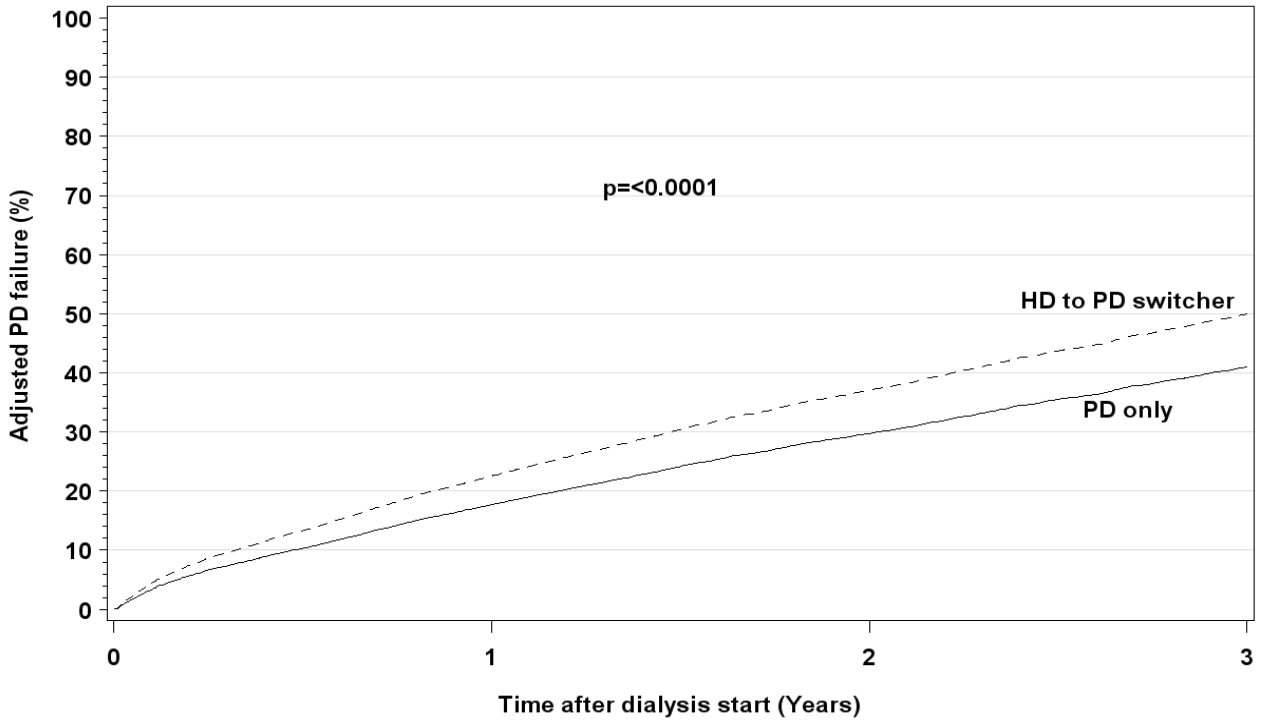
Selected Therapy-Related Factors

- CAPD vs. APD
  - No consistent difference[1,2]
  - Treatment by Indication Bias
  - CORR APD:CAPD AHR 1.02 [0.91, 1.14][3]

- Transfer from HD to PD relative to incident PD
  - Increased risk of transfer to HD:[4] AHR 1.2 [1.1-1.4]
  - Increased risk of peritonitis:[5] AHR 1.24 [1.1 to 1.40]
  - ? Patient selection
  - ? Adverse impact of HD on residual kidney function

1.Rabindranath NDT 2008
2.Mehrotra KI 2009
3. CORR unpublished
4. Lobbeddez et al CJASN 2012
5.Nessim et al CJASN 2009

