Home Dialysis University

THE LONG TERM HOME DIALYSIS PATIENT: How to keep patients on the therapy of their choice

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USF HEALTH

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Consultant: Fresenius Medical Care

Case presentation #1

A 38 yo female developed ESRD secondary to lupus nephritis. She was told that by a transplant surgeon that she should not do peritoneal dialysis because she would gain weight and not be eligible for a kidney transplant. First attempt at AVF in her non-dominant, left arm was unsuccessful and she elected to have left upper extremity AVG.

She was briefly on in-center HD but quickly elected to do home hemodialysis. She worked full time but was also an amateur off, off, off, off Broadway actress. She is 5'5" and weighed 140 pounds. She had some residual renal function. She was started on 5d/week SDHD but after 2 years she became overwhelmed with HHD and could not keep up with her work and after work activities and still find time to do SDHD. She melodramatically refused to do in-center HD.

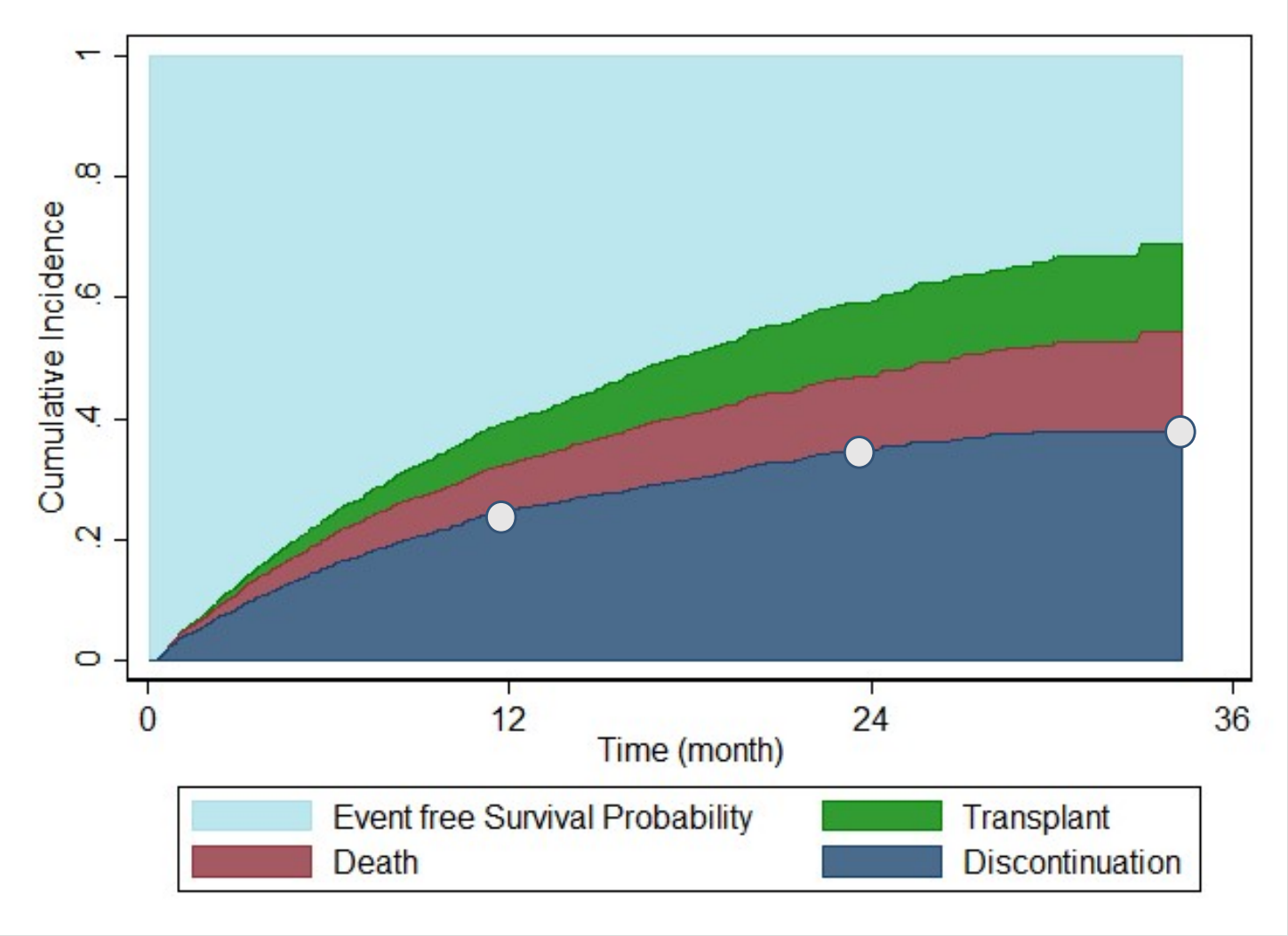
What are her options?

Goals

- How do we improve long term success of home dialysis patients?
  - Improve technique survival
  - Improve patient survival
    - Treat comorbidities that contribute to illness and death
  - Maintain psychological well-being of patients and their partners and prevent burnout

HHD Discontinuation
Seshasai, et al. AJKD 2016

24.9% 1-year discontinuation rate



Determinants of Peritoneal Dialysis Technique Failure In Incident US Patients

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

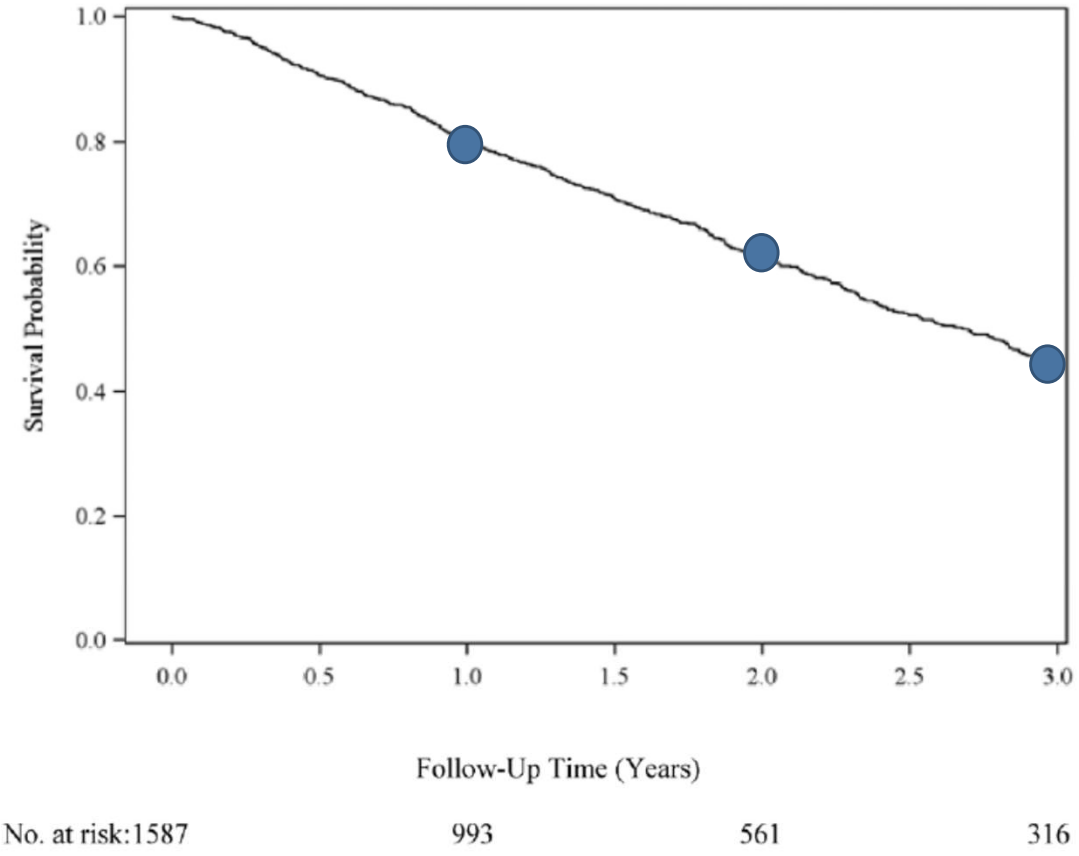


Figure 2 — Technique survival in patients initiating peritoneal dialysis. The Kaplan–Meier actuarial technique survival at 1, 2, and 3 years was 80.2%, 61.2%, and 45.2% respectively. Median survival was 2.7 years. Failure was defined as a switch from peritoneal dialysis to hemodialysis lasting 30 days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

