Universitair Ziekenhuis Brussel

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Peritoneal membrane testing: *routine* testing is not useful in 2016

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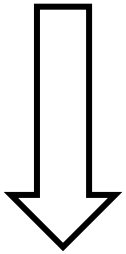
Peritoneal membrane testing

= **physiological evaluation** of a peritoneal membrane

- solute transport characteristics
- water transport characteristics



1. Determine the optimal PD treatment strategy
2. Follow individual membrane changes over time

"Individual physiology"-based medicine

Peritoneal membrane testing

= **physiological evaluation** of a peritoneal membrane

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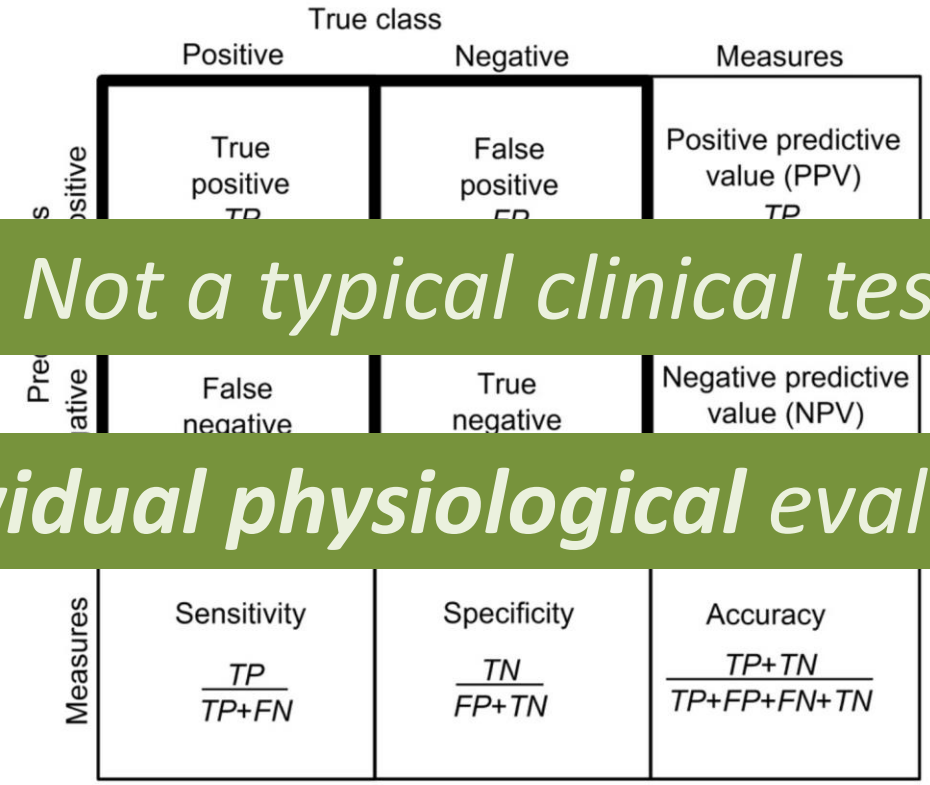


Not a typical clinical test

***Individual physiological** evaluation*

Physiology-based medicine

Low transporters

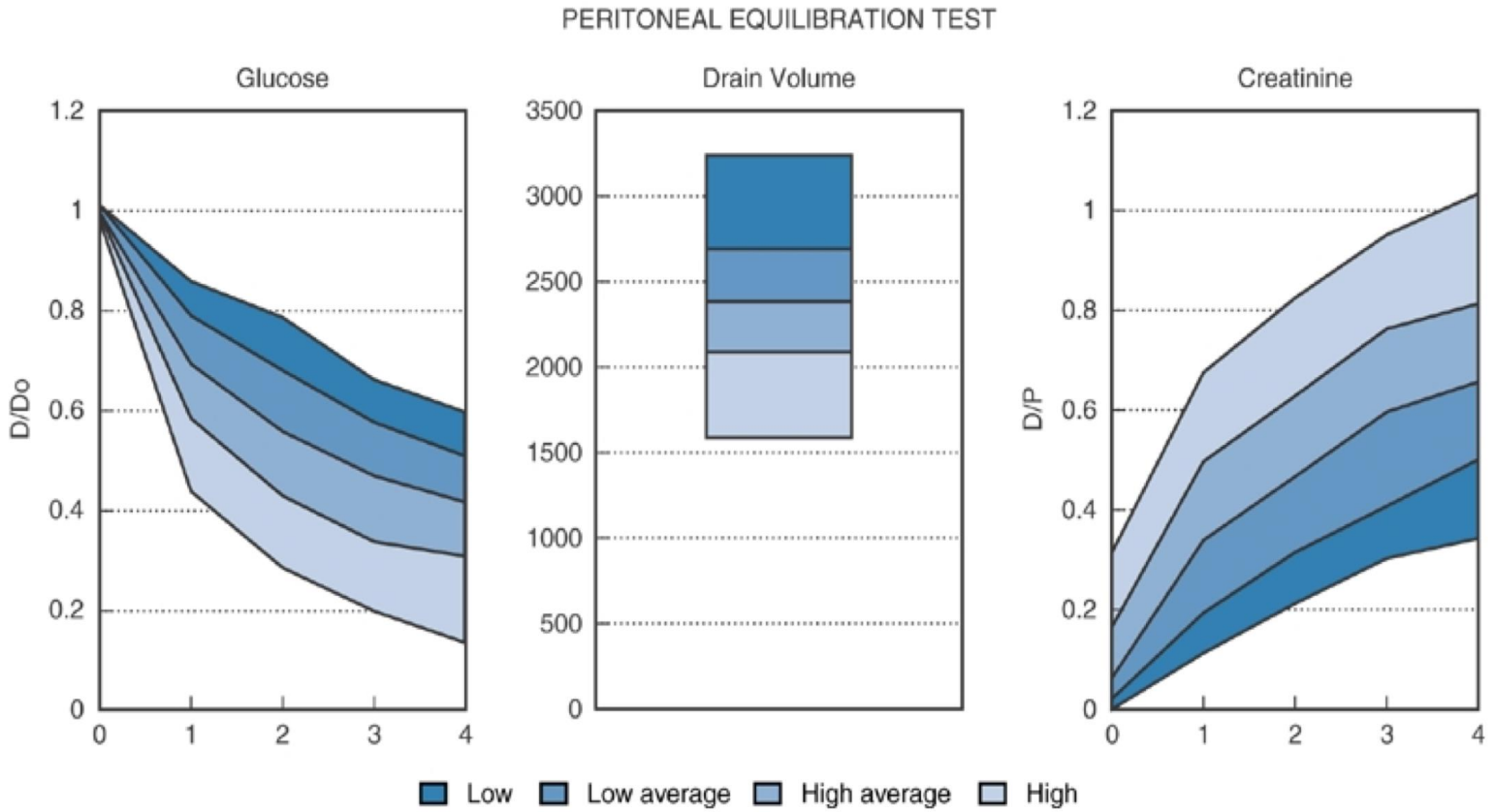
≈ smaller effective peritoneal membrane surface area

≈ lower numbers of small pores

High transporters

≈ larger effective peritoneal membrane surface area

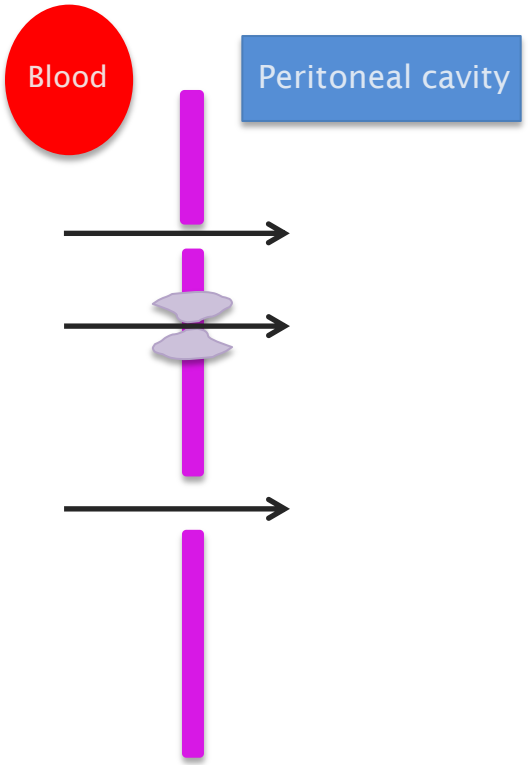
≈ higher numbers of small pores



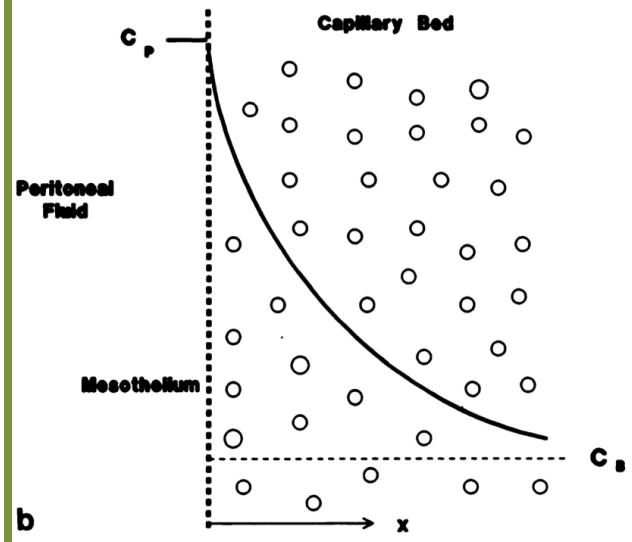
Twardowski Z et al. Blood Purification, 1989

