

After Euro BCM,  
What are the first lessons from  
iPOD study ?

R Azar

C H Dunkerque

(avec la courtoisie de FMC )

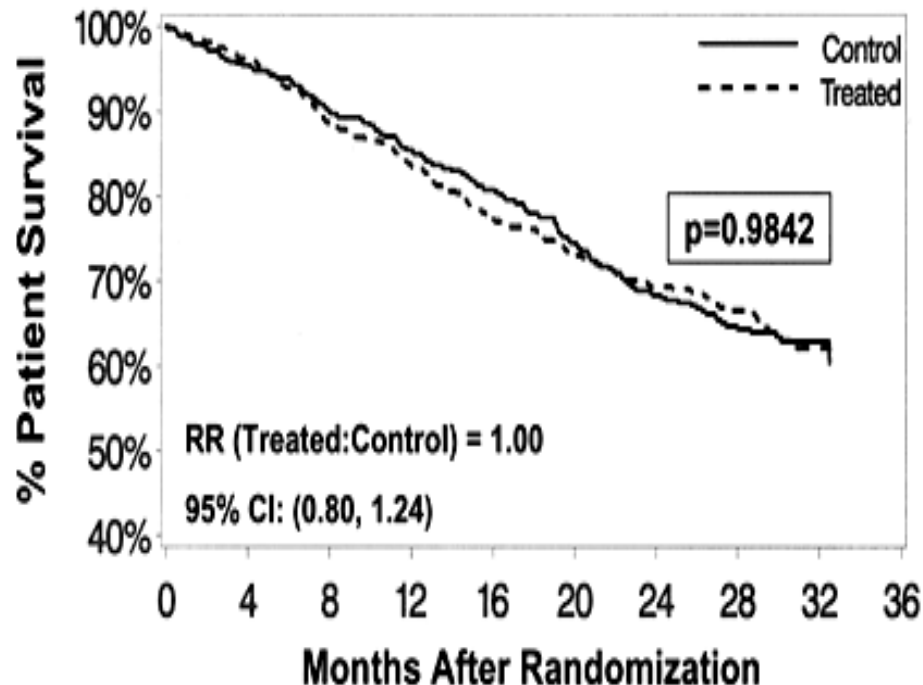
# Plan

**1** Hyperhydratation en dialyse péritonéale

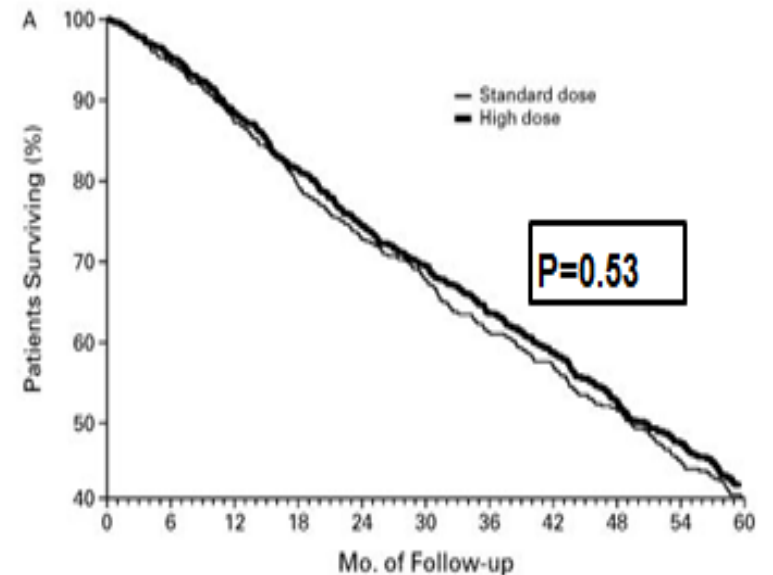
**2** Etude IPOD-PD study : The initiative of patient outcomes in peritoneal dialysis study

## ADEMEX, a Prospective, Randomized, Controlled Trial

= Effects of Increased Peritoneal Clearances on Mortality Rates in Peritoneal Dialysis:



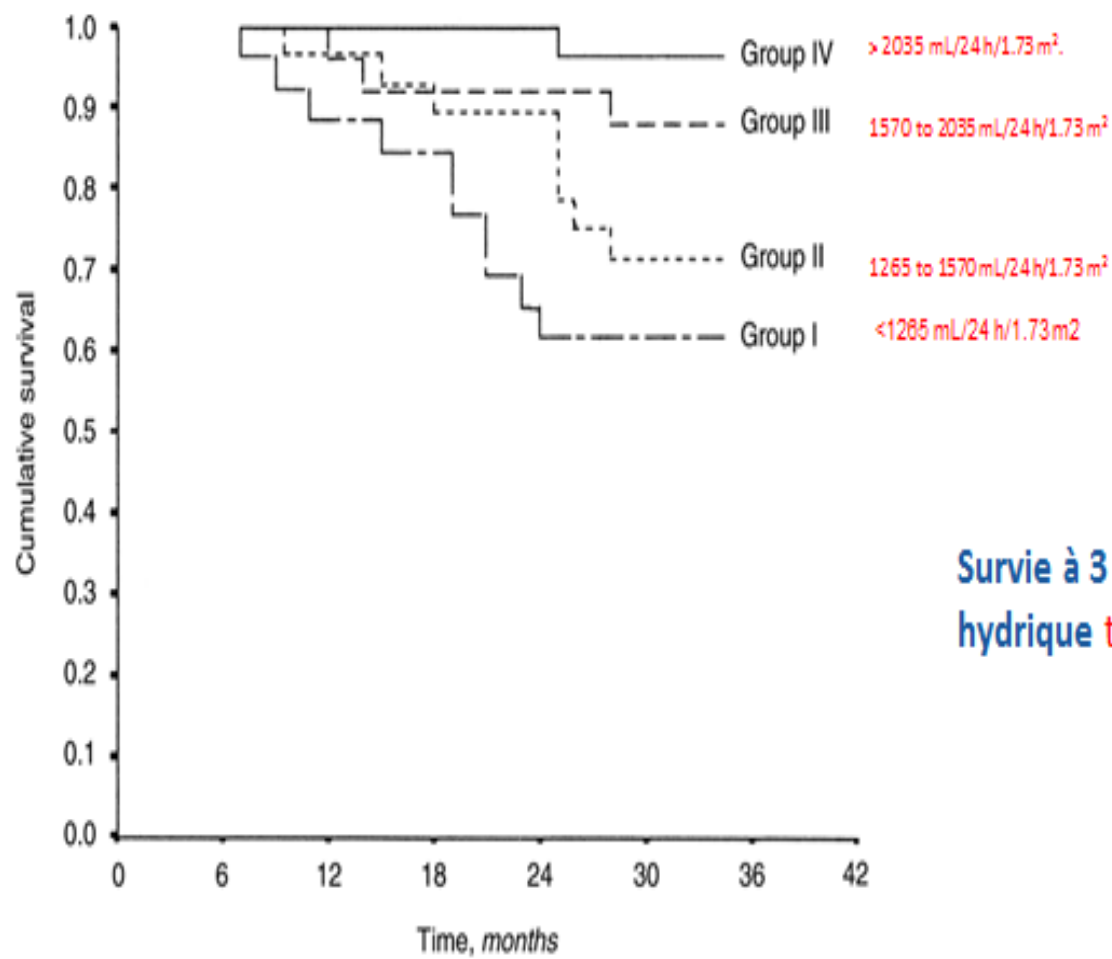
## Effect of Dialysis Dose and Membrane Flux in Maintenance Hemodialysis



No. AT RISK

Standard dose	854	759	630	524	451	382	315	253	197	149
High dose	857	753	637	538	470	399	327	266	219	166

