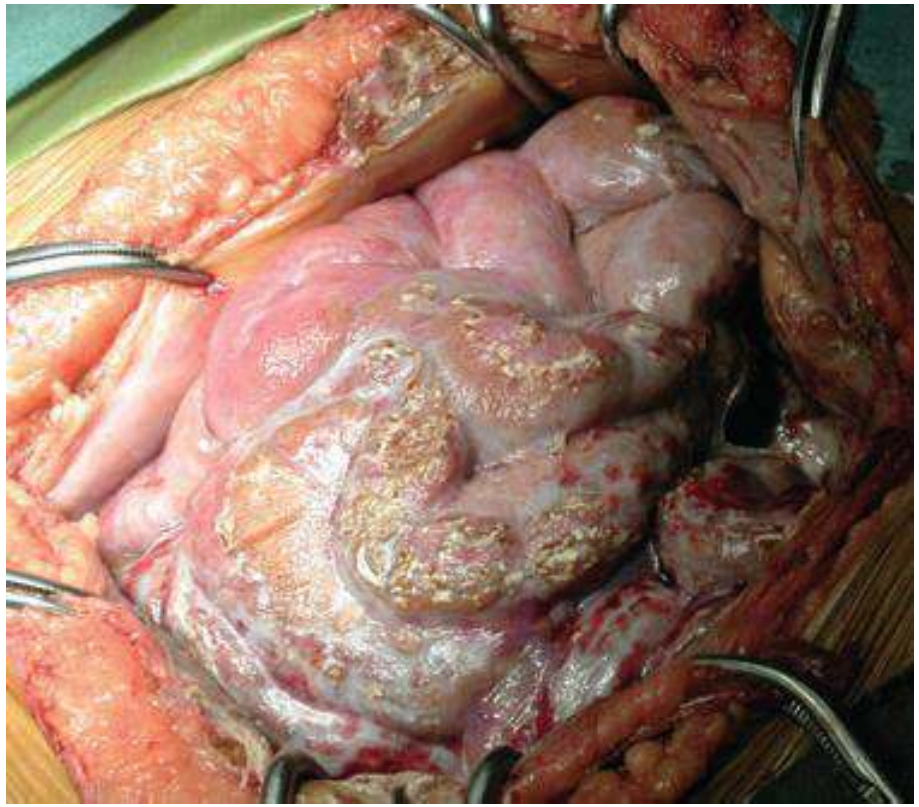
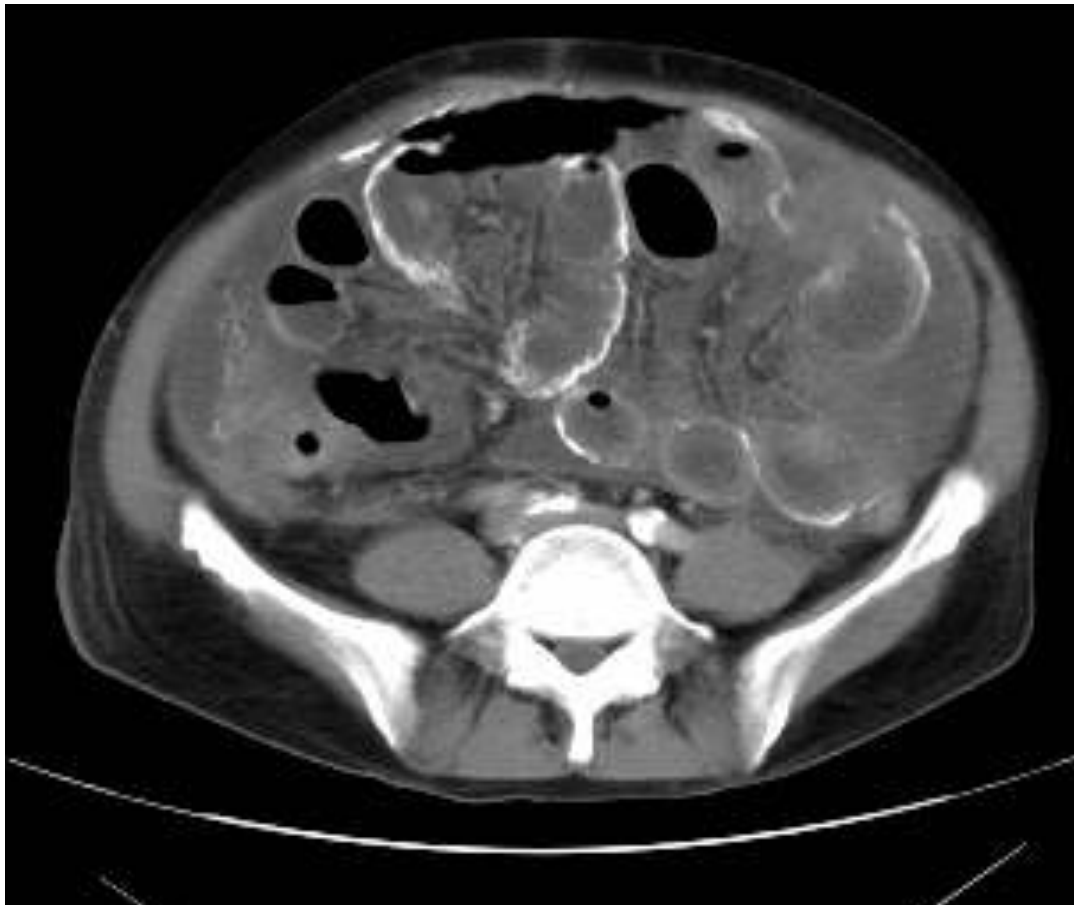
Length of Time on PD: Is There a Limit?

Professor Edwina Brown

Imperial College Renal and Transplant Centre

Hammersmith Hospital, London, UK





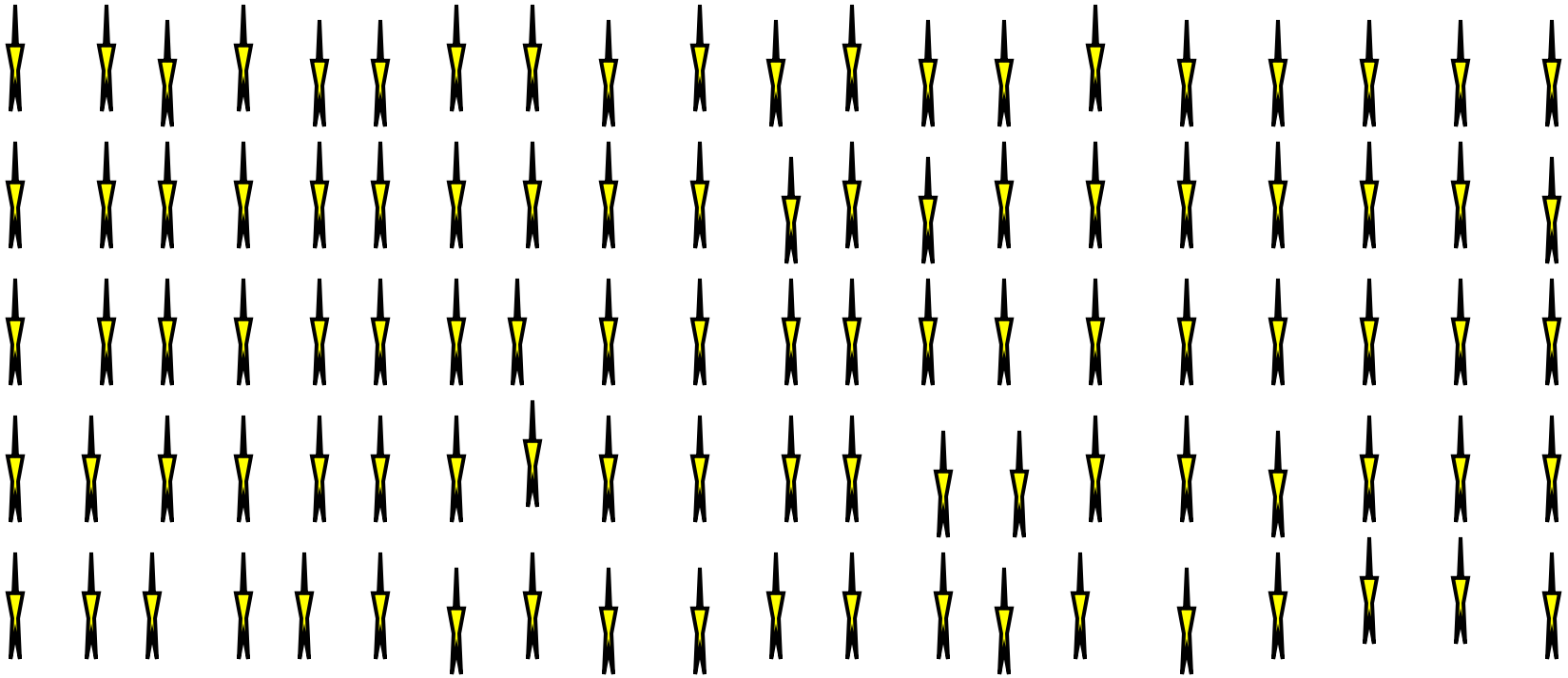
Predicting Individual Risk for Encapsulating Peritoneal Sclerosis - Challenges

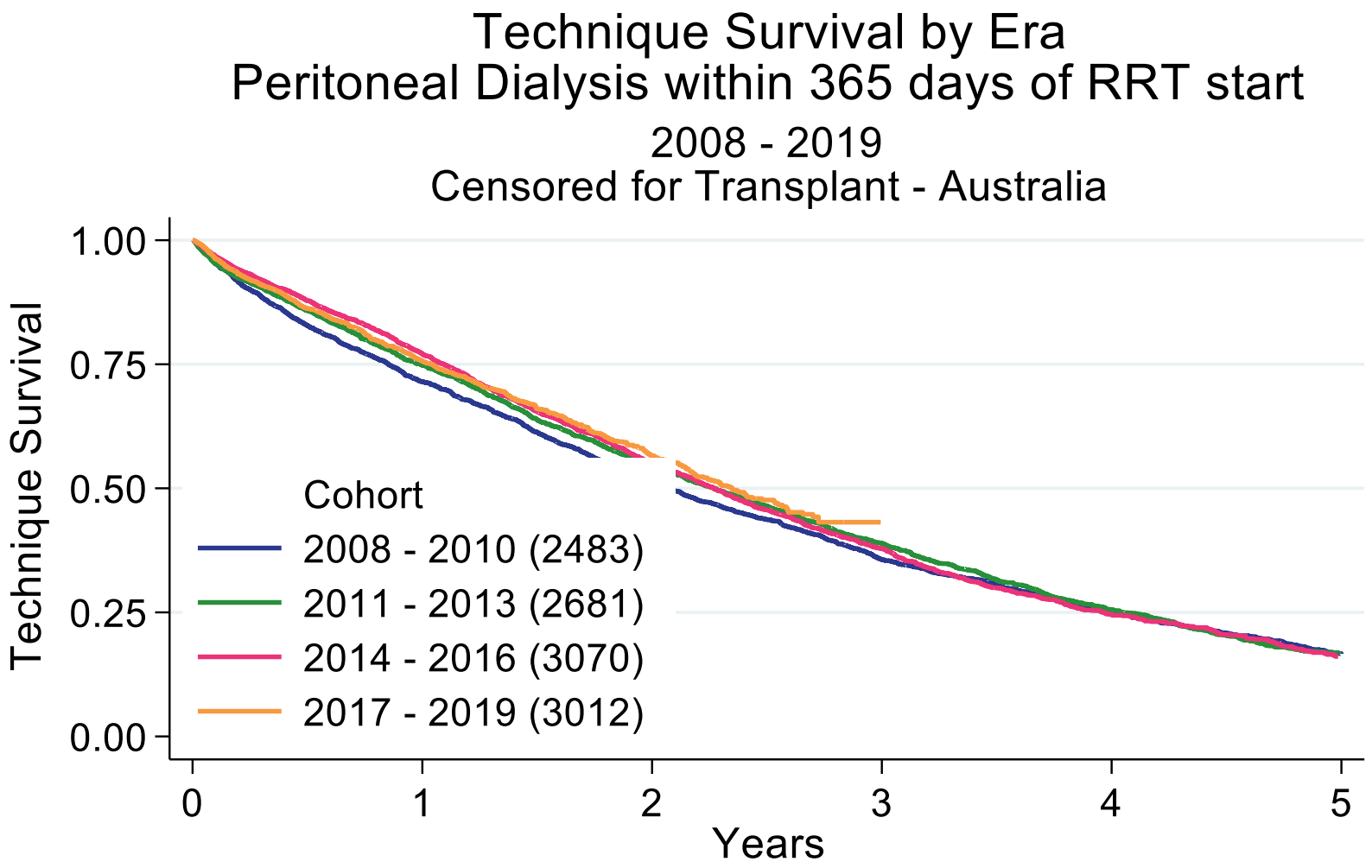
- Comprehension of risk
- What is prevalence of EPS?
- Predictors of EPS
  - Clinical
  - Biomarkers
- Competitive risks
- Predicting individual risk - suggestions

What is risk of EPS?

- What proportion of PD patients remain on PD for >5 years?
- What is risk of developing EPS at 5 years?
- What is risk of developing EPS at 8 years?
- What are risks of transferring to HD?
- What are outcomes of EPS?

