PATIENT FOCUSED PD PRESCRIPTION
A CASE BASED APPROACH

ISPD NAC 2021
Annual Dialysis Conference

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Disclosures

- Medical Director of government agency called Ontario Renal Network
- Occasional (once a year) honoraria from Baxter Global for talks

THIS TALK

- PD Prescription – what factors should you consider?
- Case Histories to demonstrate clinical points

THREE DRIVING FORCES IN PATIENT MEDICAL CARE PLAN

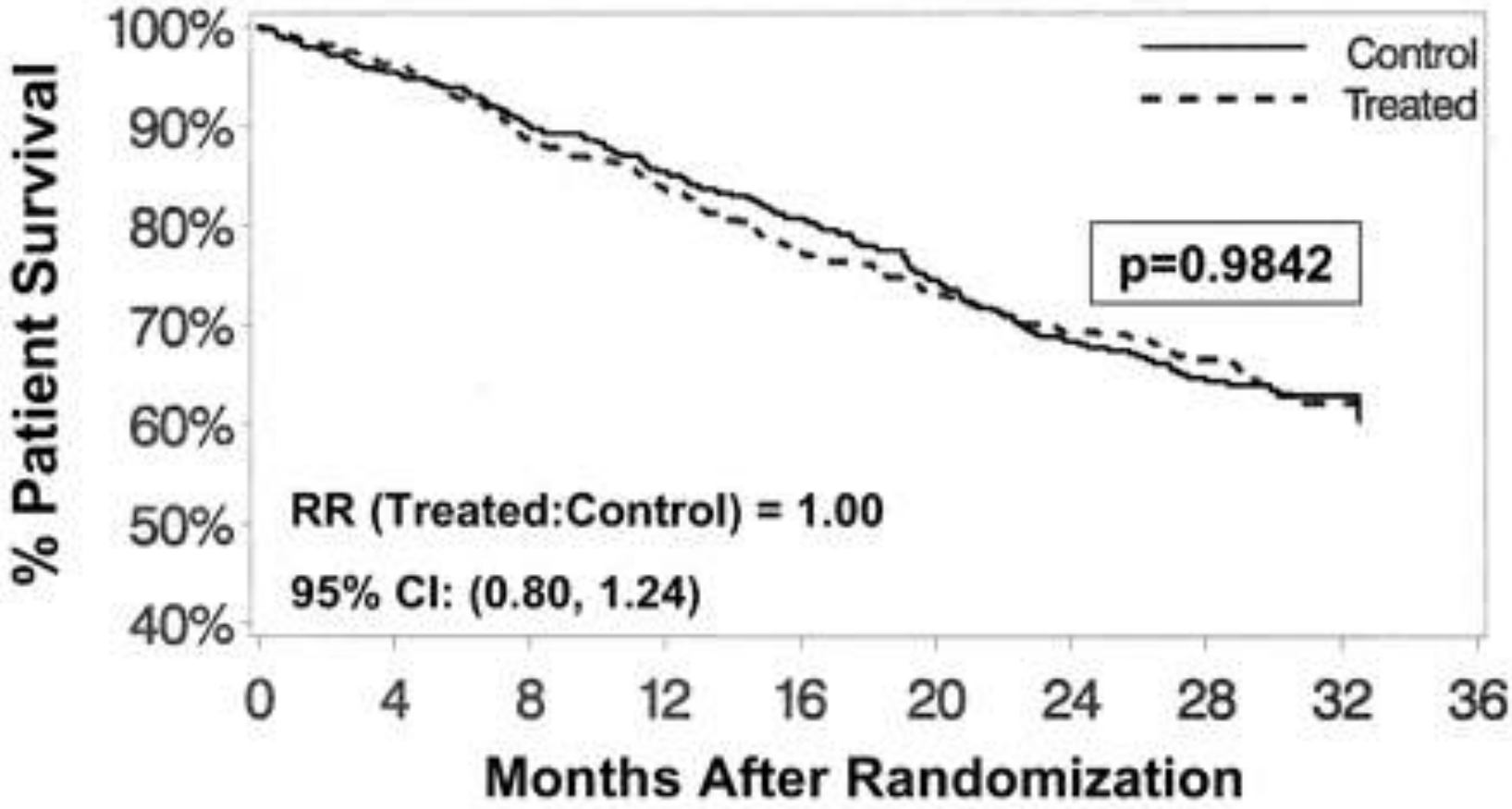
- Evidence based medicine
- Cost / cost effectiveness
- What the patient wants

Every decision should take these 3 factors into account

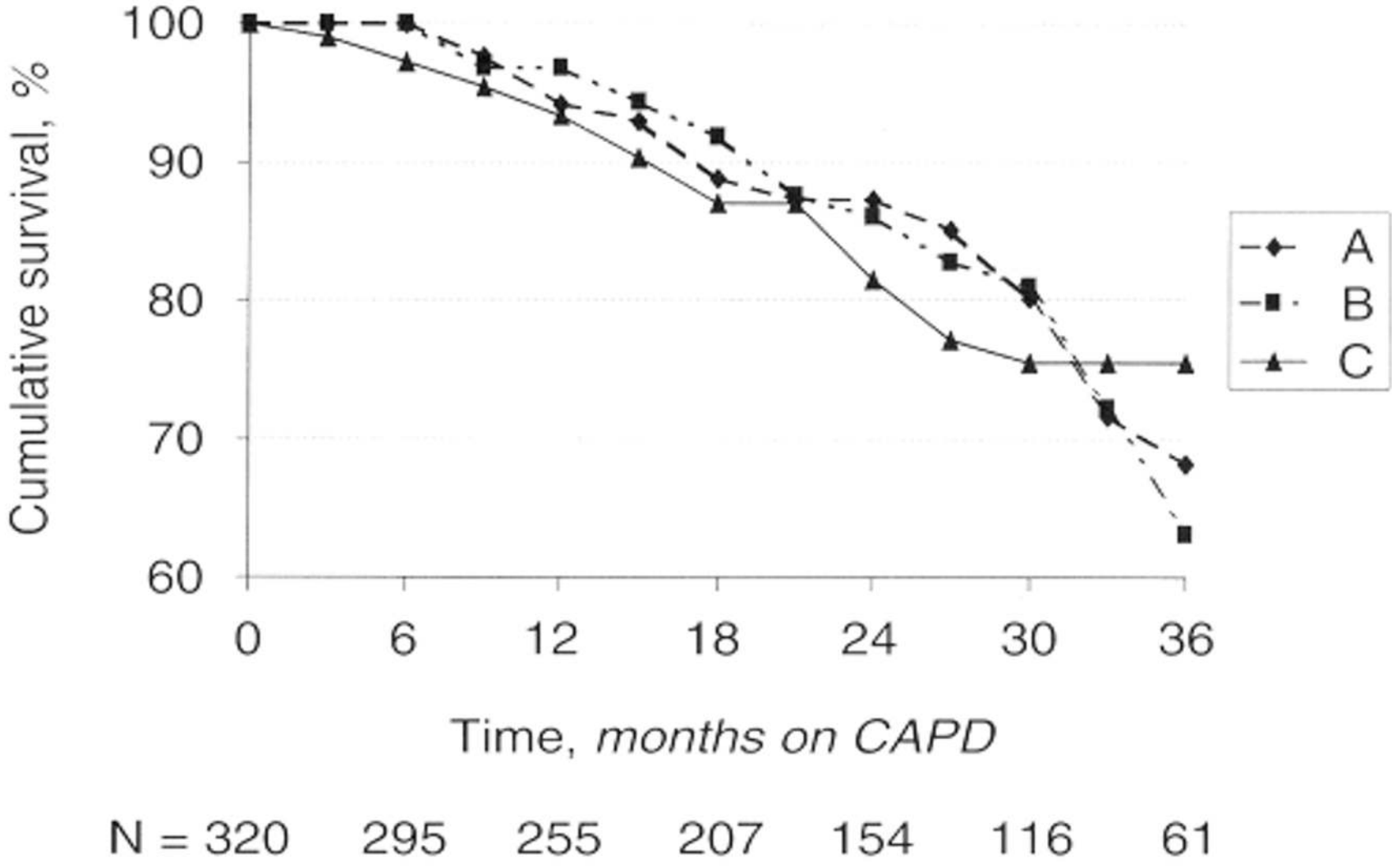
What Does Evidence Based Medicine Tell Us About Peritoneal Dialysis Prescription?

