WESTERN CANADA PD DAYS

Protein and Energy: Are PD Patients Different?

Vicky Ngo RD
Providence Health Care

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Outline

1. Understand the prevalence of malnutrition in PD populations and why the requirements are important to us
2. Review current guidelines on protein and energy requirements and its limitations
3. Comparison to other renal replacement modalities
4. Challenges of meeting these requirements
5. Strategies to “fill in” the gap

Protein-Energy Malnutrition (PEM)

- PEM - one of the strongest risk factors of adverse outcomes in pts with ESRD who undergo maintenance dialysis treatment.
- Inadequate amount of protein and energy intake is an important determinant of PEM.
- PD pts consistently have been shown to have reduced intake, with most pts not reaching their recommended daily intake of kcal, protein

Prevalence of Protein-Energy Malnutrition (PEM)

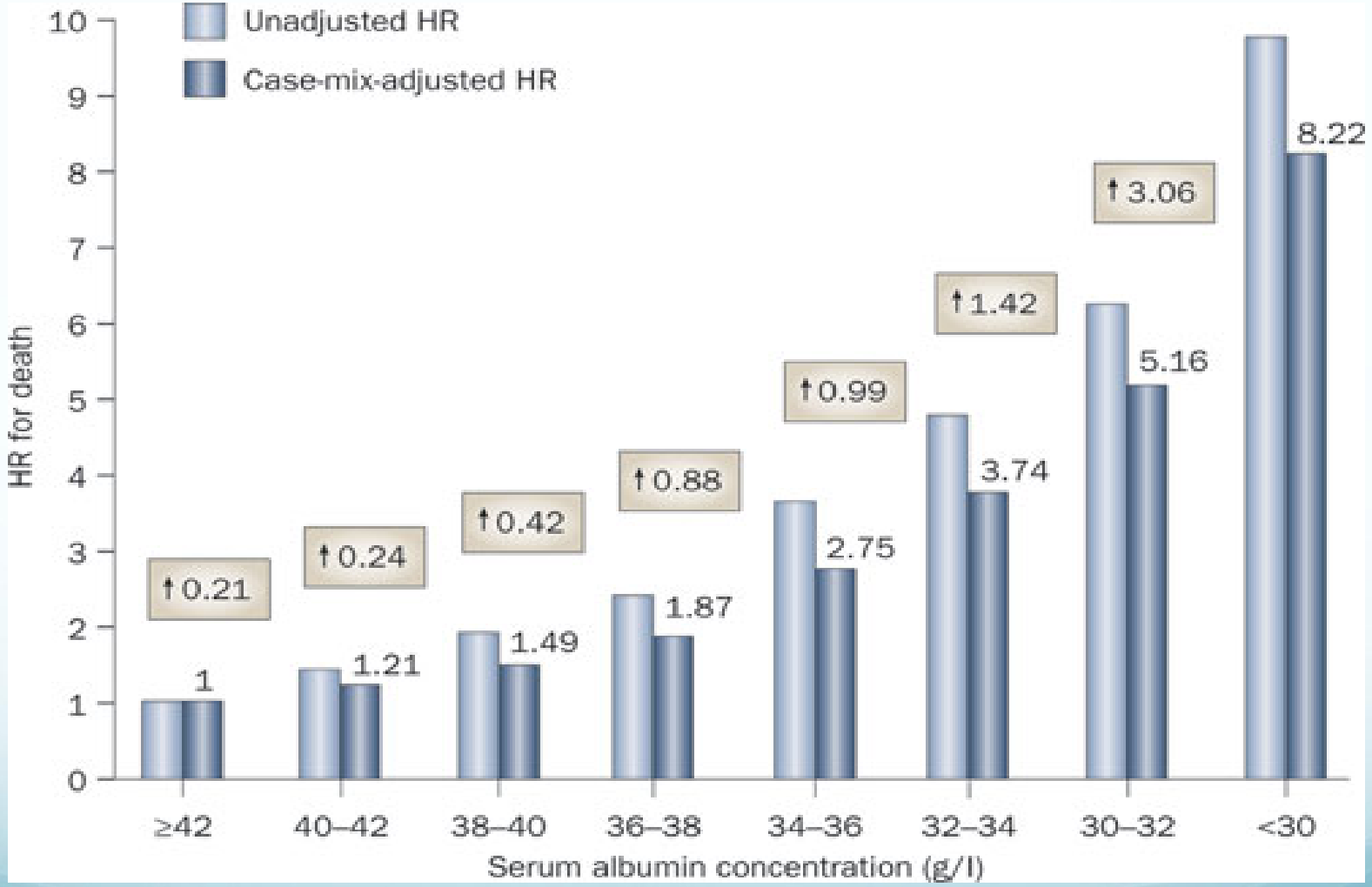
Prevalence of Malnutrition in Peritoneal Dialysis (PD) Patients—Cross-sectional Study by Subjective Global Assessment