Models of peritoneal membrane transport

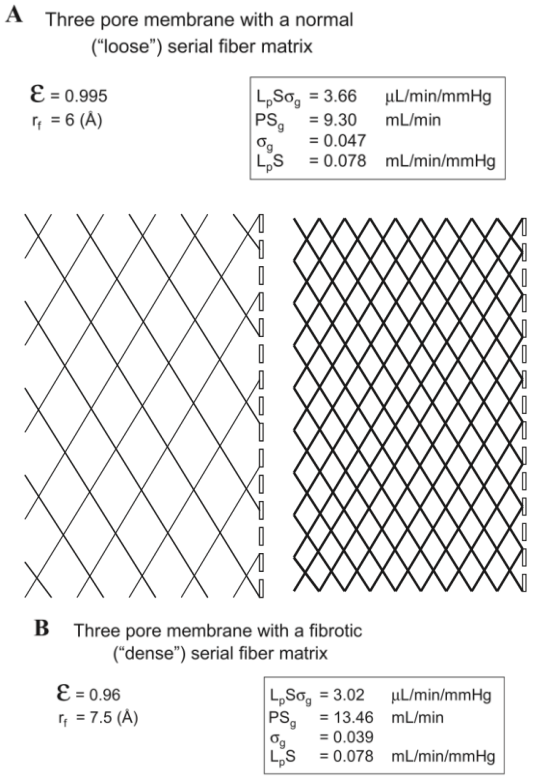
3-pore model



Distributed model



Serial/fiber matrix model



Rippe B et al. KI 1991
Flessner MF. JASN 1991
Rippe B et al. Am J Physiol Renal Physiol 2007

Physiology-based medicine

Low transporters

≈ smaller effective peritoneal membrane surface area

≈ lower numbers of small pores

High transporters

≈ larger effective peritoneal membrane surface area

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Development of cyclers and APD treatment regimens

Introduction of icodextrin

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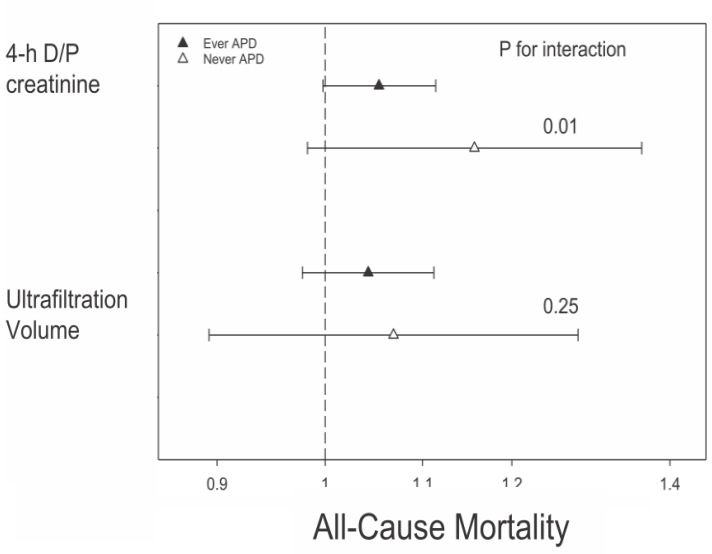
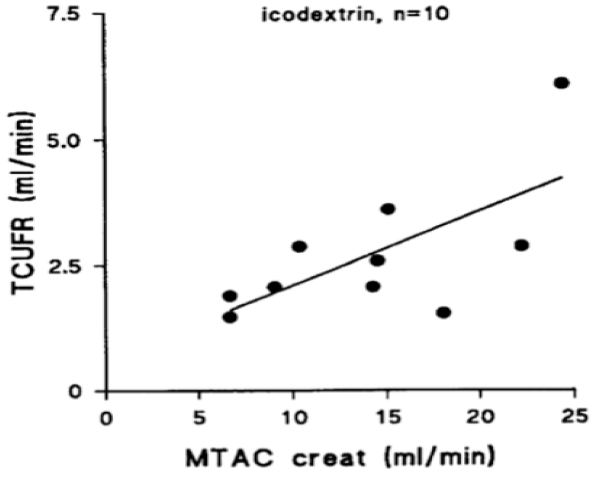
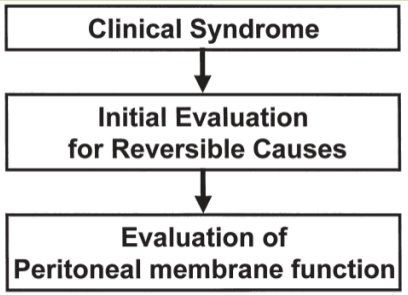




Mehrotra R et al. CJASN 2015; Krediet R.T. in *Nolph and Gokal's textbook of PD*. 2009

EVALUATION AND MANAGEMENT OF ULTRAFILTRATION PROBLEMS IN PERITONEAL DIALYSIS



A patient's membrane transport status should be evaluated by the standard peritoneal equilibration test (PET).

A PET should be performed approximately 4 weeks after initiating peritoneal dialysis, but no earlier.

PETs should be repeated at 2 years and then annually. PETs should be repeated earlier if there is clinical evidence of fluid overload with a significant decrease in ultrafiltration, hypertension or elevated serum urea levels, particularly in those patients who have had episodes of peritonitis.

KIDNEY HEALTH AUSTRALIA CARI GUIDELINES

2006 Updates Clinical Practice Guidelines and Recommendations

National Kidney Foundation KDOQI KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE

3.2 Baseline peritoneal membrane transport characteristics should be established after initiating a daily PD therapy.

3.3 Data suggest that it would be best to wait 4 to 8 weeks after starting dialysis to obtain this baseline measurement.

3.4 Peritoneal membrane transport testing should be repeated when clinically indicated (see Table 15).

THE RENAL ASSOCIATION founded 1950

We recommend that peritoneal membrane function should be monitored regularly (6 weeks after commencing treatment and at least annually or when clinically indicated) using a peritoneal equilibration test (PET) or equivalent. Daily urine and peritoneal ultrafiltration volumes, with appropriate correction for overfill, should be monitored at least six-monthly. (1C)

CANADIAN SOCIETY OF NEPHROLOGY GUIDELINES/RECOMMENDATIONS

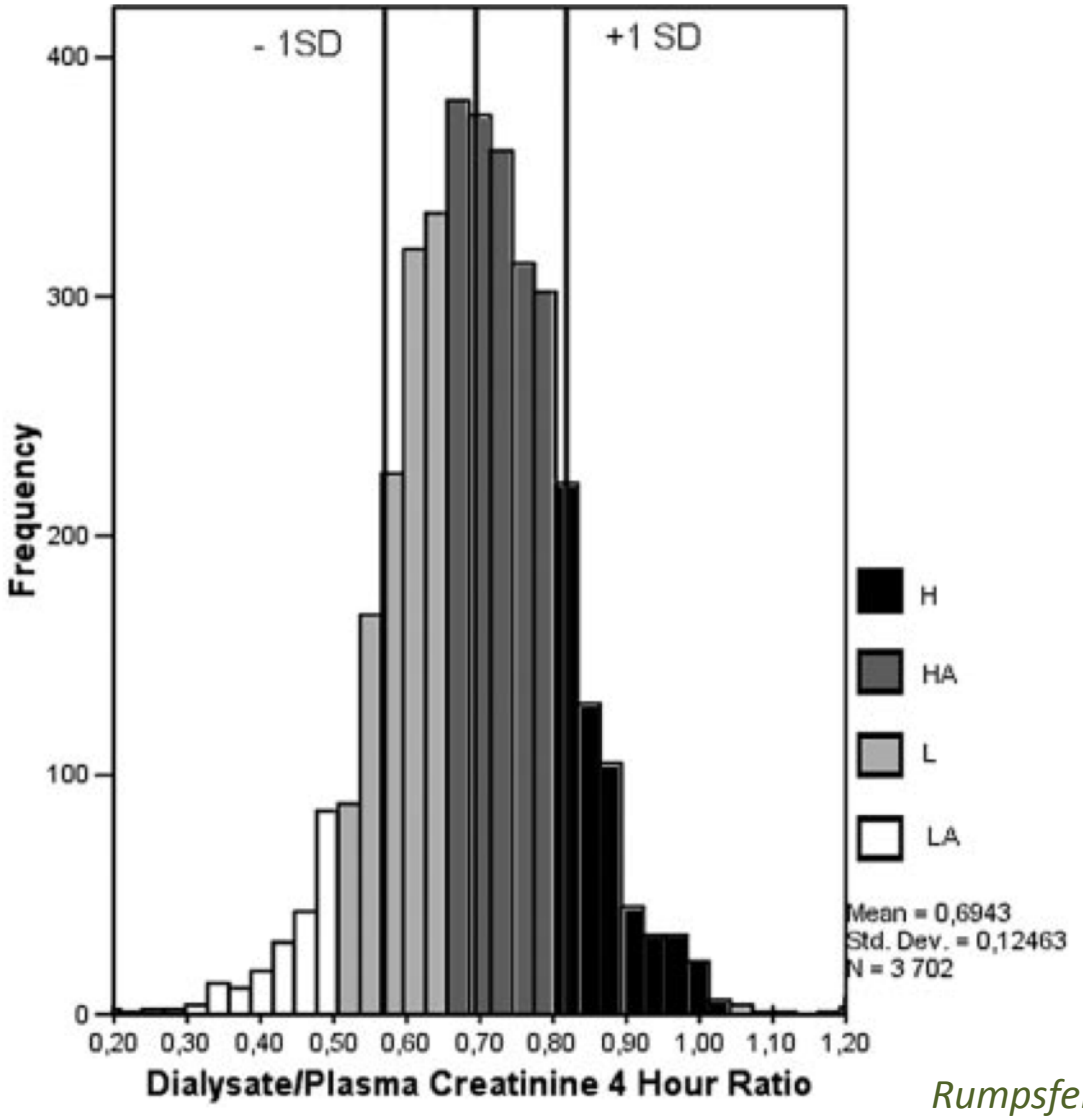
3.1.2 A 2.5% or 4.25% dextrose PET should be carried out no sooner than 4 weeks after initiation of PD. This test should be subsequently repeated if there are unexplained or unexpected changes in volume status or UF (opinion).