ADEMEX SURVIVAL CURVES

Paniagua et al JASN 2002



Cumulative Patient Survival in the 3 Groups
Lo et al KI 2003



WHAT EVIDENCE BASED MEDICINE DOES TELL US

That icodextrin may improve some surrogate outcomes

- Volume-related e.g. LVH, ECF volume (Davies JASN 2003, Konings KI 2003)
- Metabolic e.g. HgbA1C, Lipids (Paniagua PDI 2009, Li JASN 2013)

PREVIOUS GUIDELINES

- Try and achieve a total Kt/V clearance of 1.7 per week but recognize that evidence is modest and so take into account other factors when prescribing (KDOQI 2006, ISPD 2006, CSN 2011)
- For long dwells in patients where volume status or metabolic issues are important, use Icodextrin (CSN 2011)

ISPD PD PRESCRIPTION GUIDELINES 2020

- International ISPD Committee with nurse and 'patient' participation (Brown EA PDI 2020)
- 'Goal Directed High Quality Dialysis' is 'in' and 'Adequacy of Dialysis' is 'out'
- Consistent with KDIGO Consensus Conference on Dialysis Initiation, Modality Choice and Prescription (Chan et al KI 2019)
- Also with SONG PD initiative on priorities of people on PD emphasizing 'life participation' endpoint (Manera CJASN 2019)

Guidelines

PERITONEAL DIALYSIS INTERNATIONAL

Peritoneal Dialysis International
2020, Vol. 40(3) 244–253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DOI: 10.1177/0896860819895364
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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]

HIGH QUALITY GOAL DIRECTED PD

- Person Centered PD with Shared Decision Making and awareness of individual 'Goals'
- Symptoms, well being, quality of life and treatment burden
- Residual function, volume status and nutrition
- Limitations of clearance-based prescribing in isolation given weak evidence base
- Individualized Clearance Goals for each person

PERSON CENTRED CARE

- **What the patient wants**
- A dominant idea in health care delivery
- Unbiased guidance from care providers
- Involves family and/or friends
- Considers person's preferences and values, culture, family, social situation

The NEW ENGLAND JOURNAL of MEDICINE

Shared Decision Making — The Pinnacle of Patient-Centered Care

Michael J. Barry, M.D., and Susan Edgman-Levitan, P.A.

PERSON CENTERED CARE

- How does this apply to Peritoneal Dialysis?

FREQUENT CHARACTERISTICS OF PEOPLE WITH ESKD

- Socioeconomically disadvantaged
- Limited life expectancy
- Major burden of disease
- Very impaired quality of life
- Many value quality over quantity of life

Trajectories for People on Dialysis

Trajectory	Focus on Survival	Focus on Quality of Life
Transplant Trajectory	++++	++
Long Term Dialysis Trajectory	+++	+++
Semi Palliative Dialysis Trajectory	++	++++

GOAL DIRECTED PERSON FOCUSED PD

Participation in PD prescription

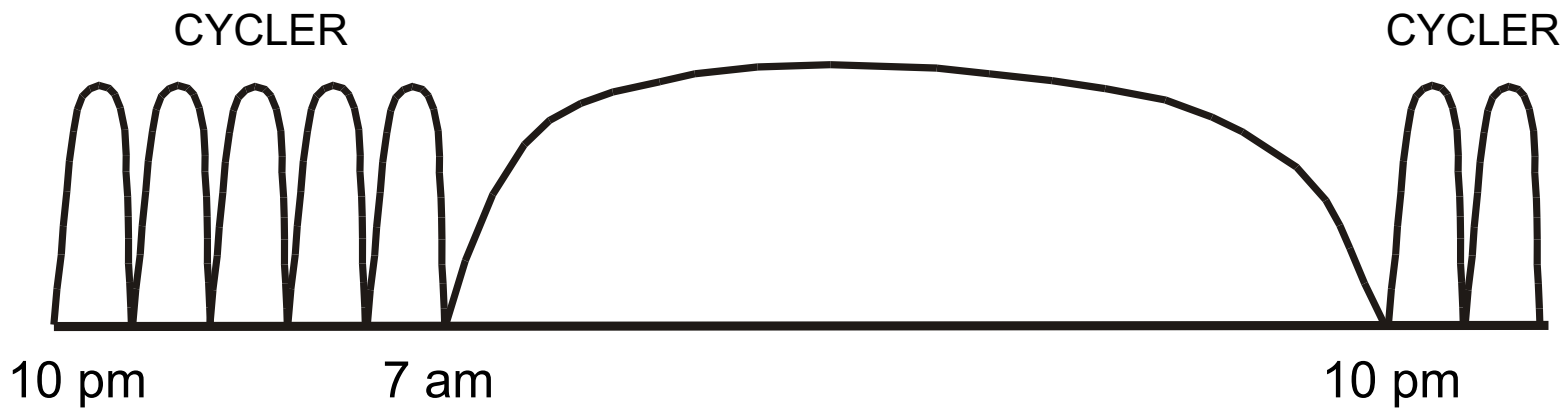
- Incremental PD
- Low intensity PD
- Glucose sparing PD