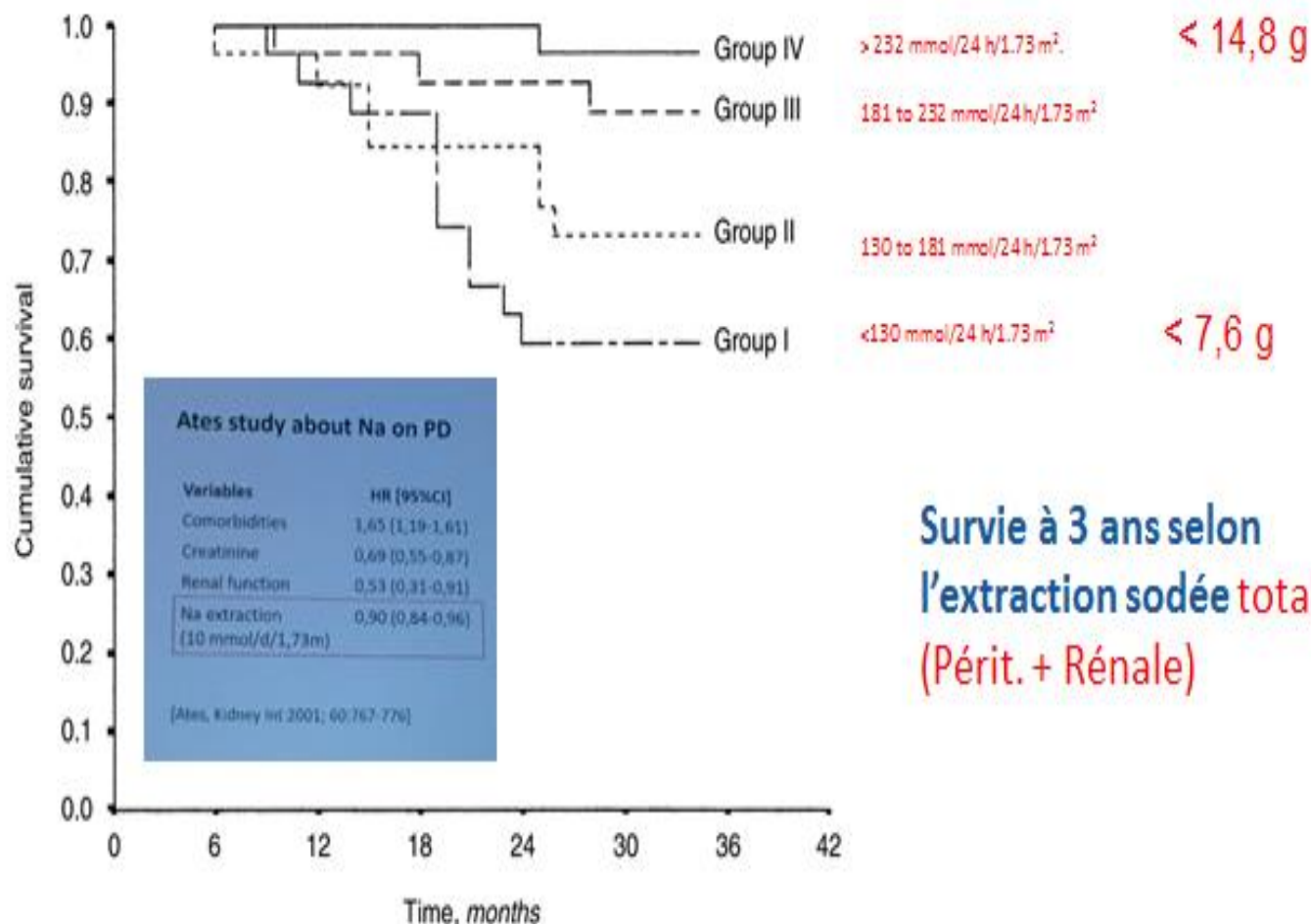
# EPIDEMIOLOGIE



Survie à 3 ans selon l'extraction  
hydrique totale (Périt. + Rénale)