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%**

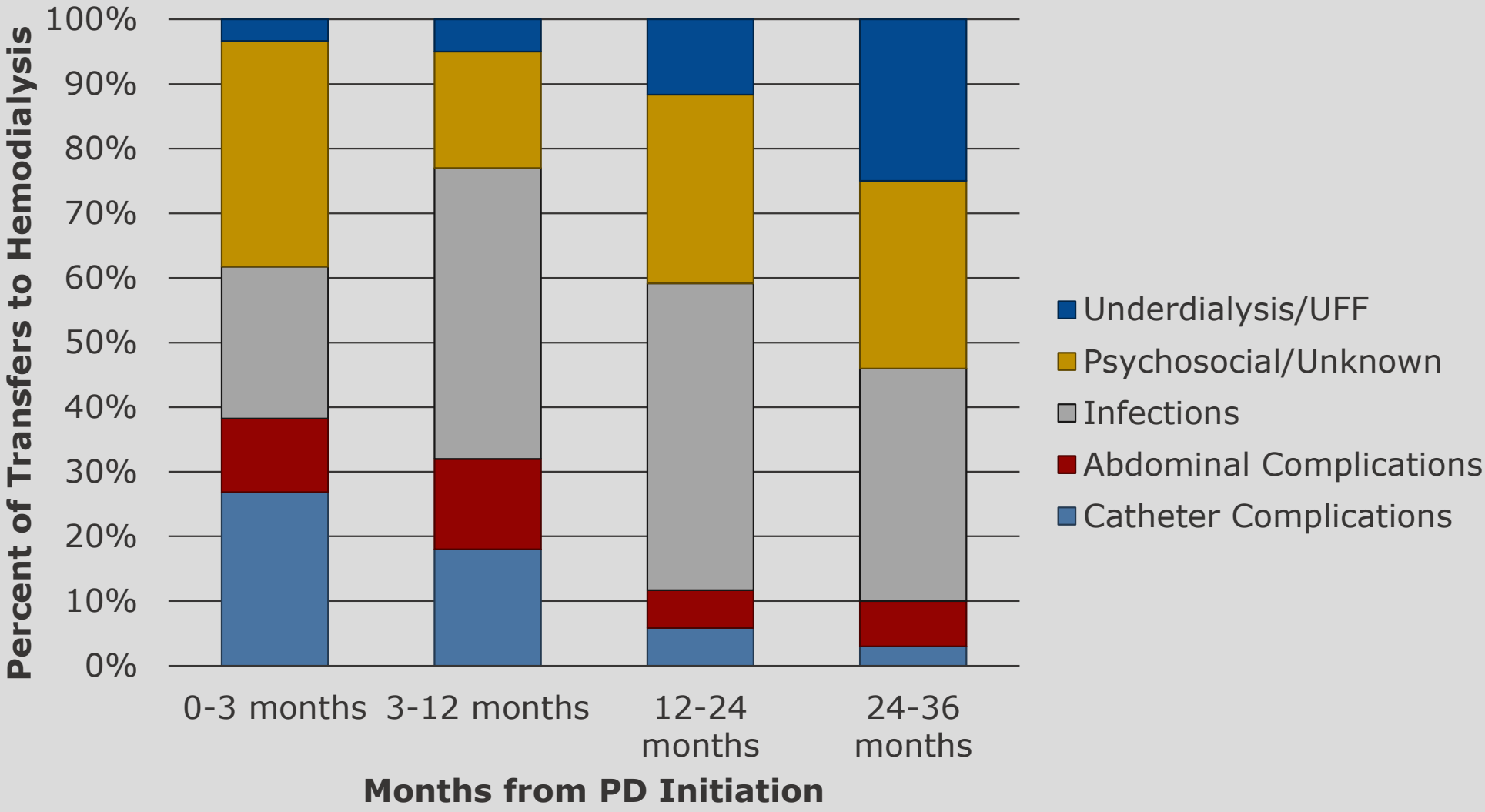
†Data adjusted for risk factors; ‡Estimated from published distribution

10y= 48%

Courtesy Dr. Anjali Saxena

Causes of Modality Change Vary by Time on Therapy

Kolesnyk et al PDI March 2010 – Vol 30, No 2

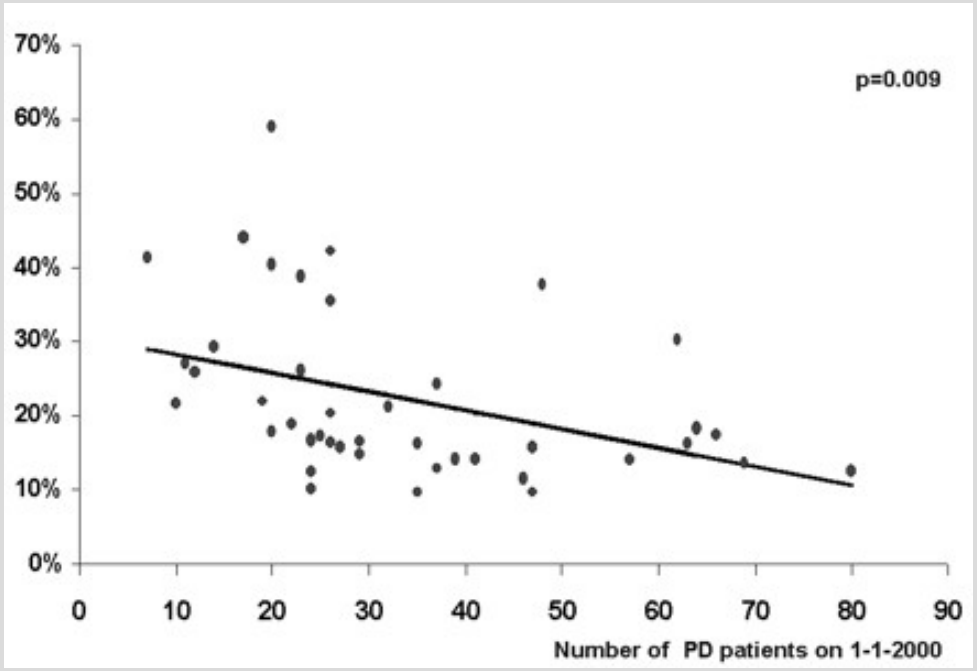


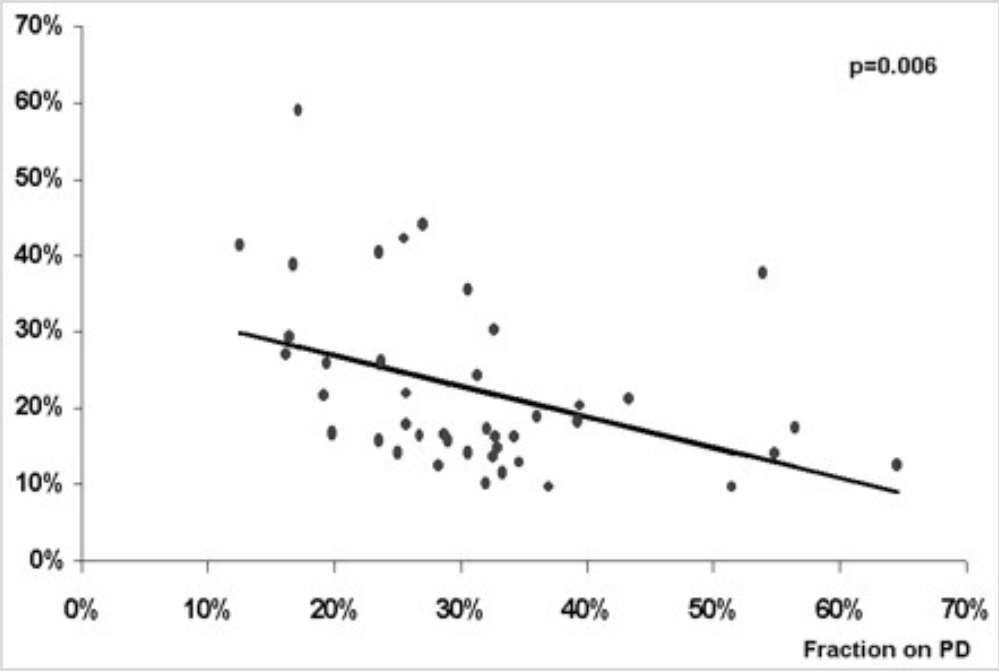
How do we improve long term success of home dialysis patients:
Get a good start!

- Prior to dialysis
  - Excellent CKD care
  - Excellent modality education
  - Early referral to transplant (eGFR<20)
  - Timely placement of access by an experienced surgeon
- Develop a quality home dialysis program
  - Provide the right infrastructure
  - Cultivate the best staff
  - SIZE COUNTS

The Center Effect

Huisman, Nephrol Dial Transpl 17: 1655-1660, 2002

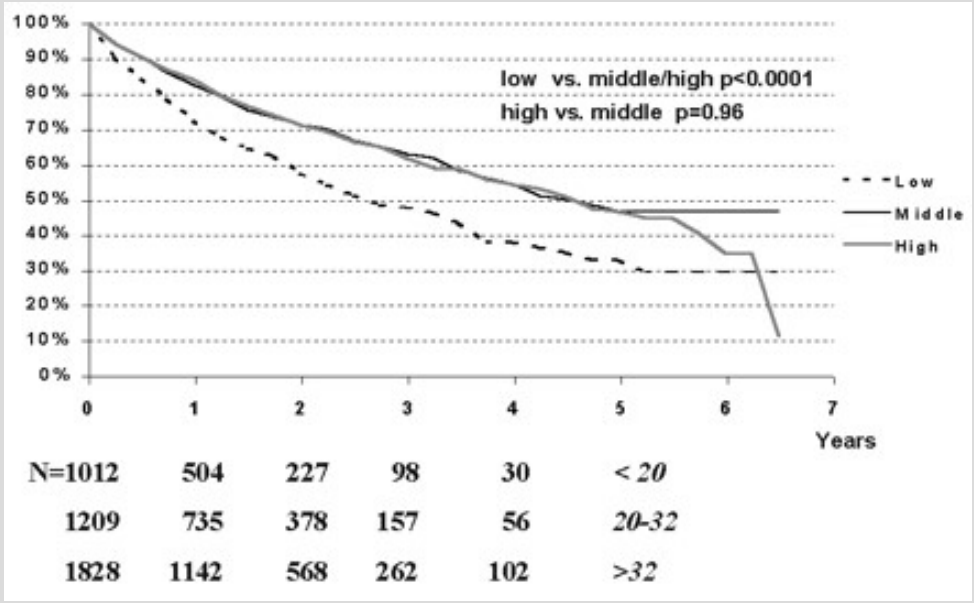




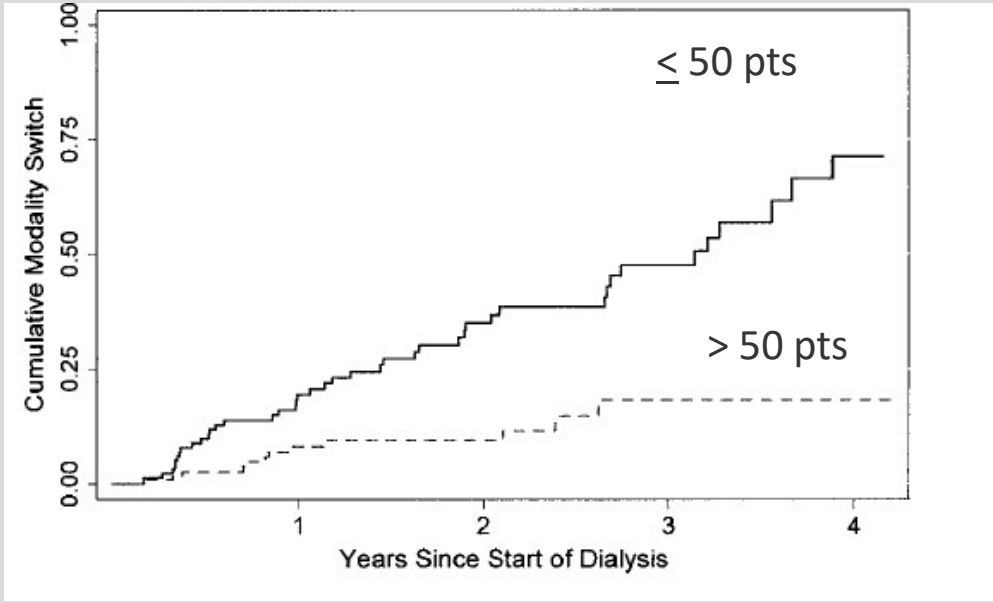
Technique Failure

More than 20 PD patients is the key, but >50 may be better!