CASE ONE

- 52 year old woman starts APD for ESRD due to ADPCKD, weight 60 kgs, PET HA
- 5 x 2L + 2L day dwell
- At 3 months Kt/V is 3.1 (1.8 pKt/V + 1.3 rKt/V)
- She feels well and volume status is good
- She asks can she go ‘day dry’

"Day Dry" APD

APD with Long Day Dwell (CCPD)



HIGH Kt/V
CHOICES

1. Bad idea – you cannot get too much dialysis!
2. Bad idea – you need middle molecule clearance from the day dwell
3. Bad idea – you will need day dwell eventually so get used to it now
4. Good idea – go ‘day dry’

HIGH Kt/V
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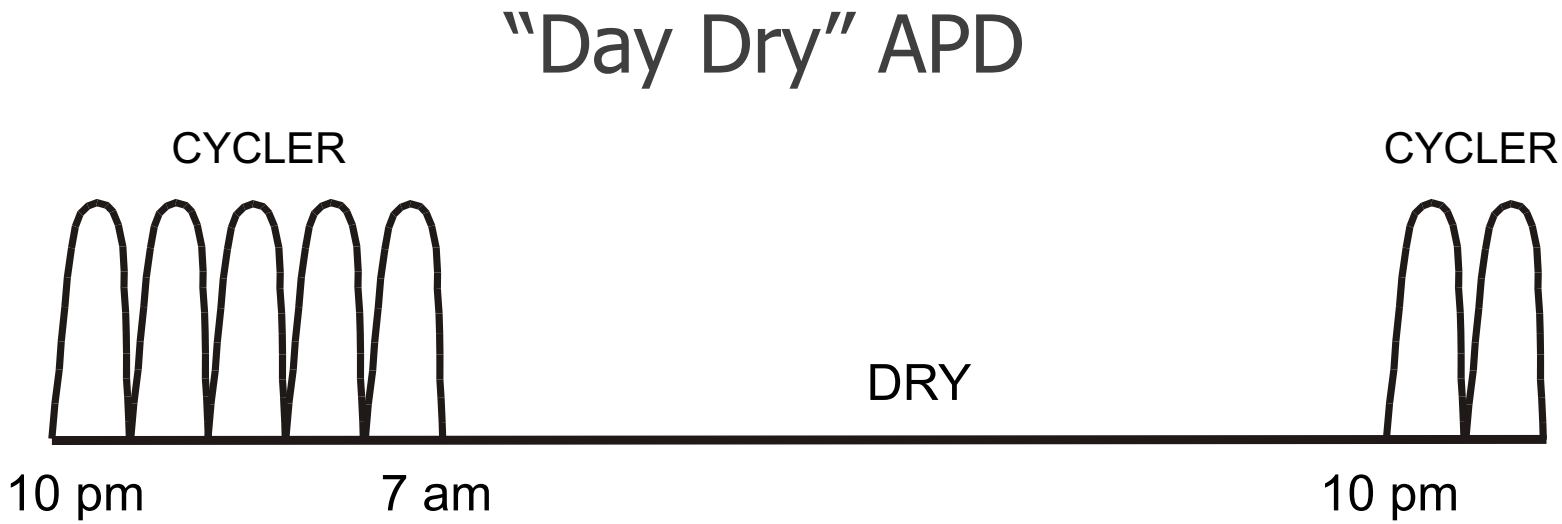
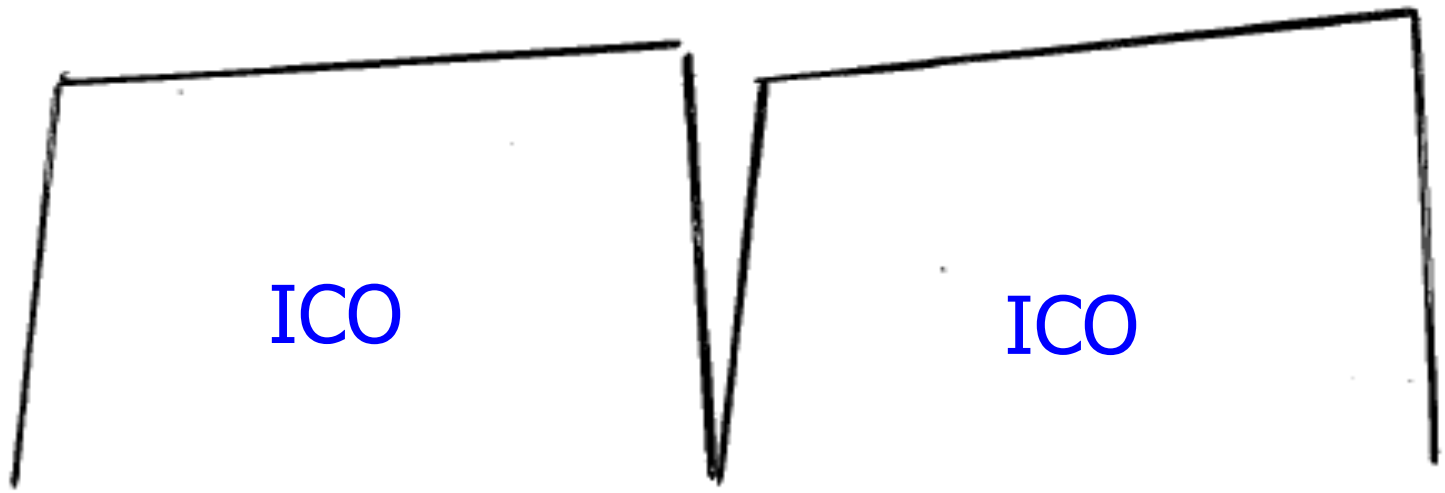
INCREMENTAL APD



INCREMENTAL CAPD
CAPD 3 X 2 L DAILY

CAPD – 2 DWELLS DAILY
Usually with Icodextrin*



*Not FDA approved

INCREMENTAL PD PRESCRIPTIONS

CAPD

- 3 x 2 L daily
- 1 x 2L daily (often Icodextrin)
- 2 x 2L daily (often Icodextrin)
- 1.5 L dwells

APD

- 'Day dry' APD
- APD 5 or 6 days a week
- APD for 5 or 6 hours each night (or day)

Guidelines

PERITONEAL DIALYSIS INTERNATIONAL

Peritoneal Dialysis International
2020, Vol. 40(3) 320–326

DOI: 10.1177/0896860819895362
journals.sagepub.com/home/pdi

Incremental peritoneal dialysis

Peter G Blake[1], Jie Dong[2,3,4,5] and Simon J Davies[6]

INCREMENTAL PD
Definition ISPD 2020

1. Less than a standard CAPD or APD prescription*

2. Peritoneal clearance < goal (e.g. Kt/V 1.7 weekly) but total clearance > goal

3. Clear intention to increase peritoneal clearance if and when total clearance falls below goal

*Standard CAPD = 4 x 2 L daily
*Standard APD = At least 8 L total solution daily including at least 1 day dwell