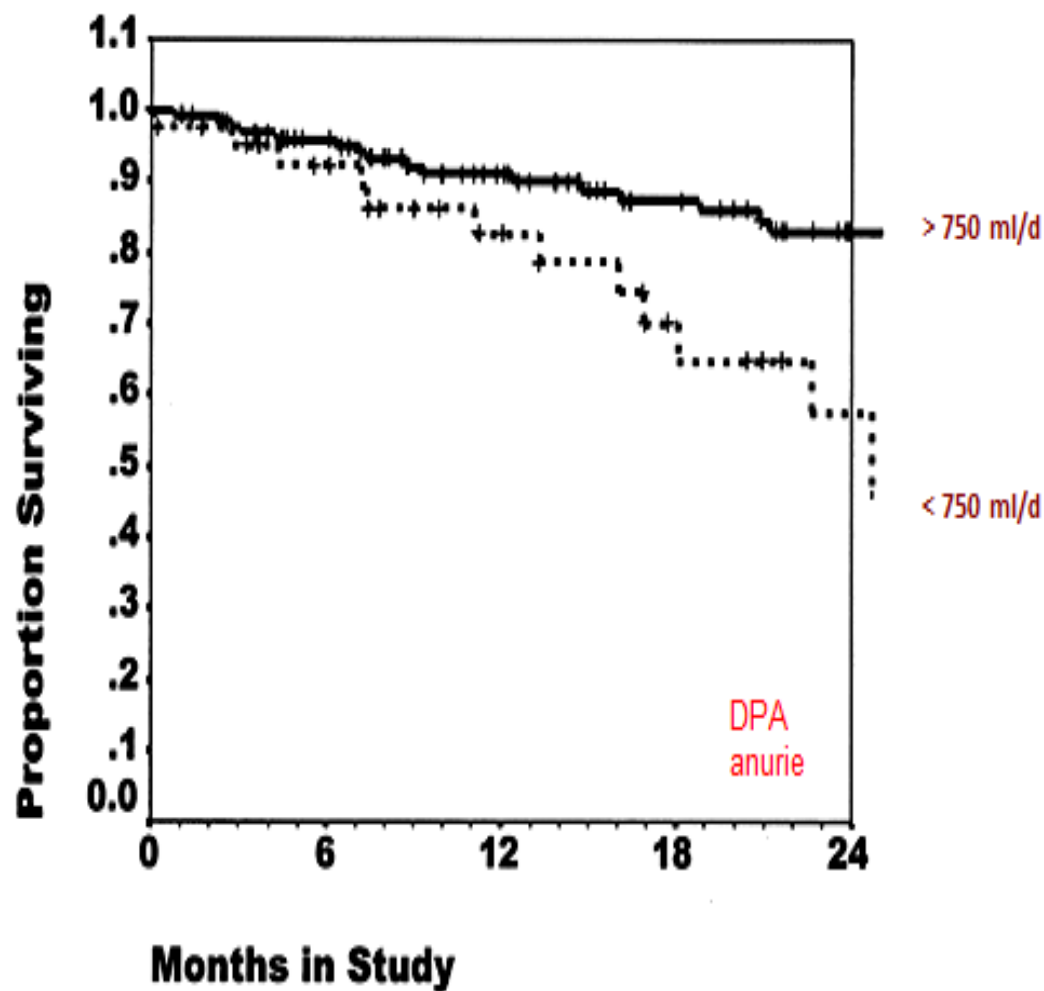
The four groups are defined as: group I,  $< 1265 \text{ mL}/24 \text{ h}/1.73 \text{ m}^2$ ; group II,  $1265 \text{ to } 1570 \text{ mL}/24 \text{ h}/1.73 \text{ m}^2$ ; group III,  $1570 \text{ to } 2035 \text{ mL}/24 \text{ h}/1.73 \text{ m}^2$ ; and group IV,  $> 2035 \text{ mL}/24 \text{ h}/1.73 \text{ m}^2$ .

# EPIDEMIOLOGIE



The four groups are defined as: group I, <130 mmol/24 h/1.73 m<sup>2</sup>; group II, 130 to 181 mmol/24 h/1.73 m<sup>2</sup>; group III, 181 to 232 mmol/24 h/1.73 m<sup>2</sup>; and group IV, > 232 mmol/24 h/1.73 m<sup>2</sup>.

# EPIDEMIOLOGIE



Survie Patient  
Anuriques en DPA :

The European APD  
Outcome Study

## Recommandations officielles : quelles cibles?

### ISPD

Ultrafiltration is predictive of survival in anuric APD patients

Study (EAPOS) : baseline ultrafiltration below 750 mL/day was associated with poorer survival

Ultrafiltration analyzed as a continuous variable was a significant factor for survival in the time-dependent analysis of anuric patients in NECOSAD .