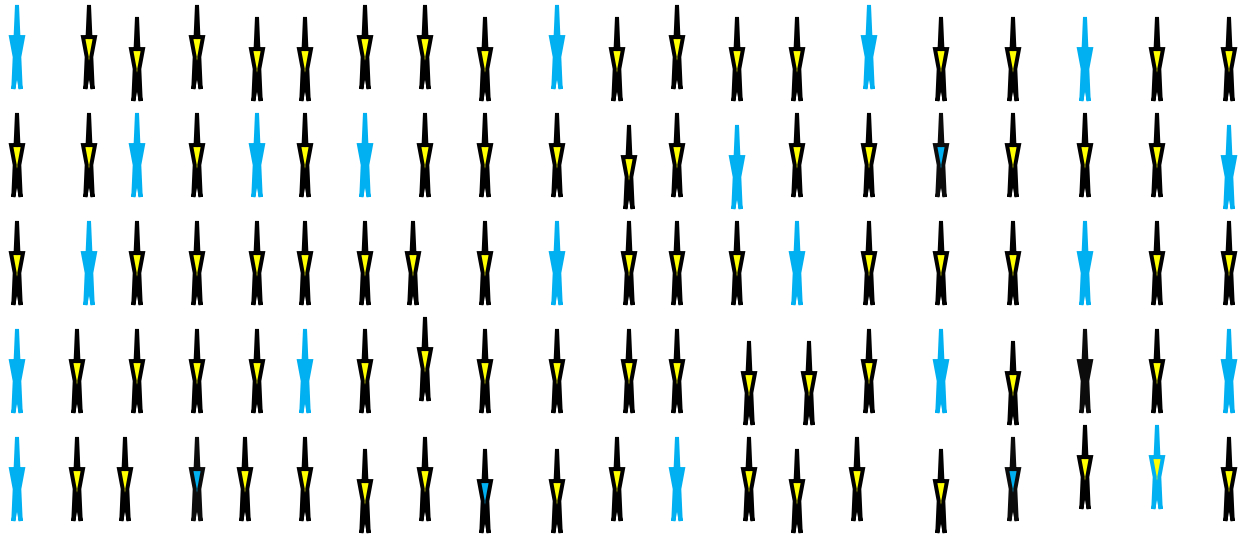
Proportion of incident patients on PD at 5 years



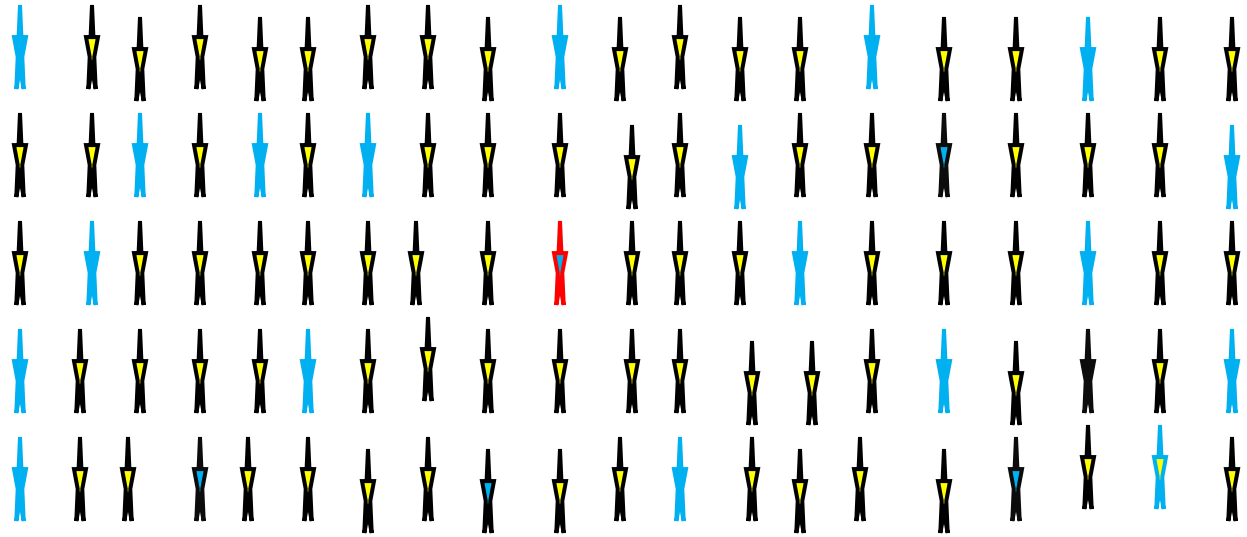


2020 ANZDATA Annual Report, Figure 5.13.1

Proportion of incident patients on PD at 5 years?



Risk model of EPS in patients starting on PD if prevalence is 5% at 5 years



Predicting Individual Risk for Encapsulating Peritoneal Sclerosis - Challenges

- Comprehension of risk
- **What is prevalence of EPS?**
- Predictors of EPS
  - Clinical
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- Predicting individual risk - suggestions

What is prevalence of EPS?

- Not an easy question
  - Varies between countries
  - Varies over years
  - Onset of clinical EPS provoked by stopping PD
  - Related to length of time on PD so prevalence lower in PD populations with shorter duration of PD
    - high transplant rate
    - older patients with poor prognosis

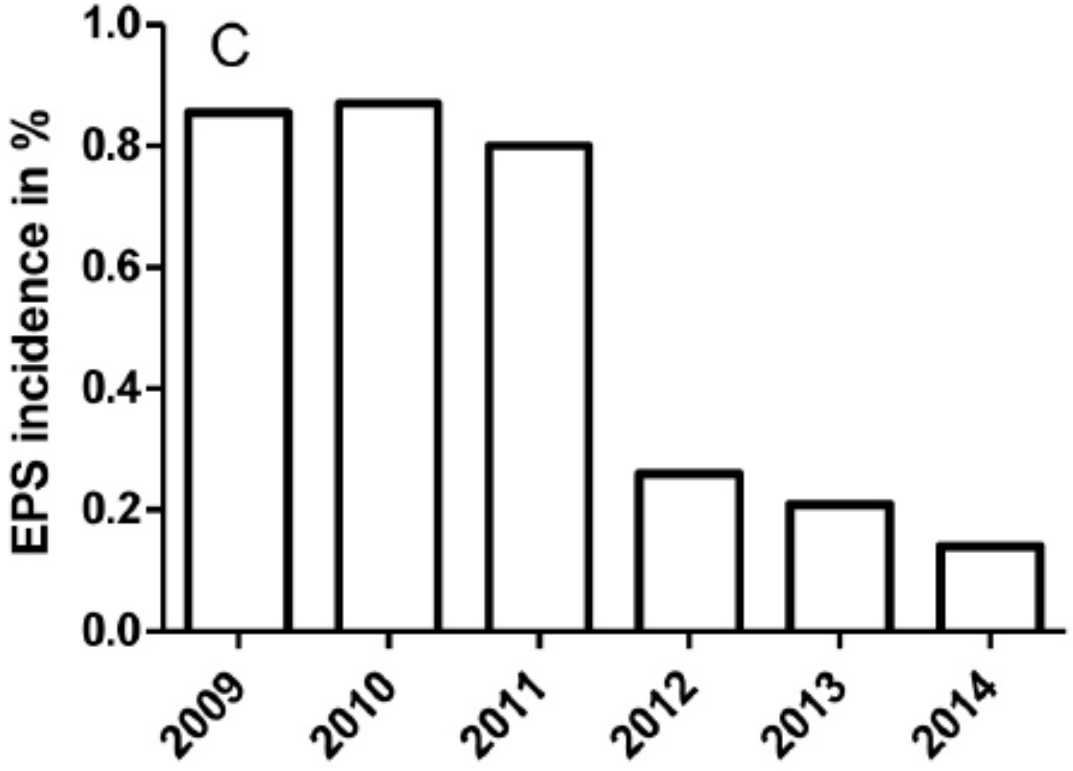
Historic Registry Data

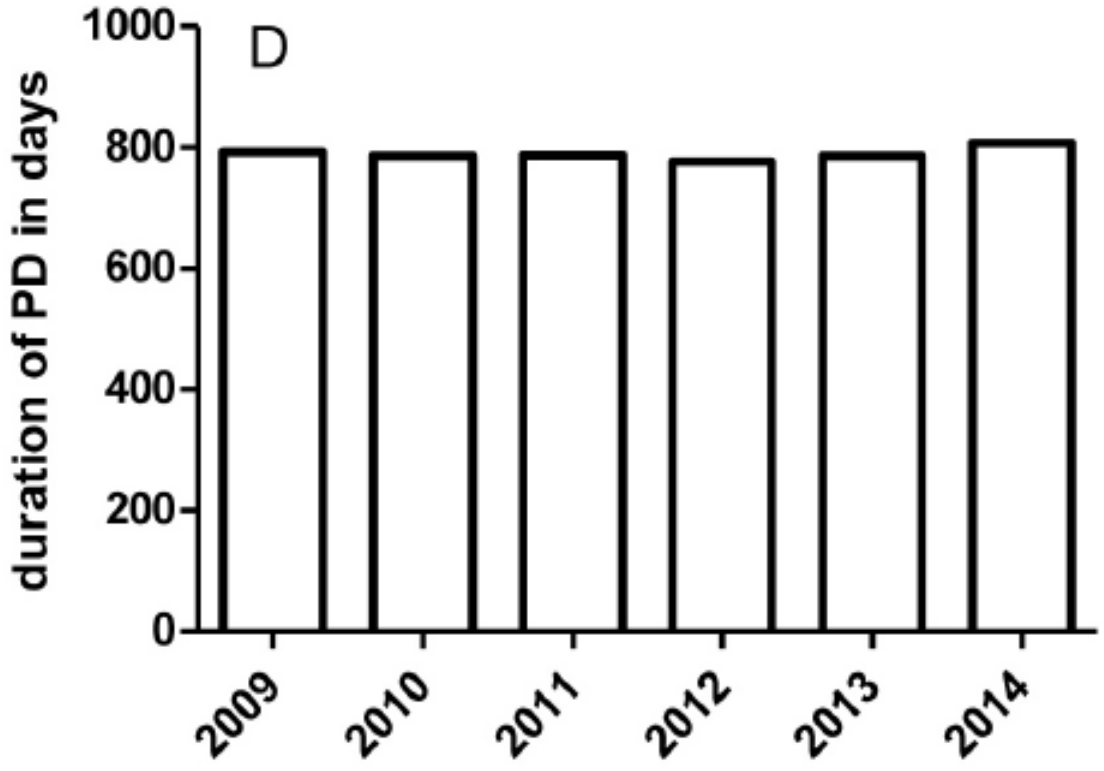
- ANZDATA Johnson et al, Kid Int 2010
  - overall prevalence 1.8%
  - incidence at 3, 5, and 9 years was 0.3%, 0.8% and 3.9%
  - 79% patients on PD at time of diagnosis
- Japan Kawinishi, PDI 2005
  - overall prevalence 2.5%
  - incidence at 3, 5, 8 and 15 years was 0%, 0.7%, 5.9% and 8.6%
- Scotland Brown M, CJASN 2009
  - incidence at 5 years was 8.1%
  - 72% diagnosed after stopping PD

Is incidence of EPS declining?

- Data shown relates to period 2005-2011
  - Greatly increased awareness during this period
  - Flurry of publications
  - Position statement from ISPD 2009
- In recent years
  - Lower use of high concentration dextrose dialysis
  - Higher use of biocompatible dialysate
  - Higher rate of transplantation in many countries
  - (Changes in manufacturing process?)

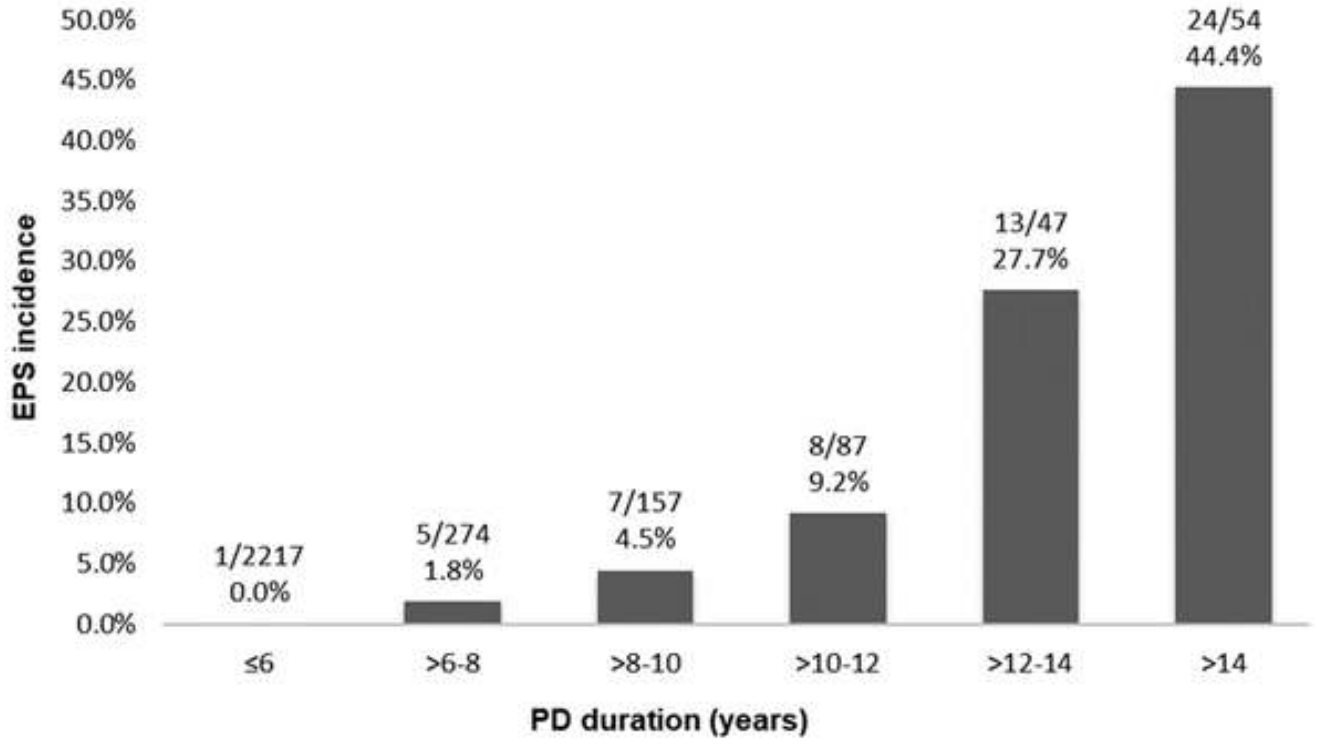
Decline of EPS incidence in Netherlands





Betjes et al, PDI 2017

PD duration and EPS incidence - Taiwan



PD duration	≤6	>6-8	>8-10	>10-12	>12-14	>14
Odds ratio	0.0	1 (Ref)	2.5	5.5	20.6	43.0
P value	0.001		0.1	<0.01	<0.001	<0.001

Tseng CC, Chen JB, Wang IK, Liao SC, Cheng BC, et al. (2018) Incidence and outcomes of encapsulating peritoneal sclerosis (EPS) and factors associated with severe EPS. PLOS ONE 13(1): e0190079. https://doi.org/10.1371/journal.pone.0190079
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0190079