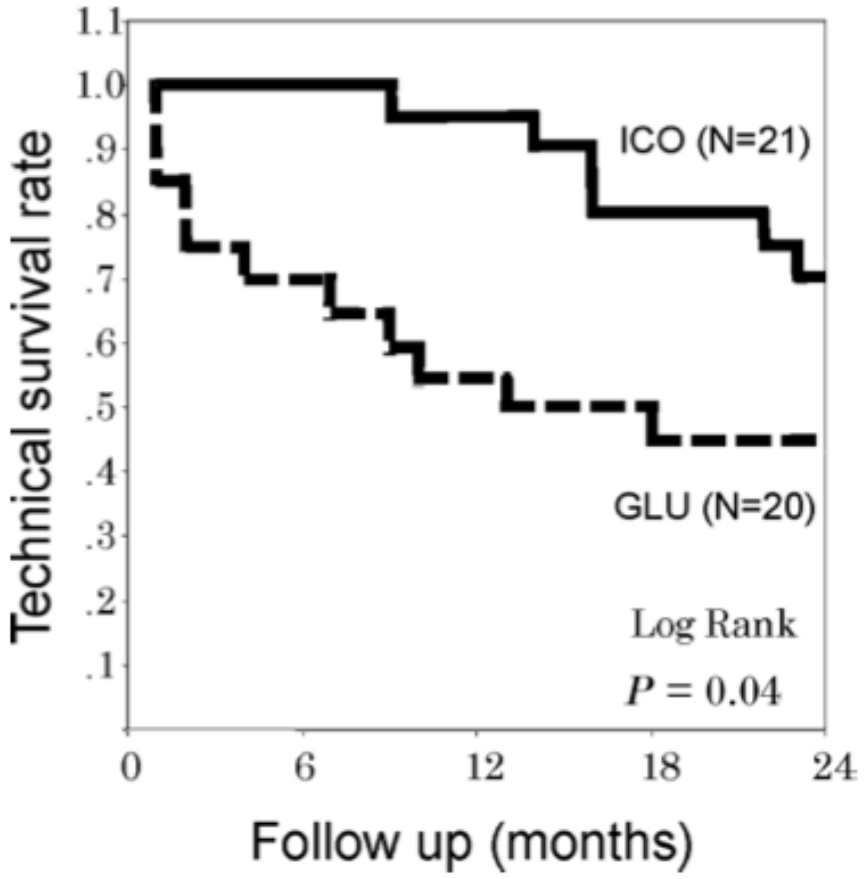
Transfer to PD From HD



		All-Cause Technique Failure
Overall		
PD Only		1.0
HD To PD Switch	Within 90 days	1.31 [1.17, 1.45]
	Between 91-180 days	1.45 [1.26, 1.68]
	Between 181-365 days	1.17 [0.98, 1.39]