Technique Survival



Huisman, Nephrol Dial Transpl 17: 1655-1660, 2002



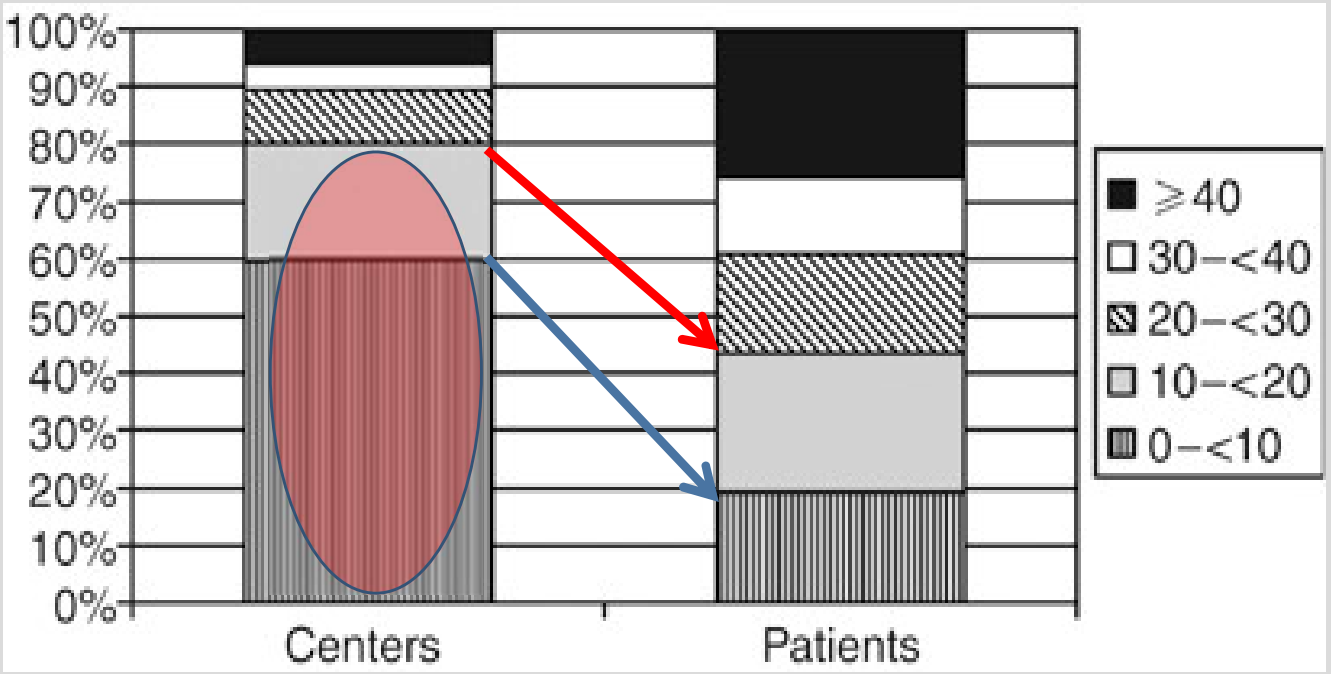
Plantinga et al PDI 29:285, 2009

Most U.S. programs are too small

Mujais S, et al. *Kidney Int.* 2006;70(suppl):S21-S26.

80% Centers have < 20 patients. Those centers take care of 43% of all PD patients

60% Centers have < 10 patients.



Distribution of centers by center size and proportions of PD patients treated in each individual center size category.

Why Size Matters

- Ability to:
  - Individualize therapy
  - Improve knowledge base
  - Gain nursing / MD experience (nephrologists, surgeons, etc)
  - Problem solving, easier with more experience
- CQI is broader, i.e. more diverse
- Staffing
- Better outcomes measured as:
  - Technique survival
  - Patient survival

Long-Term Home Dialysis Success

- **Long term effectiveness of modality**
  - **Preservation peritoneal membrane**
  - Peritonitis
  - Dialysis access
    - PD Catheter malfunction
    - HD access

  } Addressed

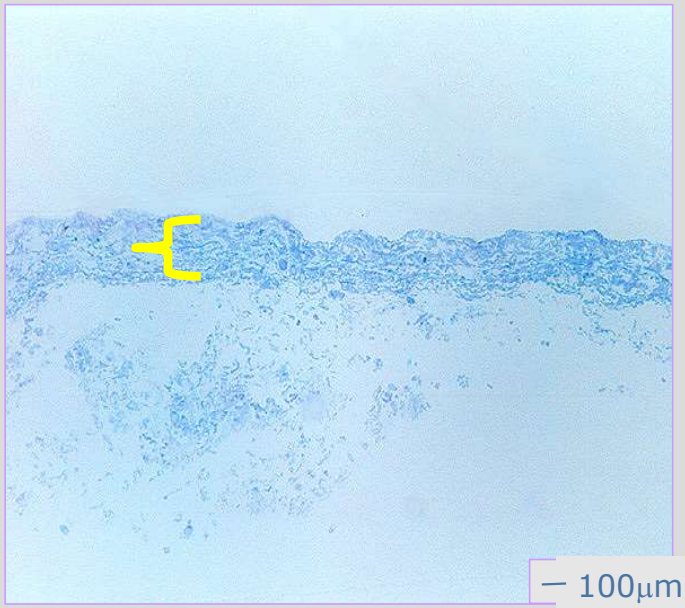
- **Improve patient survival**
  - Cardiovascular disease
  - Volume overload
  - Loss residual renal function
  - Metabolic derangements
- **Maintain patient and partner psychological well being**

Current Concepts About Membrane Changes Over Time

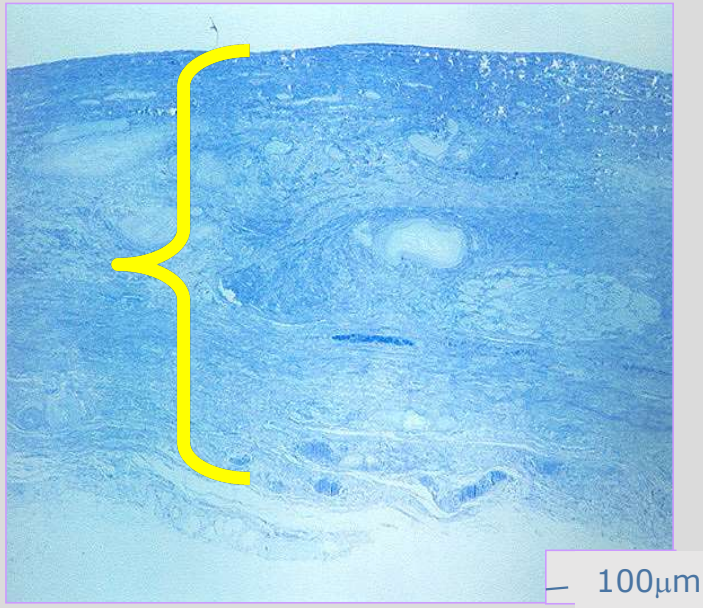
- The vasculopathy includes vascular proliferation, increasing "effective" peritoneal surface area
  - Responsible for some patients becoming more rapid transporters over time
- The submesothelial fibrosis physically obstructs the movement of water across the membrane
  - For any given osmotic gradient there will be less ultrafiltration
- So the long-term patient has a double-whammy:
  - More rapid transport status and dissipation of the glucose osmotic gradient
  - Less ultrafiltration for any given osmotic gradient