PLOS ONE

Predicting Individual Risk for Encapsulating Peritoneal Sclerosis - Challenges

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- **Predictors of EPS**
  - **Clinical**
  - **Biomarkers**
- Competitive risks
- Predicting individual risk - suggestions

Predictors of EPS

- Clinical
  - Time on PD
  - Membrane transport on PET
  - Use of high strength dextrose
  - Residual renal function
  - Loss of ultrafiltration
- Biomarkers
  - Dialysate cytokines, e.g., IL6, Ca-125, CCL18
  - Genetic markers

Clinical characteristics of EPS patients compared to group matched for duration of PD

	EPS (n=17) (median and IQ range)	Non-EPS (n=34) matched for PD duration (median and IQ range)	P value
Age (years)	53 (49-66)	59 (51-72)	0.21
Total duration PD (months)	76 (46-94)	71 (51-87)	0.18
Glucose exposure (mmol/24h)	**1226 (1052-2076)**	**857 (530-1452)**	**0.0014**
Urine output (ml/24h)	**40 (0-364)**	**602 (179-1277)**	**0.0025**
D/P creatinine	**0.83 (0.74-0.9)**	**0.71 (0.42-0.78)**	**0.0028**
Peritonitis episodes	1 (0.5-1.5)	1 (0.5-1.5)	0.45
Ultrafiltration failure (% and CI)	**47 (23-71)%**	**18 (5-30%)**	**0.02**

Goodlad C et al, PDI 2014

Predicting Individual Risk for Encapsulating Peritoneal Sclerosis - Challenges

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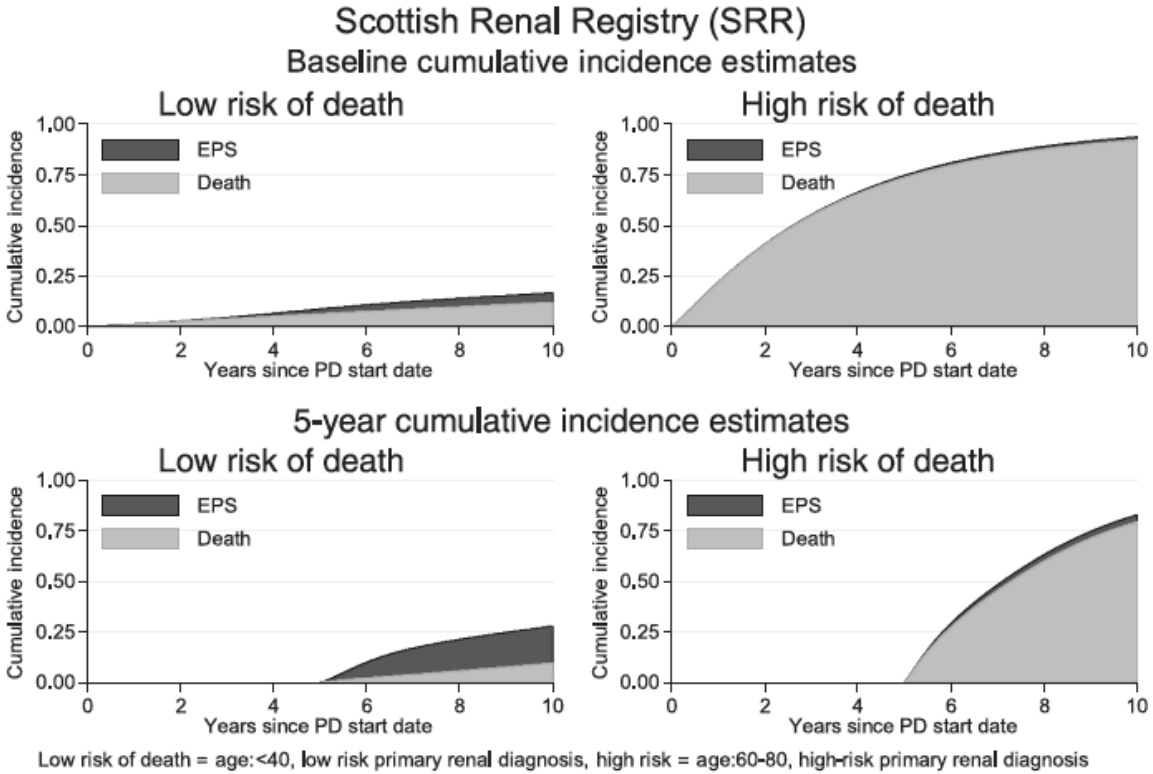
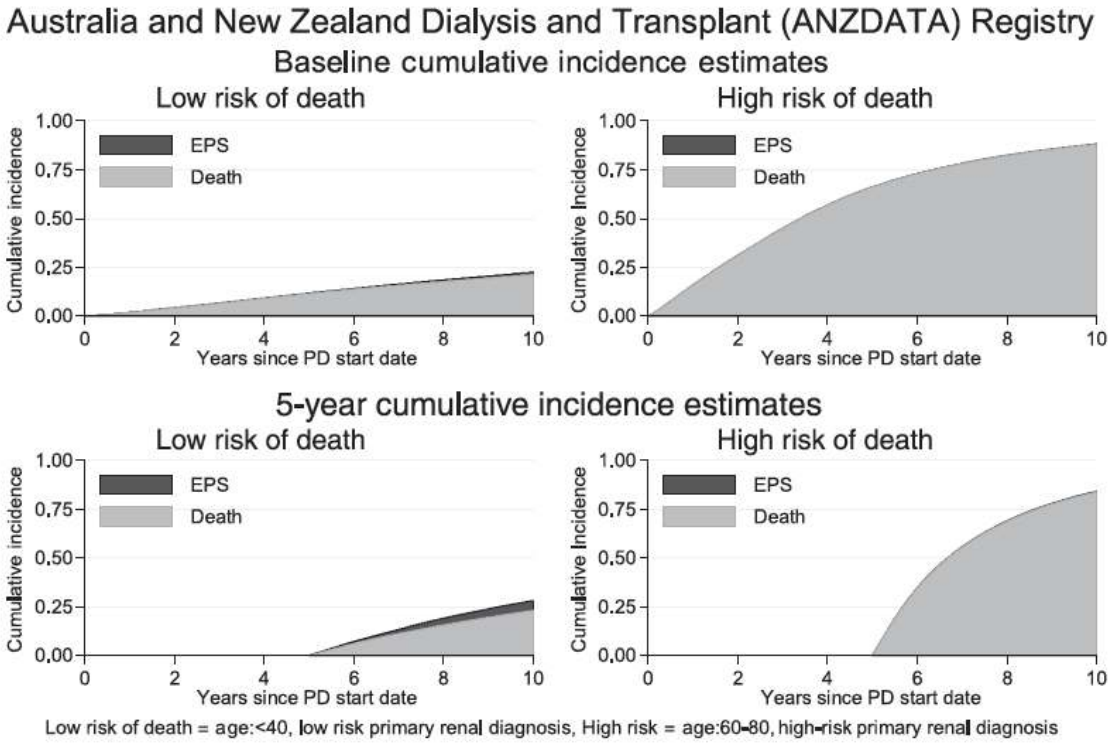
- **Competitive risks**
- Predicting individual risk - suggestions

Competitive risks

- Many older and comorbid patients could be at higher risk of dying than of getting EPS, even if they have factors suggestive of high risk of developing EPS

EPS risk country specific and can be predicted by age, using age, primary renal disease and duration of PD





Lambie M et al, Nephrol Dial Transplant 2019; 34: 1585

Predicting Individual Risk for Encapsulating Peritoneal Sclerosis - Challenges

- Comprehension of risk
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- Competitive risks
- **Predicting individual risk - suggestions**

Predicting individual risk

- Younger age and low comorbidity
- On PD > 5 years
- Loss of residual renal function
- High D/P
- Loss of ultrafiltration
- High glucose exposure

Peritoneal Dialysis International

Peritoneal Dialysis International, Vol. 37, pp. 362–374
www.PDIConnect.com

0896-8608/17 $3.00 + .00

ISPD GUIDELINES/RECOMMENDATIONS

LENGTH OF TIME ON PERITONEAL DIALYSIS AND ENCAPSULATING PERITONEAL SCLEROSIS — POSITION PAPER FOR ISPD: 2017 UPDATE

Edwina A. Brown,[1] Joanne Bargman,[2] Wim van Biesen,[3] Ming-Yang Chang,[4] Frederic O. Finkelstein,[5] Helen Hurst,[6] David W. Johnson,[7] Hideki Kawanishi,[8] Mark Lambie,[9] Thyago Proença de Moraes,[10] Johann Morelle,[11] and Graham Woodrow[12]

https://ispd.org/ispd-guidelines/

ISPD position statement: CONCLUSION

- Encapsulating peritoneal sclerosis is a rare condition. There is no evidence to withhold PD as a treatment option because of fear of development of EPS. There is insufficient evidence to support a single rule about optimal length of time on PD to avoid the risk of EPS

Brown EA et al. Perit Dial Int 2017

ISPD position statement: CONCLUSION

- Each long-term patient needs to be considered individually, taking into account the following factors:
  - Age and prognosis of patient;
  - Length of time on PD;
  - Quality of PD (dialysis adequacy, ultrafiltration, peritonitis frequency);
  - Access to and suitability for transplantation;
  - Potential risk of HD in the particular patient (hemodynamic stability, vascular access); and
  - Quality of life of the patient.

Brown EA et al. Perit Dial Int 2017

Knowledge / Wisdom

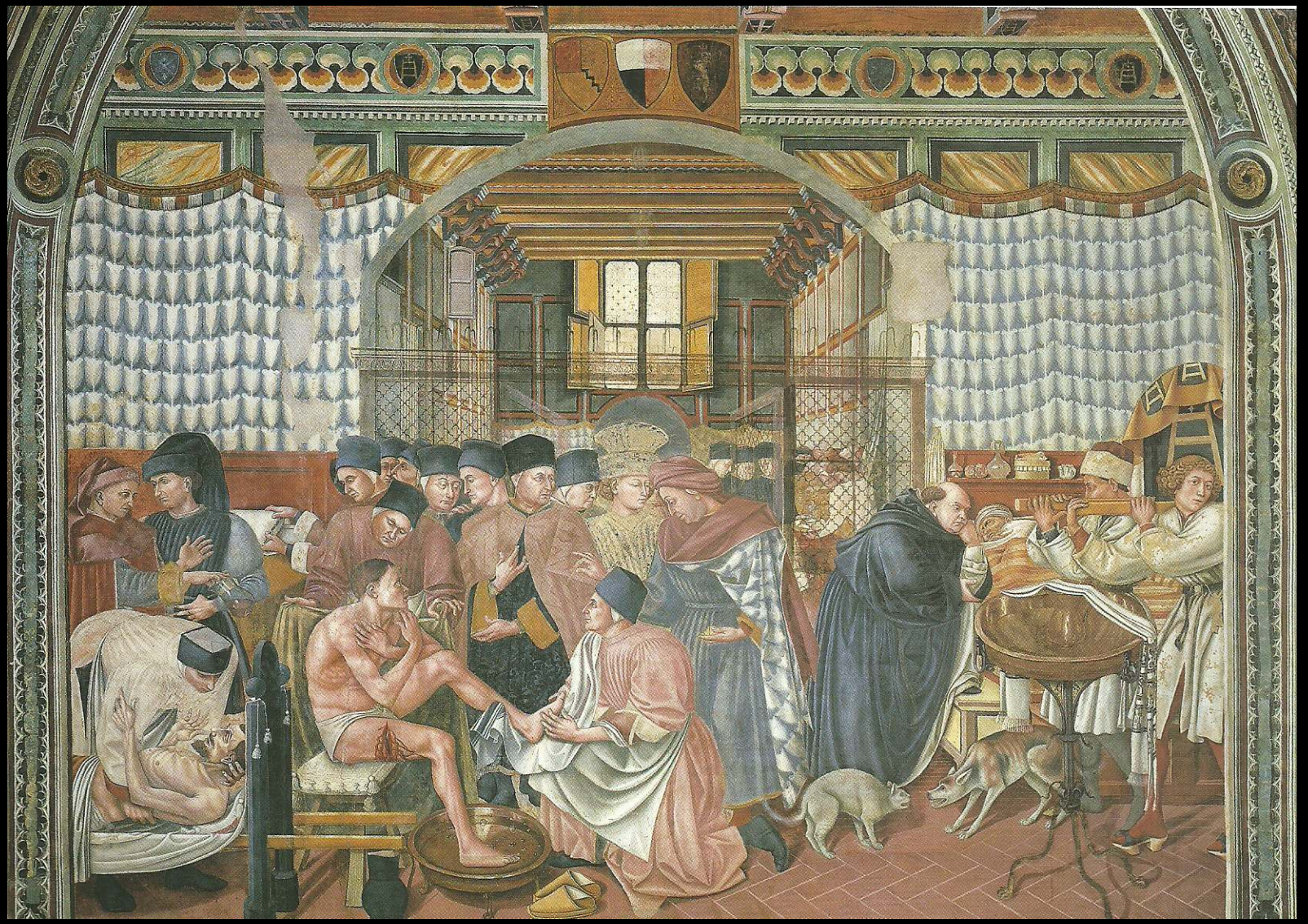
Knowledge is knowing a tomato is a fruit.