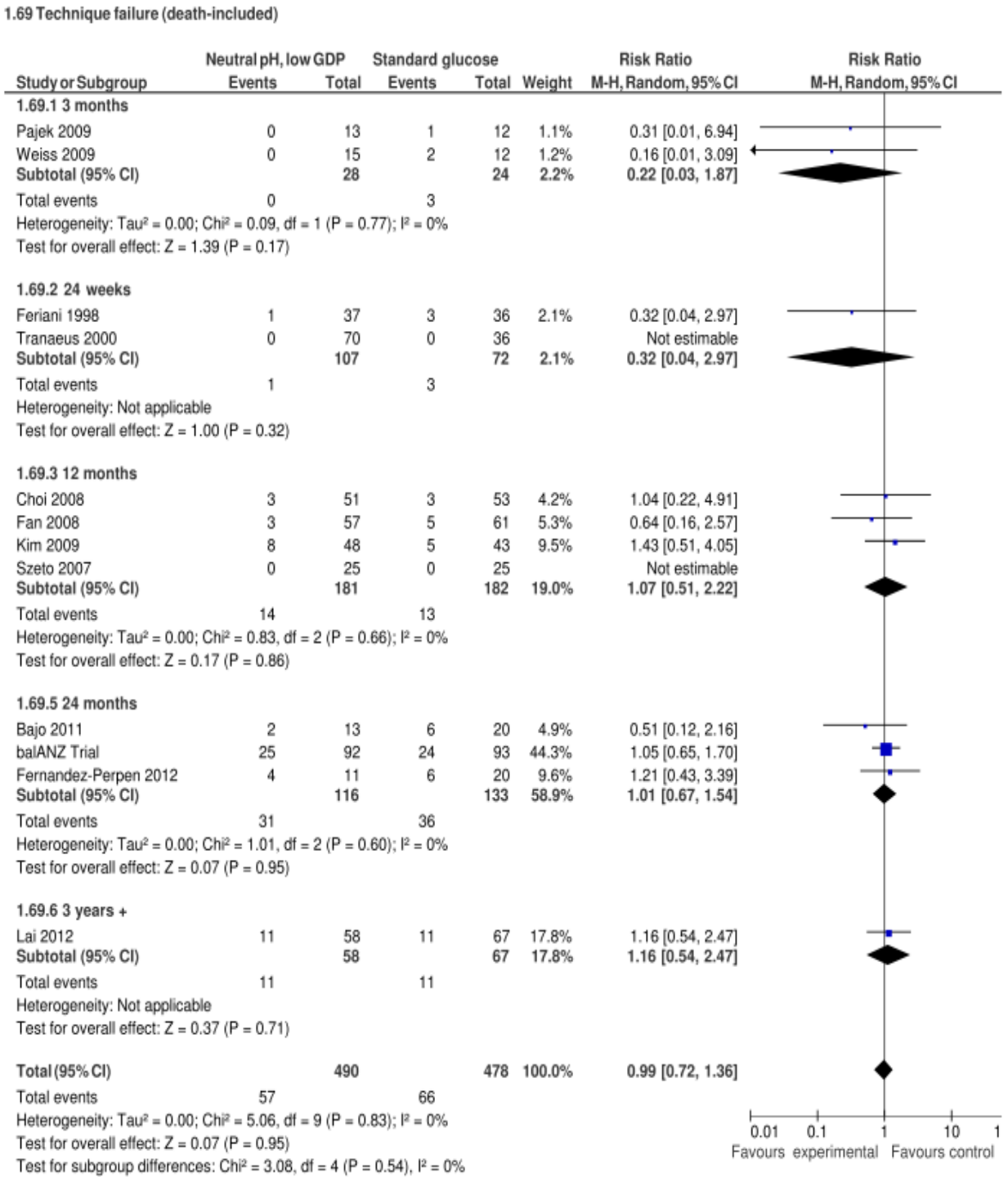
Perl… Nessim et al Unpublished

Impact of Icodextrin Use on Technique Survival



Takatori CJASN 2011

Impact of Neutral-PH Low GDP PD Solutions on Technique Survival



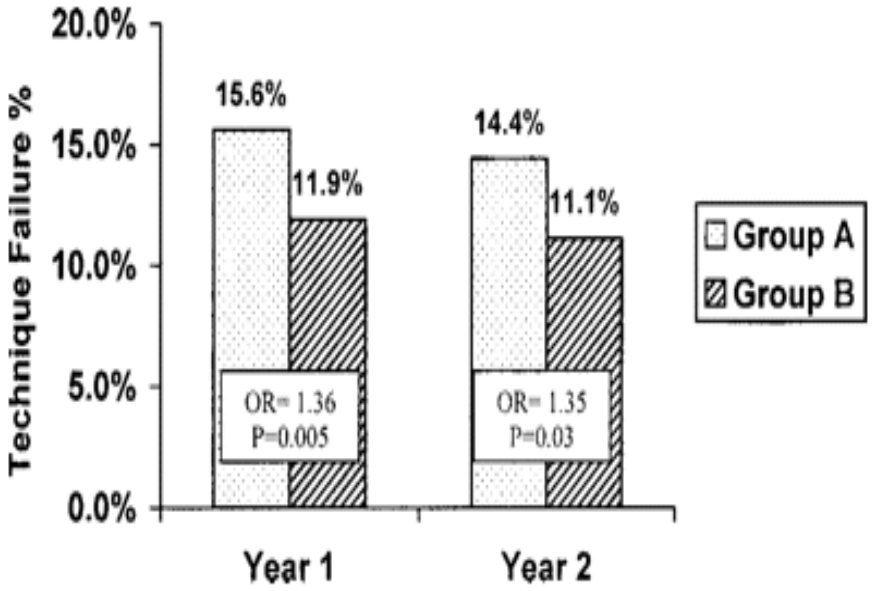
Impact of Peritoneal Membrane Transport Characteristics on The Risk of Transfer to HD

Transport Type	Risk of Technique Failure
High (n=628)	0.88 (0.64-1.21)
High-average (n=1936)	1.17 (0.95-1.44)
Low-average (n=1145)	1.02 (0.77-1.35)
Low (n=96)	1.24 (0.67-2.29)