Reference	Patients (*n*)	Mean age (years)	Mean duration of PD (months)	Region	Malnutrition (%) Mild-to-moderate	Severe
Young *et al.*, 1991 (3)	224	53.4	32.2	Europe and North America	32.6	8.0
Cianciaruso *et al.*, 1996 (11)	224	60.2	28.0	Italy	34.9	7.4
CANUSA, 1996 [a] (6)	680	54.3	—	Canada, U.S.A.	44.6	4.2
Jansen MA *et al.*, 2001 (12)	75	56.0	9.5	Netherlands	49	
Kang *et al.*, 1999 [b] (13)	147	46.7	44.7	Korea	28.6	1.0
Chung *et al.*, 1999 (14)	98	47.9	22.3	Korea	44.9	2.0
Kumano *et al.*, 2000 [c] (15)	259	50	50.4	Japan	26.2	3.0
Wang *et al.*, 2001 (16)	247	55	37	Hong Kong	40.1	2.5
Kang *et al.*, 2002 [b] (17)	127	50.7	67.3	Korea	34.7	6.3

[a] Baseline assessment of incident patients.
[b] These two studies were performed at the same center with a 2-year interval.
[c] Study used "subjective judgment," including an assessment of general condition, objective symptoms, and laboratory findings.

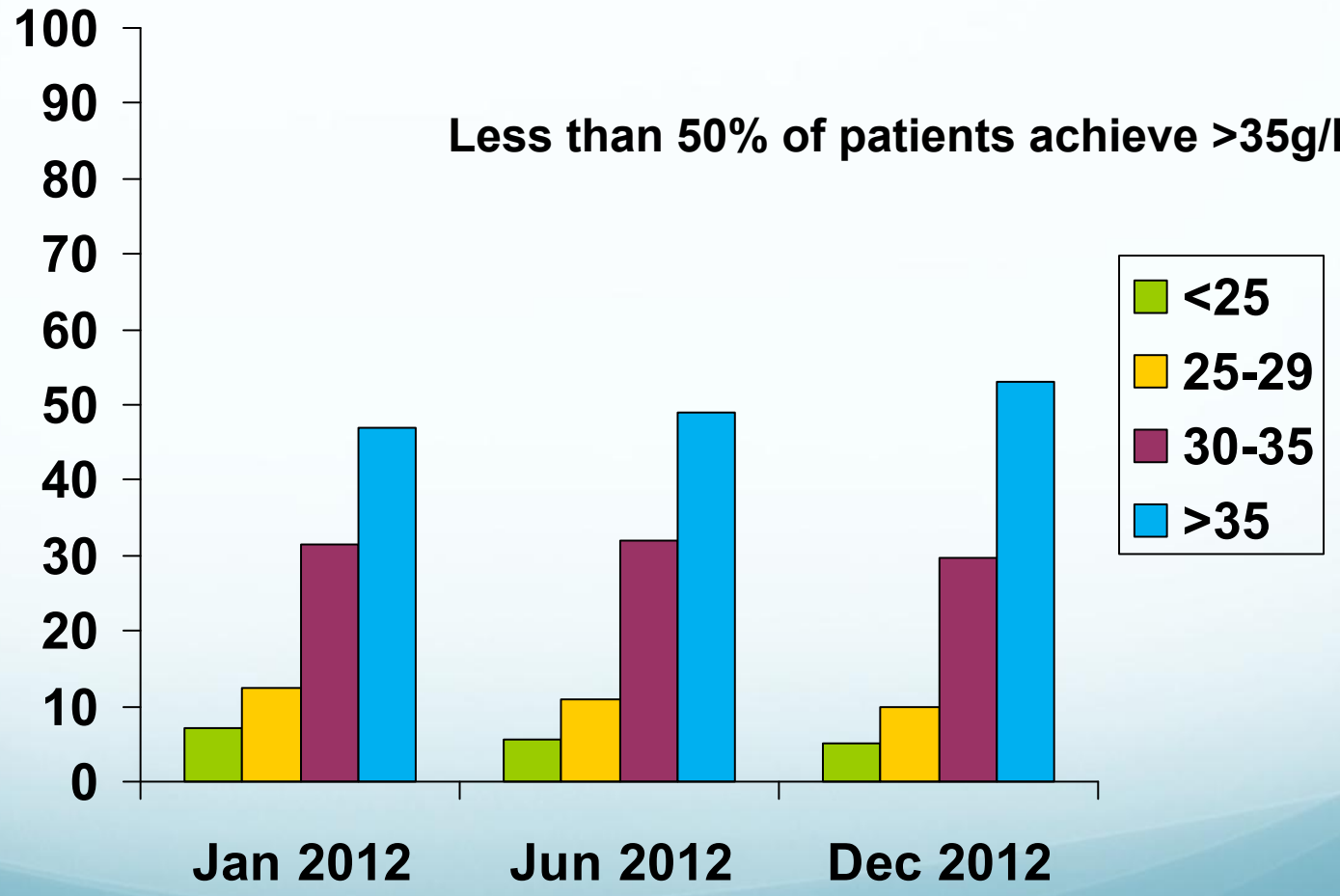
Kang et al Perit Dial Int 2003; 23(S2):S58-S64