Morphological Changes in the Peritoneal Membrane

Normal peritoneal membrane



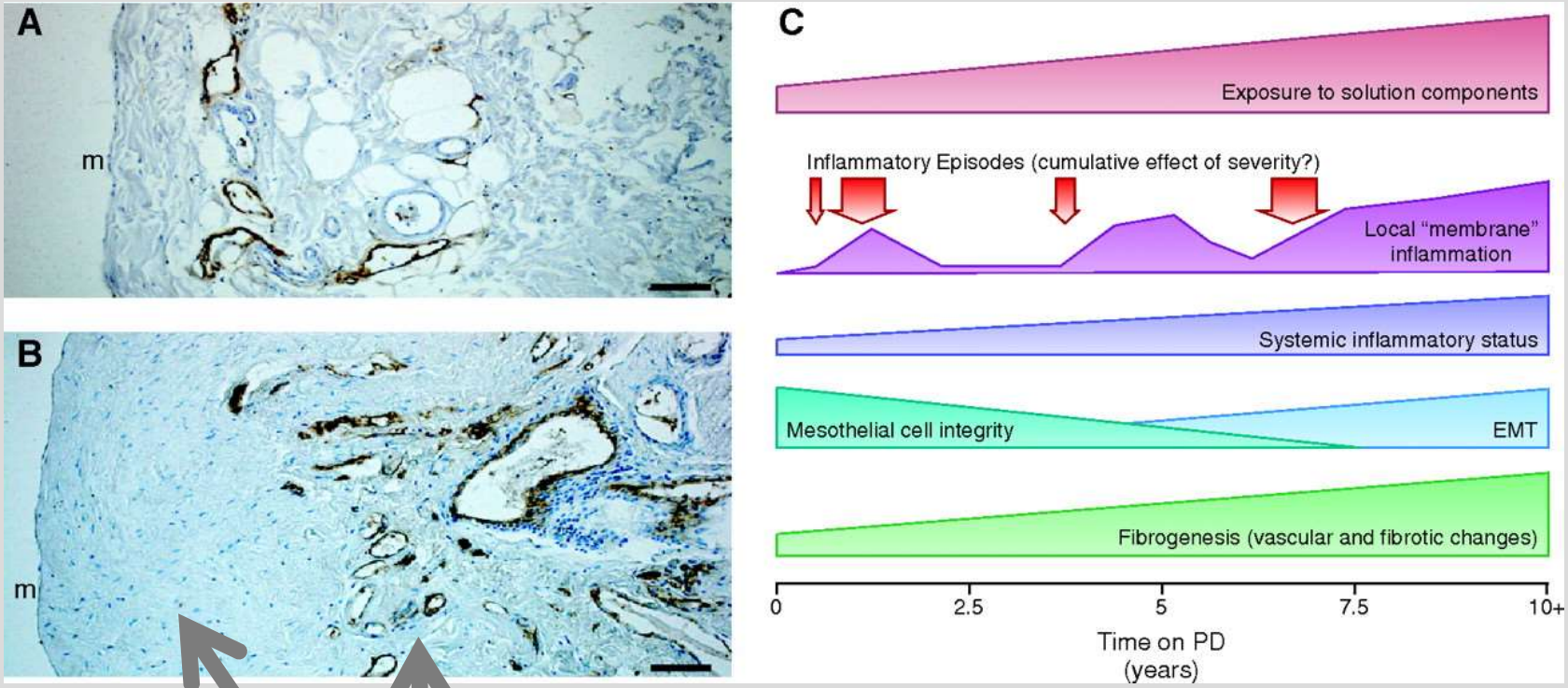
peritoneum >5 years PD



Williams et al. Cardiff Peritoneal Biopsy Registry

Long-term changes in the peritoneal membrane
Devuyst O et al. JASN 2010;21:1077-1085

Initiation of PD



After 5 years

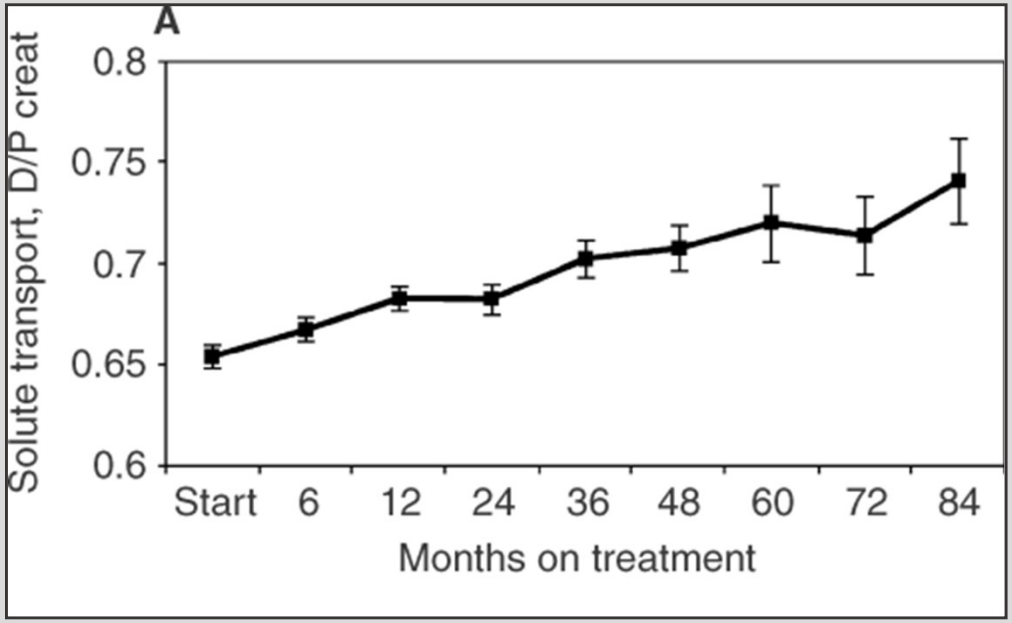
Fibrosis

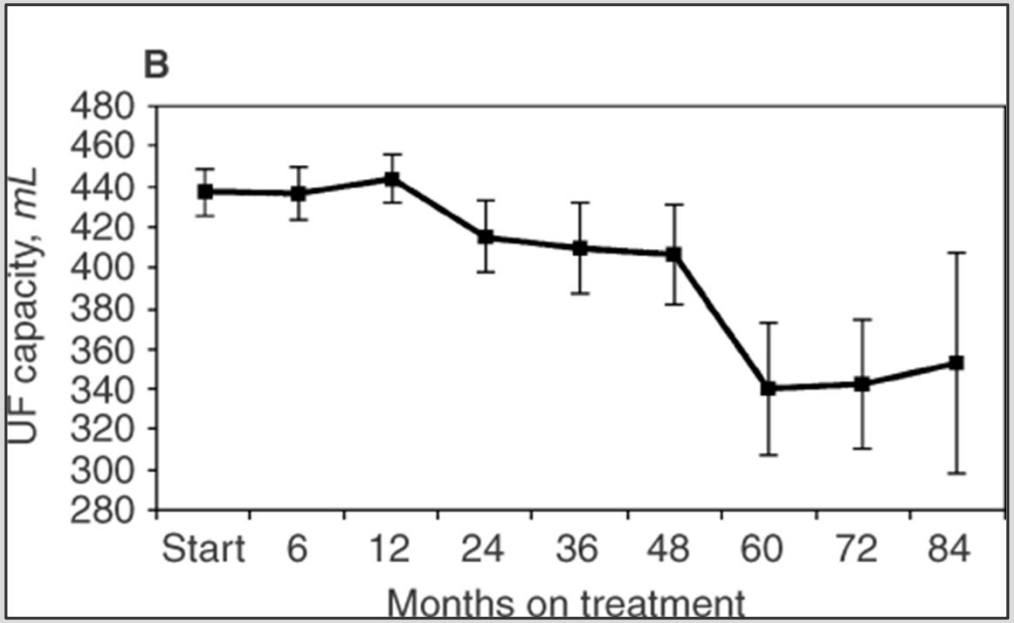
New blood vessel formation

Functional Consequences of Peritoneal Membrane Damage

Davies, Kidney Int 2004; 66: 2437-2445

↑ capillary density → ↑ effective peritoneal surface area → ↑ peritoneal solute transfer rate





Baseline: 574 subjects

One-year: 299

Seven-year: 27

Proposed Causes of Membrane Changes

- "Uremia"
- Recurrent peritonitis
- **Exposure to dialysate - bioincompatible**

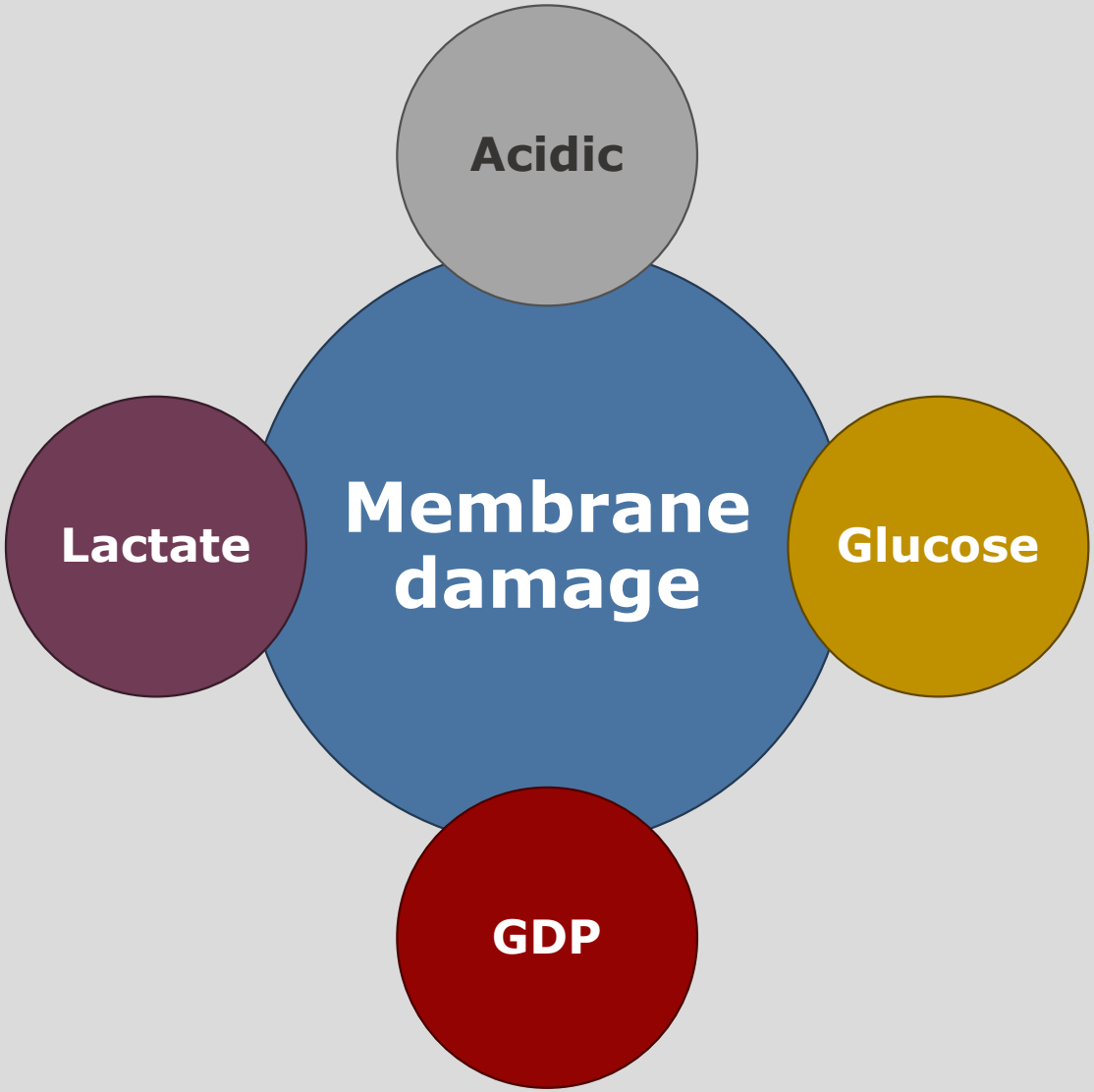
Definition of BIOCOMPATIBLE:

compatible with living tissue or a living system by not being toxic, injurious, or physiologically reactive and not causing immunological rejection