Johnson et al NDT 2010

Impact of PD Centre Size

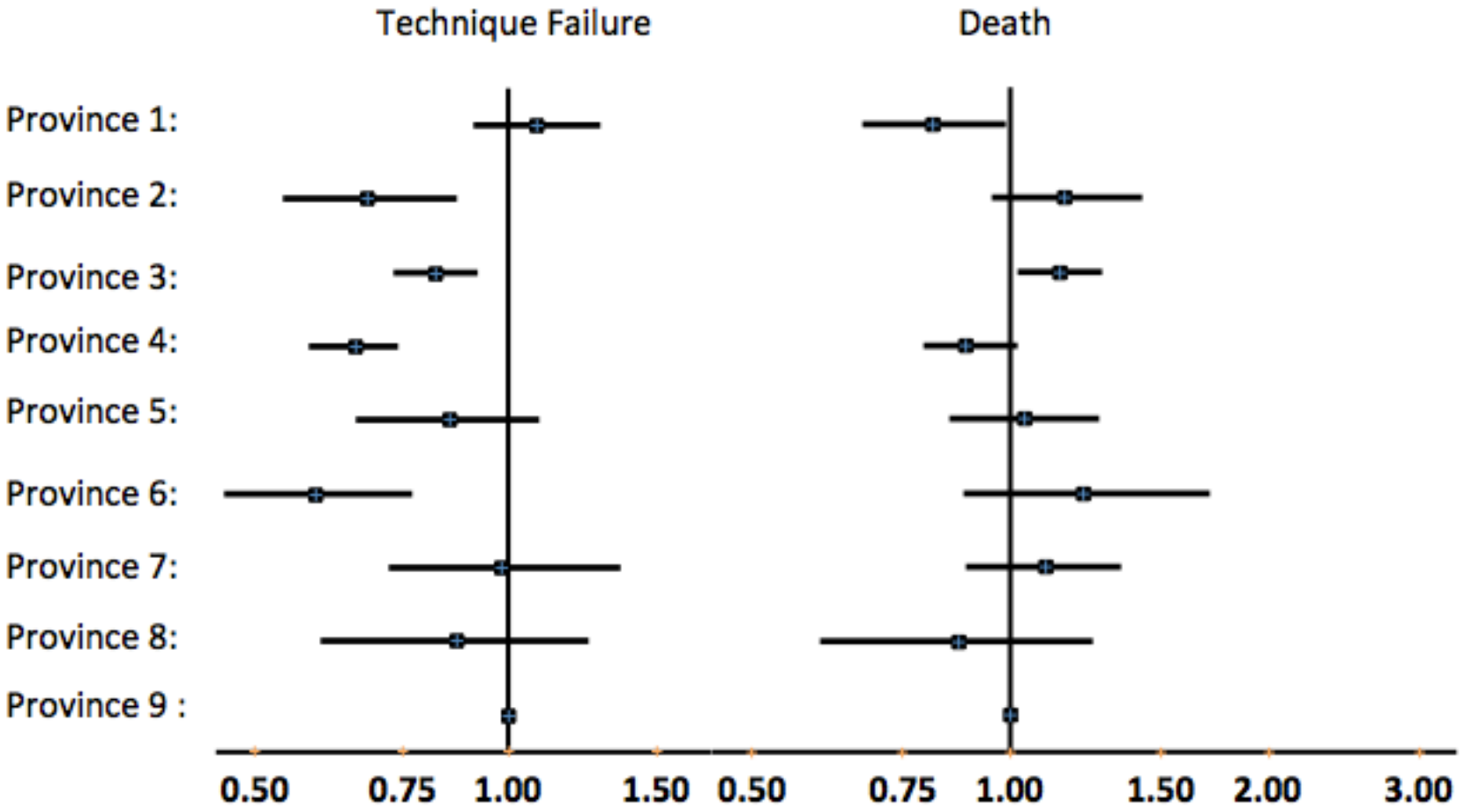
- Consistent and strong independent predictor of transfer to HD in Canada, USA, Australia and The Netherlands
- Associated with improved adherence to clinical practice guidelines
- Larger centers may have improved practices, knowledge and resources