INCREMENTAL PD

- Rationale is that if Kt/V 1.7 due to PD alone is acceptable, surely Kt/V 1.7 due to combination of pKt/V and rKt/V is sufficient and indeed is better
- ADEMEX showed that increasing pKt/V within usual therapeutic ranges is not helpful
- Middle molecule clearance is not an issue here because residual renal function provides far more than PD ever could

ADVANTAGES OF INCREMENTAL PD

- Less work for person on PD +/or caregivers and hopefully more 'life participation'
- Less glucose exposure
- Less mechanical stress on patients
- Costs less
- Many never require full prescription
- Patient centered approach

DISADVANTAGES OF INCREMENTAL PD

- Need to monitor residual renal function every 3 to 6 months*
- Sometimes difficult to augment prescription when person has got used to incremental prescription e.g. addition of day dwell
- No RCT to validate incremental PD

* Some programs do not consistently collect urine and instead use clinical judgement, or urine volume estimates, or serum creatinine, or symptoms

PROTECTING RESIDUAL RENAL FUNCTION Enables Incremental PD

- ACEIs or ARBs
- Avoid aminoglycosides if there is residual renal function
- Use contrast with discretion
- Do not volume deplete patients

CASE TWO

- 86 year old man has diabetic ESRD, on day dry APD 5 x 1.9 L x 18 months but losing urine output and Kt/V falls to 1.5 weekly; he is not eating so well and his energy is mediocre
- You add 2 L day dwell but he complains of being distended and uncomfortable and says his appetite is worse

CASE TWO

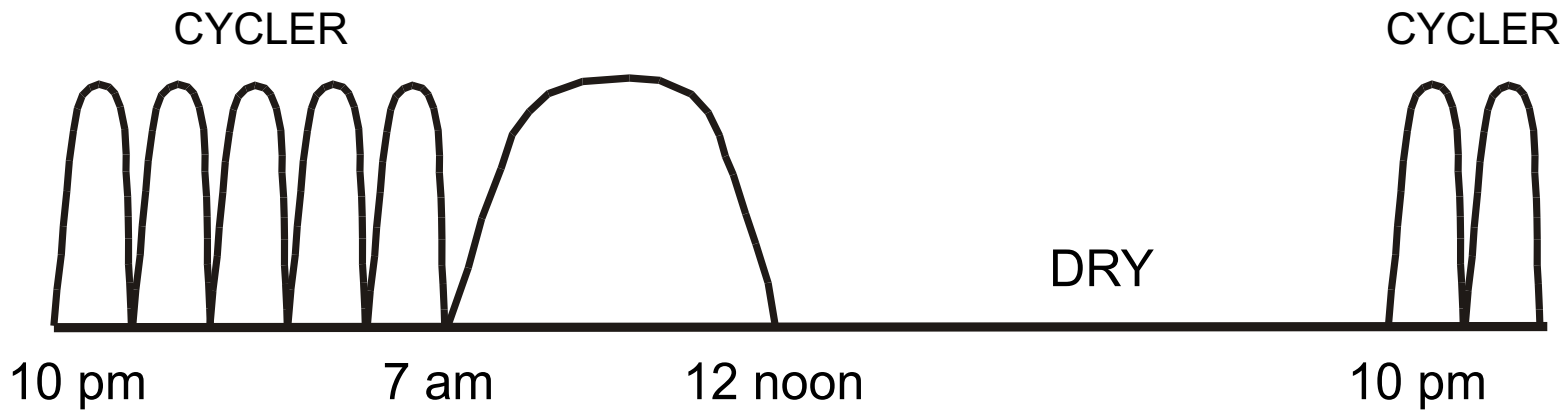
- You try 1.5 liters but he is still uncomfortable – he feels worse since you added day dwell

- Options?

CASE TWO
OPTIONS

- Try 1 liter day dwell
- How about 1.5 L for 4 hours only as last bag option or as evening dwell?
- Resume ‘day dry’ APD but go up to 15 L i.e. 7 x 1.9 L
- Go back to 10 L ‘day dry’ prescription
- How to decide?

APD with Morning Day Dwell



APD with Evening Day Dwell

CASE TWO
KEY POINTS

- Dialysis is about quality as well as quantity of life
- Evidence for survival benefit of Kt/V 1.7 versus lower is suggestive and not conclusive
- At age 86, survival in ESKD is limited regardless
- Time for Goal Directed PD based on Shared Decision Making

CASE TWO
OPTIONS

- Consult with patient and family
- Try 1 liter day dwell
- How about 1.5 L for 4 hours only as last bag option or as evening dwell?
- Resume ‘day dry’ APD but go up to 15 L
- Go back to 10 L ‘day dry’ prescription

CASE THREE

- 80 year old woman has diabetic ESRD on APD 3 x 2 L + 2 L day dwell + 2L dwell each evening x 2 years
- Worsening heart failure, hypotension and progressively deteriorating health, losing vision and hearing
- Quality of life is poor according to patient and PD is very hard work

CASE THREE

- You discuss discontinuation of dialysis but patient says her family – husband and 2 daughters would be very upset – and she was not ready for this
- Could she have less dialysis and skip a few days a week?

PALLIATIVE DIALYSIS

- Low intensity dialysis – may be HD x 2 weekly with less fluid off or 'day dry' APD
- Ignores clearance targets or volume status and concentrates on quality of life and symptom burden – Goal Directed PD
- Alternative to stopping dialysis for those not quite ready or able

PALLIATIVE DIALYSIS

- Very little published on this
- Ethical issues for some – 'death by underdialysis' – but this patient is dying anyway
- Reimbursement issues re Kt/V in U.S.?
- Uncomfortable for some health care professionals

CASE THREE

Decision:

- Cycle for 8 hours nightly
- 1 L day dwell
- One night and day off a week
- Passes away after 4 months

CASE FOUR

- 64 year old woman with diabetic ESRD is on PD for 6 months
- Blood work shows Urea 28 (10 mmol/L), Cr 6 (530 micmol/L), K 3.0
- Patient advised to liberalize K intake but K 3.1 4 weeks later
- Why might K be low despite ESKD?

CONTRIBUTORS TO LOW K

- Furosemide and metolazone
- Low K diets in CKD
- Poor nutritional intake
- Glucose loading and hyperinsulinemia shifting

CASE FOUR

- Initial response to K 3.0

1. Not a problem – does not affect outcome and may even be protective
2. Put on high K diet
3. Stop furosemide if taking
4. Start K supplements
5. Start an ACEI or ARB if not already taking

WHY TREAT LOW K?