-Merriam-Webster Medical Dictionary

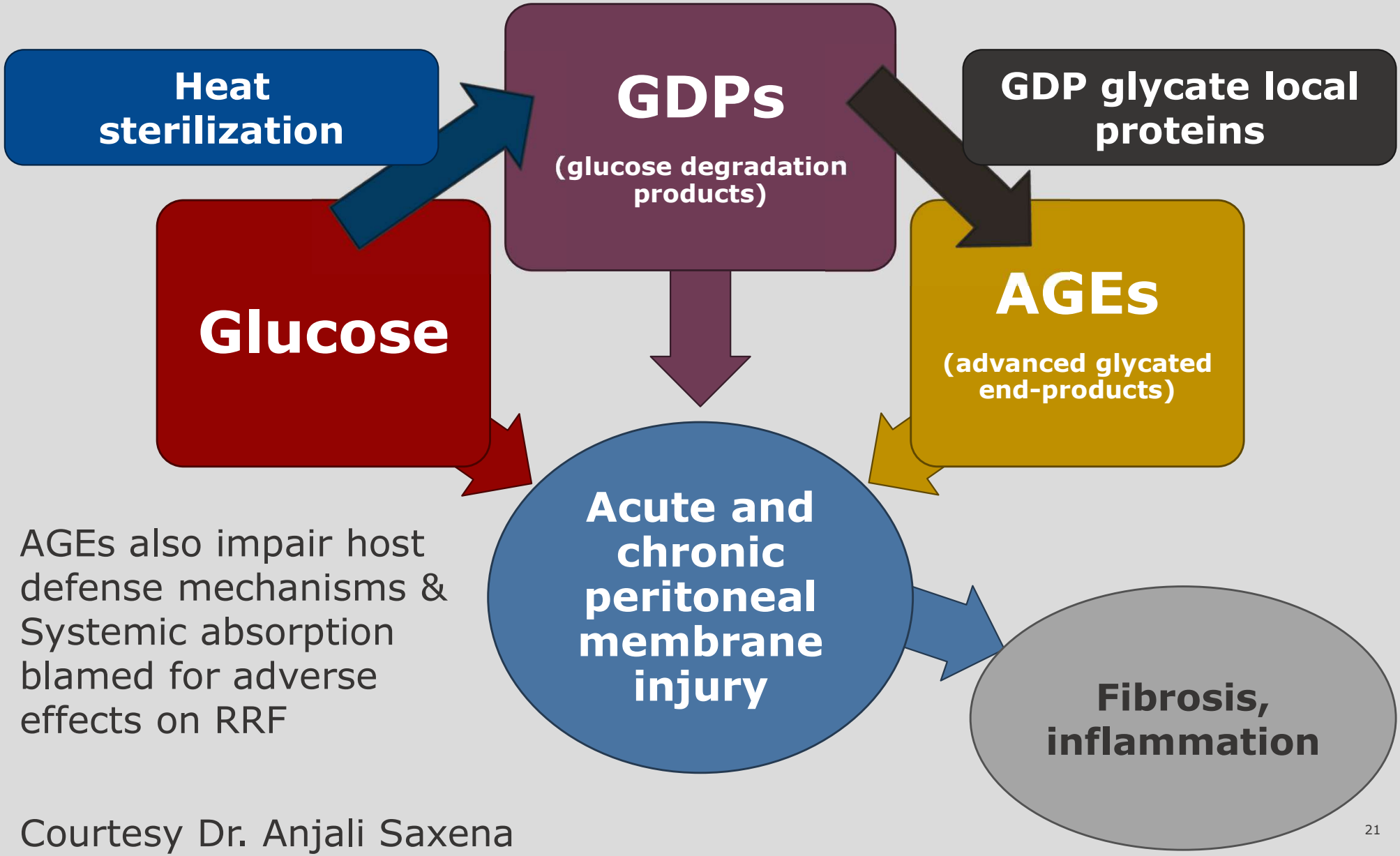
Courtesy Dr. Anjali Saxena

Damaging Components of PD Fluid



Courtesy Dr. Anjali Saxena

Adverse Effects of Glucose-based PD Solution



AGEs also impair host defense mechanisms & Systemic absorption blamed for adverse effects on RRF

Courtesy Dr. Anjali Saxena

Is Glucose Exposure the Cause?

- Even hemodialysis and CKD patients have abnormal peritoneal membranes

BUT

- Animal models show similar changes when the membrane is exposed to hypertonic glucose
- Glucose inhibits mesothelial cell proliferation and causes intracellular damage *in vitro*

Peritoneal Glucose Exposure Associated Membrane Changes

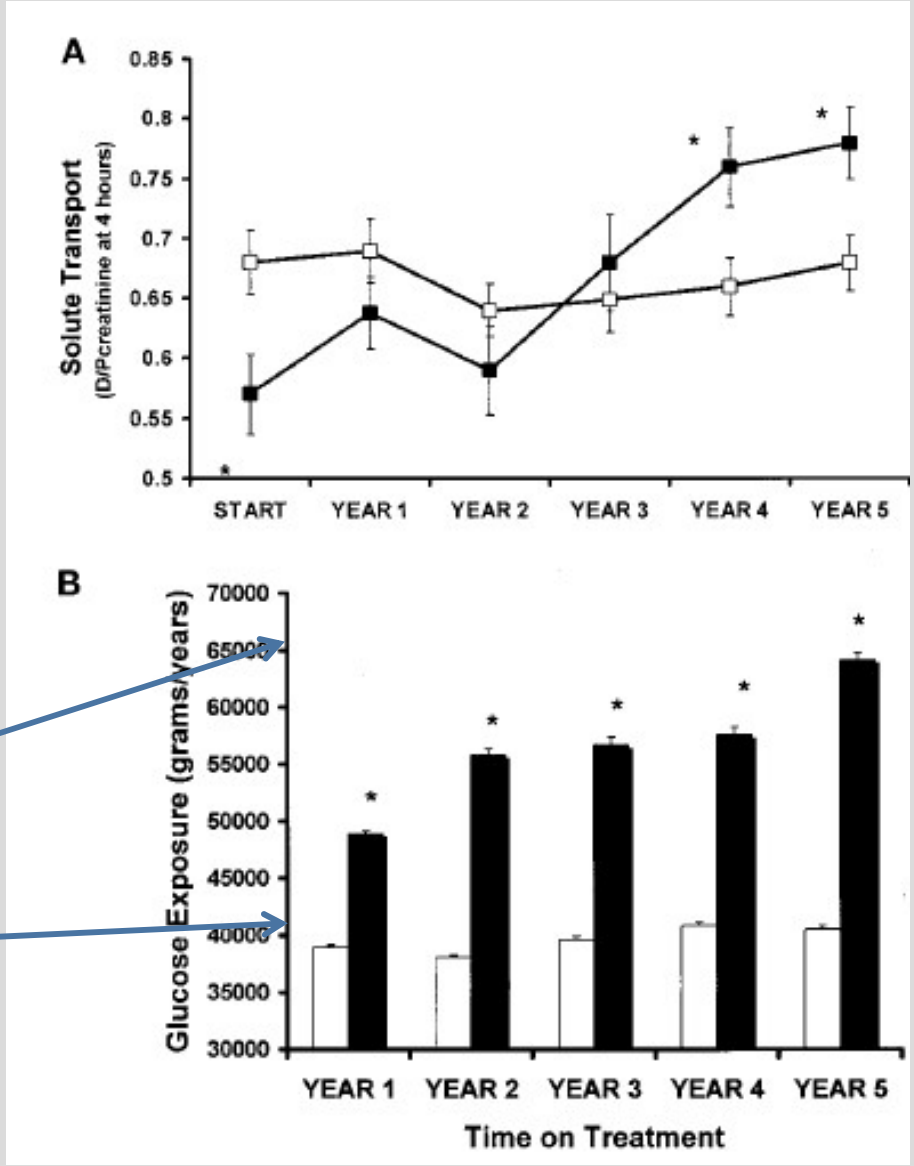
Davies et al. JASN 12:1046, 2001

- All pts completed 5 yrs of PD
- Filled squares and bars are those who D/Pcr rose (N =9)
- Open squares and bars are those with stable D/Pcr (N=13)
- Conclusion
  - Hypertonic dextrose may cause alterations in peritoneal membrane function

65000~ 4x2L 2.5%

40000~ 4x2L 1.5%

Benefit of incremental PD?



Mitigating Membrane Damage

- Less glucose
- Pharmacological interventions to preserve the membrane?
- Biocompatible solutions
- Membrane rest

Reasons To Consider Use Of ACEI or ARB In PD Patients

- BP control
- CV risk reduction
- Preservation of RKF
- Prevention of membrane changes?