Group A ≤ 25 patients
Group B > 25 patients

Afolalu, PDI 2009

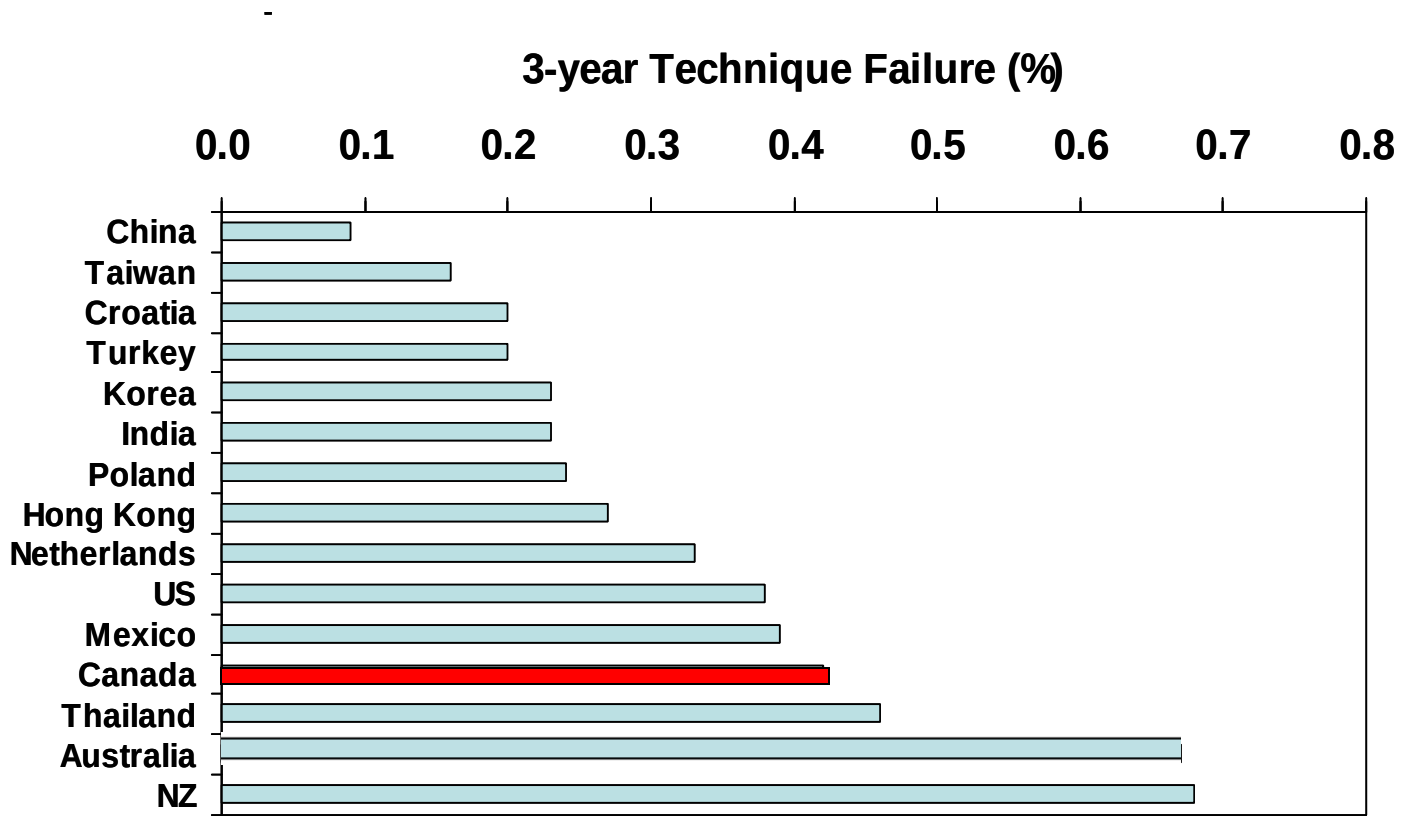
Regional Variation in Rates of Transfer to HD