Baseline Serum Albumin Concentration and Survival in Patients on Hemodialysis



Kalantar-Zadeh, K. et al. Nephrol. Dial. Transplant. 20, 1880–1888 (2005)

Albumin Level of PD Patients (BC Province)



Protein Requirement for Healthy Subjects

- DPI= 0.8g/kg/d by DRA Committee in US[1]
- 1.01-1.08g/kg/d (Japan Welfare Ministry)

- Minimum: 0.58g/kg/d by FAO (food and Agriculture Organization of UN), WHO (World Health Organization)[2]

[1]. Pellet LP, Am J Clin Nutr 51:723-737, 1990

[2]. World Health Organization Technical Report Series 724, 1985

Compared to Different Modalities (Protein Losses)

- PD> HD> CKD – due to protein losses into PD dialysate are higher than hemodialysate
- Peritoneal protein losses – average 5-15g/day [1]
- Total protein ~9-12g, 6-8g albumin daily, and more during episodes of peritonitis[2]
- HD- Amino acids losses ~ 4-9g in fasting state; 8-12g post prandially, protein losses in negligible[2].

[1] Movilli E et al. Nephrol Dial Transplant 1995;10: 514-518
[2] Blumenkrantz MJ et al. Kidney Int 1981; 19:593-602

Contribution of Dialysate Protein & Amino Acids Losses

Gahl GM, et al, Annals of Internal medicine 1981:94: 643-646

N=5 CAPD Germany
Result: Protein losses in CAPD (~10g/d)

Wystke, M et al, Perit Dial Int 2007; 27:192-195

Netherlands N=9 (APD) 4-7 exchanges/night

1) **Protein losses significantly & independently related to the number of night time exchanges and the duration of dwell.**

2) **Protein + amino acids losses =15 % of dietary N intake** ***(avg:0.14g/kg/d dialysate Protein; 0.015g/kg/d dialysate amino acids).***

Example: 50 kg PD pt= 7g protein, 0.75g amino acids

Summary of Individual Studies on Protein Requirement (after year 2000)

Aguirre Galindo 2003	Achieved better adherence to high protein diet with use of supplements but no indication of optimal protein intake
Chen 2008	Improved pre□albumin with protein intake 1.2g kg/day compared to 0.8g kg/day
Chow 2003	Mean protein intake 1.37 (range 0.26□2.92)g/kg associated with mild to moderate malnutrition by SGA in 79% subjects
Dong 2011	<0.73g/kg – associated with PEW, worst outcome; 0.73-0.93g/kg: negative nitrogen balance and risk of peritonitis; >0.93g/kg favourable long term outcomes
Gonzalez□Espinoza 2005	Trend to improved SGA with protein intake of 1.7 g/kg/day in the intervention group compared to usual (1.0g/Kg/day) intake
Sutton 2007	Dietary intake 0.93□1.01g/kg/day protein and 23.4□25.7Kcal/kg/day associated with no significant change in nutritional status
Wang 2007	Protein intake ≥1.17g /Kg/day and total energy intake 29.6 Kcal/kg/day associated with optimal SGA scores. Malnutrition associated with protein intake 0.92 to 1.06 g/kg/day

****references on the last page of presentation**

Dietary Protein Intake (DPI) NKF K/DOQI - 2000

PD (clinically stable)

- 1.2-1.3 g/kg/d (no less than 1.2 g/kg/d)
- At least 50% of DPI should be of high BV protein

Unless DPI of 1.2 g/kg/d demonstrated adequate, 1.3g/kg/d should be prescribed

2000 Update National Kidney Foundation KDOQI

DPI European Best Practice Guidelines (EBPG) 2005

- DPI> 1.2 g/kg/d: Not achieved by most PD; no impact on malnutrition or preserve status
- DPI of 1-1.2 associated with neutral or +N balance,
- DPI >1.0 g/kg/d: Sufficient in most CAPD pts (based on N-balance study)
- Warned against <0.8g/kg/d

Dombros N et al. Nephrol Dial Transplant 2005 Dec 20 Suppl 9:ix28-ix33

Recommended Dietary Protein Intake by Different Expert Groups

European Best Practice Guidelines (ENPG) 2005[1]	**≥ 1.0g/kg/d**
NKF K/DOQI (2000)	**1.2-1.3g/kg/d** **> 50% HBV protein**
Australian Evidence Based Practice Guidelines for the Nutritional Management of CKD, 2006 [2]	**1.2□1.4g/kg IBW** **>50% HBV protein** **(Peritonitis: at least 1.5g/kg/d)**
European Society of Parenteral and Enteral Nutrition (ESPEN)	**1.2-1.5g/kg/IBW (additional 0.1-0.2g/kg/d if peritoneal inflammation occurs) 50% HBV protein**