1. Predisposes to peritonitis
2. Associated with cardiac death
3. Associated with infectious mortality

Goal here may be oriented around improving nutrition and serum potassium

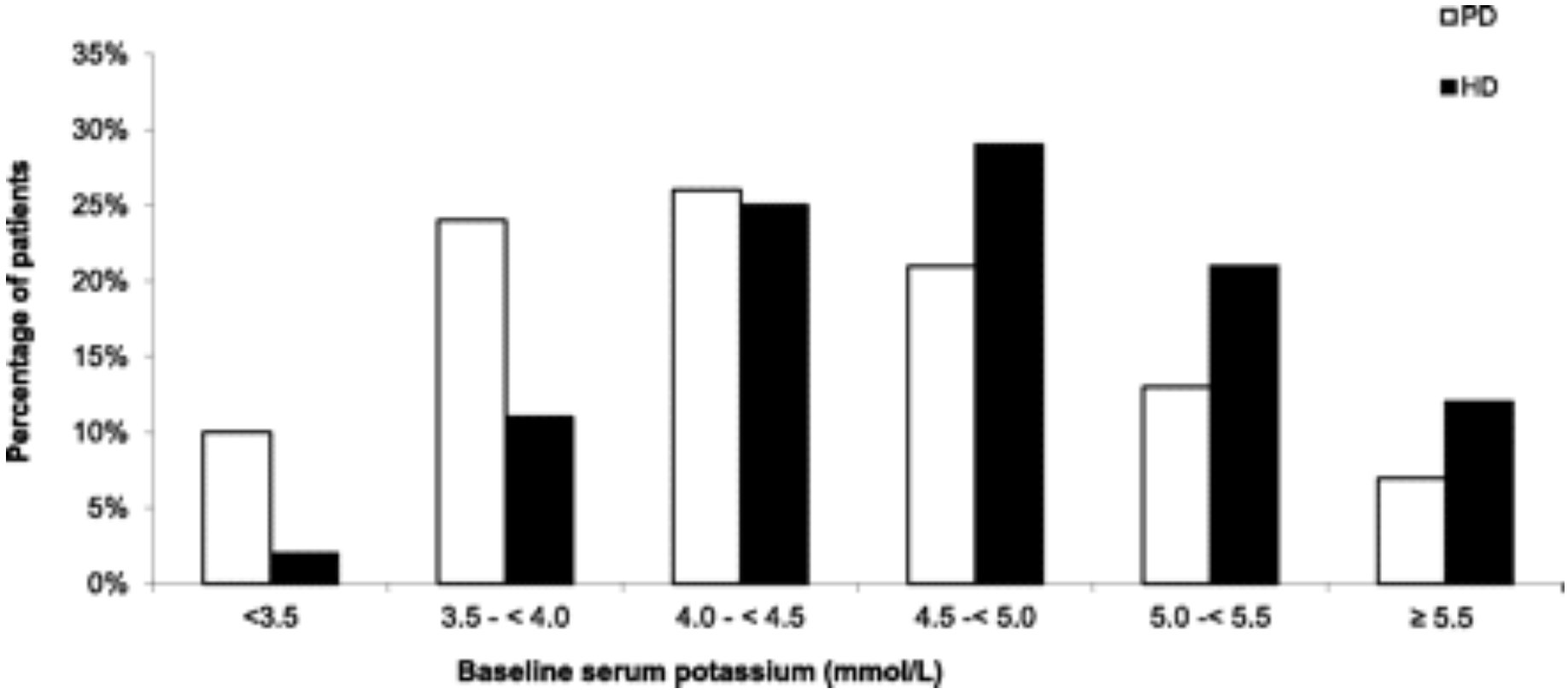
Serum Potassium and Cause-Specific Mortality in a Large Peritoneal Dialysis Cohort

Klara Torlén,[*†] *Kamyar Kalantar-Zadeh,*[†‡§] *Miklos Z. Molnar,*[†§‖] *Tania Vashistha,*[†] *and Rajnish Mehrotra*[¶]

Previous papers from Hong Kong and Taiwan showed associations of hypokalemia with mortality (Szeto AJKD 2005) and peritonitis (Chuang NDT 2009) in PD

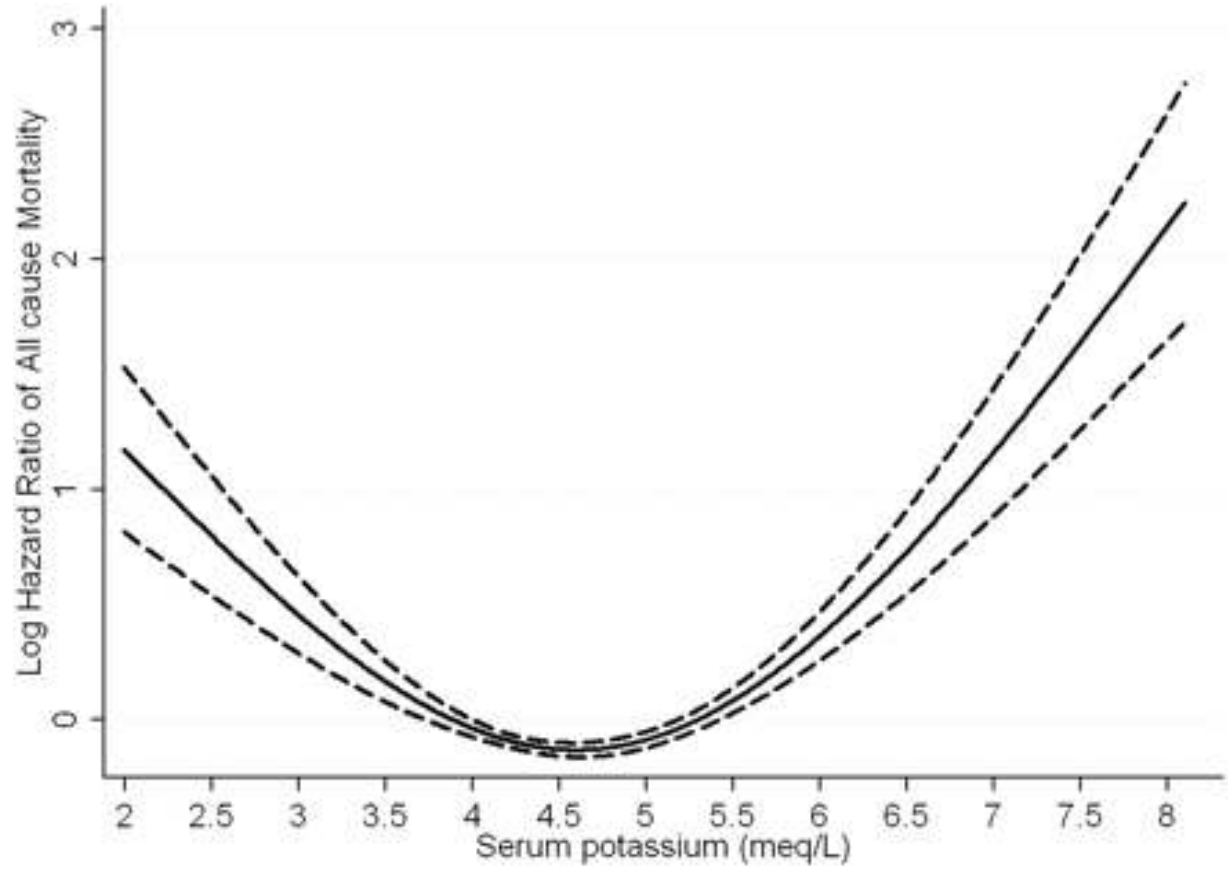
Tested this in huge US Da Vita database 2001-06
10,468 PD + 111,651 HD