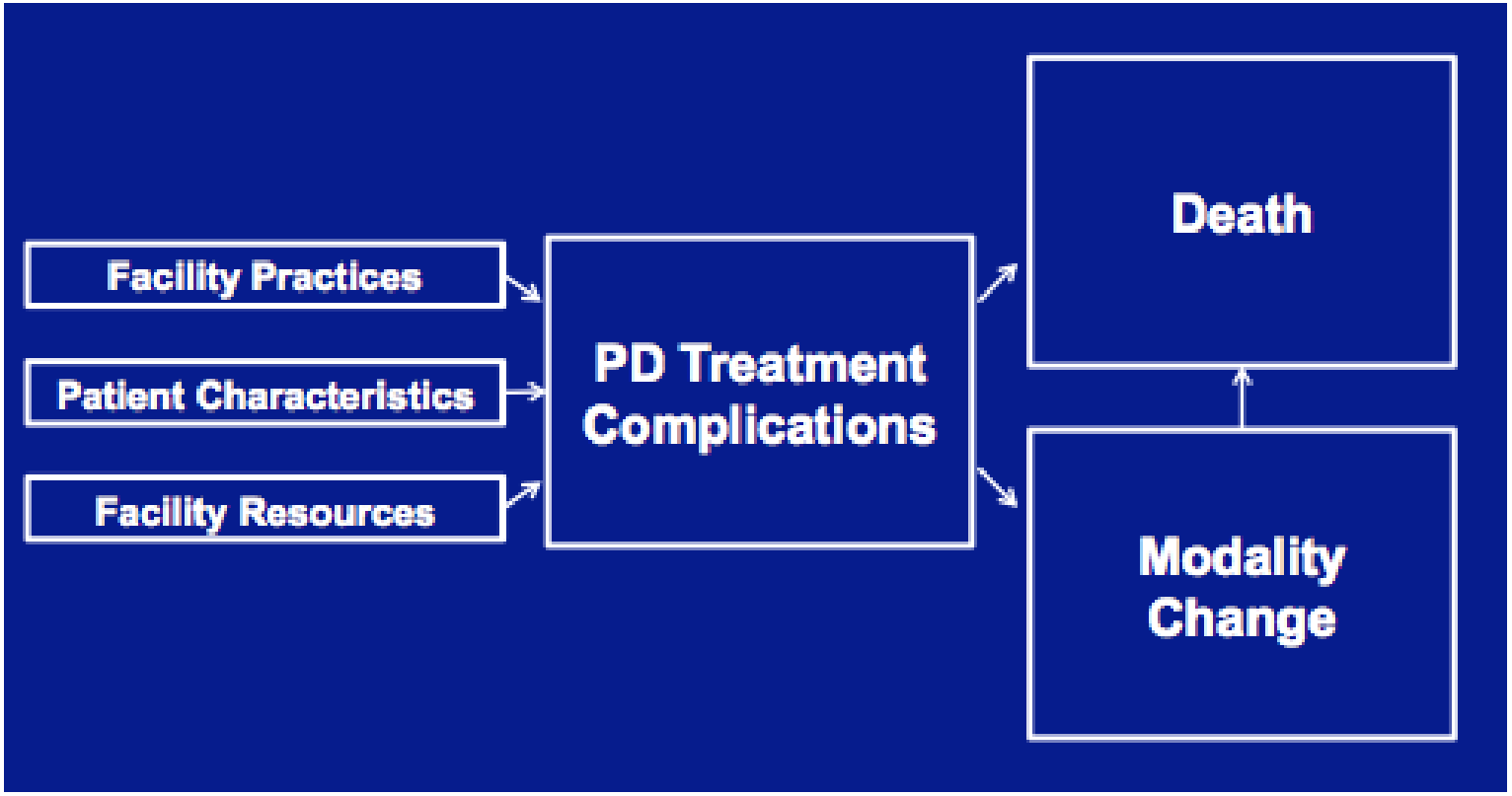
Adjusted for age, race, sex, body mass index, end stage renal disease comorbidity index, primary diagnosis, PD modality (Automated PD vs. Continuous ambulatoryPD)

Perl unpublished data

International Variation in Rates of Technique Failure



Putting It All Together



WCN Milan: A Special Birthday

Objectives

- Understand the reasons for discontinuation of PD therapy
- Understand Trends in PD Technique Failure in Canada
- Review patient, therapy and facility-specific risk factors for transfer to HD from PD
- Introduce The Peritoneal Dialysis Outcomes Practice Patterns Study (PDOPPS) as a Means to Recognize Modifiable Causes of Peritoneal Dialysis Technique Failure

Design and Implementation

PDOPPS – Scientific Approach

1. *Describe variation in practice* and monitor trends by following nationally representative samples of peritoneal dialysis facilities

2. *Identify best practices* by analyzing variations in practice and outcomes

3. *Translate* (communicate) key findings to improve clinical care

Study Goal

- The primary scientific goal of PDOPPS is to identify optimal practices to maximise time on PD treatment, without compromising patient survival and morbidity