Wisdom is not putting it in a fruit salad

Miles Kingston

Patient story

- 72 yr old Afro-Caribbean woman with SLE since 1988 – **now on PD for 13 years**
- **Started PD Dec 2007**; suspended on transplant list since 2011 - TIAs
- Increasing cognitive impairment and occasional falls; on assisted PD since 2011
- 1 exchange 2.27% overnight; icodextrin day time dwell
- PET June 10 0.72; Aug 11 0.68; Oct 13 0.80
- Now anuric; admitted a few times with fluid overload and chest infection – but none for 2 years
- Good UF when adding in 2nd icodextrin manual exchange
- Lives in 3 generation female family – loves talking about her 5 year old granddaughter



Bartolo: Care and government of the sick(1440-1443)
SIENA – Pilgrim's Hall, Ospedale di S Maria della Scala

Creating Long-term PD Success

Anjali Bhatt Saxena, MD FASN

Clinical Associate Professor of Medicine, Stanford University

Director of Peritoneal Dialysis, Santa Clara Valley Medical Center, San Jose, CA

Patient And Technique Survival in Long-term Cohort Studies of PD

Davies et al, KI 54, 2207-2217, 1998; and Han et al, PDI 27, 410-412, 2007 and PDI 29 Sup 3, 2008

	Mean age	% with DM	5-yr patient survival	5-yr technique survival
Maiorca et al, 1991	56.2	20.2%	**50%**	**70%†**
Rotellar et al, 1991	47	18%	**60%**	**64%**
Lupo et al, 1994	58.4	13%	**48%**	**58.5%**
Maiorca et al, 1996	62	13%	**60%†**	**72%**
Kawaguchi et al, 1997	47.6	13.8%	**50%**	**55%**
Fenton et al, 1997	63‡	31.9%	**35%**	**n/a**
Davies et al, 1998	58.8	14.8%	**55%**	**70%**
Han et al, 2007	48.9	27.8%	**69.8%**	**71.9%**

†Data adjusted for risk factors;
‡Estimated from published distribution

10y= 48%

PD technique survival:

Shen JI, Mitani AA, Saxena AB *et al.* PDI 33: 155-166, 2011

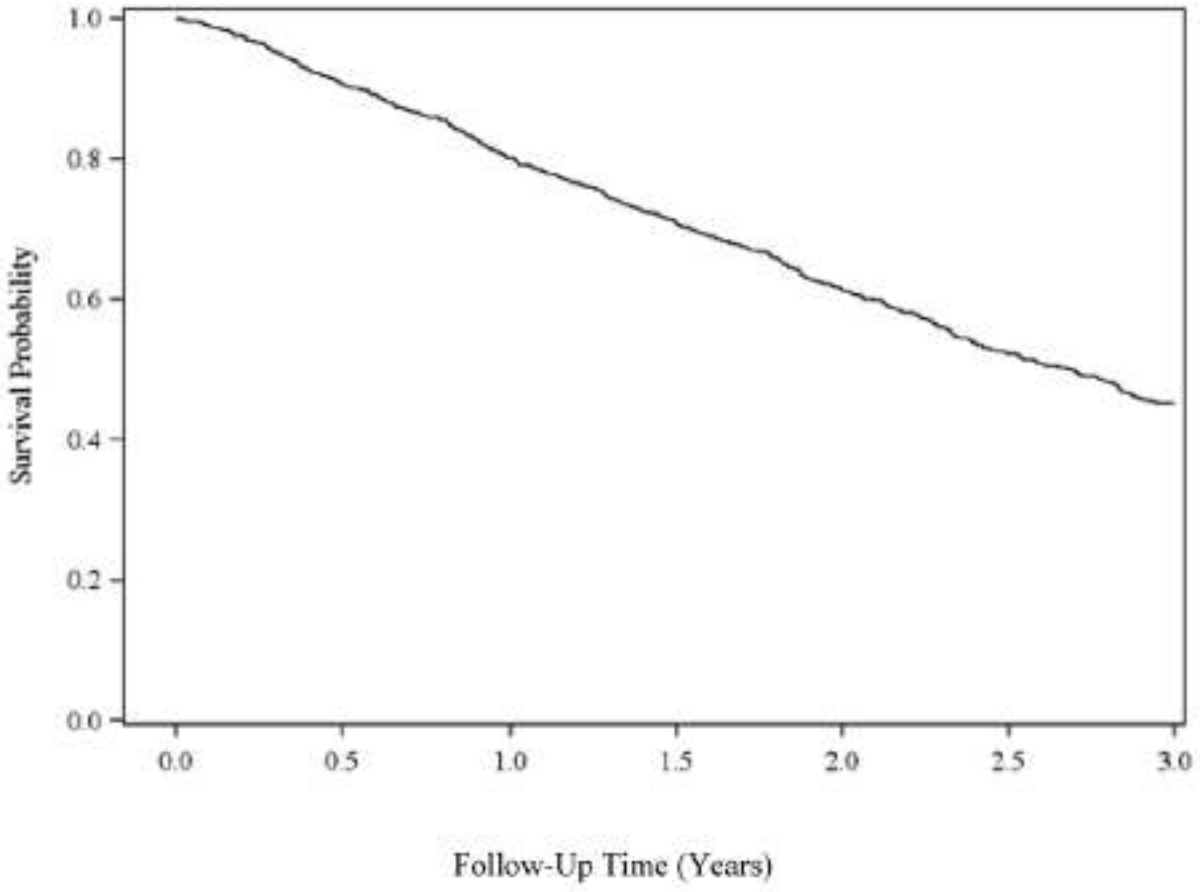


Figure 2 — Technique survival in patients initiating peritoneal dialysis. The Kaplan–Meier actuarial technique survival at 1, 2, and 3 years was 80.2%, 61.2%, and 45.2% respectively. Median survival was 2.7 years. Failure was defined as a switch from peritoneal dialysis to hemodialysis lasting 30 days or more.

PD: What Happens to Prevent Long-term PD Success?

Causes of Techniques Failure in Long-term Cohort Studies of PD

Davies et al, KI (54), 2207-2217, 1998; and
Han et al, PDI(27), 410-412, 2007

	Recurrent peritonitis	UF failure	Solute Removal	Choice/ not coping
Maiorca et al, 1991	48.8%	22.1%		13%
Lupo et al, 1994	29%	16.4%		11%
Maiorca et al, 1996	37%	9%	9%	37%
Kawaguchi et al, 1997	13.6%	23.5%	-	15.2%
Davies et al, 1998	54%	27%	-	17%

Increasing long-term PD Success

-Peritonitis prevention and prompt management

-Reduce catheter malfunction

-Prevent/treat volume overload promptly

-Identify psychosocial risks and barriers to

Peritonitis – Limit The Duration of Inflammation to Protect The Peritoneum

-prompt diagnosis

-prompt treatment

-follow-up surveillance

Peritonitis – Limit The Duration of Inflammation to Protect the Peritoneum

Chow et al. CJASN 1:768, 2006

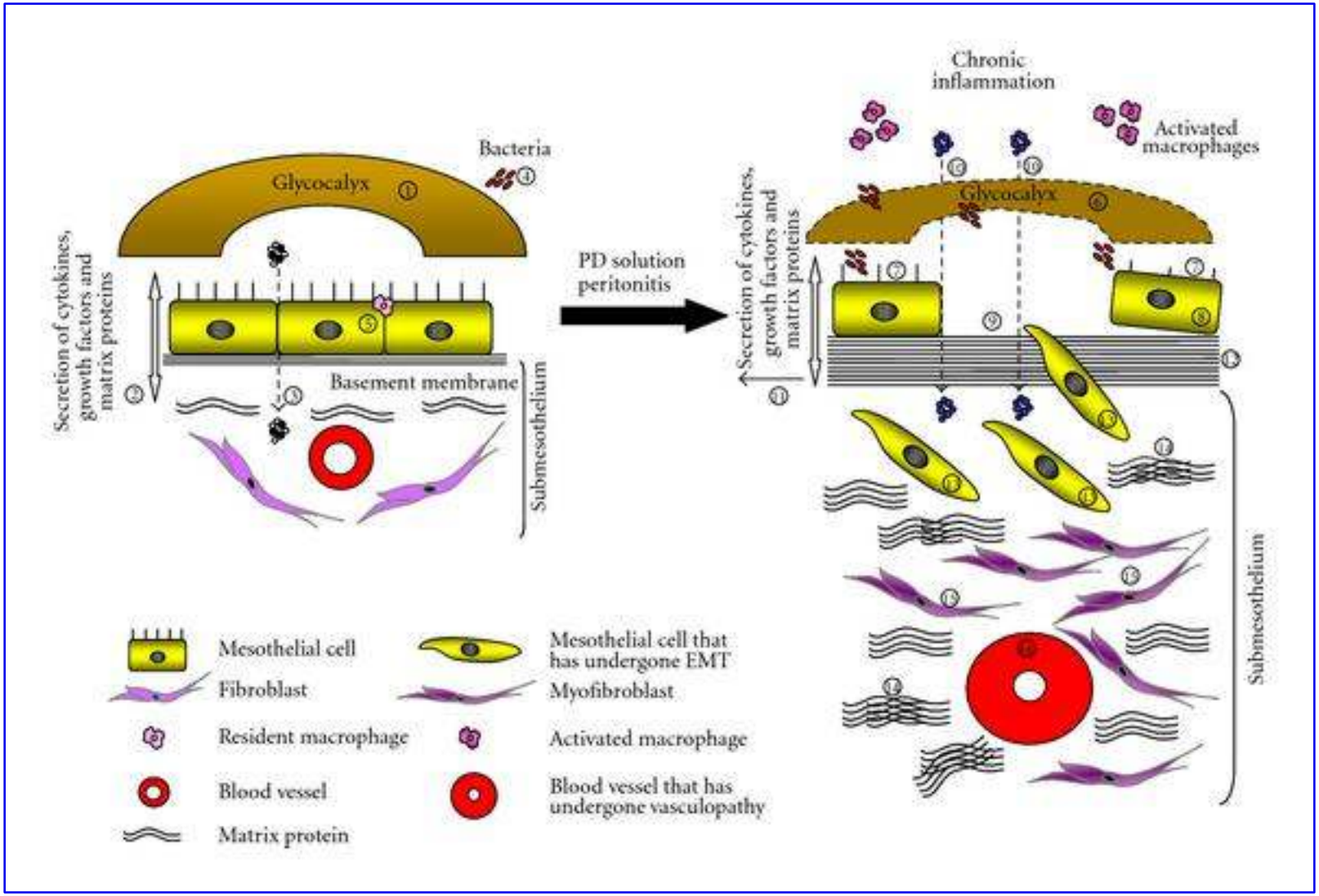
Yang et al. Perit Dial Int 28:361, 2008

A persistently elevated cell count should prompt you to reconsider antibiotic and prepare for possible catheter removal

- → Evaluate follow-up cell counts

Peritonitis Damages The Peritoneum

Yung S and Chan TM. *Mediators of Inflammation* Volume 2012 (2012), Article ID 484167



Prognostic Value of Effluent Cell Counts

Chow *et al* CJASN 1:768, 2006

- 565 consecutive episodes in Hong Kong
- **Day 3 effluent cell count > 1000 indicates a 64% likelihood of treatment failure**
  - Should be a clear sign to tool up/prepare for catheter removal in the next few days
- Other predictors of treatment failure:
  - Infection with gram negatives only, mycobacterium, pseudomonads, fungi, longer duration on PD, diabetes

Prognostic Value of Effluent Cell Counts in Peritonitis

Yang *et al.* Perit Dial Int 28:361, 2008

- 579 episodes in Taiwan
  - Catheter removal group –
    - Average # days with PDE cell count > 100/μL = 8.6
  - Catheter preserved group
    - Average # days with PDE cell count > 100/μL = 4.8
    - P<0.001

**Initial cell count not different b/w groups*

Prognostic Value of Effluent Cell Counts in Peritonitis

Krishnan *et al.* PDI 2002; 22:573–581

- 399 episodes of peritonitis in 191 patients on PD in Toronto
  - Number of days the PD effluent cell count remained > 100/μL independently predicted the outcome of an episode of peritonitis.

Prognostic Value of Effluent Cell Counts

Chow *et al.* CJASN 1:768, 2006

Yang *et al*. Perit Dial Int 28:361, 2008

- Persistently elevated cell count should prompt you to prepare for possible catheter removal
- Evaluate follow-up cell counts
- Other predictors of possible treatment failure:
  - Infection with gram negatives only, mycobacterium, pseudomonas, fungi, longer duration on PD, diabetes, concomitant exit site or tunnel infection

Determinants of Catheter Loss in 401 Single-Organism Peritonitis Episodes

TABLE 5
Determinants of Peritoneal Dialysis (PD) Catheter Loss by Multivariate Logistic Regression Analysis Among Single-Organism Peritonitis ($n = 401$)

Parameter	Odds ratio	95% CI	*p* Value
Duration on PD	1.01	1.00–1.024	0.031
Serum albumin level	0.43	0.20–0.92	0.029
Duration of effluent leukocyte count remaining above 100/μl	1.14	1.08–1.21	<0.001
Etiology			
Concomitant exit-site infection	5.44	1.25–23.61	0.024
Concomitant tunnel infection	11.09	2.71–45.41	0.001
Abdominal catastrophe	5.98	0.98–36.35	0.052
Causative organism			
Pseudomonas sp	3.08	0.82–11.52	0.095
Anaerobes	27.17	1.77–418.35	0.018
Fungi	28.76	9.06–91.24	<0.001

Prevention of Peritonitis

- Patient Training and Technique
- Connectology
- Certain catheter care
  - Prophylactic antibiotics at time of catheter insertion
  - Down-going exit site
- Prophylactic antibiotics at time of certain procedures

Antibiotic Prophylaxis

- **Dental Procedures**

OXFORD
UNIVERSITY PRESS

From: ***Intravenous amoxicillin/clavulanate for the prevention of bacteraemia following dental procedures: a randomized clinical trial***

J Antimicrob Chemother. 2016;71(7):2022-2030. doi:10.1093/jac/dkw081

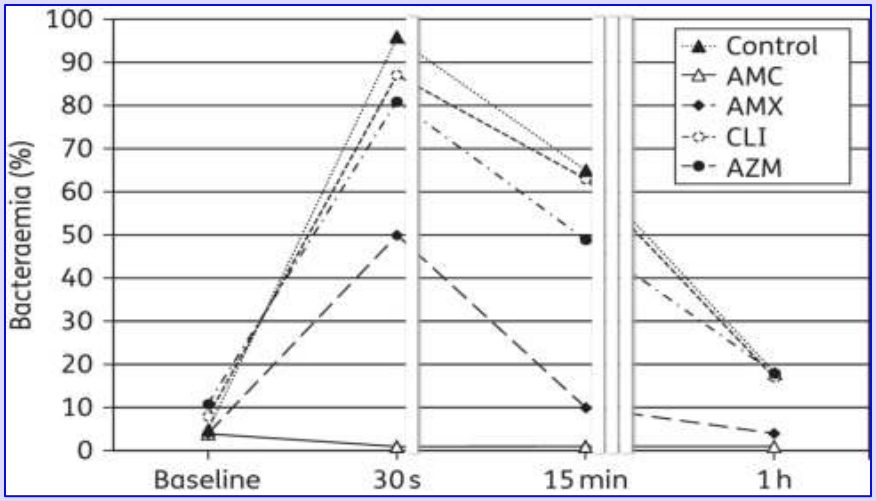


Figure Legend:

Incidence of bacteraemia (%) in the five study groups at baseline and at three timepoints following dental extractions. Control, control group; AMC, amoxicillin/clavulanate group; AMX, amoxicillin group; CLI, clindamycin group; AZM, azithromycin group; Baseline, blood sample drawn under basal conditions; 30 s, blood sample drawn 30 s after completing the dental extractions; 15 min, blood sample drawn 15 min after completing the dental extractions; 1 h, blood sample drawn 1 h after completing the dental extractions.