ISPD Guidelines. *Perit Dial Int* 2006; 26:520–522

### ERA EDTA

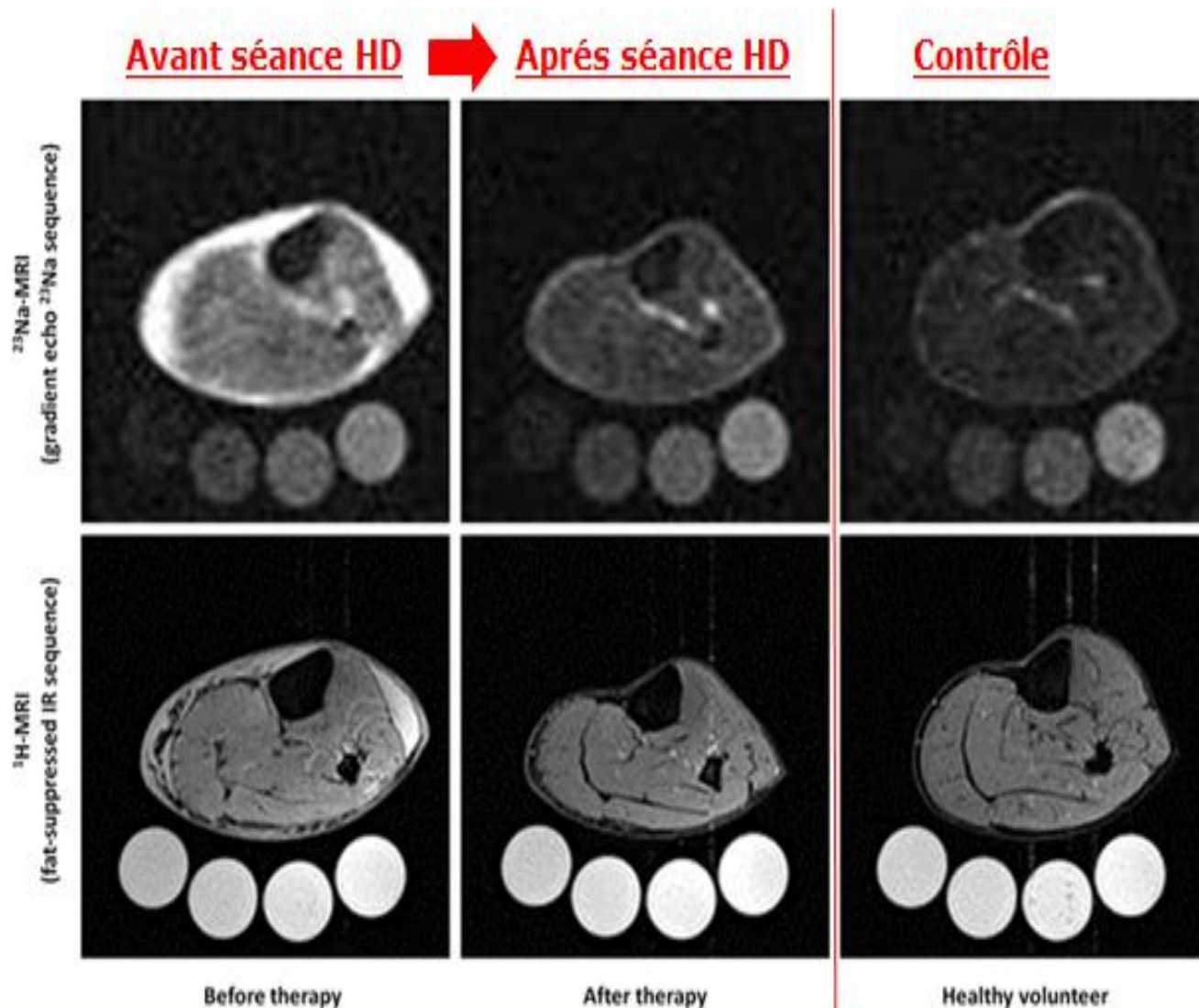
The minimum peritoneal target for net ultrafiltration in anuric patients is 1.0 L/day. (Evidence level B)

The presence of residual renal function can compensate when these peritoneal targets are not achieved. (Evidence level C)

*Nephrology Dialysis Transplantation*, 20, suppl\_9, 1  
December 2005

# Nouvelles données sur le Sel : Rôle du sel "non osmotique"?....

- IRM du mollet
- Patient en HD
- DT2





# Nouvelles données sur le Sel : Rôle du sel "non osmotique"?....


## Etude de Cohorte de patients IRC ND

- Pas d'association entre « Na<sup>+</sup> non osmotique » et DFG
- Pas d'association avec l'OH (BCM)