Standardizing Data Definitions: Causes of Switch to HD

Level 1	Level 2
Infection related	Acute severe Refractory Relapsing Recurrent Exit site infection only Tunnel infection
Catheter related problems	Fibrin Omental wrap Adhesions Catheter misplaced Cause unclear Cuff extrusion Catheter fell out
Problems with solute/water clearance	Inadequate clearance - defined by either Kt/V or creatinine clearance Inadequate clearance - phosphate clearance Uraemic symptoms/poor nutrition Loss of RRF Patient size UF failure - PET defined Unable to remove excess body water Unwillingness to prescribe more dialysate glucose to achieve sufficient UF Excess fluid removal

Lambie et al, ASN abstract 2012

Standardizing Data Definitions: Causes of Switch to HD

Level 1	Level 2
Peritoneal leaks/hernia	Scrotal oedema Pleuro-peritoneal leak Abdominal wall Elsewhere Inguinal Peri-umbilical Elsewhere
Psychosocial/medical	Patient choice/"burn out" Carer choice/"burn out" Change in circumstance (e.g. death of carer, change in job etc) Severe Depression Physical incapacity Cognitive impairment
Risk of, or diagnosis of, Encapsulating peritoneal sclerosis (EPS)	Diagnosed EPS Time on PD GI symptoms but not formally diagnosed with EPS
Other	Haemoperitoneum Intra-abdominal pathology Other reason not included elsewhere

PDOPPS: Initial Countries

- First wave (2013):
  - US
  - UK
  - Canada
  - Japan
- Anticipate other countries soon:
  - Investigators seeking funding locally

PDOPPS: Procedures & Data

- Sampling
  - Facilities – National samples of PD facilities (with ≥15 patients), by stratified random sampling
  - Patients – Samples of prevalent and incident* patients
- 3000+ patients
- Follow for 3+ years, including ≥4 mos. after permanent transition to HD
- Detailed clinical data, as well as patient and physician/nurse surveys

PDOPPS: Primary and Secondary Outcomes

Primary Outcome:

- All Cause PD Technique Failure

Secondary Outcomes:

- All-cause mortality
- Cause specific PD technique failure:
  - Inadequate clearance
  - Infection-related
  - Psychosocial-related
  - Catheter-related*
  - Mechanical-related*