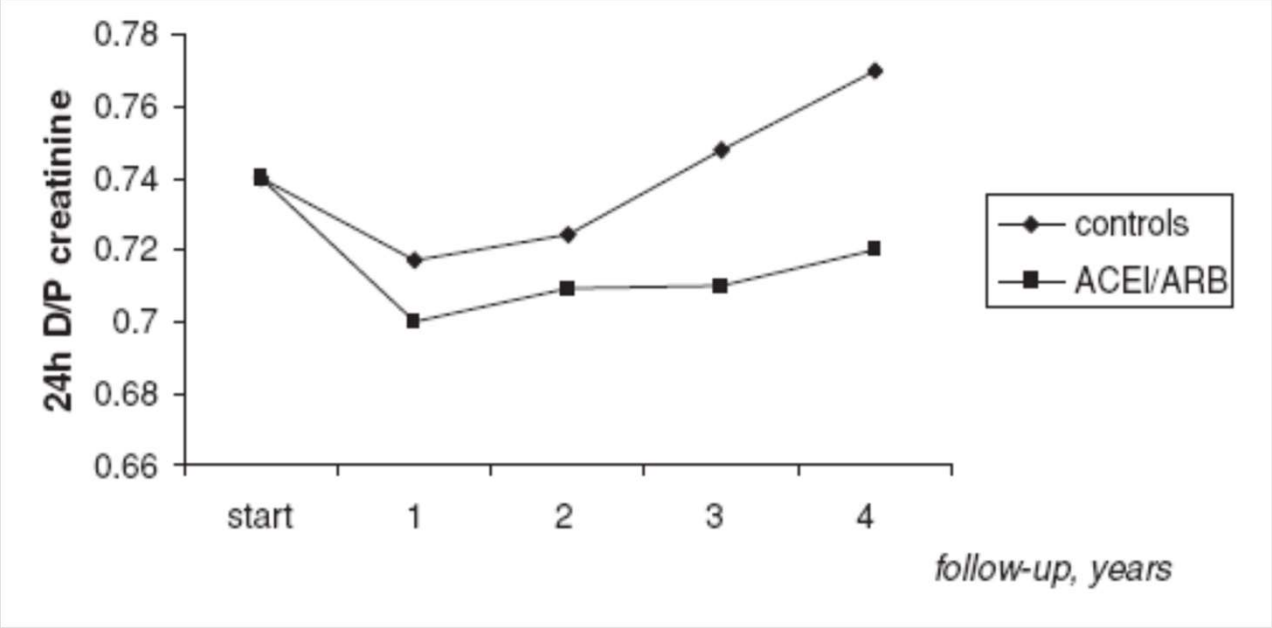
The Rationale For ACEI/ARBs Protection of Peritoneum

- Angiotensin II is a growth factor in the development of renal fibrosis
- The effects of Angiotensin II are likely to be mediated by TGF_{β}
- ACE inhibitors attenuate the renal expression of TGF_{β} in patients with IgA nephropathy (Park et al. NDT 18:1115, 2003)

RAAS Blockade and Membrane Transport Changes

Kolesnyk et al. NDT 216:1, 2008

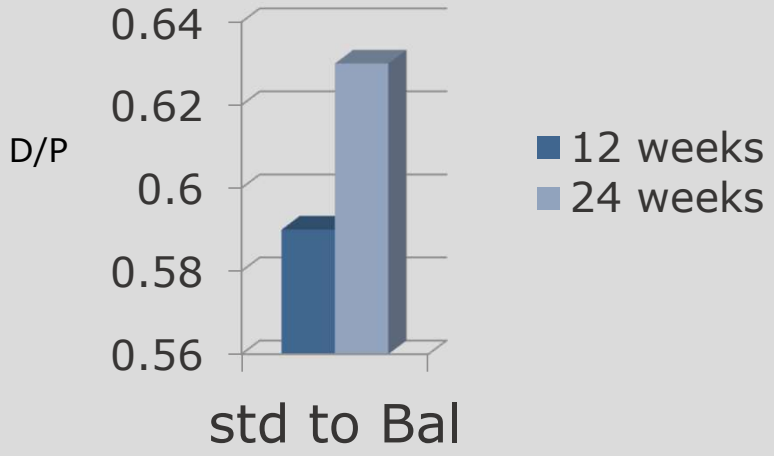
- Multicenter (38 units) observational cohort
- Started CAPD 1997-2006
- Stay on for 2 years
- Use between 8 and 10 L/day
- 97 no ACE or ARB: 120 on ACE or ARB > 3 months

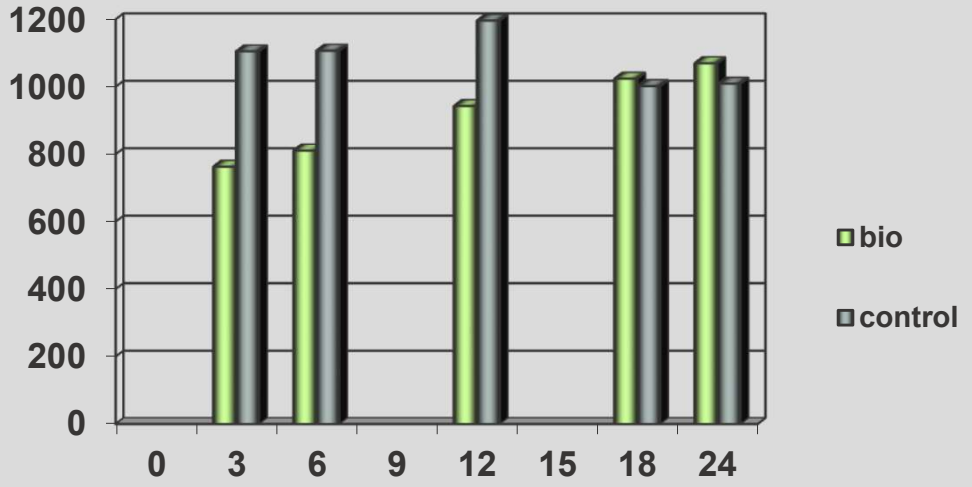


What about new biocompatible solutions?

Johnson et al J Am Soc Nephrol 2012; Kidney Int 2004 66: 408-18

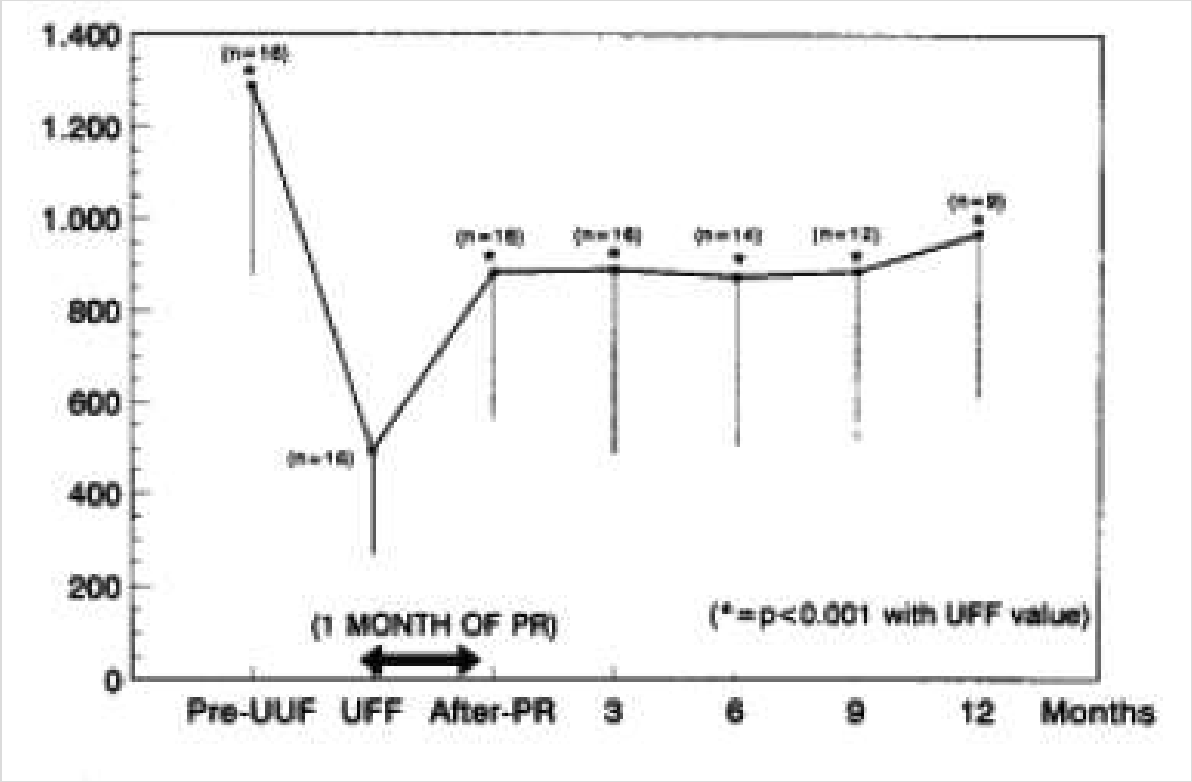
- Biocompatible
  - Neutral pH (contains bicarbonate)
  - Low degradation products
- Solute transport (D/P creat): Increase
- Fluid removal UF: Decrease
- Decrease time to first peritonitis
- Mixed results on peritonitis rates
- Better preservation residual renal function





Membrane Resting: Improvement in UF?

De Alvaro (Selgas) et al Adv PD 9:56, 1993



- 25 rest periods in 16 pts (4 weeks of no PD)

  15 regained UF ability (improved from 500 to 900 mL/day)

- Benefit lasted > 12 months

Long-Term Home Dialysis Success

- Long term effectiveness of modality
  - Preservation peritoneal membrane
  - Peritonitis
  - Dialysis access
    - PD Catheter malfunction
    - HD access
- **Improve patient survival**
  - **Cardiovascular disease**
  - Volume overload
  - Loss residual renal function
  - Metabolic derangements
- Maintain patient and partner psychological well being