**Mais association indépendante avec l'HVG....**

### Sodium extraction, GFR, hydration and CKD

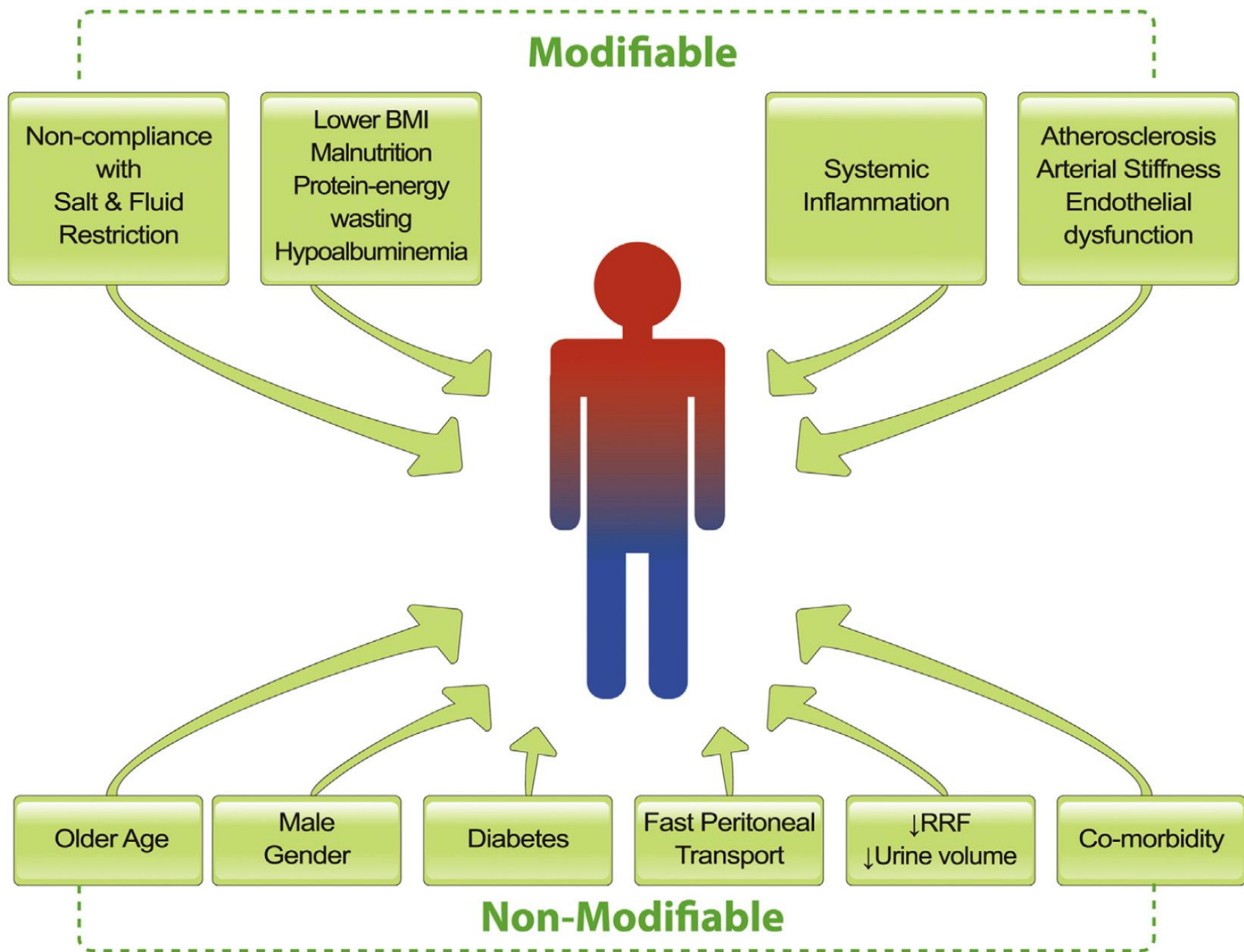
#### Covariates associated with Left Ventricular Mass