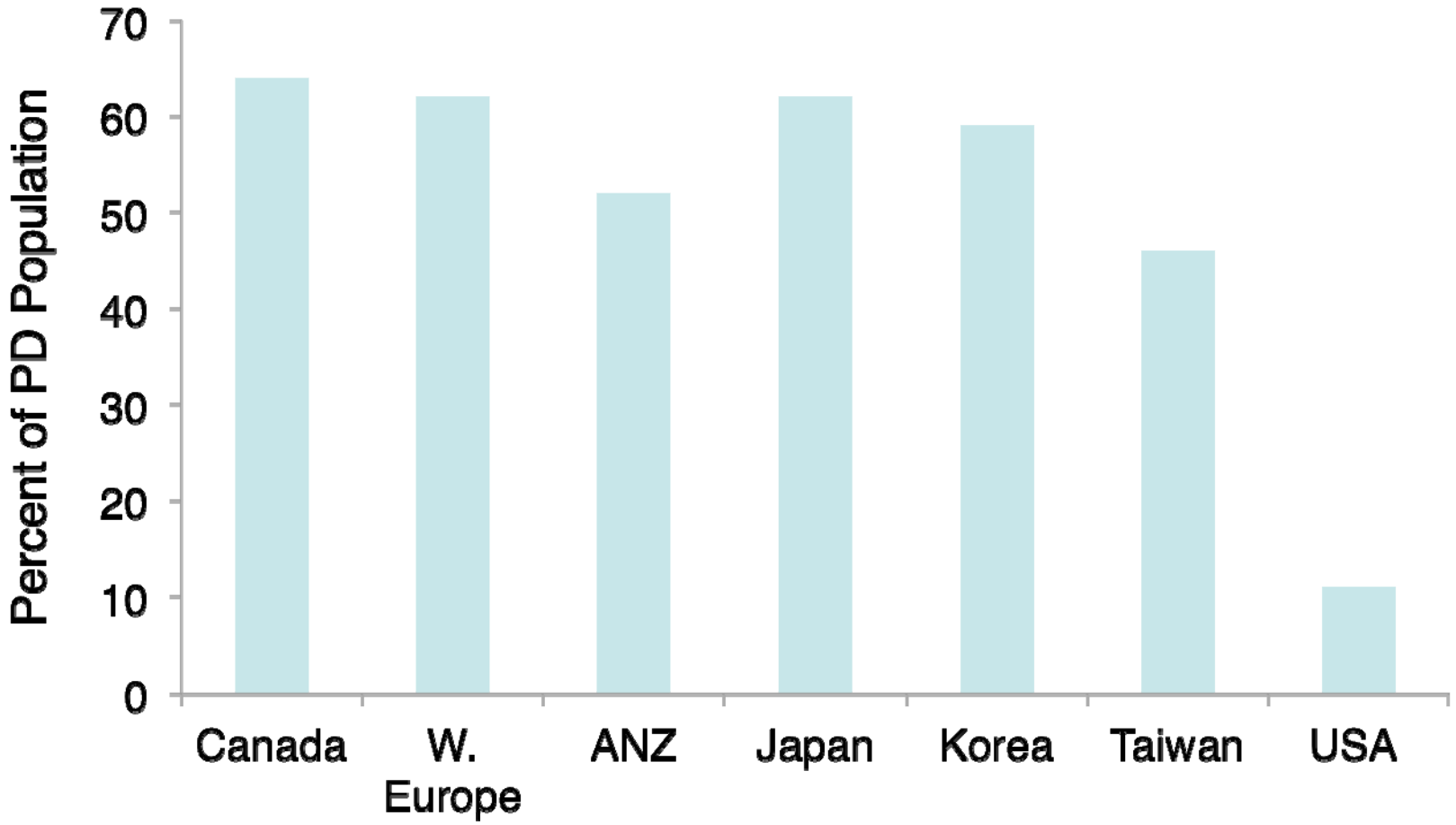
Secondary Outcomes:

- PD related complications:
  - Hospitalizations
  - PD-related infections
  - Residual kidney function decline/anuria
  - PD access intervention
- Patient-reported outcomes (PRO)
- Clinical/laboratory measures:
  - Peritoneal membrane function: transport Status, UF capacity
  - Metabolic/inflammatory: Lipids, HbA1C, CRP

PDOPPS: ISPD Work Groups

- Infection: Prevention and Management
- PD catheter Access and function
- Clinical application of PD therapy
- Dialysis Prescription and Fluid Management
- Patient Support
- Patient training and Education

Icodextrin: Variability In Absolute Use by Country



Source: Baxter Healthcare: previous 18 months

Impact of Icodextrin Use on PD Technique Survival: PDOPPS Proposed Analysis

Hypothesis:

Because glucose exposure appears to contribute to peritoneal membrane changes, the use of icodextrin early in PD therapy will reduce the risk of all-cause PD technique failure*

Exposure:

Facility incident use of icodextrin:
-early use of icodextrin among incident patients within the first 6 months of PD therapy

Outcome:

Primary:
-All cause technique failure
Secondary:
-Technique failure due to inadequate ultrafiltration and dialysis inadequacy
-Mortality

Adjustments:

- -demographics
- -comorbidities
- biochemistry
- -membrane function
- --residual kidney function
- modality (APD / CAPD)
- -low GDP solution use
- -Glucose exposure
- Facility characteristics

Summary (I)

- Causes of technique failure variable and poorly understood and variability captured across registries
- Likely that multiple causes in any given patient with psychosocial causes under appreciated
- Little change in technique survival in Canada in the last 15 years with the exception of patients > 65

Summary (II)

- Complex interplay between facility, patient and therapy characteristics that lead to risk of transfer to HD
- Need to better understand the impact of each and modifiable practices on the risk of transfer to HD
- PDOPPS: an international research program to understand modifiable causes of PD technique failure

Thank you

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- Jeffrey Perl
- Ronald Pisoni
- Fritz Port
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Industry/Country Sponsors

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- Fresenius USA
- Japanese Society of PD

DOPPS Dialysis Outcomes and Practice Patterns Study

St. Michael's Inspired Care. Inspiring Science.

Arbor Research Collaborative for Health

International Society for Peritoneal Dialysis