Cardiovascular

- BP
- Volume

} Addressed

- Lipids - 3 studies
  - 4D
  - AURORA
  - SHARP

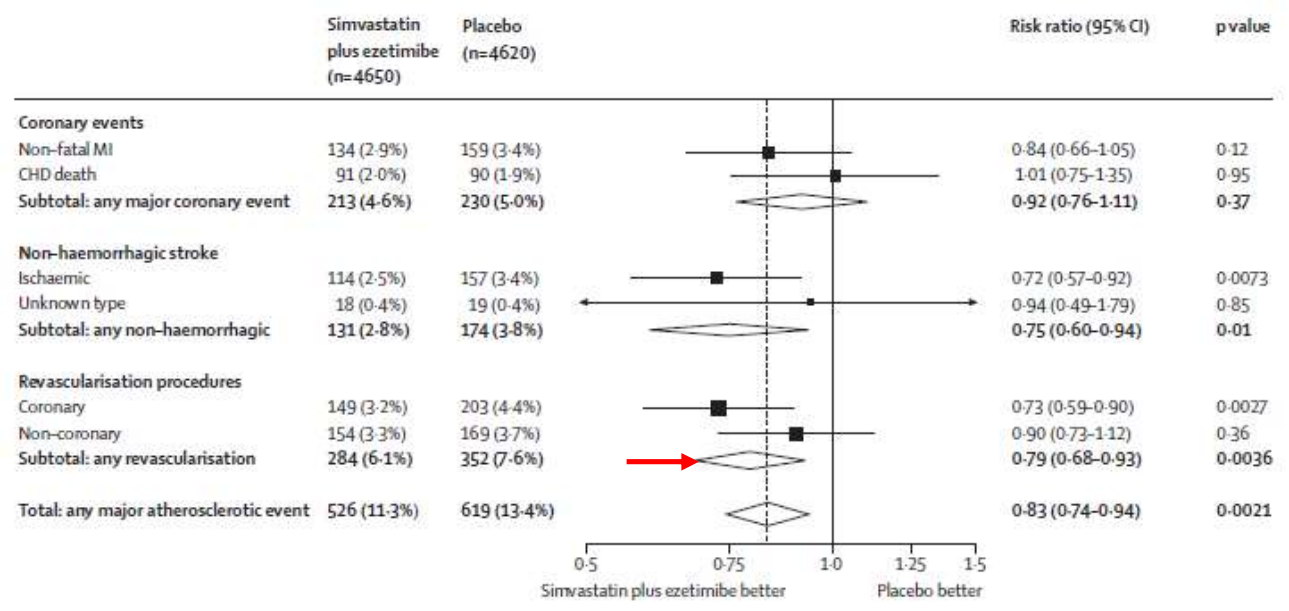
Lipid Trials in CKD and ESRD

	N	Population	Inclusion	Treatment	Outcome	Conclusion
4D **Wanner et al, N Engl J Med 2005; 353:238-248**	1300	• Hemodialysis	• 18-80 years • DMII • LDL-C: 2.1-4.9mmol/L • No CV events x 3 mos	Atorvastatin 20 mg vs. placebo	**Composite:** • Cardiac death • non-fatal MI • stroke	• Atorvastatin had **no significant** effect on composite end point in diabetic HD patients
AURORA **Fellstrom et al, N Engl J Med 2009; 360:1395-1407**	2776	• Hemodialysis	• 50-80 years	Rosuvastatin 10 mg vs. placebo	**Composite:** • Cardiovascular death • non-fatal MI • stroke	• Rosuvastatin lowered LDL but had **no significant** effect on composite end point
SHARP **Baigent et al, Volume 377, Issue 9784, P2181-2192, 2011**	**9000**	• CKD (3-5) • Hemodialysis (n=1275) • **Peritoneal Dialysis (n= 258)**	• >40 years • No hx of CAD • Uncertainty regarding • LDL lowering therapy	Simvastatin 20mg/ Ezetimibe 10 mg vs. placebo	**Composite:** • Coronary death • non-fatal MI • Non-hem. Stroke • Revascular iz.	Entire group and CKD non dialysis had benefit. CKD dialysis no effect CKD PD maybe

Cardiovascular disease: SHARP study

Baigent, C et al, Lancet 77:2181-2192

Reduced incidence of major cardiovascular events in treated group

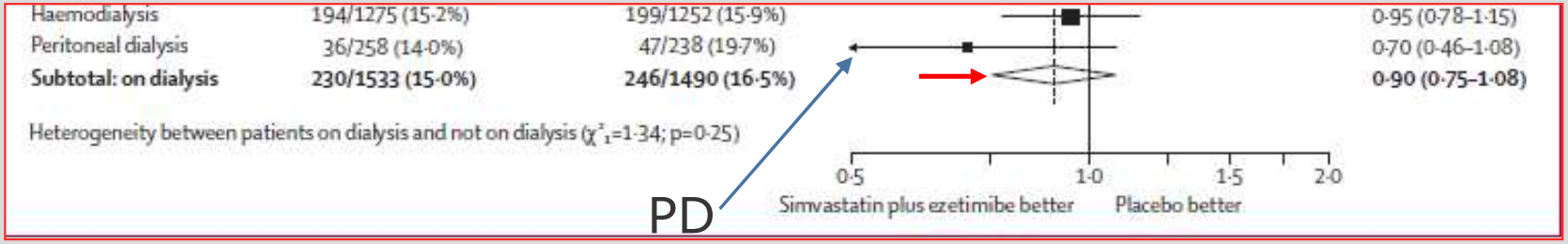


	Simvastatin plus ezetimibe (n=4650)	Placebo (n=4620)	Risk ratio (95% CI)	p value
Coronary events				
Non-fatal MI	134 (2·9%)	159 (3·4%)	0·84 (0·66–1·05)	0·12
CHD death	91 (2·0%)	90 (1·9%)	1·01 (0·75–1·35)	0·95
Subtotal: any major coronary event	**213 (4·6%)**	**230 (5·0%)**	**0·92 (0·76–1·11)**	**0·37**
Non-haemorrhagic stroke				
Ischaemic	114 (2·5%)	157 (3·4%)	0·72 (0·57–0·92)	0·0073
Unknown type	18 (0·4%)	19 (0·4%)	0·94 (0·49–1·79)	0·85
Subtotal: any non-haemorrhagic	**131 (2·8%)**	**174 (3·8%)**	**0·75 (0·60–0·94)**	**0·01**
Revascularisation procedures				
Coronary	149 (3·2%)	203 (4·4%)	0·73 (0·59–0·90)	0·0027
Non-coronary	154 (3·3%)	169 (3·7%)	0·90 (0·73–1·12)	0·36
Subtotal: any revascularisation	**284 (6·1%)**	**352 (7·6%)**	**0·79 (0·68–0·93)**	**0·0036**
Total: any major atherosclerotic event	**526 (11·3%)**	**619 (13·4%)**	**0·83 (0·74–0·94)**	**0·0021**

0·5 0·75 1·0 1·25 1·5

Simvastatin plus ezetimibe better | Placebo better

Dialysis patients no benefit



Haemodialysis	194/1275 (15·2%)	199/1252 (15·9%)	0·95 (0·78–1·15)
Peritoneal dialysis	36/258 (14·0%)	47/238 (19·7%)	0·70 (0·46–1·08)
Subtotal: on dialysis	**230/1533 (15·0%)**	**246/1490 (16·5%)**	**0·90 (0·75–1·08)**

Heterogeneity between patients on dialysis and not on dialysis (χ^2_1=1·34; p=0·25)

PD

0·5 1·0 1·5 2·0

Simvastatin plus ezetimibe better | Placebo better

Long-Term Home Dialysis Success

- Long term effectiveness of modality
  - Preservation peritoneal membrane
  - Peritonitis
  - Dialysis access
    - PD Catheter malfunction
    - HD access
- Improve patient survival
  - Cardiovascular disease
  - Volume overload
  - Loss residual renal function
  - Metabolic derangements
- **Maintain patient and partner psychological well being**

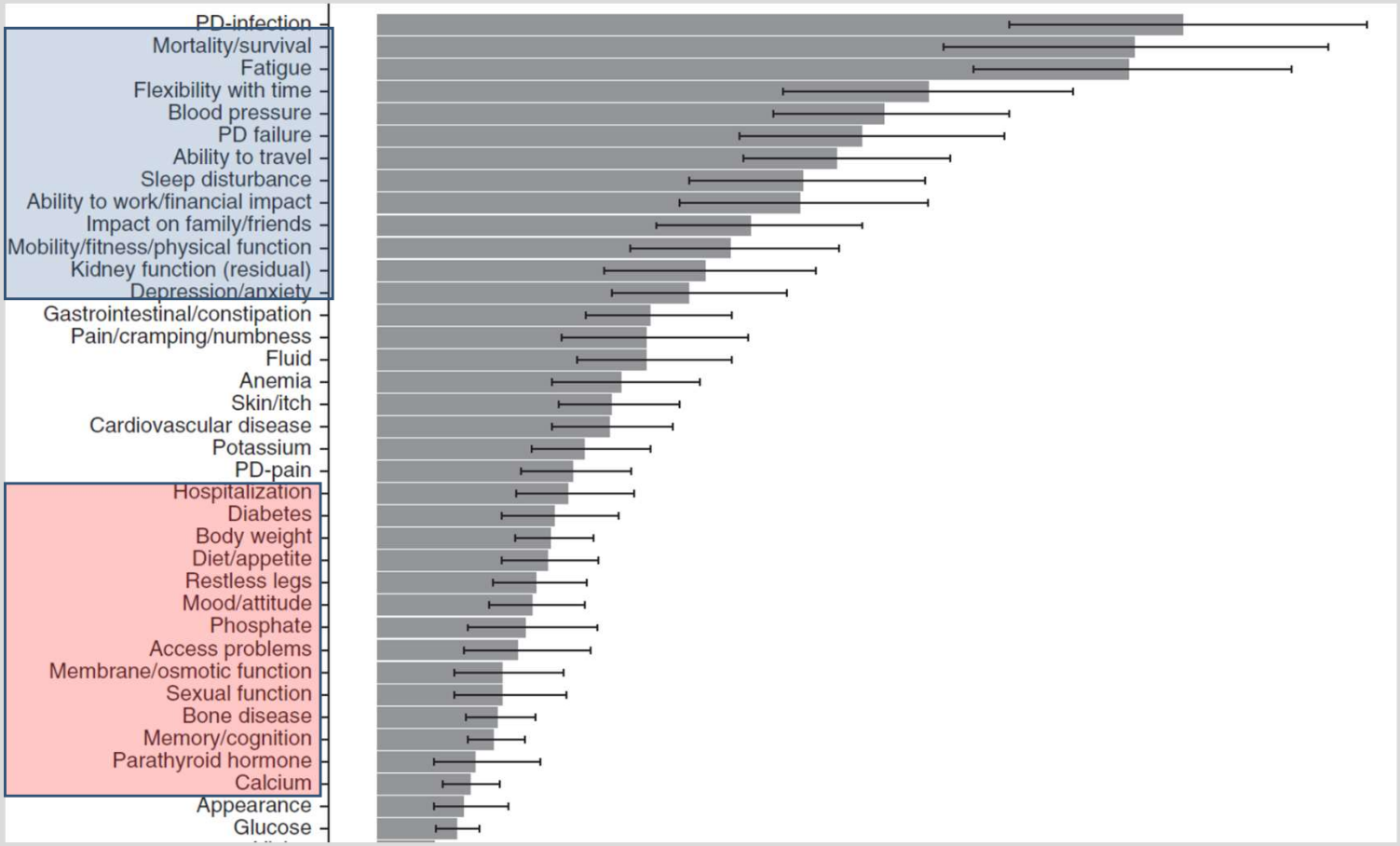
Quality of Life

Causes of technique failure
"Modality switch or discontinuation rate"