Antibiotic Prophylaxis

- **Colonoscopy or GYN procedures**:
  - Ampicillin + cipro (or gent) + flagyl
  - Aminoglycoside overnight + Oral Metronidazole +/- ampicillin 1 gram PO
  - Fluconazole added in GYN procedures???

- **Perform procedure with dry abdomen, try to be dry for 12-24h afterwards**

Risk of Peritonitis after Colonoscopy

Yip T *et al.* PDI 27(5), 2007

- 77 CAPD patients underwent 97 colonoscopies in Hong Kong between 1994–2006
  - 18 cases given antibiotics → no peritonitis
  - 79 cases without antibiotics →
    - 4 early peritonitis (within 24h)
    - 1 after 5 days
    - Having bx or polypectomy not assoc with greater risk
- 6.3% risk of peritonitis after colonoscopy if not given prophylactic antibiotic

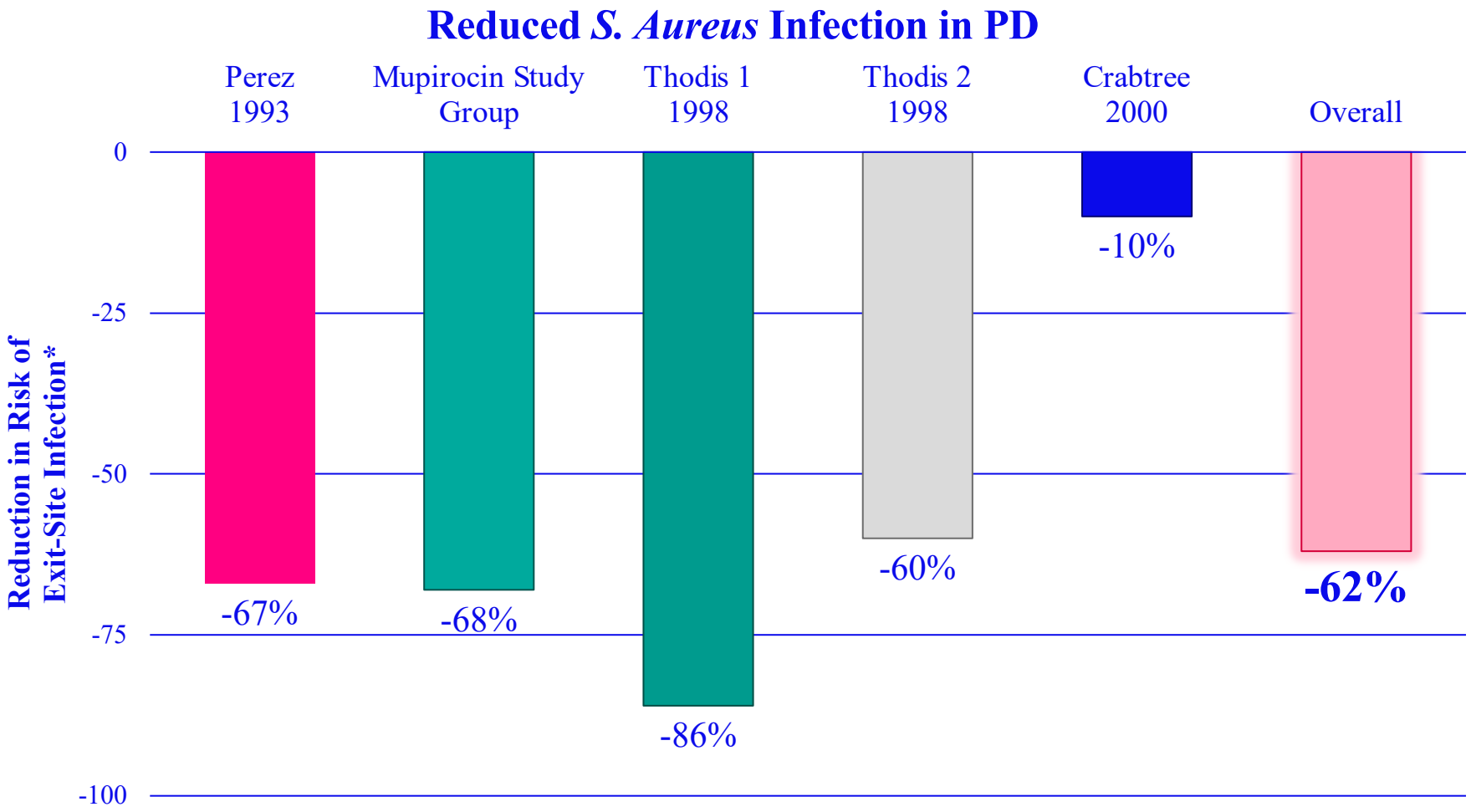
Upper GI Procedures

- Upper endoscopy
  - 4 cases in literature
  - gram positive AND gram neg
  - Cirrhotic patients with ascites are often prophylactic antibx peri-EGD to prevent SBP and bacteremia
  - Higher infection risk with ERCP, variceal treatment.

Prevention of Peritonitis

- Patient Training and Technique
- Connectology
- Certain catheter care
  - Prophylactic antibiotics at time of catheter insertion
  - Down-going exit site
- Prophylactic antibiotics at time of certain procedures
- Avoidance of constipation
- Exit-site care

Approaches to Reduce Exit-Site Infections
Mupirocin Prophylaxis
Tacconelli E et al. Clin Infect Dis. 2003;37:1629-1638.

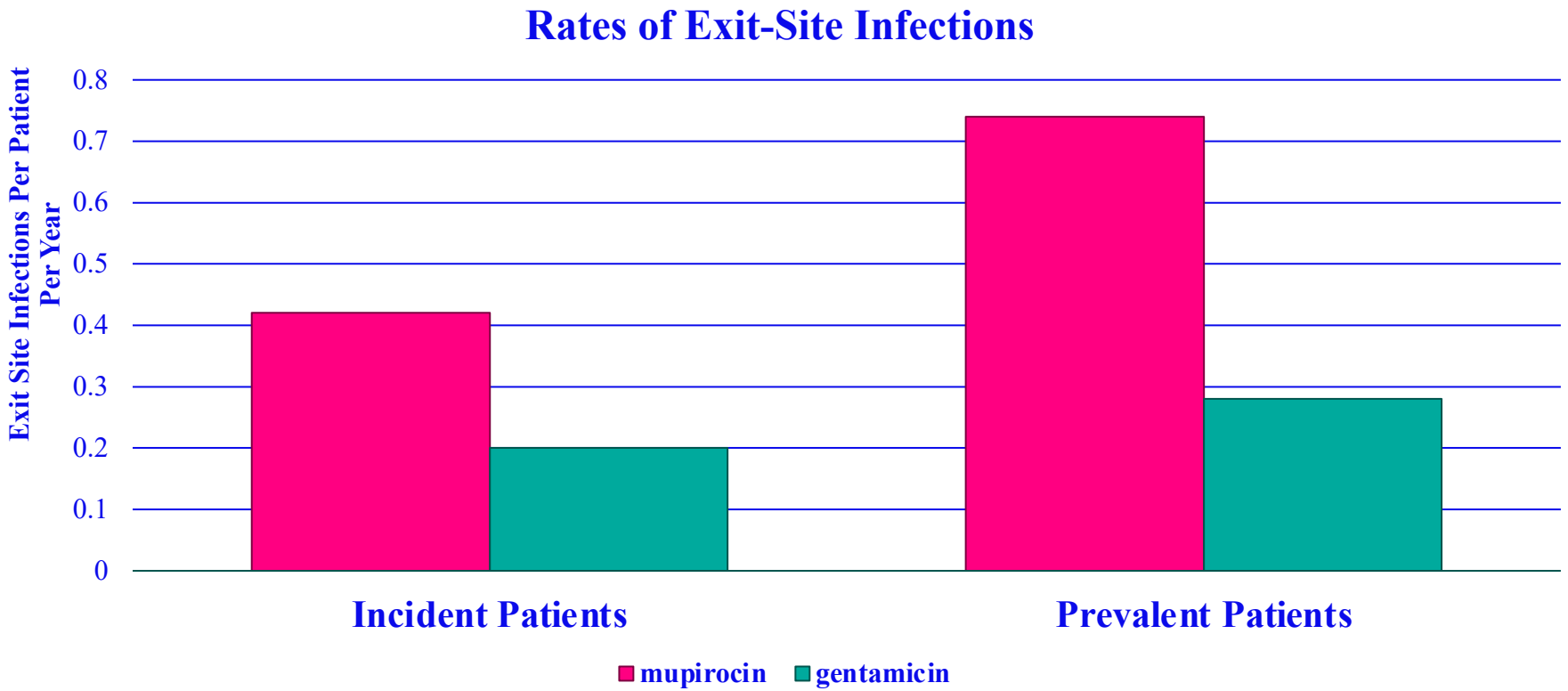


*Risk of exit-site infection, mupirocin : without mupirocin.

†P<0.001 vs placebo or no treatment.

Approaches to Reduce Exit-Site Infections
Gentamicin Prophylaxis
Bernardini J et al. J Am Soc Nephrol. 2005;16:539-545.

Fewer gram-negative exit site infections in PD



**P < 0.01 vs mupirocin*

Preventing peritonitis - other

- Observational data: regular lactulose reduces peritonitis rate
  - Asfar B *et al.* PDI 30: 243-6, 2010

- Treat hypokalemia: hypokalemia associated with increased risk for peritonitis
  - Chuan YW *et al.* NDT 24:1603-8, 2009
  - Shu KH *et al.* NDT 24: 1289-92, 2009

Increasing long-term PD Success

-Peritonitis prevention and prompt management

-Reduce catheter malfunction

-Prevent/treat volume overload promptly

-Identify psychosocial risks and barriers to long-term PD

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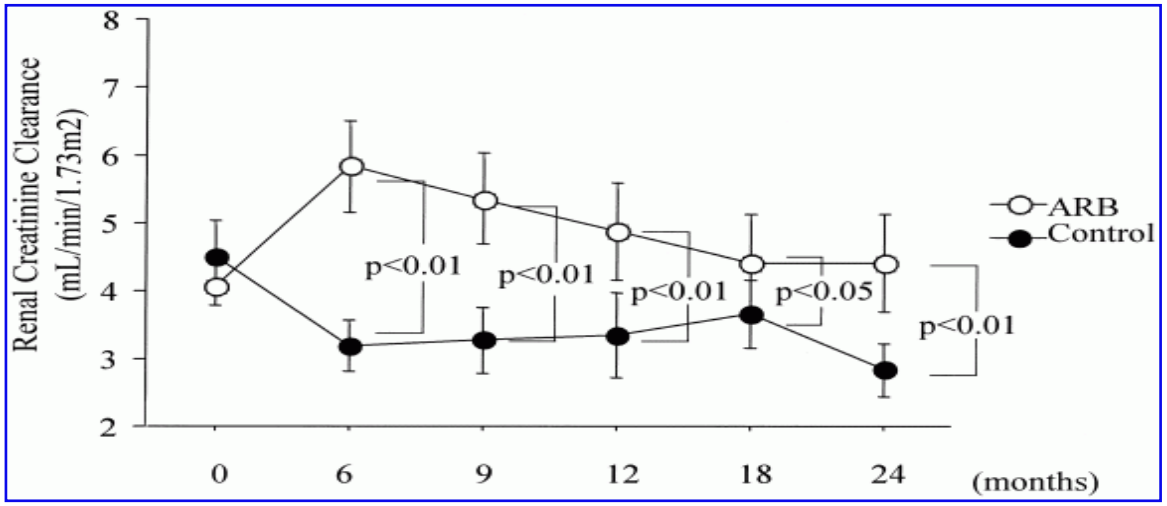
Maintain Residual Kidney Function (RKF) Benefits RKF

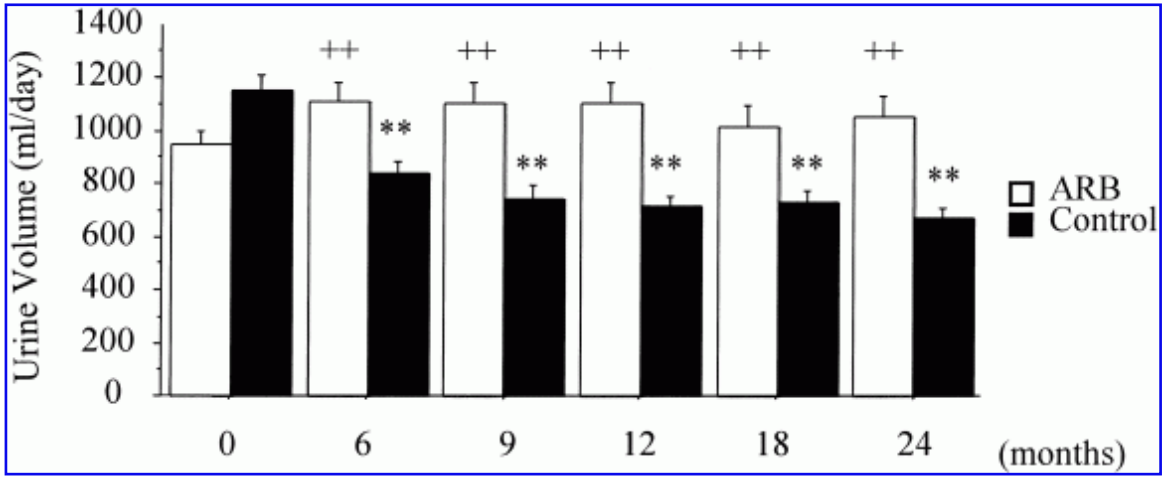
- Improved sodium removal
- Better fluid management
  - You can avoid hypertonic dialysate
- Improved MMW solute clearance
  - Including phosphorus

How to Preserve Residual Renal Function

- Avoid hypertonic dialysate
- Reduce systemic inflammation
- ACE inhibitors and angiotensin receptor blockers (ARB's) can slow down deterioration of renal function

Preservation of Residual Kidney Function with Angiotensin Receptor Blockers
Suzuki et al, Am J Kidney Dis 2004