SERUM K AND MORTALITY IN PD
Torlen et al CJASN 2012



SERUM K AND MORTALITY IN PD
Torlen et al CJASN 2012

Da Vita
Data
N = 10,468



PD AND SERUM K

- Low K and High K associated with worse outcomes in PD – all causes of mortality
- Low K more common and so more important
- But is it the low K that causes adverse outcomes or is it the conditions that cause it? (e.g. poor nutrition)

PLOS | ONE

2015

RESEARCH ARTICLE

Low Serum Potassium Levels Increase the Infectious-Caused Mortality in Peritoneal Dialysis Patients: A Propensity-Matched Score Study

Silvia Carreira Ribeiro[1], Ana Elizabeth Figueiredo[2], Pasqual Barretti[3], Roberto Pecoits-Filho[1], Thyago Proenca de Moraes[1]*, all centers that contributed to the BRAZPD II study[¶]

BRAZPD II Study
5,707 patients with > 90 days PD
Used propensity scores to assess if effect of K is Causation or just association

PD AND SERUM POTASSIUM CONCLUSION

- Strong association between low K (also high K) and mortality in multiple studies
- Robust even with propensity matching suggests causation and not just association
- Strong justification to be more aggressive treating low K in PD

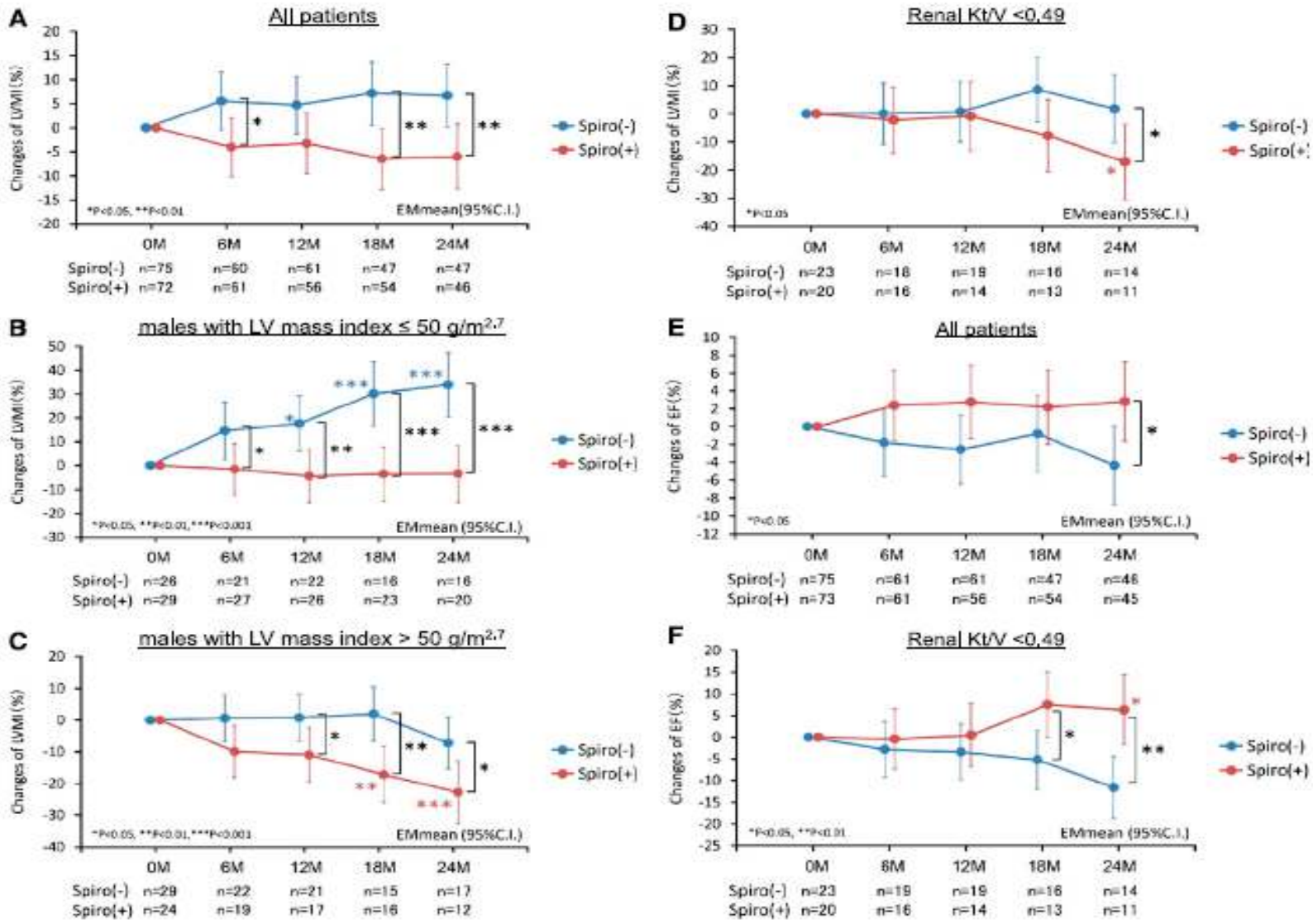
Long-Term Effects of Spironolactone in Peritoneal Dialysis Patients

Yasuhiko Ito,* Masashi Mizuno,* Yasuhiro Suzuki,* Hirofumi Tamai,† Takeyuki Hiramatsu,‡ Hiroshige Ohashi,§ Isao Ito,‖ Hirotake Kasuga,¶ Masanobu Horie,** Shoichi Maruyama,* Yukio Yuzawa,†† Tatsuaki Matsubara,‡‡ and Seiichi Matsuo,* on behalf of the Nagoya Spiro Study Group

JASN 2016
Randomized controlled multicentre trial
158 PD patients on ACEI or ARB – Not CHF
Spironolactone 25 daily or not (open label)
Primary endpoint - LV mass

Trial positive for LV mass and EF

SPIRONOLACTONE PREVENTS LVH AND PROTECTS EF IN PD PATIENTS Ito et al JASN 2016



The Safety and Efficacy of Mineralocorticoid Receptor Antagonists in Patients Who Require Dialysis: A Systematic Review and Meta-analysis