Clinically stable PD patients

[1] Dombros N et al, Nephrol Dial Transplant. 2005 Dec 20 suppl 9:ix28-ix33

[2] Ash S. Nutrition and Dietetics 2006; 63 (Suppl s2): s33-s45

Protein Requirement Limitations

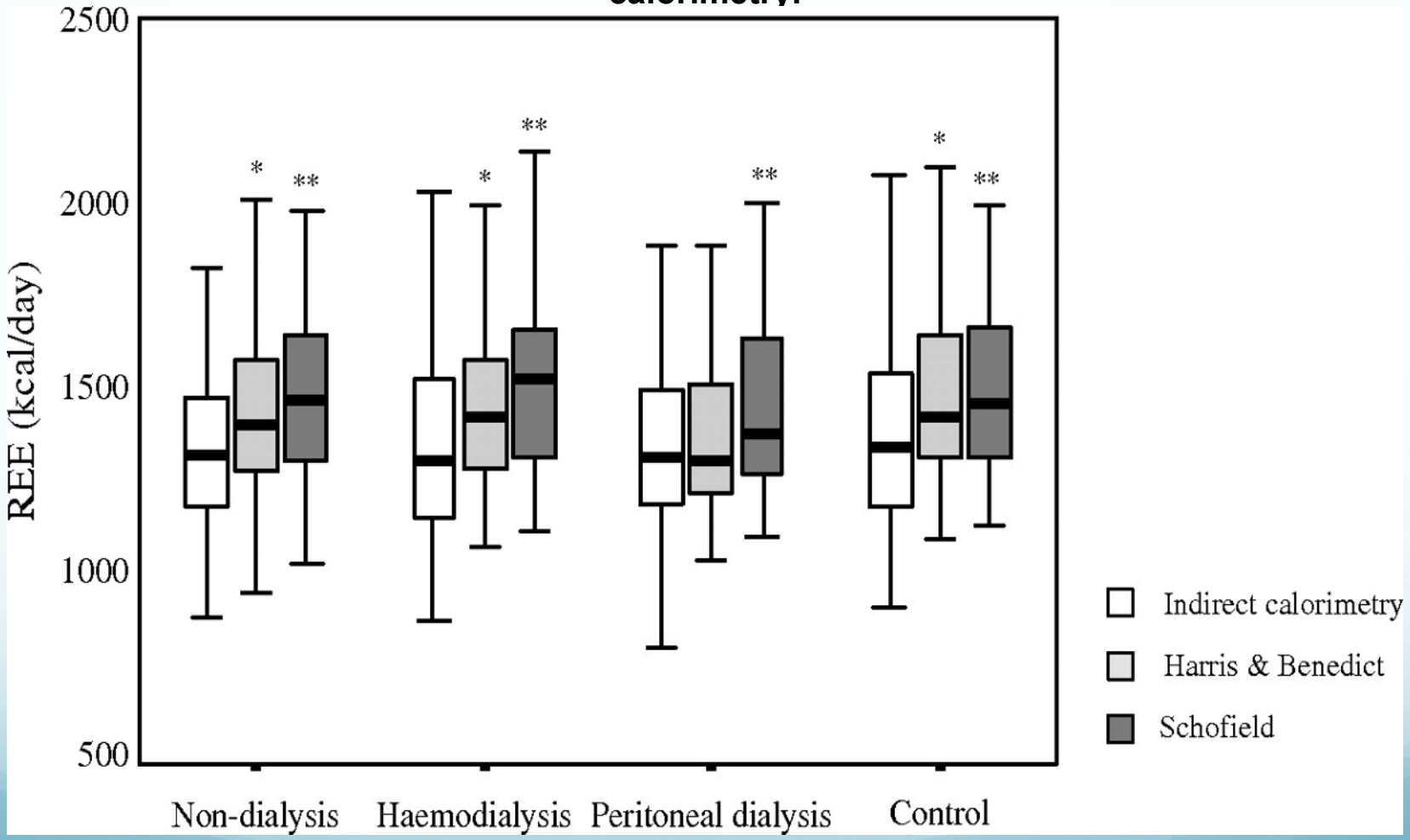
- Small sample size, not randomized control trial, short duration, dissimilar in design
- Diverse range of population and different ethnicity/age/ BMI/muscle mass
- Lack of detail on factors required to examine protein requirements (body weight-IBW, edema-free, DPI, physical activity)

Energy Requirements

- Assessment of energy expenditure (REE) is important for determination of energy recommendation.
- Identify factors associated with a disease that could modify the requirement.
- Calories absorbed from PD dialysates (CAPD, CCPD)

REE Prediction Equations

REE predicted by the equations against the reference indirect calorimetry. *P < 0.001 Harris and Benedict > indirect calorimetry; **P < 0.001 Schofield > Harris and Benedict and indirect calorimetry.