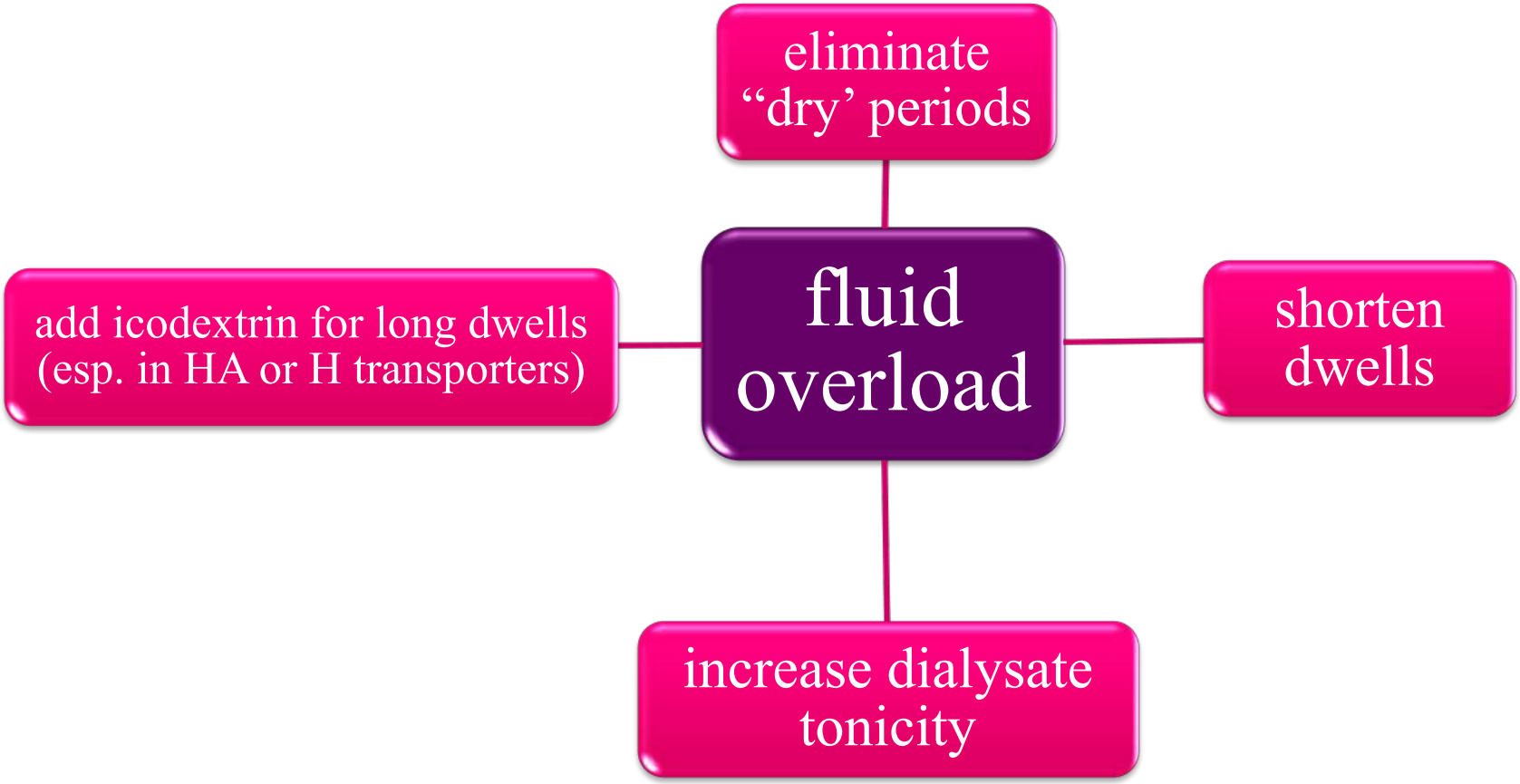


Diuretic use

Using the PET as a *guideline* for PD Rx management

transport type	small solute clearance	maximizing small solute clearance	ultrafiltration
Low (slow)	Slow	Longer dwells	Excellent
Low Average	Average	Standard PD	Average
High Average	Average	Standard PD	Average
High (rapid)	Rapid	Shorter dwells	Requires shorter dwells

PD Prescription: adjusting the Rx



Increasing long-term PD Success

-Peritonitis prevention and prompt management

-Reduce catheter malfunction

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General factors associated with home dialysis success

- Psychosocial reasons
  - loss of home
  - loss of caregiver
  - need for long-term care (SNF)
  - depression
  - major life stressors
    - Financial, death in family/friends
  - patient or care-giver “burn-out”

Strategies to Mitigate New Or Ongoing Psychosocial Concerns in home dialysis

Factors

- Depression
- Major life stressors
  - Financial, death in family/friends

Interventions

- Depression screening
- Home visits
- Patient support groups (e.g. BAAKP)
- NKF Peer-program
- Assisted dialysis

Home dialysis burnout

- definition:

mental, emotional, or physical exhaustion that leads to negative attitudes towards home dialysis, cessation of desire to continue (or assist with) home dialysis, or inability to perform it safely

PD burnout

Oveyassi JO,…Saxena AB, Tong A, Shen JI: ASN PDI 2020

- 81 patients and 45 caregivers from 9 dialysis units in Australia, Hong Kong and the US
- 14 focus groups
- transcripts analyzed thematically

PD burnout

Oveyassi JO,…Saxena AB, Tong A, Shen JI: PDI 2020

Overwhelmed by the daily grueling regimen

- "You've just had enough. It's just, you just don't want it anymore, you know. It's just like, it's such a pain in the arse to get home if you've been out for a night out or something and have to set up your machine or whatever, and emptying the bags, and all that sort of stuff. It's like oh, for goodness sake. Just, enough's enough." *(F, patient, 40s, Australia, 5 years on PD)*

- "As being the carer, it also makes you feel burnt out as well. And then there's times she doesn't feel like doing it, because – I don't blame her – it's physically draining at times. But I'm physically drained as well from work and doing other stuff as well, so then… it does make it a bit difficult when someone has a burnout." *(M, caregiver, 20s, Australia)*

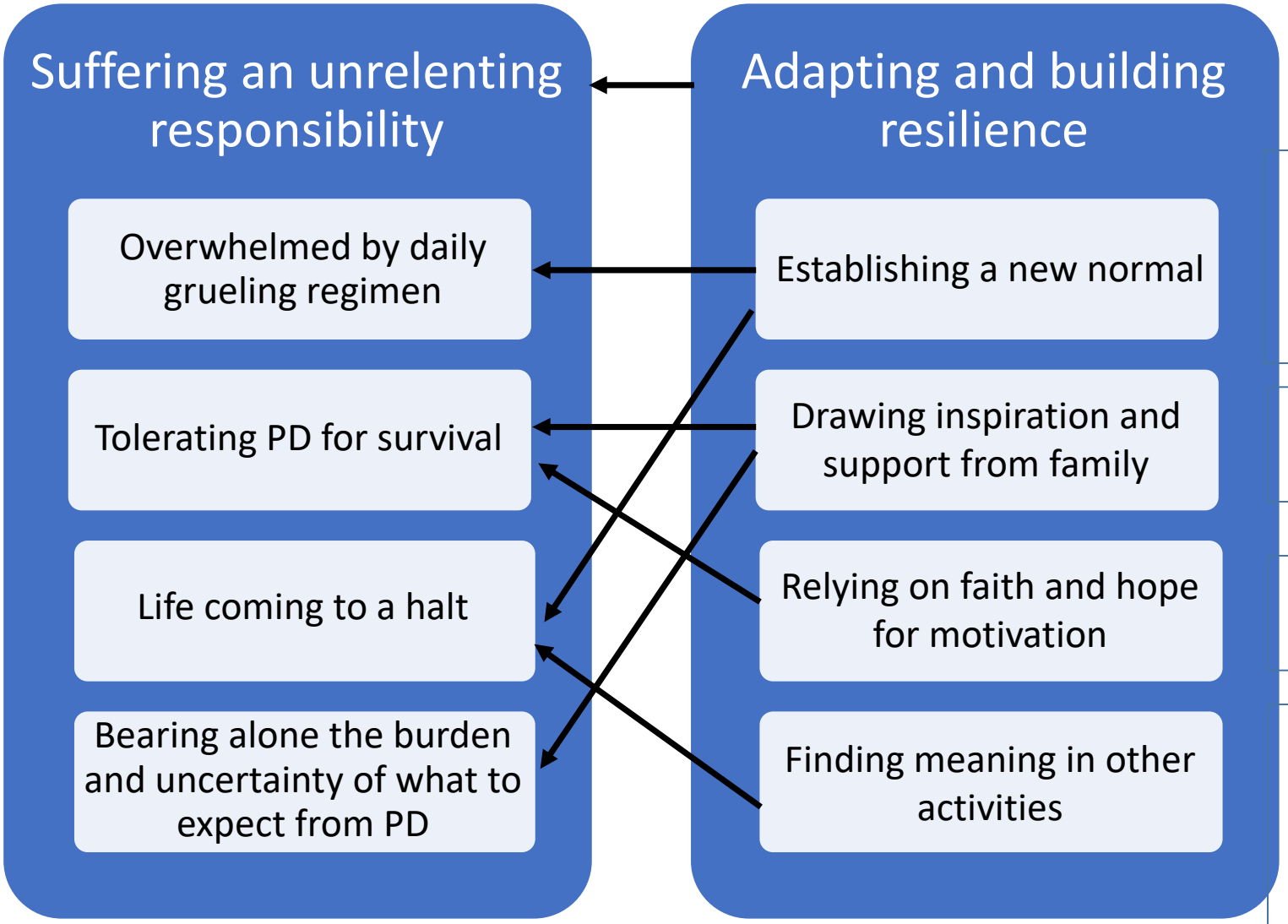
PD burnout

Oveyassi JO,…Saxena AB, Tong A, Shen JI: PDI 2020

Domain	Suggested strategies and actions
Psychological/emotional support	Routinely screen for burnout
	Offer counseling services
	Offer peer support programs
	Provide early and continuous education
Burden of time	Consider incremental dialysis
	Consider automated PD
	Consider telemedicine or home visits
Physical support	Offer assisted in-home peritoneal dialysis, if available
	Offer in-center peritoneal dialysis as respite care, if available

PD burnout - solutions

Oveyassi JO,…Saxena AB, Tong A, Shen JI, PDI 2020



Increasing long-term PD Success

-Peritonitis prevention and prompt management

-Reduce catheter malfunction

-Prevent/treat volume overload promptly

-Identify psychosocial risks and barriers to long-term PD

Clinical Management

Peritoneal Dialysis

Define Clinical Management

A sequence of steps corresponding to **clinical** tasks and decisions that are aimed at managing a patient with a specific presentation (disease)

Objectives:

- Well composed patient training program
- Clinical Management of Infection Prevention
- Peritoneal Dialysis Patient Follow-up Care
- Patient and interdisciplinary team collaboration
- After Hours Coverage for Home Dialysis Patients

Patient Training Outline

A training outline for home patients must include all aspects of self care for the patient to be successful as well as knowledgeable staff to prepare the patient for success at home.

- Dialysis procedures
- Aseptic Technique
- Care of the catheter and transfer set
- Management of exit site (routine care and assessment)
- Infection prevention
- Observation and management of complications
- Management of home supplies
- Daily assessment and reporting (vitals signs, fluid status, etc.)
- Medication administration
- Follow up care and contact

Infection Prevention: Peritonitis

- Aseptic Technique
  - sterile connections during dialysis procedures
  - reduced air flow (wearing mask, no fans, no open windows)
  - Avoidance of pets in the procedure area
- Proper Hand washing
- Monitoring of dialysis equipment and supplies
- Proper care of PD Exit site
- Preventative maintenance prior to invasive procedures
- Avoidance of constipation

Infection Prevention: Exit Site/Tunnel

- Good Hand Hygiene
- Proper cleansing of Exit site
- Frequent assessment of exit site – reporting areas of concern
- Use of antibacterial/antimicrobial agent
- Securing of catheter to prevent trauma
- Change dressing/perform exit site care If site gets wet or dirty

Patient Follow-up Care:

- Initial and PRN Home Visits
- Minimum of monthly clinical visit:
  - Exit site evaluation
  - Medication reconciliation
  - Vital signs/fluid balance/nurse assessment
  - Routine education
  - Distribution of ancillary supplies
  - Physician, Nurse, social worker, dietitian review
  - Review of home records report
- Frequent phone contacts with primary care nurse

Interdisciplinary Care:

It is vital for all care team members, especially the patient, to collaborate in forming an appropriate plan of care.

- Routine follow-up by physician, primary nurse, dietitian and social worker
- Care Plan Meetings:
  - Initial (within 30 days of start)
  - 3 month (follow up)
  - Annual
  - Unstable (as needed)
- Assessments performed by care members prior to care plan meetings to assess for any new or changes in information.