“Physiology-based” medicine
or
“Individual physiology”-based medicine?

Are the general physiological principles of peritoneal transport so difficult to adopt in a single patient that individual testing is always warranted?

Why could routine peritoneal membrane testing in all individuals treated with peritoneal dialysis be useful?

General facts on membrane characteristics



Rumpsfeld M et al. JASN 2006

Individual physiological membrane testing

is useful in clinical practice if it:

- is simple and affordable
- impacts the treatment strategy
- is a stronger predictor of outcomes compared to clinical parameters
- prevents long-term complications of PD

Cost of a routine PET

- *Dialysate* 1 (or 2) x 2.0L bag
- *Dialysate samples* around € 30
- *Blood samples* around € 5
- *Nurse* at least 4hrs availability
- *Patient* transport, unavailability for work
- *Hospital* accommodation

Imagine your hospital has 50/50 PD/HD patients

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is useful in clinical practice if it:

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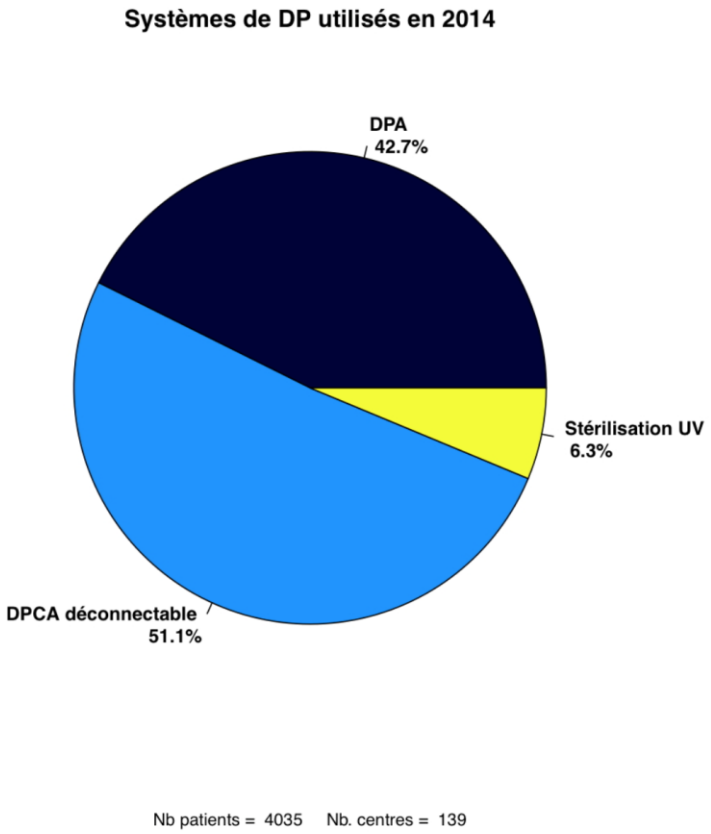
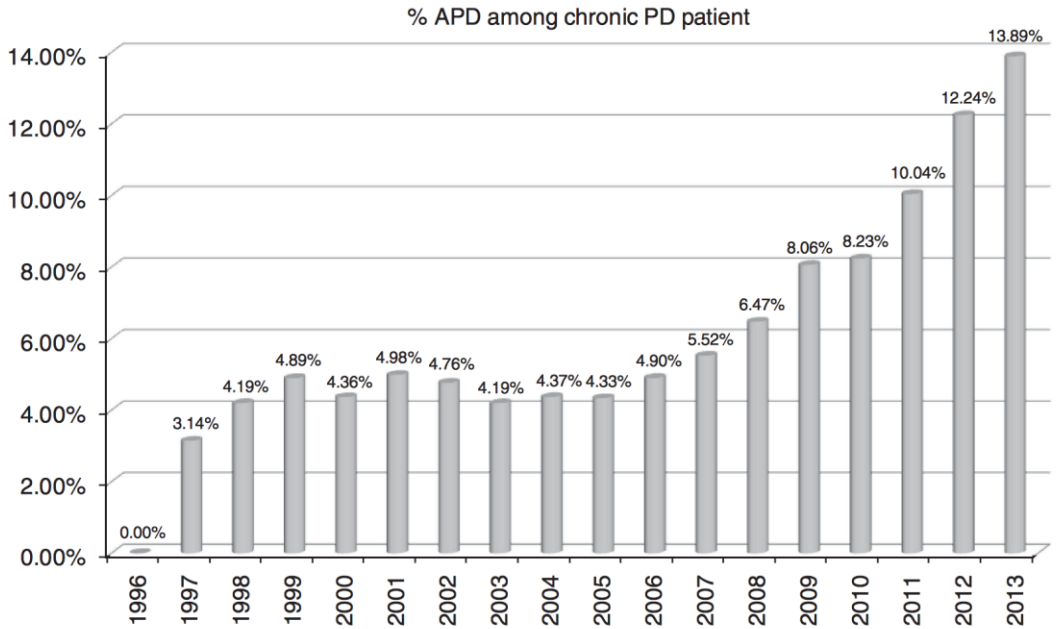
Proportion of CAPD and APD use

France



www.rdplf.org

Hong-Kong



Leung CB et al. KI Suppl 2015

Proportion of CAPD and APD use

Comparison of peritoneal dialysis practice patterns and outcomes between a Canadian and a Chinese centre

	Canadian patients	Chinese patients
Age (y)	58.8 ± 17.8	54.4 ± 16.2
CVD (%)	42.2	14.2
RKF (ml/')	6.77 ± 4.43	3.52 ± 2.67
Residual urine output (mL)	889 ± 622	1010 ± 684
S Albumin (g/L)	36.8 ± 4.8	34.6 ± 4.8
D/P creat	0.71 ± 0.09	0.68 ± 0.13
PD treatment V (L)	8.0 (1.5 – 17)	6.0 (2.0 – 8.0)
CAPD use (%)	**38.7**	**100**
Icodextrin use	**30.1**	**0**

Fang W et al. NDT 2008

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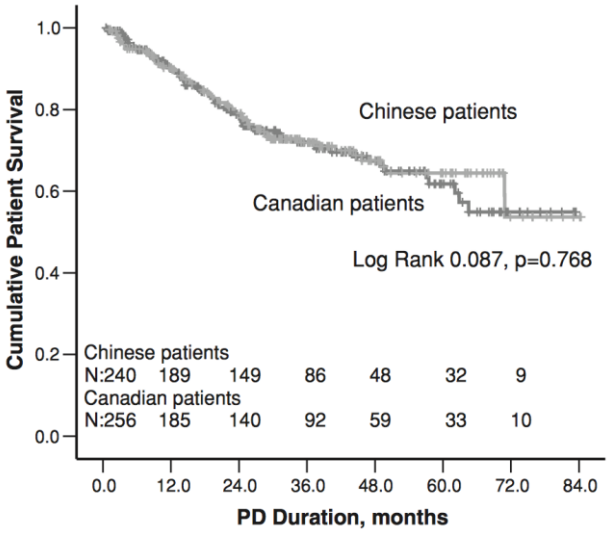

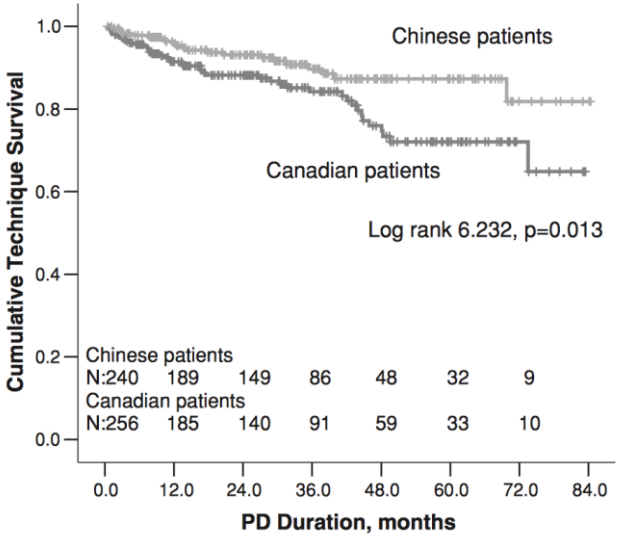

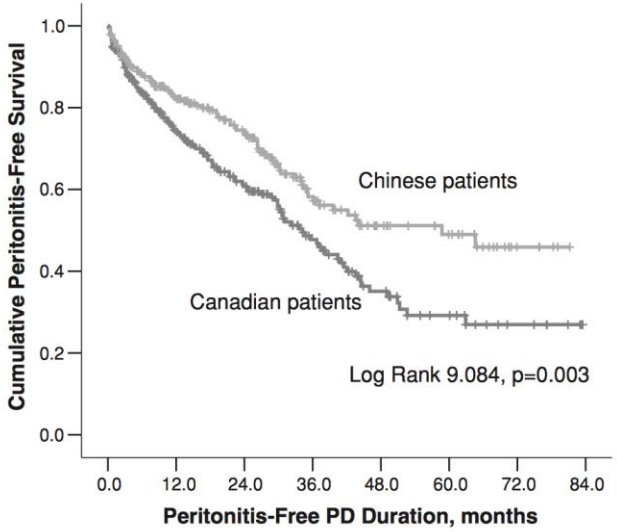

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(*) independent predictors of survival in overall cohort

Fang W et al. NDT 2008

US and ANZ observational data

Variable	Low/Slow (*n*=1634)	Average (*n*=6954)	High/Fast (*n*=1555)	All (*n*=10,142)
D/P creatinine, mean [range]	0.46±0.05 [0.30–0.52]	0.65±0.07 [0.53–0.77]	0.84±0.05 [0.78–1.13]	0.65±0.12 [0.30–1.13]
Use of APD, %				
Initial	58	52	48	52
Ever through follow-up	87	88	87	88