Kamimura M A et al. Nephrol. Dial. Transplant. 2011;26:544-550

Guidelines for Energy Requirements

EBPG 2005 and European Consensus[1]	**35 kcal/kg* (< 60 yrs)** **30 kcal/kg* (> 60 yrs)** ***standard body weight**
NKF/KDOQI 2000[2]	**35 kcal/kg/d < 60 yrs** **30-35 kcal/kg/d > 60 yrs**
Australian Evidence Based Practice Guidelines for the Nutritional Management of CKD, 2006[3]	**30□35 kcal/kg IBW**
European Society of Parenteral and Enteral Nutrition (ESPEN)	**35 kcal/kg/d**

Includes energy intake from nutrients absorbed from dialysate

[1] Francesco L et al, Nephrol Dial Transplant 2002; 17:563-572
[2] 2000 Update National Kidney Foundation KDOQI
[3]Ash S. Nutrition and Dietetics 2006; 63 (Suppl s2): s33-s45

Calories from PD Dialysate

- Depends on dextrose concentration, dwell time, number/volume of exchanges, types of PD
- Estimation dextrose absorption: *60-70%* with CAPD; *~50%* CCPD.
- Pts with normal peritoneal transport capacity, ~60% of dialysate glucose load is absorbed / ~ 100-200g glucose/d (~ 340-680 kcal/d)[2]
- Calories could account for more than 1/3 of daily needs.

[1] **Burkhart J. Semin Dial. 2004; 17:498-504**
[2] **Heimburger O et al, Kidney Int 1992 May 41(5): 1320-32**

Resting Energy Expenditure (REE) of PD = Healthy Population?

- REE are similar to those of normal adults 35kcal/kg – positive nitrogen balance could only be attained with EI > 30 kcal/kg/d [1]

- Cross-sectional study of 37 PD pts (Brazil) and controls' EE by indirect calorimetry found REE was similar between groups[2]

[1] Bergstrom J et al, Kidney Int 1993; 44: 1048-1057

[2] Bazanelli AP et al. Perit Dial Int 2006 Nov-Dec 26(6) 697-704

REE (Higher in PD)

Wang A et al. Hong Kong

- Loss of RRF (far outweighing that of other factors, including DM, CVD, C-reactive protein, S-alb) is associated with increased REE

- Rationale – Loss of RFF: increases uremia, inflammation, with increased risk CVD

Wang A et al. J Am Soc Nephrol 15: 3134-3143, 2004

Energy Requirement Limitations

- Age difference but not race – How about those with PEW, obesity, elderly?
- No simple biomarker exists to determine the energy intake (EI) of an individual
- Dietary self-reporting methods are largely used to assess EI in epidemiological surveys and in clinical studies (accuracy?)

Summary of Guidelines of PI &EI

	Protein	Energy
European Best Practice Guidelines (ENPG) 2005	**> 1.0g/kg/d**	**35 kcal/kg* (<60 yrs)** **30 kcal/kg* (>60 yrs)** *standard body weight
NKF K/DOQI (2000)	**1.2-1.3g/kg/d** **> 50% HBV protein**	**35 kcal/kg/d <60 yrs** **30-35 kcal/kg/d >60 yrs**
Australian Evidence Based Practice Guidelines for the Nutritional Management of CKD, 2006 (4)	**1.2□1.4g/Kg IBW** **>50% HBV protein**	**30□35 Kcal/Kg IBW**
European Society of Parenteral and Enteral Nutrition (ESPEN)	**1.2-1.5g/kg/IBW** (additional 0.1-0.2g/kg/d if peritoneal inflammation occurs) >50% HBV protein	**35 kcal/kg/d**

Comparison to Other Modalities

	Pre-Dialysis	HD	PD	Transplant
Protein (g/kg/d)	0.8-1.0 >50% HBV	1.2 >50% HBV	1.2-1.3 >50% HBV	1.3-1.5 (1st 6-8 wk) Long term: 1.0
Energy (kcal/kg/d)	35 <60yr 30-35 >60yr	35 <60yr 30-35 >60yr	35 <60yr 30-35 >60yr	Sufficient to maintain optimal weight

Points to consider

- No studies exist to determine whether provision of additional protein and calories to reach target recommendations will change the outcomes of mortality and morbidity.
- No randomized , prospective, controlled trials have been carried out to examine this question.
- Main risk of increasing protein/calorie intake= need to increase in dialysis dose, of PO4 binder therapy

Challenges

- Typical patient intake compared to healthy individual.