Kevin Quach, MSc,[1] Lyubov Lvtvyn, MSc,[1] Colin Baigent, FRCP,[2] Joe Bueti, MD,[3] Amit X. Garg, MD, PhD,[4,5] Carmel Hawley, MBBS, MMedSci,[6,7] Richard Haynes, DM,[2] Braden Manns, MD, MSc,[8,9] Vlado Perkovic, MD, PhD,[10] Christian G. Rabbat, MD, MSc,[11] Ron Wald, MDCM, MPH,[12] and Michael Walsh, MD, PhD[1,11,13]

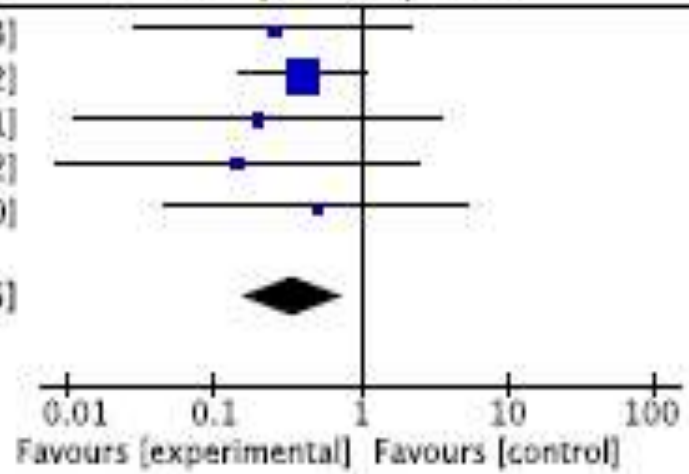
Systematic Review
Identified 9 RCTS (8 spironolactone)
5 HD, 3 PD, 1 Both
829 patients

MRAs REDUCE CARDIAC MORTALITY
66% EFFECT

Study or Subgroup	MRA Events	MRA Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Ito 2013	1	78	4	80	13.3%	0.26 [0.03, 2.24]
Matsumoto 2014	5	157	12	152	60.3%	0.40 [0.15, 1.12]
Taheri 2009	0	8	2	8	7.5%	0.20 [0.01, 3.61]
Taheri 2012	0	9	3	9	7.8%	0.14 [0.01, 2.42]
Walsh 2015	1	77	2	77	11.1%	0.50 [0.05, 5.40]
Total (95% CI)		**329**		**326**	**100.0%**	**0.34 [0.15, 0.75]**
Total events	7		23			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.77$, $df = 4$ ($P = 0.94$); $I^2 = 0\%$

Test for overall effect: $Z = 2.67$ ($P = 0.008$)

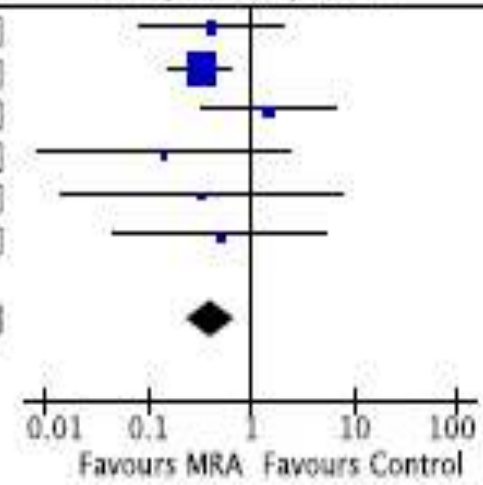


MRAs REDUCE ALL CAUSE MORTALITY
60% EFFECT

Study or Subgroup	MRA Events	MRA Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Ito 2013	2	78	5	80	11.4%	0.41 [0.08, 2.05]
Matsumoto 2014	10	157	30	152	63.7%	0.32 [0.16, 0.64]
Taheri 2009	3	8	2	8	13.1%	1.50 [0.34, 6.70]
Taheri 2012	0	9	3	9	3.7%	0.14 [0.01, 2.42]
Vukusich 2010	0	33	1	33	2.9%	0.33 [0.01, 7.90]
Walsh 2015	1	77	2	77	5.2%	0.50 [0.05, 5.40]
Total (95% CI)		**362**		**359**	**100.0%**	**0.40 [0.23, 0.69]**
Total events	16		43			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.98$, df = 5 (P = 0.55); $I^2 = 0\%$

Test for overall effect: Z = 3.28 (P = 0.001)

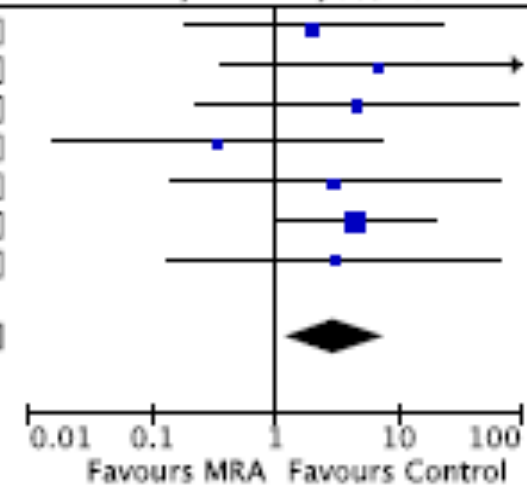


MRAs INCREASE RISK OF HYPERKALEMIA x 3 EFFECT

Study or Subgroup	MRA Events	MRA Total	Placebo Events	Placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
Ito 2013	2	78	1	80	15.2%	2.05 [0.19, 22.17]
Matsumoto 2014	3	157	0	152	9.9%	6.78 [0.35, 130.14]
Ni 2014	2	40	0	36	9.5%	4.51 [0.22, 90.96]
Taheri 2009	0	8	1	8	9.2%	0.33 [0.02, 7.14]
Taheri 2012	1	9	0	9	9.1%	3.00 [0.14, 65.16]
Walsh 2015	9	77	2	77	38.3%	4.50 [1.00, 20.15]
Yongsiri 2015	1	12	0	12	8.9%	3.00 [0.13, 67.06]
Total (95% CI)		**381**		**374**	**100.0%**	**3.05 [1.21, 7.70]**
Total events	18		4			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.72$, df = 6 (P = 0.84); $I^2 = 0\%$

Test for overall effect: Z = 2.35 (P = 0.02)



18/381 (4.7%) v 4/374 (1.1%)

Rise of 0.16 mmol/l in 13 weeks in 1 study

CASE FOUR

- Response to K 3.0

1. Put on high K diet
2. Continue furosemide if helping
3. ACEI or ARB if not already taking
4. Start MRA – spironolactone 25–50 mg daily
5. Latter preferable to impalatable K supplements

CASE FIVE

- 60 yr old male with ESRD of unknown cause weighing 90 kg is on APD 5 x 2L + 2 L day dwell x 6 mths; baseline PET shows he is an average transporter
- After 6 months on PD he up to 100 kgs
- Transplant team say they will not list him unless he loses 10 kgs
- An approach ?