Mehrotra R et al. CJASN 2015

Variable	Total Population (n = 3702)	Breakdown by Transport Category				
		Low (n = 185)	Low-Average (n = 1055)	High Average (n = 1848)	High (n = 614)	Crude P Value
Received APD	1231 (33.3%)	52 (28.1%)	295 (28.0%)	641 (34.7%)	243 (39.6%)	< 0.001
D:P Cr 4 h	0.69 ± 0.12	0.42 ± 0.08	0.59 ± 0.04	0.72 ± 0.05	0.88 ± 0.08	< 0.001

Rumpsfeld M et al. JASN 2006

Characteristic	APD (n = 142)	CAPD (n = 486)	P-value
D/P Cr 4h	0.88 ± 0.09	0.87 ± 0.07	0.2

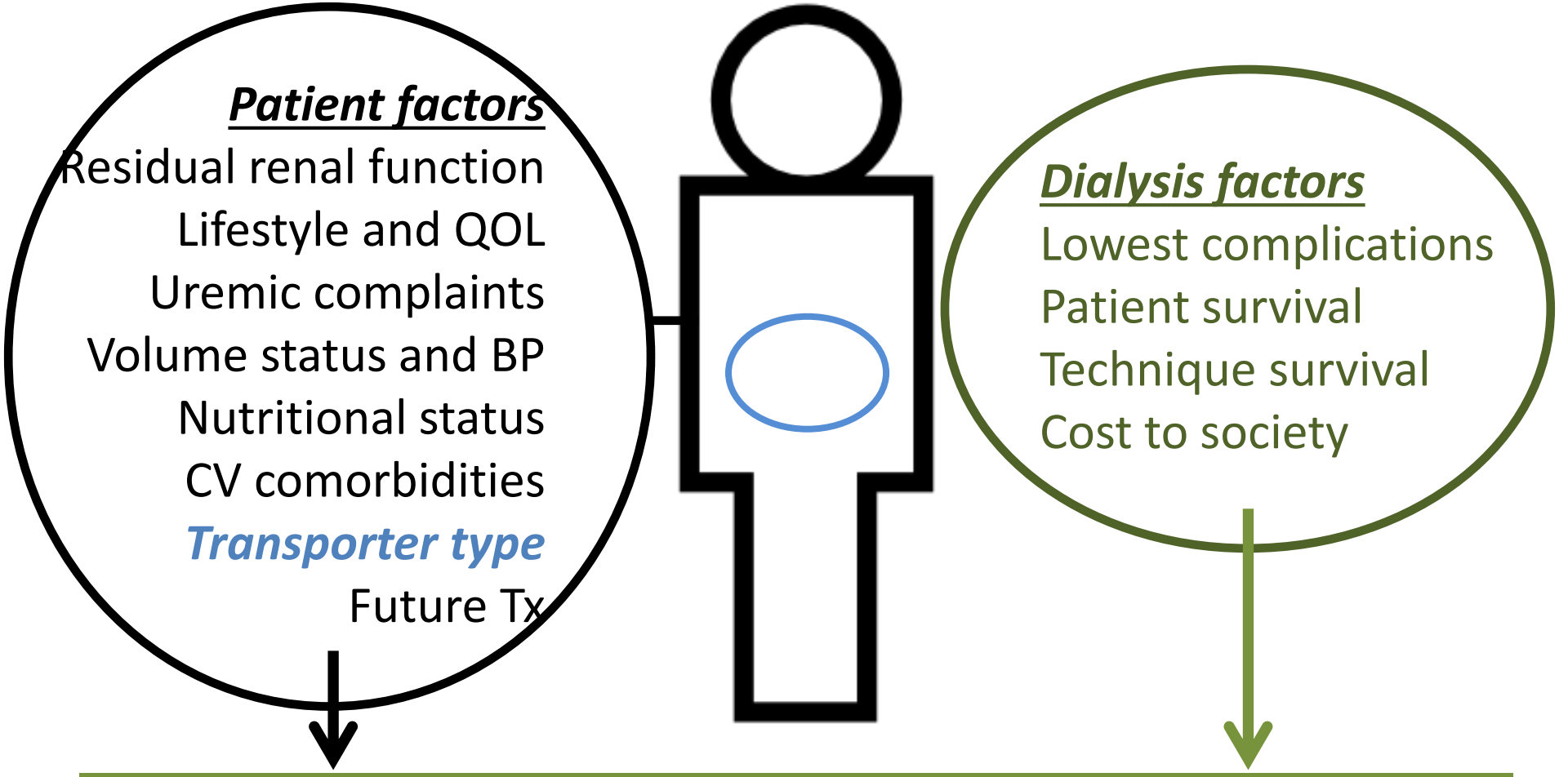
Johnson DW et al. NDT 2010

PET-adjusted PD prescription

No interventional trials

evaluating the effects of treatment changes according to peritoneal membrane characteristics

The optimal PD strategy



PD modality
dwell V – dwell time – dialysate

Individual physiological membrane testing

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- is simple **YES!** and affordable **RATHER NOT!**
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- prevents long-term complications of PD

Clinical parameters and patient outcomes

Solute clearance

Variable	Relative Risk	95% Confidence Limit
Ccrp (5 L/wk per 1.73 m^2 greater)	1.00	0.898–1.105
GFR (5 L/wk per 1.73 m^2 greater)	0.88	0.829–0.943

Bargman JM et al. JASN 2001

Variable	Actuarial survival RR	95% CI	*p* Value
Peritoneal Kt/V (↑ 0.1)	0.94	0.89–0.99	0.03
Residual GFR (↑ 1 mL/min/1.73 m^2)	0.80	0.73–0.88	0.0001

Szeto CC et al. PDI 2004

Clinical parameters and patient outcomes

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SN 2001

ACE-I
Avoid volume depletion
Avoid nephrotoxic agents

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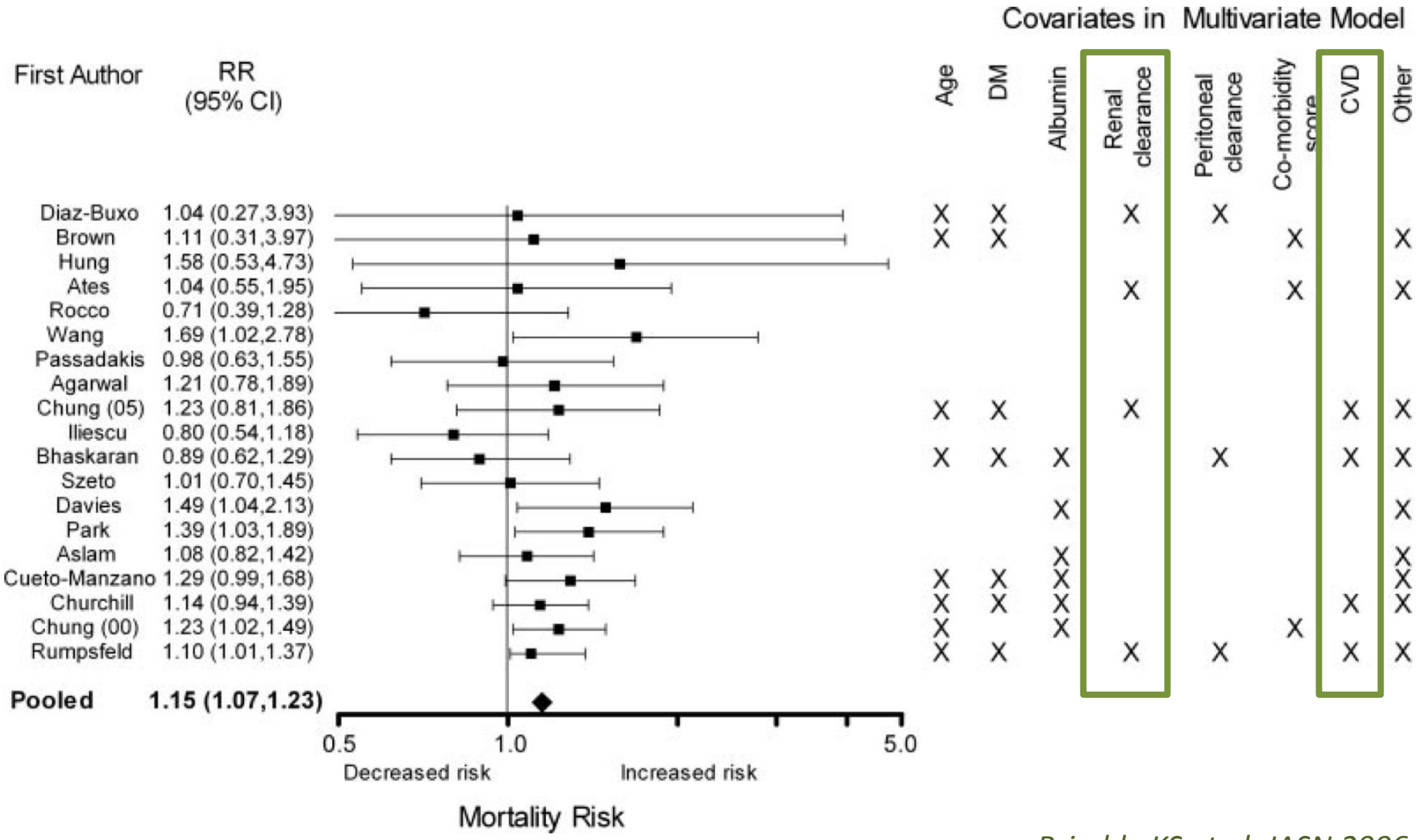
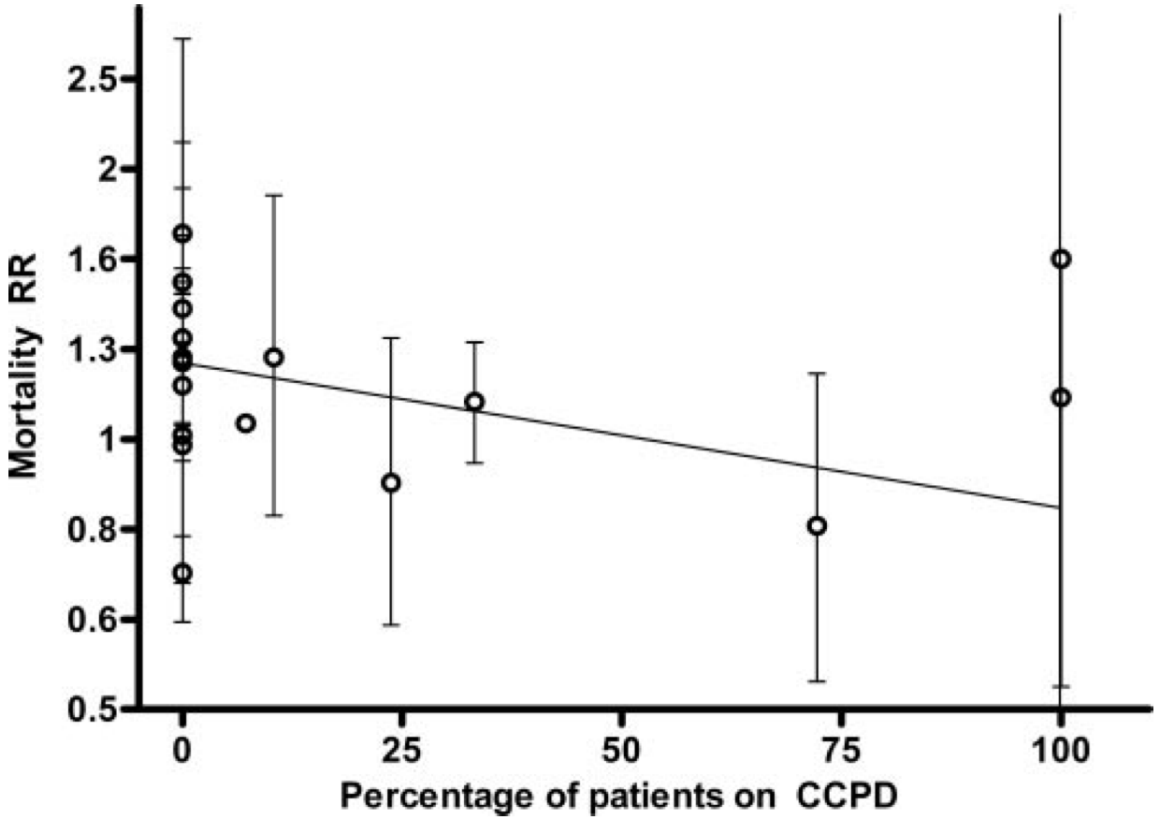
Solute transport characteristics