	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%

Patient and Caregiver Priorities for Outcomes in Peritoneal Dialysis

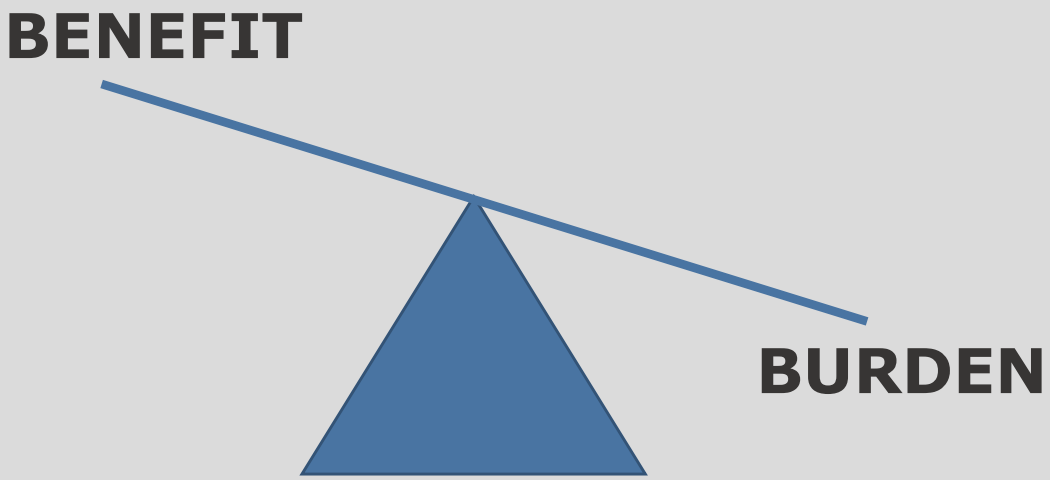
Manera, KE, et al CJASN :4 (1) 74-83. 2019



Modality Choice: Patient Perspective

- Why do patients choose Home Dialysis?
  - Seek better outcomes (BP, phosphate, volume status)
    - Maybe but not primarily
  - Feel better
    - Yes but they won't know until they try it
  - **They need or want to**
    - **Driven by quality of life decisions!**

Why do patients stay on home dialysis? The benefit outweighs the burden!



Always minimize burden and maximize benefit

Burden = everything associated with treatment!

Patient – centric: TEAM EFFORT!

Psychological or Social Factors Affecting Home Dialysis Success

- Patient or care-giver "burn-out"
  - Decreased motivation to perform self-dialysis
  - First discussion at CQI/patient review meetings is from Social Worker
- Depression
- Major life stressors
  - Financial, death in family/friends
- Development of a new disability (blindness, amputation, CVA)
- **You won't know about psychosocial stress unless you ask**
  - Ask even if you think everything is OK

Decrease burden for PD patients

- Incremental PD
  - Dry day
  - Less days per week
  - Days off
    - A day off even if anuric
- Patient friendly PD regimen
  - Incorporate patient's lifestyle into prescription
    - Dry abdomen to exercise
    - Dry abdomen if feels full when eating dinner
  - Minimize required interventions for patient
    - Less visits to clinic
    - Repeat labs only when absolutely need (for patient benefit not number crunchers)

Decrease burden for PD patients

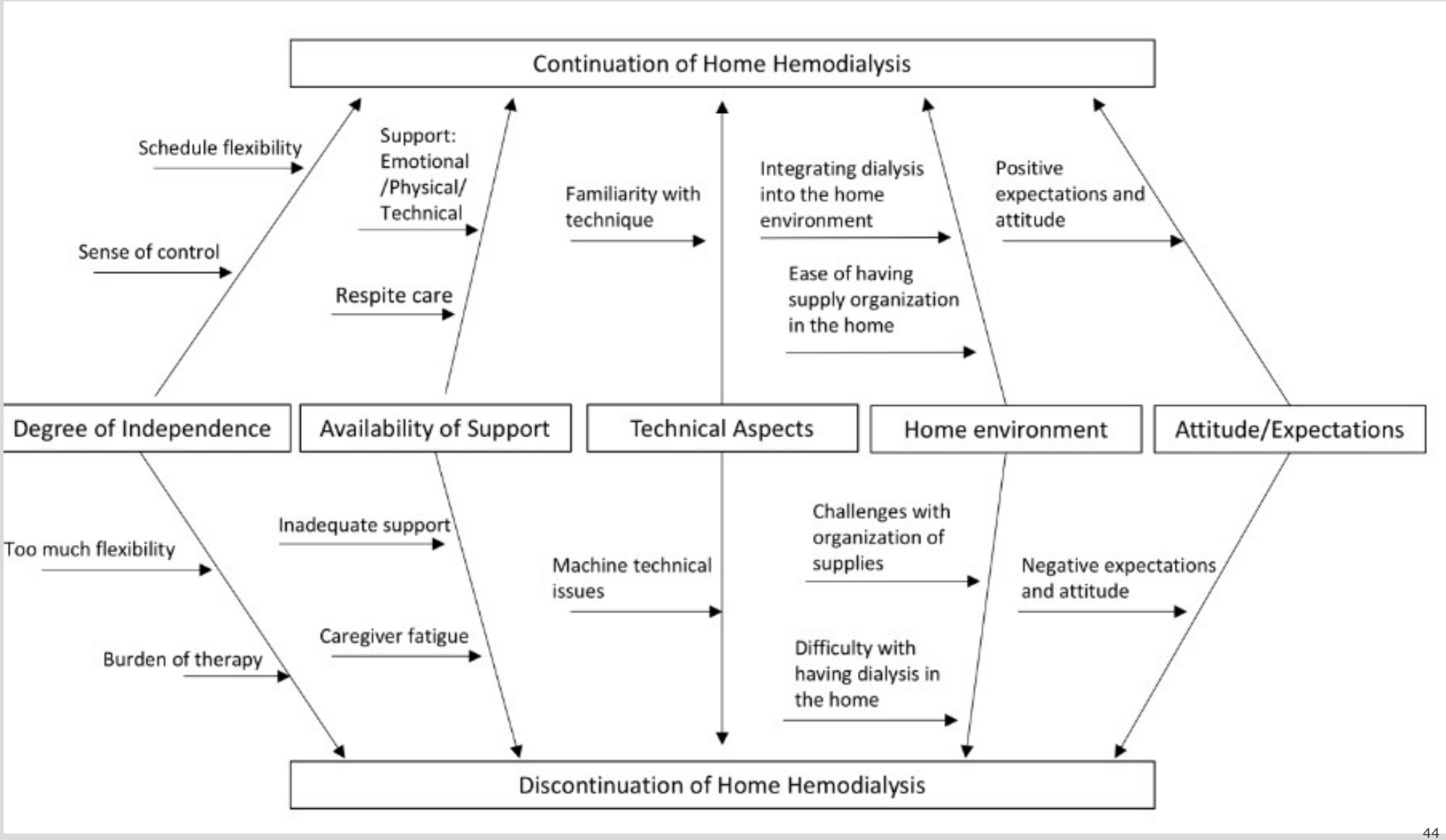
- Be flexible
  - Random days off
  - "What would you like to do that you think you cannot because of PD"
- Respite in-clinic PD
- Home assist PD
- Revisit barriers to transplant
  - Obesity – consider bariatric surgery
  - Chronic volume expansion and decrease cardiac function – consider HHD

Why Do Long-Term HHD Patients Switch to Facility-based Dialysis?

- Medical Inability to Perform HHD
  - Cognitive
  - Physical
  - Both
- Loss of Caregiver Ability to Perform HHD
- Loss of home environment to support HHD
- Vascular access challenges
- Patient / Family / Care partner burnout

Qualitative factors ⟶ HHD discontinuation

Seshasai, RK et al, Hemodial Int, 23:139, 2019



Decrease burden for HHD patients

- Modify prescription
  - Days off
  - Less time per treatment
  - Part time - care partner
  - Hybrid home vs. in-center
- Caregiver and/or patient respite
- Home assisted HD
- Nocturnal HHD
- Revisit transplantation options

Integrated Care in ESRD

- Timely transitions from PD to HD can improve long-term outcomes
- In patients with PD technique failure, but no change in overall functioning, transition to home HD allows for continuation of independence and autonomy
- *Planned transitions* are optimal
- Transition points may not be predictable, nevertheless, timely modality transfer optimizes outcomes

Case presentation #1

A 38 yo female developed ESRD secondary to lupus nephritis. She was told that by a transplant surgeon that she should not do peritoneal dialysis because she would gain weight and not be eligible for a kidney transplant. First attempt at AVF in her non-dominant, left arm was unsuccessful and she elected to have left upper extremity AVG.

She was briefly on in-center HD but quickly elected to do home hemodialysis. She worked full time but was also an amateur off, off, off, off Broadway actress. She is 5'5" and weighed 140 pounds. She had some residual renal function. She was started on 5d/week SDHD but after 2 years she became overwhelmed with HHD and could not keep up with her work and after work activities and still find time to do SDHD. She melodramatically refused to do in-center HD.

What are her options?

Case presentation #1

- She should have started dialysis on PD
  - She had residual renal function and burden of therapy would have been less.
  - She may have received a transplant while on PD
  - Her arm will be scarred forever!
- Options:
  - Nocturnal HHD
  - In-center Nocturnal
  - PD

- She elected to do PD and was transplanted 2 years later

Questions?