  (Example of 70kg male)
- PD dialysate volume – gastric fullness, satiety
- Glucose absorbed from dialysate and dwell time – anorexia.
- Multiple comorbidities and dietary restrictions.

Challenges

- Actual protein intake: ~ 0.95-1.0g/kg/d;

  Energy intake: ~ 23-28 kcal/kg/d[1]

- Japanese study by Yoshihiko[2]: Compliance to protein recommendation is low ~77.3%; EI~85%

[1] Cianciaruso B et al. Am J Kidney Dis 26: 475-486, 1995

[2] Yoshihiko K et al. Contrib Nephrol. Basel, Karger 2007, vol 155, pp72-81

Strategies to “Fill In” the Gap

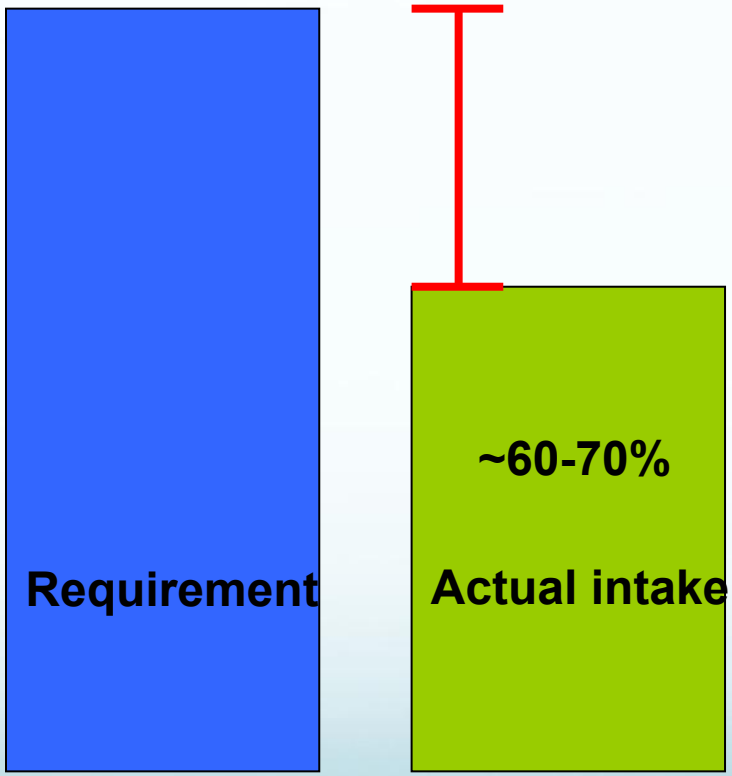
EI
REE
EEPA

Nutrient loss during dialysis

Inflammation

Hypercatabolic illness

Endocrine disorders



Anorexia

PD dialysis

Catabolism

Acidosis

Inflammation

1. Oral Nutritional Supplementation

- Boudville et al 2003: Australia n=13
- Substitution of food supplements for regular food with no net gain in calories or protein intake
- Meta-analysis of all oral supplement trials suggested that oral supplement improved serum albumin levels in patients with severe energy wasting[1]
- Oral nutritional supplements, protein powder

[1] **Stratton RJ et al. Am J Kidney Dis 46:387-405, 2005**

Nonrandomized Trials in Patients Undergoing Peritoneal Dialysis

Table 4 | Nonrandomized trials in patients undergoing peritoneal dialysis

Study	Intervention modality, duration and study design	Patients and condition (*n*)	Results and conclusions
Shimomura *et al.* (1993)[76]	Protein dessert with high biological value (0.1–0.3 g/kg daily) for >6 months	CAPD (18) No control arm	Increased serum levels of total protein, albumin, prealbumin, transferrin, total amino acids, EAA/non-EAA ratio, Kt/V urea, PCR Albumin levels rose from 32.5 g/l to 33.1 g/l in patients given the dessert, whereas patients in the control group had an albumin level of 38.8 g/l and 37.7 g/l before and after the study period, respectively
Patel & Raftery (1997)[77]	Standard ONS (Protein Forte [Fresenius Kabi, Bad Homburg, Germany] and Ensure® Plus [Abbott Nutrition, Columbus, OH, USA]) vs routine care for 8 weeks	PD (22) Case (10) Control (12)	Increased serum albumin levels, nPCR, DPI and DEI in the group taking supplements Significant difference in BMI and protein intake between the groups
Heaf *et al.* (1999)[78]	Standard ONS (Fortimel [Nutricia, Schiphol, The Netherlands]) vs usual diet for 10 weeks	PD (42) Case (12) Control (30) Albumin concentration <36 g/l	No improvement in nutritional status; albumin levels decreased in both groups Condition worsened in half of patients because of nausea
Boudville *et al.* (2003)[79]	CKD-specific ONS (Nepro®, Abbott Nutrition) vs calorie-free placebo; crossover design	PD (13) Baseline albumin concentration 34.8 g/l	Drinking the supplement 2 h before lunch resulted in a significant increase in total caloric intake as compared with during the placebo visit (843 kcal vs 430 kcal, respectively; $P<0.001$) and protein intake (41.3 g vs 27.6 g, respectively; $P=0.006$)
Teixidó-Planas *et al.* (2005)[80]	Non-CKD-specific ONS (Protenplus®, Fresenius); multicenter, randomized study for 6–12 months	PD (70) Case (35) Control (35)	Increased total lymphocyte count in the 'intention to treat' analysis In the 'as treated' analysis (9 cases, 20 controls): increased body weight ($P<0.03$), triceps skinfold thickness ($P<0.01$), mid-arm-muscle circumference ($P<0.03$), lean body mass ($P<0.002$), creatinine generation rate ($P<0.002$) in the group taking the supplement High noncompliance rate: 15 patients stopped ONS