Brimble KS et al. JASN 2006

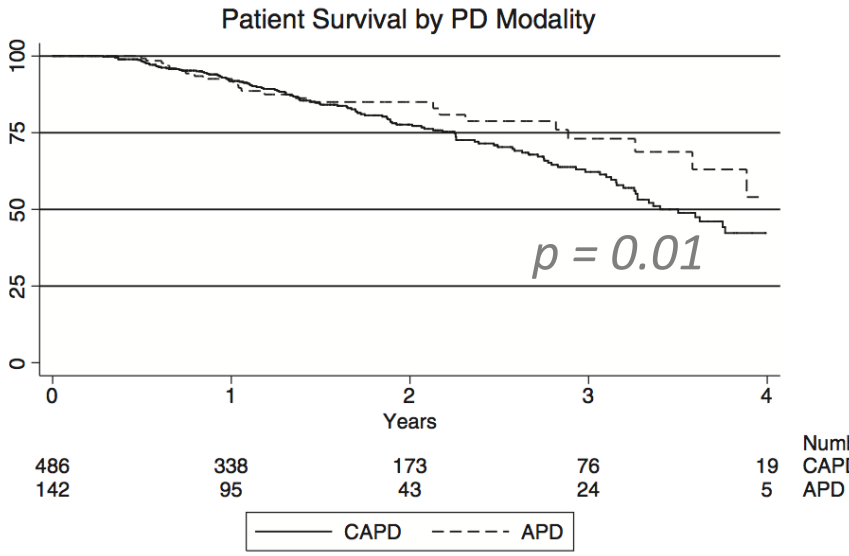
Solute transport characteristics

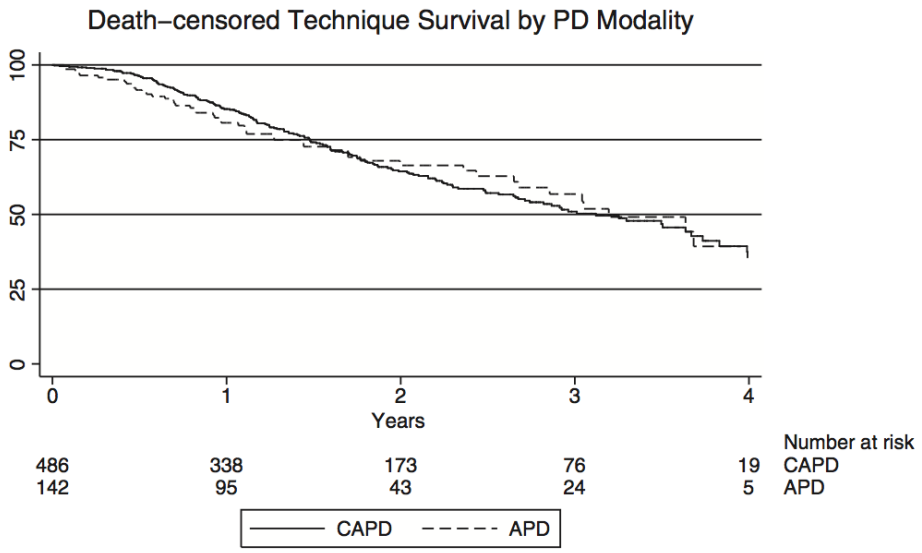


Brimble KS et al. JASN 2006

Solute transport characteristics

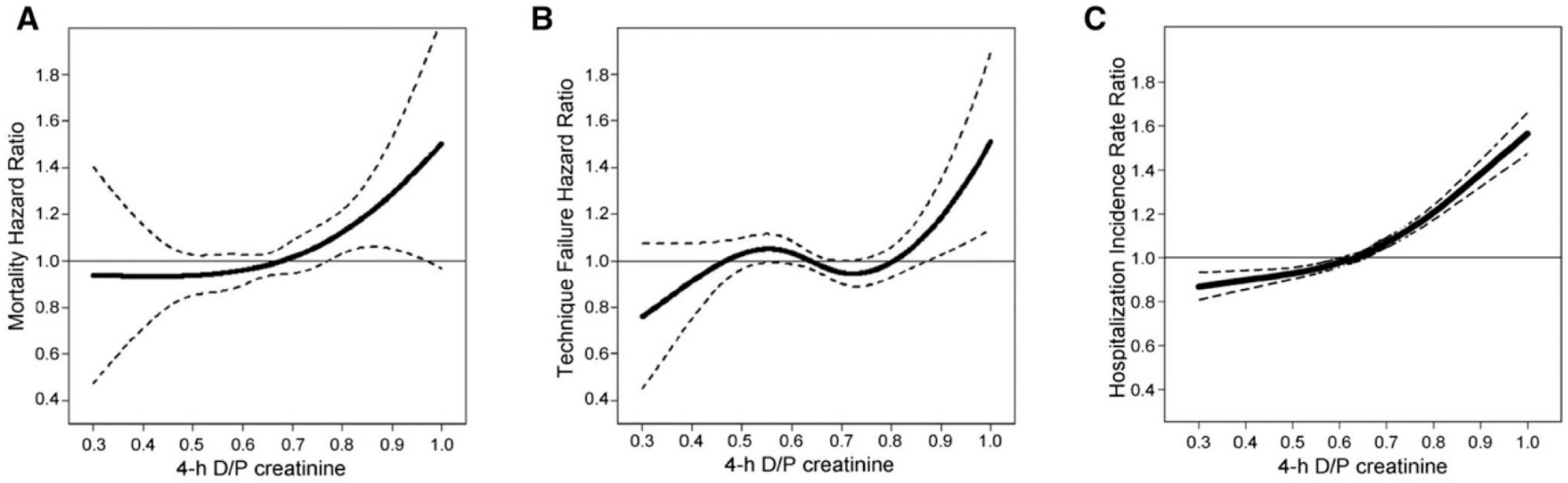
High transporters from ANZDATA Registry





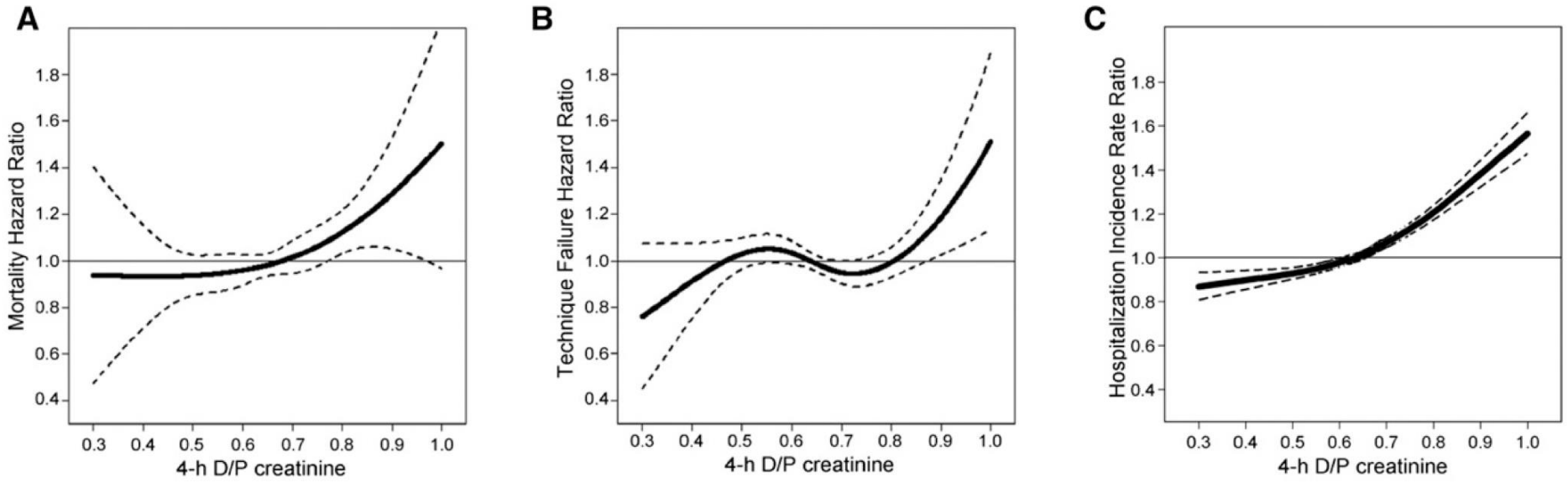
Johnson DW et al. NDT 2010

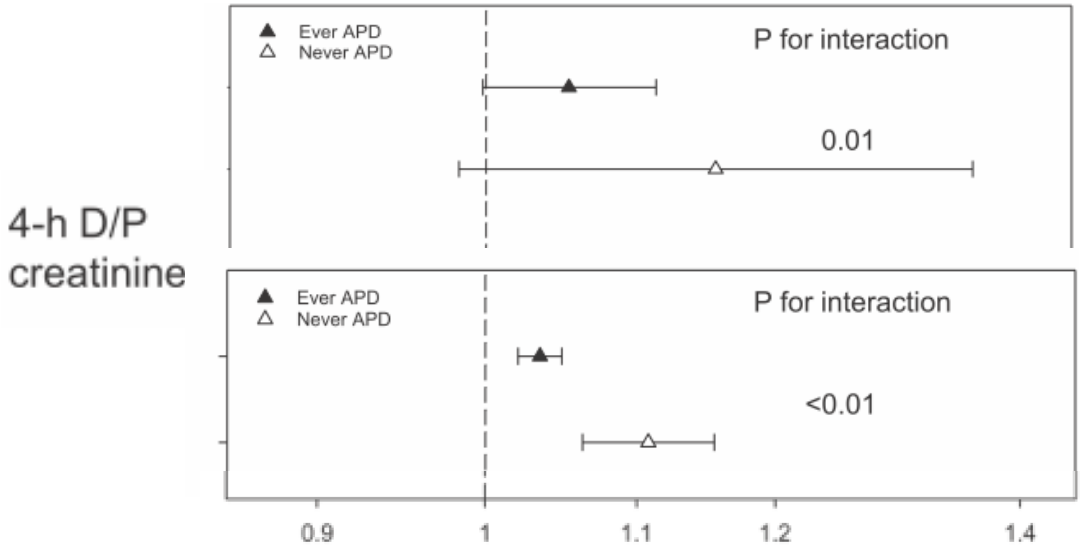
Solute transport characteristics



Mehrotra R et al. CJASN 2015

Solute transport characteristics





Mehrotra R et al. CJASN 2015

Solute transport characteristics

Differences in survival between CAPD and APD-treated high transporters:

Is volume control a predictor of survival?

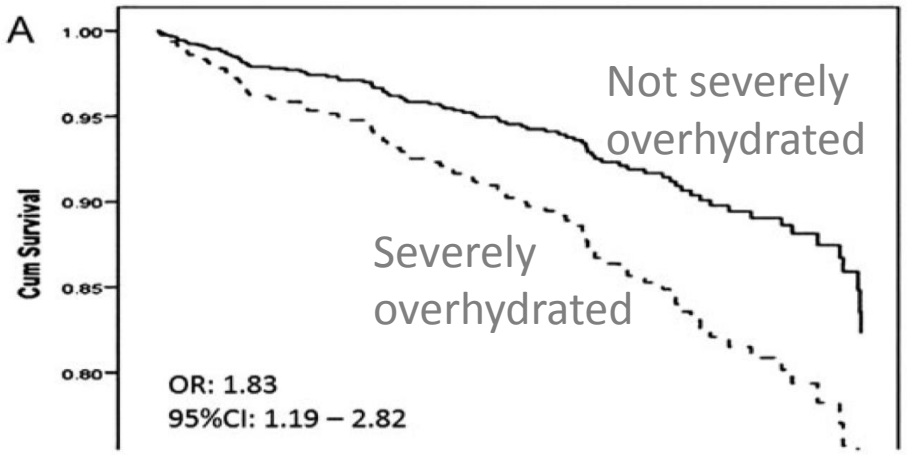
Are PET-UF results a predictor of survival?

Clinical parameters and patient outcomes

Water removal – volume control

Variable	Relative Risk	95% Confidence Limit