After Hours Coverage/Contact:

- Home patients need the support and direction available to them if and when complications arise.
- Vital for 24 hour nurse access

References:

- IGI Global. 1988-2021. https://www.igi-global.com/dictionary/clinical-management-workflow/54637

Hypoalbuminemia in Peritoneal Dialysis

Saturday March 6, 2021

Dr. David Ward MD FRCPC, Nephrologist

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Conflict of Interest

- Grants/Research Support: N/A
- Consulting Fees: Astra Zeneca, Janssen Canada, Otsuka Canada, Amgen
- Speakers' Bureau: Janssen Canada, Otsuka Canada
- Ownership Interest/Shareholder: N/A
- Royalty/Patent Holder: N/A

Objectives (A.K.A by the end of this talk participants will…)

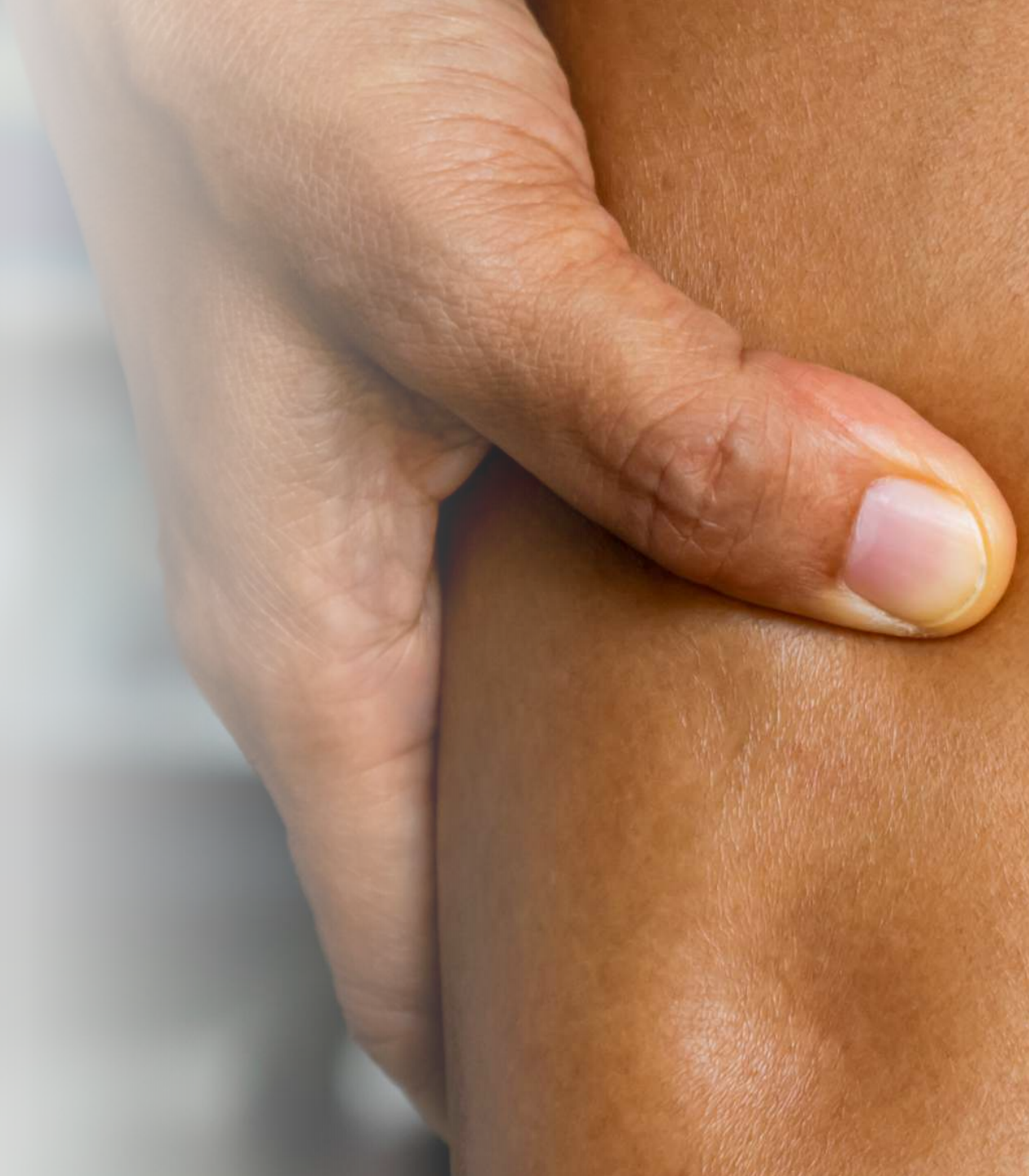
- Be able to describe the causes of hypoalbuminemia in PD patients and why it is common
- Understand the risks associated with hypoalbuminemia in PD patients
- Describe potential strategies that can mitigate hypoalbuminemia in PD patients

Outline

- Complications (knot of cables) – why should I care
- Epidemiology/Etiologies – how does it happen (image graph)
- Management (tool chest) – what can I do about it

What is albumin?

- 585 amino acids, MW 66kDa made in liver, T1/2 ~20days
- Binds drugs, metals, fatty acids, cholesterol, bile, hormones
- Osmotic pressure
- Free radical scavenger, may reduce oxidative stress
- Roche M et al. FEBS Lett. 2008;582:1783-1787
- Often used as a nutritional marker of adequate protein intake



Physiology of Albumin (Protein Balance) in PD

- Intake 1.2-1.3g/kg/day
- Effluent losses 5-15g/day; albumin is lost through large pores.
  - Any individual's rate will be driven by total surface area and % large pores Krediet RT et al PDI 1993:13S31
  - Higher losses in high transporters

- Urinary losses
- Hepatic production 12-15g/day – can increase synthesis to match losses keeping albumin level normal
  - Suppressed in inflammation De Mutsert R et al J Ren Nutr 19:127 2009

Does low albumin = malnutrition or low protein intake?

- In non-inflamed adults, serum albumin may remain normal until extremes of malnourishment (BMI<12 or starvation >6 weeks)
  - Lee J et al. AM J Med 2015;128:1023.e1-22
- In MDRD (eGFR 25-55) pts on low protein diet (0.58g/kg vs 1.3g/kg) followed over 2.2y saw albumin levels RISE (p<0.001) even though other markers of nutrition declined (e.g. arm muscle area)
  - Kopple JD et al KI 1997;52:778

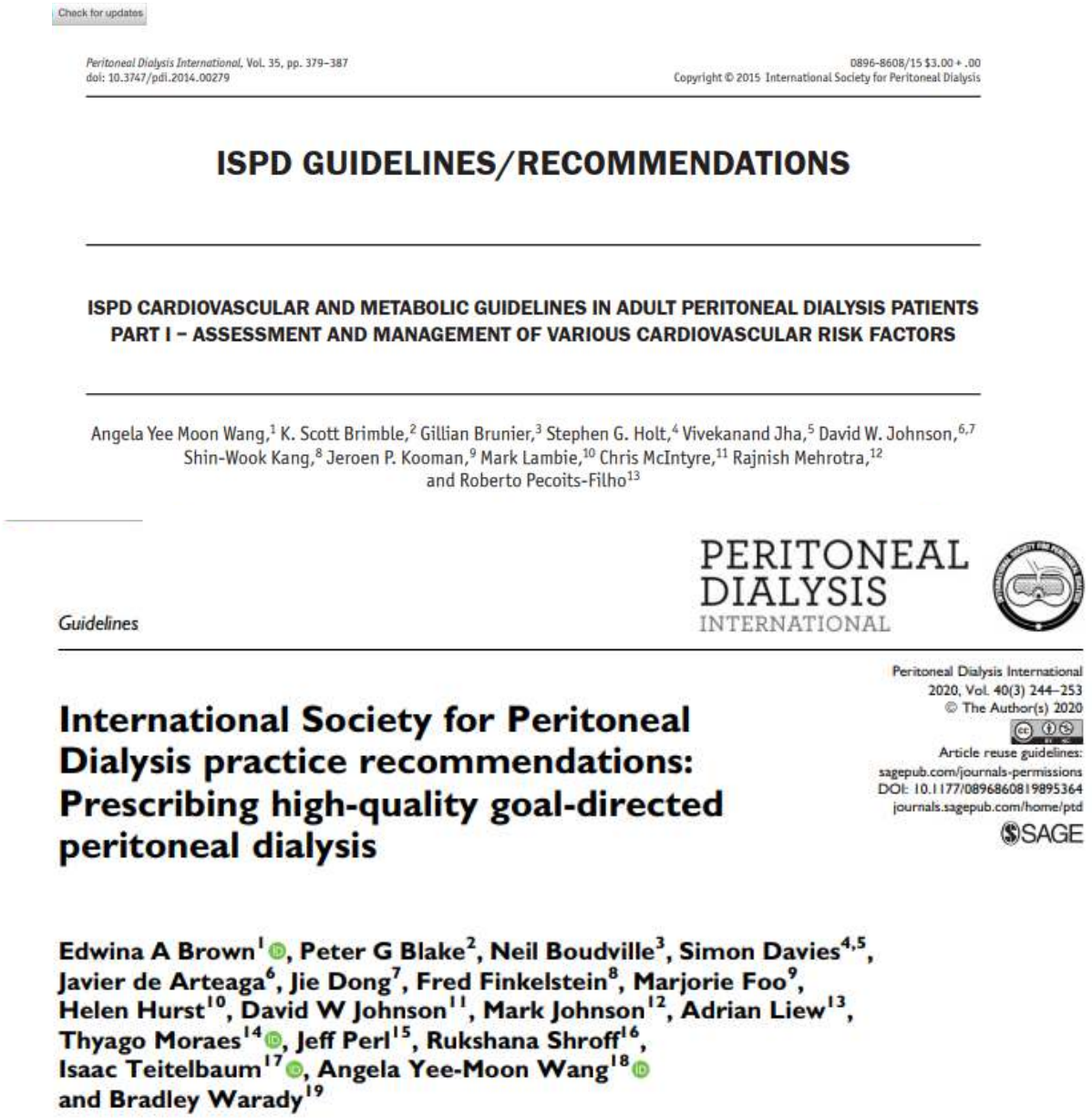
Is albumin an adequate nutritional marker in PD?

- 2008 International Society for Renal Nutrition and Metabolism (ISRNM) diagnostic criteria for malnutrition include
  - Biochemical parameters **(e.g. albumin <3.8g/dL)**
  - Body mass (e.g. BMI<23, total fat <10%, unintentional weight loss)
  - Muscle mass (e.g. reduced mid-arm muscle circumference area, low Screat)
  - Dietary intake (e.g. unintentional dietary protein intake <0.8g/kg/d)

- GUIDELINE 2.5. PROTEIN-ENERGY WASTING
  - 2.5.1 We suggest nutritional status be assessed within 6 – 8 weeks after commencement of peritoneal dialysis, and monitored regularly at least once every 4– 6 months for peritoneal dialysis patients. (ungraded)

- Headline Recommendations
- 3.3. Nutritional status

  b) Biochemical plasma markers including potassium, bicarbonate, albumin, phosphate should be regularly measured



Check for updates

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0896-8608/15 $3.00 + .00

ISPD GUIDELINES/RECOMMENDATIONS

ISPD CARDIOVASCULAR AND METABOLIC GUIDELINES IN ADULT PERITONEAL DIALYSIS PATIENTS PART I – ASSESSMENT AND MANAGEMENT OF VARIOUS CARDIOVASCULAR RISK FACTORS

Angela Yee Moon Wang,[1] K. Scott Brimble,[2] Gillian Brunier,[3] Stephen G. Holt,[4] Vivekanand Jha,[5] David W. Johnson,[6,7] Shin-Wook Kang,[8] Jeroen P. Kooman,[9] Mark Lambie,[10] Chris McIntyre,[11] Rajnish Mehrotra,[12] and Roberto Pecoits-Filho[13]

Guidelines

PERITONEAL DIALYSIS INTERNATIONAL

Peritoneal Dialysis International
2020, Vol. 40(3) 244–253

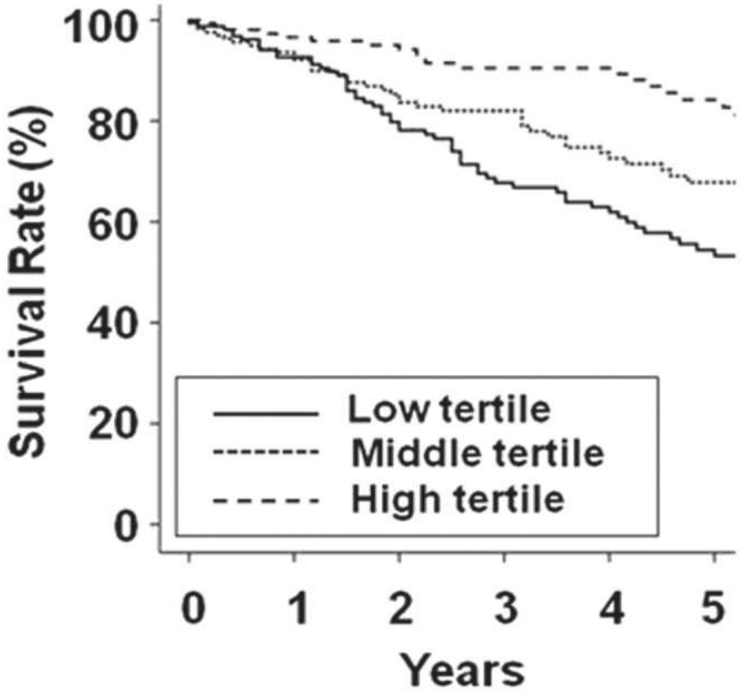
DOI: 10.1177/0896860819895364
journals.sagepub.com/home/ptd
SAGE

International Society for Peritoneal Dialysis practice recommendations: Prescribing high-quality goal-directed peritoneal dialysis

Edwina A Brown[1], Peter G Blake[2], Neil Boudville[3], Simon Davies[4,5], Javier de Arteaga[6], Jie Dong[7], Fred Finkelstein[8], Marjorie Foo[9], Helen Hurst[10], David W Johnson[11], Mark Johnson[12], Adrian Liew[13], Thyago Moraes[14], Jeff Perl[15], Rukshana Shroff[16], Isaac Teitelbaum[17], Angela Yee-Moon Wang[18] and Bradley Warady[19]

Even if it doesn't mean malnutrition – it's common

- If use just albumin; up to 63% of PD patients may be considered malnourished
  - Mehrotra R et al Am J Kidney Dis 2011;58(3)418
- If you are concerned about malnutrition consider
  - Subjective global assessment
  - Mid-arm circumference
  - Dietary history
  - Geriatric nutritional risk index (Kang SH et a
    - Multivariate HR for mortality lower albumin (<3.7 1.661
    - Available on MD calc



Complications of hypoalbuminemia

Risk factor for kidney failure: Hypoalbuminemia in Non-dialysis CKD

- IgA (adj RR 1.89 (1.37-2.6) for every 1.0g/dL decrease below 4.1g/dL)
  - Kawai Y et al PLoS One 2018;13:e0196655
- DKD – RENAAL; independent risk factor, even if UACR ≥2g/g
  - Keane W et al CJASN 2006;1:761
- Kidney Failure Risk Equation 8 variable (age, sex, eGFR, albuminuria, serum calcium, serum phosphate, serum bicarbonate, serum albumin) more accurate than 4 variable
  - Tangri N et al JAMA 2011;3015(15):1553

Hypoalbuminemia in PD patients

- Per 1-g/dL decrease in Albumin
  - Trend to 38% incr (0.87-2.20) mortality PD population; Dutch Study of 700 patients mean albumin 3.3g/dL 246 on PD, 2y mortality 21%
  - Not driven by markers of malnutrition (SGA or low protein intake) but effect was altered by inflammatory status
  - De Mutsert, R et al. J Ren Nutr 2009;19:127.