Abbreviations: CAPD, continuous ambulatory peritoneal dialysis; CKD, chronic kidney disease; DEI, dietary energy intake; DPI, dietary protein intake; EAA, essential amino acid; nPCR, normalized protein catabolic rate; ONS, oral nutritional supplement; PD, peritoneal dialysis.

Kalantar-Zadeh, K. *et al.* (2011) Diets and enteral supplements for improving outcomes in chronic kidney disease
Nat. Rev. Nephrol. doi:10.1038/nrneph.2011.60

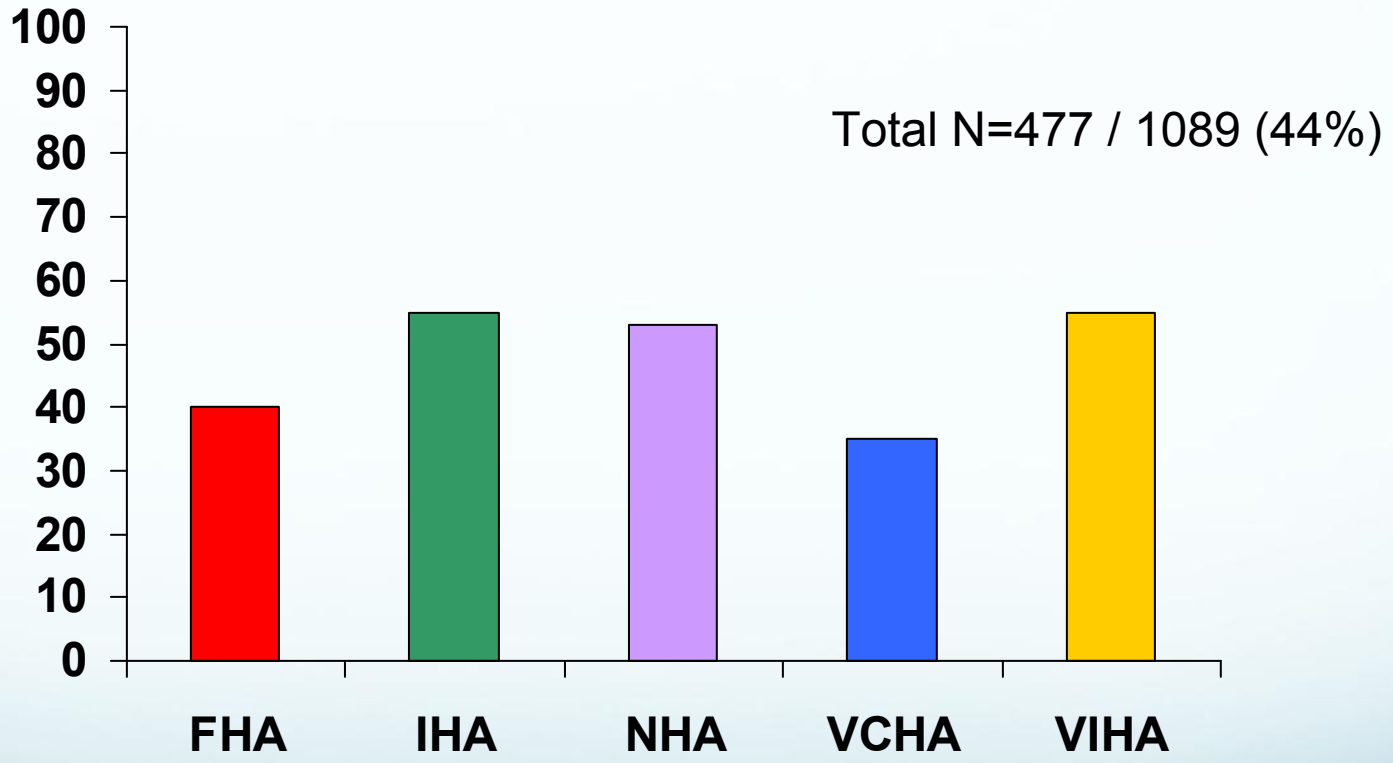
Effects of Oral Supplements on Nutritional Status in Patients on Peritoneal Dialysis