Ccrp (5 L/wk per 1.73 m^2 greater)	1.00	0.898–1.105
GFR (5 L/wk per 1.73 m^2 greater)	0.88	0.829–0.943
Urine volume (250 ml daily greater)	0.64	0.508–0.800

Bargman JM et al. JASN 2001



O'Lone EL et al. NDT 2014

Clinical parameters and patient outcomes

Water removal – volume control

TABLE 2
Predictors of Survival in Anuric Patients

EAPOS [Ref. (5)]	NECOSAD [Ref. (6)]	Hong Kong [Ref. (7)]
Age	Age	Age
Comorbidity (DM)	Comorbidity	Comorbidity (CVD)
Malnutrition (SGA C)	?	No
?	Low albumin	No
?	?	Increased CRP
Poor UF /24h	Poor UF/24h	?
No	Duration of dialysis	No
No	Kt/V <1.5/CrCl <40	No

NOT D/Pcreat

Davies SJ et al. PDI 2007

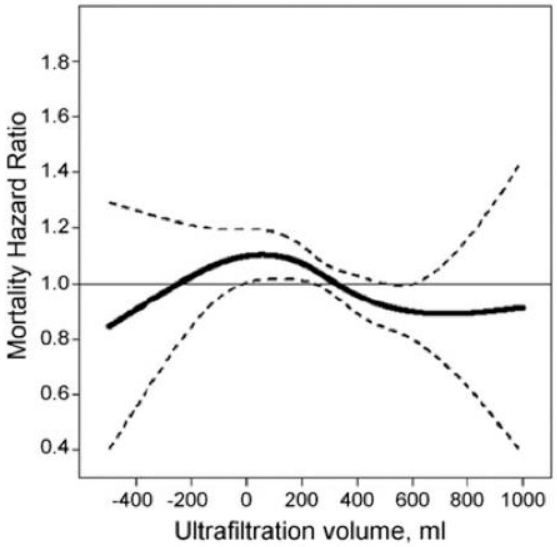
Clinical parameters and patient outcomes

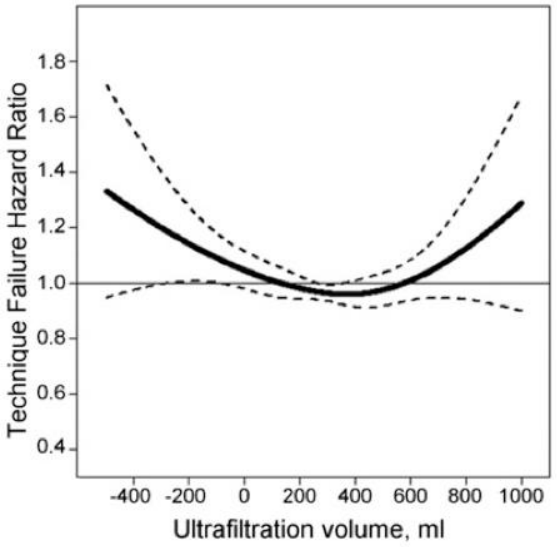
Water removal – volume control

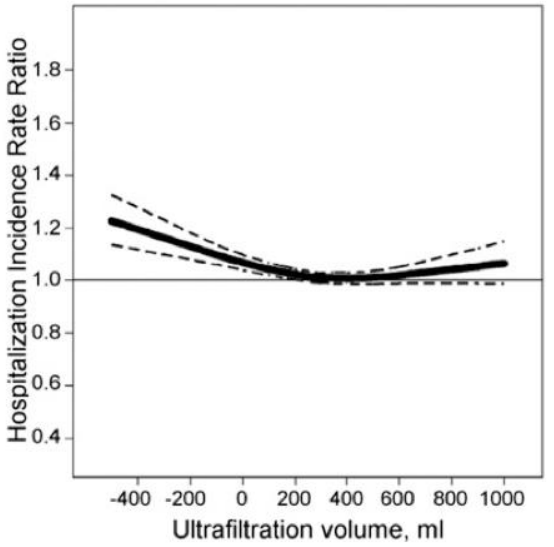
Always assess the cause(s) of overhydration:

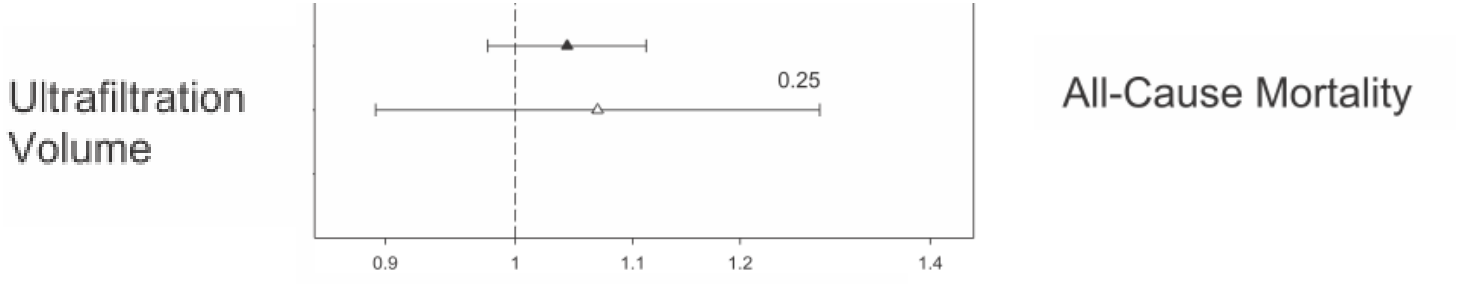
- *Residual kidney function*
- *Salt and fluid intake*
- *Poor UF:*
  - *PD KT function*
  - *Peritoneal ultrafiltration*

Water transport characteristics









Mehrotra R et al. CJASN 2015

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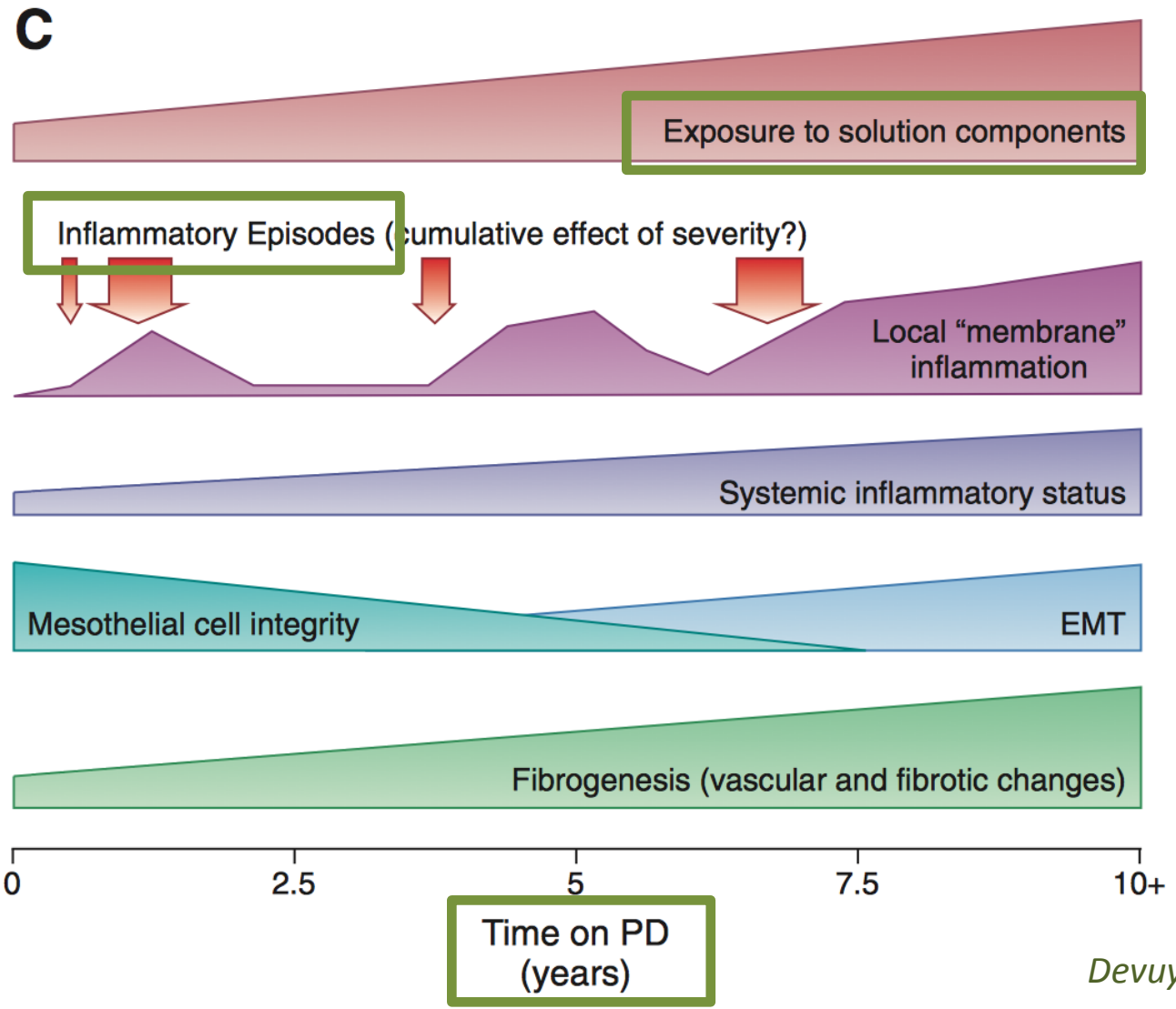
Long term peritoneal membrane changes



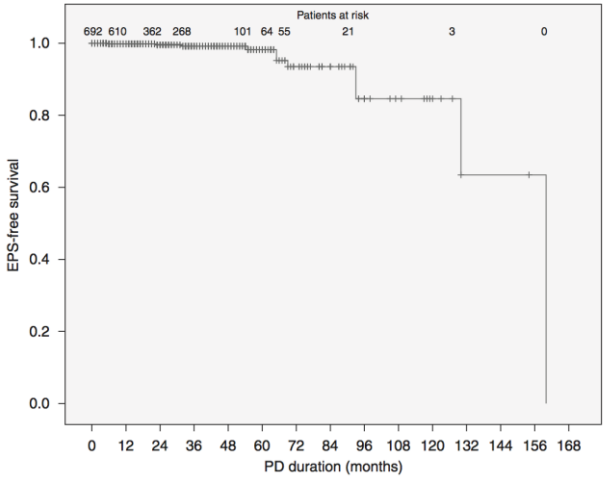
Devuyst O. JASN 2010

Peritoneal membrane fibrosis & EPS

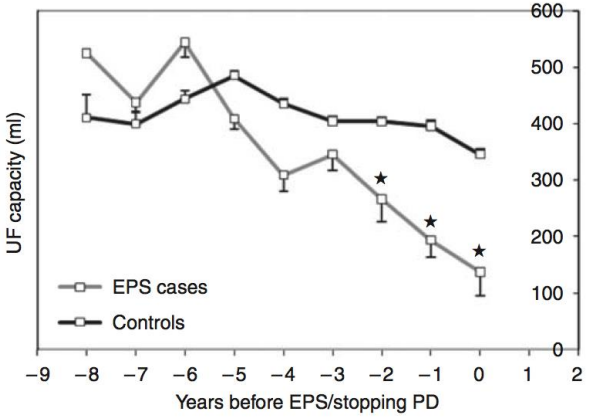
Nested case-control study on the Stoke PD cohort:

9 EPS cases/692 patients (1,3%)

Time on PD



UF



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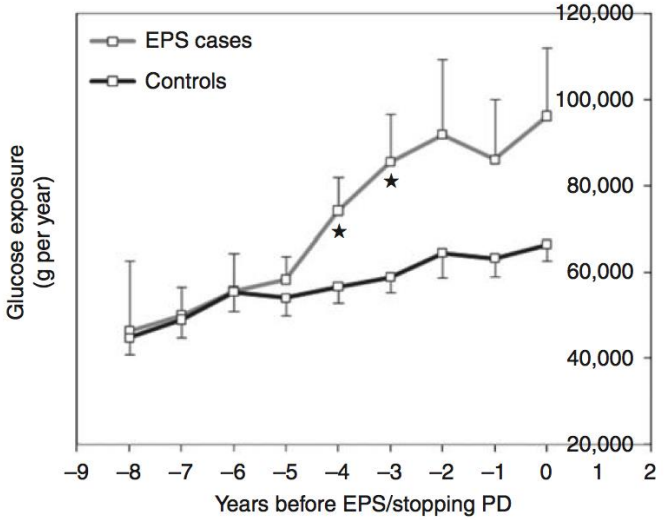
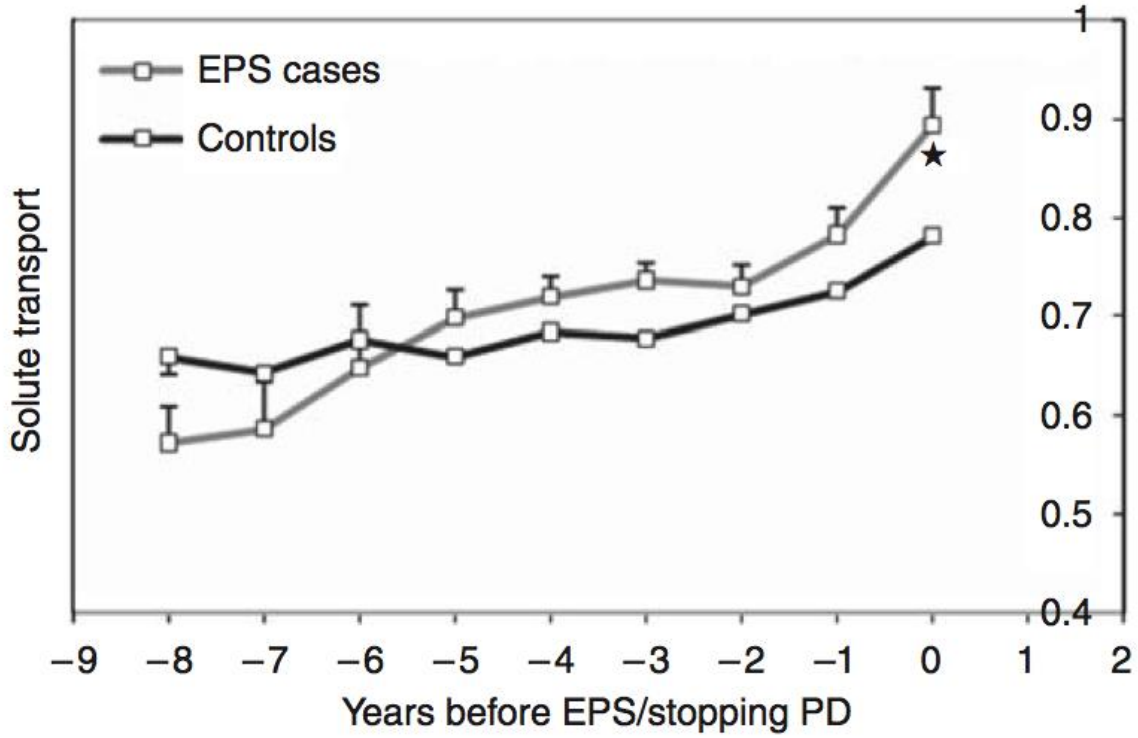
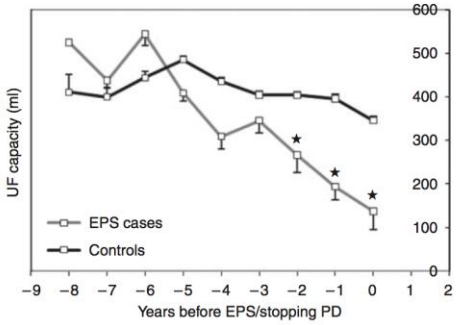
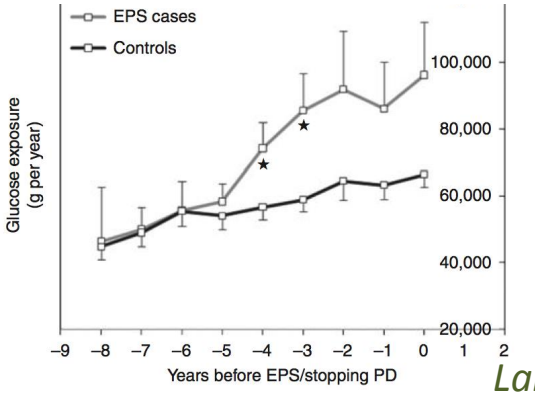