CASE FIVE

- 60 yr old male with ESRD of unknown cause weighing 90 kg is on APD 5 x 2L + 2 L day dwell x 6 mths; baseline PET shows he is an average transporter
- After 6 months on PD he up to 100 kgs
- Transplant team say they will not list him unless he loses 10 kgs
- An approach ?
- Goal here is the transplant list

CASE FIVE

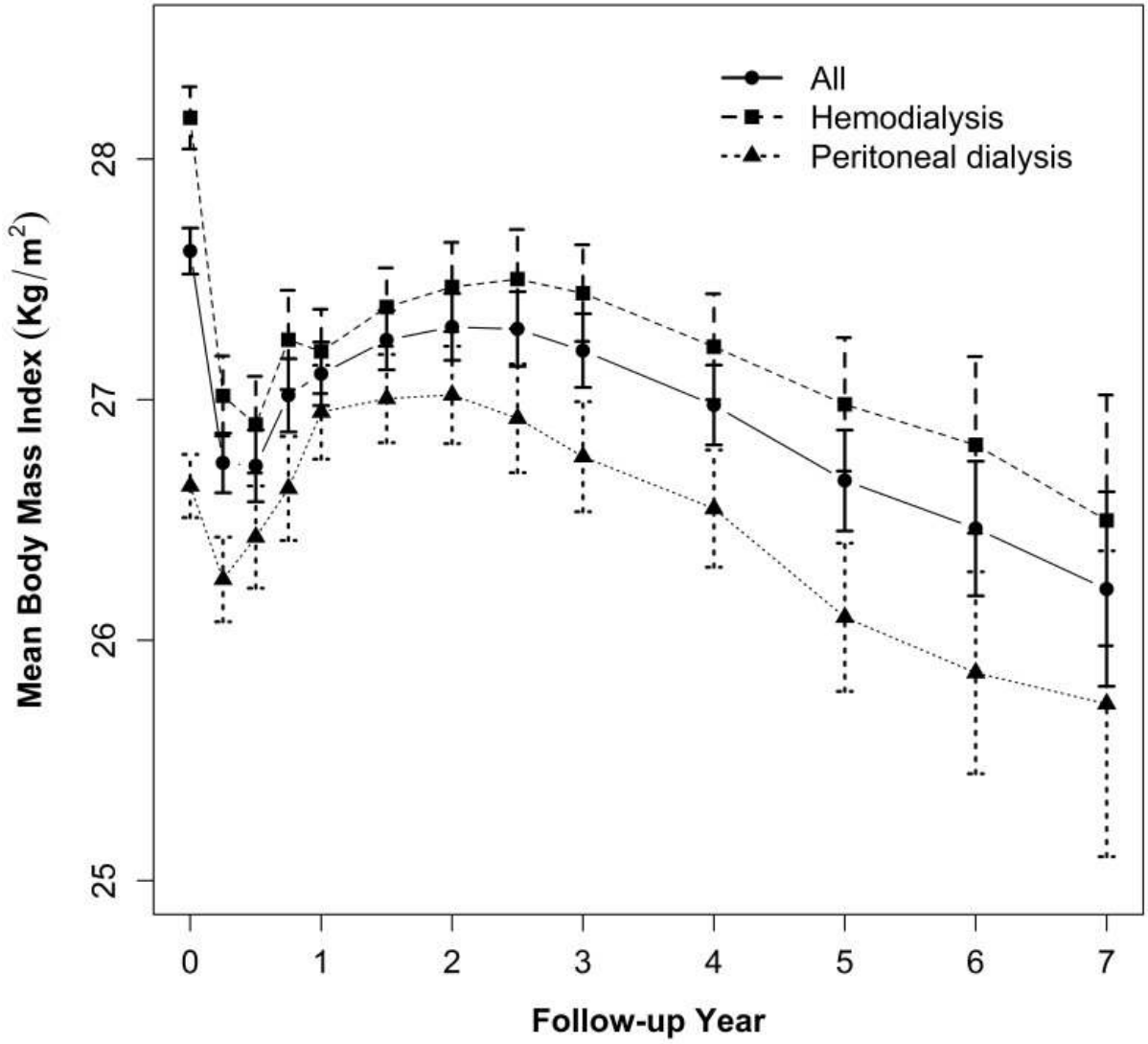
- Fluid or fat?
- Not always easy to distinguish
- Often a mix of both
- Tendency to gain weight in early months on PD
- Fluid retention more likely if residual function has declined

CHANGE IN BMI WITH TIME ON DIALYSIS

Badve et al
PLOS 2014

N = 17,022
HD 10,860
PD 6,162

ANZDATA
2001-08



CASE FIVE
Some Clinical Points

- All ankle edema is not fluid overload – some is chronic and related to venous issues or obesity or medications – new edema more significant
- All breathlessness is not pulmonary edema – deconditioning is more common
- High BP is not always a great index of fluid overload

CASE SEVEN
Some Clinical Points

- Trial and error is best approach
- Declining urine output or hypotension or increased fatigue may indicate volume depletion
- Failure to revise target weight up may lead to patient using inappropriately hypertonic solution and making obesity worse

CASE FIVE
HOW TO STOP WEIGHT GAIN

A. Glucose Sparing Strategies

1. Substitution of non-glucose solutions for glucose

2. Reducing need for glucose

B. Lifestyle changes – Diet, Exercise

CASE FIVE

GLUCOSE SPARING STRATEGIES

Reducing need for hypertonic glucose

- Salt and water restriction
- High dose diuretics
- Preserve RRF – ACEIs/ARBs
- Incremental PD – ‘day dry’ APD
- Improve glycemic control
- Realistic target weight
- 4.25% only for emergencies

CASE FIVE
GLUCOSE SPARING STRATEGIES

Substitution of non-glucose solutions for Glucose

- Icodextrin for long dwells
- Two icodextrin dwells daily*

*Not FDA approved

CASE FIVE
GLUCOSE SPARING STRATEGIES

Better to be ‘glucose sparing’ from the start, especially in obese patients

Some may need switch to HD especially if transplant eligibility is the issue

Most will stabilize with a glucose sparing approach

PD PRESCRIPTION CONCLUSION

- When clearance goals are not met and an increase in PD dose is being considered…
- There are often a number of options and a need to share decision making, to re-discuss Goals and to individualize

PD PRESCRIPTION

- We think of effect on Kt/V too much and everything else too little?
- Person Centered Goal Directed PD should individualize prescription and remember shared decision making, goals of care, quality of life, trajectory, and treatment burden including symptoms such as distension, drain pain, back pain, heartburn
- Not just the PD prescription but the medications and diet and lifestyle changes to benefit quality of life, nutrition, residual renal function
- Opportunity for engagement and shared decision making