Complications

- At start – associated with 3.24-fold (1.47-7.17 p=0.001) greater drop gfr rrf
  - Yamada S et al. Therap Apher Dial. 24(1):72-80, 2020 Feb.

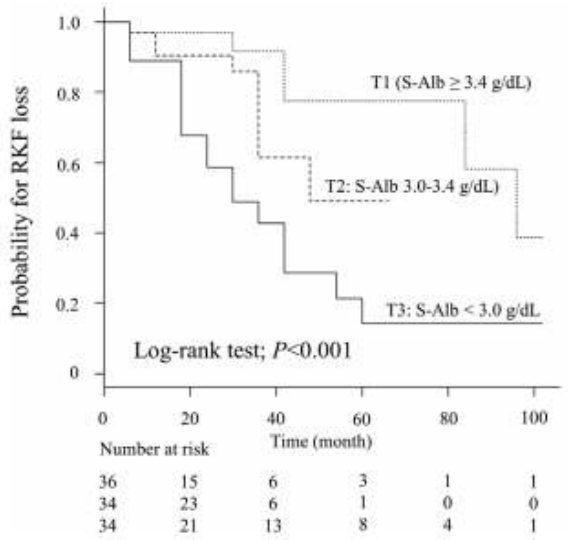


FIG. 2. Event-free survival rate for loss of residual kidney function.Patients were divided into three categories of serum albumin level, and the unadjusted Kaplan–Meier curves were compared. Log-rank test was used for the analysis. A two-sided *P* value less than 0.05 was considered statistically significant. Abbreviations: RKF, residual kidney function; S-Alb, serum albumin.

Complications

- Peritonitis; Wang Q et al AJKD 2003;41(3)664
- Marker of nutritional status
- CV events; Per 100mg/L increase in peritoneal albumin excretion HR for CV even 1.83 (1.11-3.02 p=0.018) Szeto CC et al PDI 2005
- Mortality
  - Thailand CAPD study 1177 patients; HR 0.48 (0.34-0.70) for albumin 3.0-3.4g/dL and 0.25 (0.16-0.40) for albumin >3.4g/dL
    - Vejakama P et al BMC Nephrol 2013
  - DaVita cohort of 12,171 PD patients found baseline albumin<3.0g/dL had 3 fold higher risk all-cause/CV mortality and 3.4 fold higher infection-related mortality c/w 4.00-4.19g/dL
    - Mehrotra R et al Am J Kidney Dis 2011;58(3)418

Early onset (at start) or later onset

- In a cohort of 80 CAPD patients with baseline serum albumin level, followed for up to 33 months, non survivors had initial albumin 3.1 ± 0.5 g/dL vs survivors 3.6 ± 0.5g/dL $p<0.001$
  - For every 1g/dL increase RR of mortality 0.42 (95% 0.20-0.89 p=0.024)
  - Protein losses in peritoneal fluid were not associated with baseline serum albumin or survival
  - Avram M et al. AJKD 1994;23(1):91
- If drops over time increased risk of all cause mortality (if dropped by ≥0.2g/dL
  - Mehrotra R et al Am J Kidney Dis 2011;58(3)418

What drives the associated risks of hypoalbuminemia?

- Is it reduced intake?
- Is it increased peritoneal losses?
  - Balafa O et al CJASN 2011;6(3):561
  - 257 patients
- Is it increased urinary losses?
- Is it reduced production?

Clinical implications

- If lower albumin associated with more rapid loss of RRF, and loss of renal function is associated with death and switch to other modality (HD, conservative/palliative care), does raising serum albumin mitigate these?
- In DaVita cohort of 12,171 patients, adjusted all-cause mortality was lower if albumin role by ≥0.3g/dL over 6 months
  - Mehrotra R et al Am J Kidney Dis 2011;58(3)418

Epidemiology and Etiologies

- Graph picture

Etiologies

- “False” Hypoalbuminemia
  - Dilution secondary to hypervolemia
- Reduced production
  - Normal is 12g/day
  - Negative phase reactant (thought to augment production of hepatic proteins that help immune system)
- Reduced intake (anorexia due to uremia/inadequate dialysis, delayed gastric emptying or abdominal fullness due to abdominal dialysate, glucose absorption from dialysate with or without hyperglycemia)

Etiologies

- Increased losses
  - Nephrotic range proteinuria and significant residual urine output (Seok H et al BMC Nephrol 2012; 13:171)
  - Transperitoneal albumin losses (esp when combined with serum CRP)
    - Higher CRP does not drive transperitoneal albumin losses Yeun JY, Kaysen GA AM J Kidney Dis 1997 (6):923
- Not secondary to weekly Kt/V or PCRn – appears more linked with inflammation
- ISPD 2020 guidelines Hypoalbuminemia is more common in PD compared to HD and is associated with protein energy wasting and peritoneal protein losses. Interventions are of limited utility in increasing serum albumin alone (practice point)

Can we predict which patients will develop hypoalbuminemia

- In Canadian study of 67 PD patients examining pre/post PD initiation albumin with transporter status (mean age 57.5, 36% DM) eGFR ~4mL/min
  - For H, HA, LA, L mean albumin prior to dialysis were 3.51, 3.74, 3.78, 4.04g/dL
  - Albumin decreased in all categories after initiation; 3.32, 3.5, 3.7, 3.9
  - A greater drop in albumin was thus in the high transp
  - 13.7% of variance in albumin was explained by intera membrane; it was not explained by proteinuric (etio
  - Concl: b/c H/HA have lower Salb at start, perhaps inf unifying factor for both (higher transport and lower a
  - Margetts PJ et al PDI 2000;20;14-18

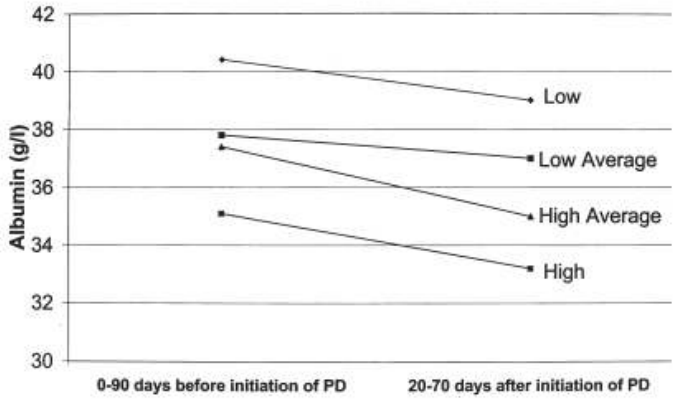


Figure 1 — Serum albumin concentration before and after the initiation of peritoneal dialysis (PD) by peritoneal transport category is plotted.

Monitoring dietary protein intake

- Normalized protein equivalent of total nitrogen appearance (nPNA – est from daily urea excretion in dialysis solution and urine)

Management strategies

- Dietary counselling/supplementation
- Avoid overhydration (dilution) – sodium restriction
- Whey protein 25% additional protein (above recommended 1.2g/kg/d)
  - 19/36 PD >12m patients with albumin <3.5 and no infection/malig/liver/GI dz
  - Dose 28.1 ± 14.3g/d split BID
  - Salb and nPNA sig increased over 12 weeks from 3.53 to 4.07g/dL
  - CRP fell from 12.35 to 10.1mg/dL
  - Hassan K Therapeutic Apheresis and Dialysis 2017;21(5)485

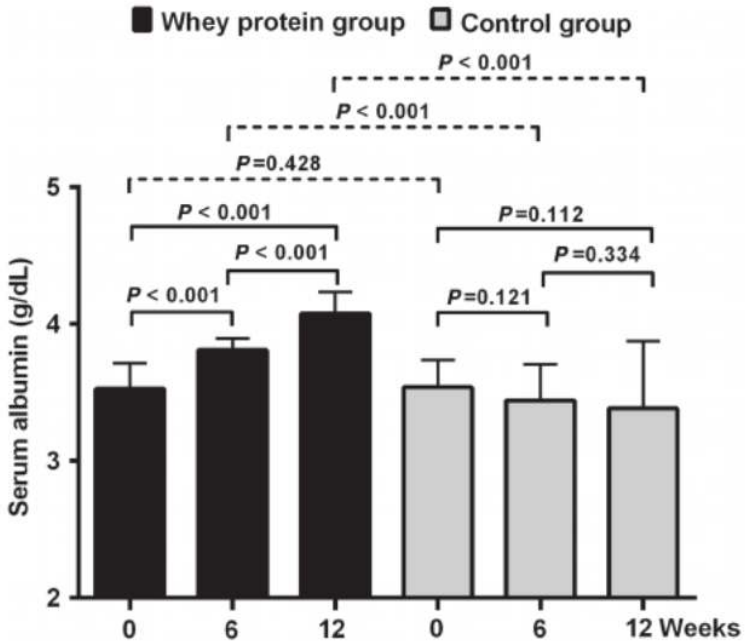


FIG. 1. The effects of whey protein supplementation on serum albumin levels compared to control group at the start of the study and at weeks 6 and 12 in hypoalbuminemic peritoneal dialysis patients.

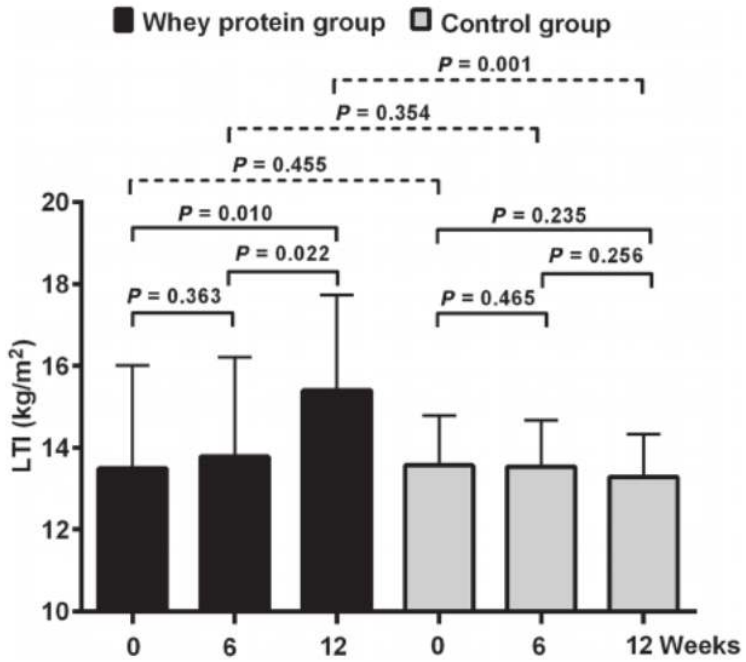


FIG. 3. The effects of whey protein supplementation on lean tissue mass index (LTI) compared to control group at the start of the study and at weeks 6 and 12 in hypoalbuminemic peritoneal dialysis patients.

Management strategies

- Does protein source matter (animal vs plant)
  - Eggs are alkaline and have low PO4 Tallman et al Nutritents 2018(10);12:1945
  - High amounts of protein (whey 46g/d or egg 70h/d) may have GI s/e that are intolerable (Jeloka et al 2013 Indian J Nephrol 21(1)1-4)
  - Consider plant based diet Cases et al Nutrients 2019(11):6
- Ensure adequate dialysis (lack of symptoms and control of metabolic risk factors such as acidosis)
- Consider increased protein intake during peritonitis 1.5g/d Ikizler et al KI 2013 (84);6:1096
- Consider increased physical activity

Management strategies

- Does changing to amino acid-based solutions help?
  - They can safely ultrafiltrate, remove urea/creat/K, and are absorbed 70-90% from solution with serum peak at 1h return to basal by 6h Oreopoulos et al 1979

TABLE 2
Clinical Studies with Amino-Acid Solutions in Adult Continuous Ambulatory Peritoneal Dialysis Patients

Author, year	Patients (n)	Selection	Duration (months)	Schedule (amino acids/all exchanges)	Result[a]
Oren (19), 1983	6	Unselected	1	2/4	Improved
Pedersen (20), 1985	6	Non diabetic	3	2/4	No change
Schilling (21), 1985	12	With peritonitis	1	2/4	No change
Dombros (22), 1990	5	Malnourished	6	1/4, overnight	No change
Young (23), 1989	8	Malnourished	3	1/4, morning	Improved
Bruno (24), 1989	6	Unselected	6	1/4, lunch	Improved
Scanziani (25), 1990	4	Diabetic	9–17	1/4	Improved
Arfeen (26), 1990	7	Non diabetic	2	2/4	Improved
Kopple (27), 1995	19	Malnourished	0.75	1–2/4	Improved
Paller (28), 1995	15	Unselected	3	1/4, lunch	Improved
Chertow (29), 1995	183	Unselected	2–19	1/4	Improved
Misra (30), 1996	18	Unselected	6	1/4, lunch	Improved
Jones (31), 1998	54	Malnourished	3	1–2/4	Improved
Maurer (32), 1996	9	Unselected	6	1/4, overnight	No change
Grzegorzewska (33), 1999	8	Unselected	6	1/4, overnight	No change

[a] Result was considered "improved" when total protein, albumin or transferrin, nitrogen balance, or total body nitrogen was statistically increased. Variation in plasma concentrations of amino acids was not, by itself, considered improvement of nutritional status.

  - Bruno M et al, PDI 2000(20)S2;166 suggest they are effective if given with a caloric load (glucose or other), acidosis is fully corrected, and patients should be malnourished based on low protein intake (only 2 RCTs highlighted)

Management Strategies – AA containing sol'n

TABLE 4

Side Effects of Amino-Acid Solutions

- Loss of appetite
- Nausea, vomiting
- Increased azotemia
- Increased acidemia
- Increased peritoneal permeability and protein loss
- Toxicity from some amino acids (?)

  Methionine → homocysteine

Objectives (A.K.A by the end of this talk participants will…)

- Be able to describe the causes of hypoalbuminemia in PD patients and why it is common
  - Highlight the link with inflammation and need for full assessment if concerned about malnutrition
  - Highlight the role of PD membrane transport; higher transport = more likely to have lower SAlb
- Understand the risks associated with hypoalbuminemia in PD patients
  - Peritonitis, mortality, loss of renal function
- Describe potential strategies that can mitigate hypoalbuminemia in PD patients
  - Increased dietary whey (1.5g/d from all sources) may decrease CRP if >20g/day
  - Eggs may also be viable
- Describe limitations of research – unclear if raising albumin alone mitigates the associated risks (e.g. CV)

Questions?