Study	Study type	Population	Interventions	Follow-up	Results
Shimomura *et al.* (1993)[109]	Nonrandomized controlled	36	Supplement of 0.1–0.3 g protein per kg per day (n=18); controls had no supplement (n=18)	6 months	↑ serum albumin, prealbumin, transferrin, plasma total amino acids, and the ratio of essential amino acids to nonessential amino acids
Heaf *et al.* (1999)[110]	No control group	14	Commercial supplement with 40 g protein per day	10 weeks	No change in serum albumin, DPI, calorie intake and nPNA
Eustace *et al.* (2000)[111]	Randomized double blind placebo-controlled	47 (18 on PD and 29 on HD)	Oral essential amino acid tablets vs placebo	3 months	No change in serum albumin level or grip strength; ↑ skinfold thickness
Aguirre Galindo *et al.* (2003)[112]	Randomized	100	High protein diet (1.4 g/kg per day) (n=50) vs calcium caseinate diet (n=50)	4 months	↑ serum albumin level and total protein in both groups
Boudville *et al.* (2003)[113]	Single blind crossover	13 on PD	Commercial supplement with 475 kcal and 16.6 g protein	ND	↑ serum albumin level, total calorie and protein intake
Teixidó-Planas *et al.* (2005)[114]	Randomized controlled	75	Commercial supplement with 20 g of protein per day	12 months	No change in serum albumin level; high rate of noncompliance and intolerance to commercial protein supplement
González-Espinoza *et al.* (2005)[115]	Randomized controlled	30	Egg albumin supplement with 30 g protein per day (n=13); control (n=15)	6 months	↑ serum albumin, total calorie and protein intake, and nPNA
Poole and Hamad (2008)[116]	No control group	190 (157 on HD and 33 on PD)	20–30 g protein and 500 kcal per day for nondiabetics; 13.8 g protein and 250 kcal per day for diabetics	3 months	↑ serum albumin (HD only); no significant improvement in PD
Moretti *et al.* (2009)[117]	Randomized crossover	49 (6 on PD and 43 on HD)	PD: 105 g protein per week; HD: 45 g protein per week	12 months	No change nPCR and ↑ serum albumin level in protein supplemented group; ↓ nPCR and serum albumin level in controls

Abbreviations: DPI, dietary protein intake; HD, hemodialysis; ND, not determined; nPNA, normalized protein nitrogen appearance; nPCR, normalized protein catabolic rate; PD, peritoneal dialysis.

Han, S.-H. & Han, D.-S. (2012) Nutrition in patients on peritoneal dialysis *Nat. Rev. Nephrol.* doi:10.1038/nrneph.2012.12

Oral Nutritional Supplement Use Across BC



Intraperitoneal Amino Acids

- Amino Acid 1.1% (Nutrineal)
- 1 bag/day – with lunch/supper to enhance absorption
- Provides 17-18g amino acids
- Expensive

Low Phosphorus to Protein Ratio Food

- Food with high amount of protein and small amount of phosphorus
- Lower PO4 level without risking malnutrition
- Example: egg white

Taylor LM. J Ren Care 2011 Mar;37(1):16-24

Noori N et al. Clin J Am Soc Nephrol 2010 Apr;5(4):683-92

Caloric-Dense Food

- Replace current food/snack with higher energy and protein content.
- Specialty high protein/energy bars, cookies, pudding
- Know what is available in the market and be creative.

Liberalize Diet Restrictions

- Set priorities
- Diabetes, low salt, lipids, PD (potassium, phosphorus)…..vegetarian…..gluten free.
- Eats while “empty”

Minimize Protein Loss

- Adequate dialysis
- Preserve peritoneal membranes
- Watch for and treat infection/inflammation/ wounds to preserve protein (albumin) in the body

Conclusion

- PD populations: Dialysate, anorexia, inflammation, dialysis prescription affects protein/energy requirement and po intake.
- Understand current evidences, guidelines and limitations.
- Protein intake should not be considered in isolation from energy intake.
- Development of valid prediction equations for estimating energy expenditure.
- Ongoing nutrition assessment and counselling to “fill in” the gap.

References

(Studies on protein requirement)

Aguirre Galindo BA et al Perit Dial Int 2003; 23: 434□9

Chen WG Journal of Chinese Integrative Medicine 2008; (5): 473□7

Chow VCY Perit Dial Int2003; (SUPPL. 2): S52□S54

Gonzalez□Espinoza L et al. Perit Dial Int 2005 Mar; 25(2): 173□80

Sutton D Journal of Renal Nutrition 2007 Sep; 17(5): 329□35

Wang AYM. Am J of Kidney Diseases 2007;(5):682□92.

Questions