Lambie ML et al. KI 2010

Peritoneal membrane fibrosis & EPS





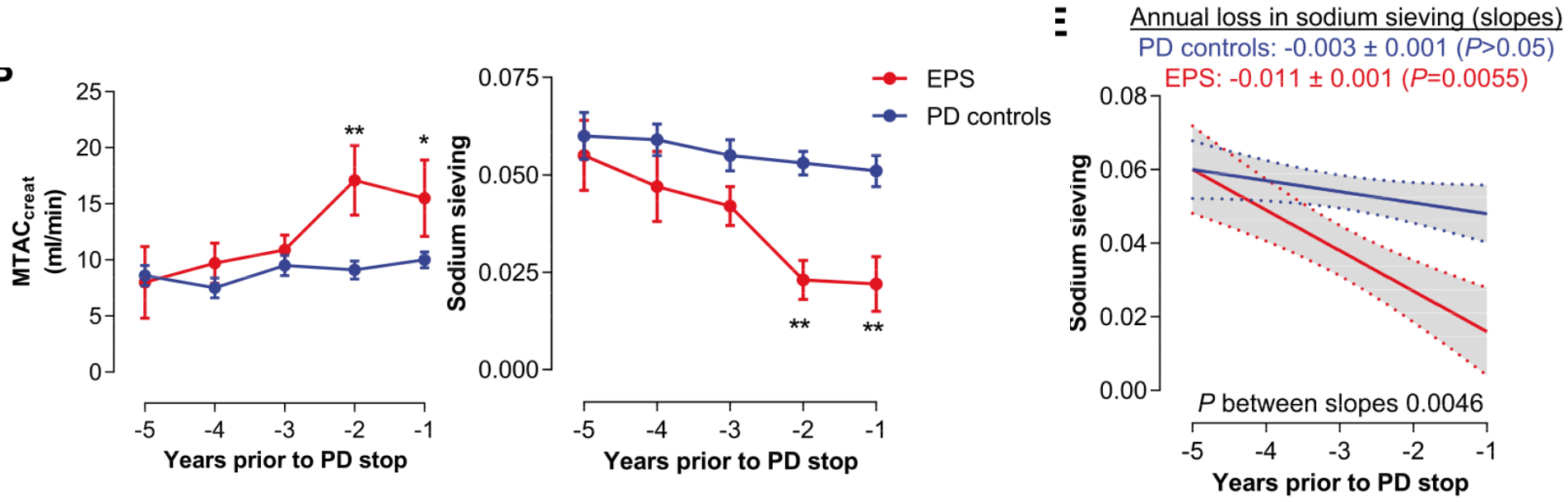


Lambie ML et al. KI 2010

Peritoneal membrane fibrosis & EPS

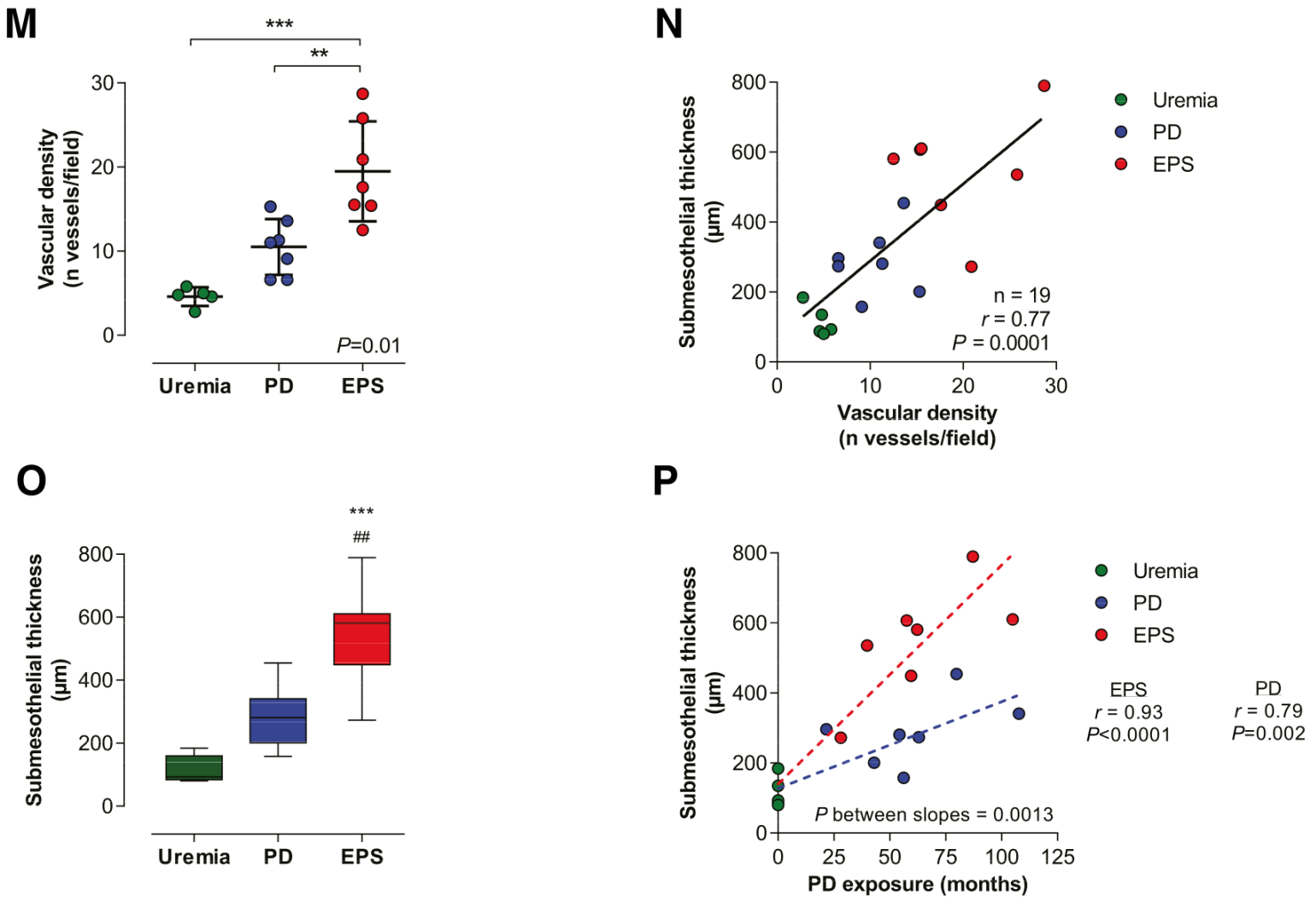
Nested case-control study on the UCL PD cohort:

7 EPS cases/234 patients (3%)



Morelle J et al. JASN 2015

Peritoneal membrane fibrosis & EPS



Morelle J et al. JASN 2015

Peritoneal membrane fibrosis & EPS

- Overall, risk for EPS is low
- Clinical factors help to identify patients at higher risk for EPS
- No interventions known to decrease the risk of EPS when peritoneal membrane tests would be abnormal

Individual physiological membrane testing

is useful in clinical practice if it:

- is simple **YES!** and affordable **RATHER NOT!**
- impacts the treatment strategy **NO!**
- is a stronger predictor of outcomes compared to clinical parameters **NO!**
- prevents long-term complications of PD **NO!**

Conclusions (1)

- Peritoneal membrane testing allows **understanding of the individual physiology of peritoneal membrane transport**.
- **Patient factors** and **clinical parameters** including PD treatment results might suggest transporter's status.
- Choice between CAPD or APD is one of **lifestyle.**

Conclusions (2)

- Peritoneal membrane testing is **time consuming** and rather **expensive**.
- **No added clinical value of routine peritoneal membrane testing in all patients**.
- Peritoneal membrane testing **might be useful in case of proven peritoneal ultrafiltration failure or for research purposes**.