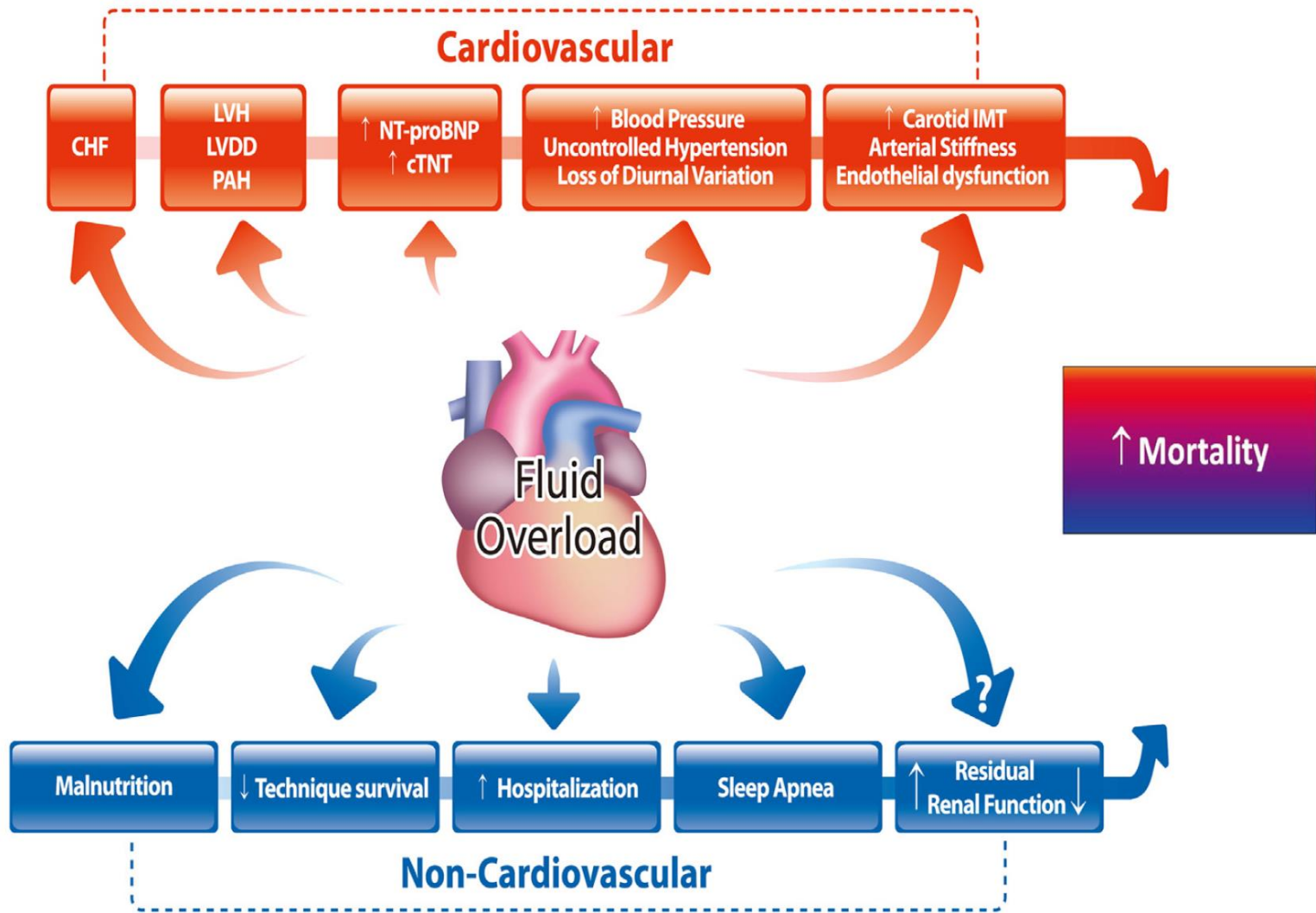
	Coefficient $\beta$	p value
Gender	- 0.30	< 0.01
Height	+ 0.33	< 0.01
24h systolic BP	+ 0.13	0.08
Skin sodium [MRI]	+ 0.33	< 0.01
OH [BCM]	+ 0.02	0.78

Skin sodium was not associated with GFR, OH [BCM]....

[Schneider MP, J Am Soc Nephrol 2017; 28: 1867-1876]



**Figure 2.** Modifiable and nonmodifiable factors influencing fluid status. BMI, body mass index.

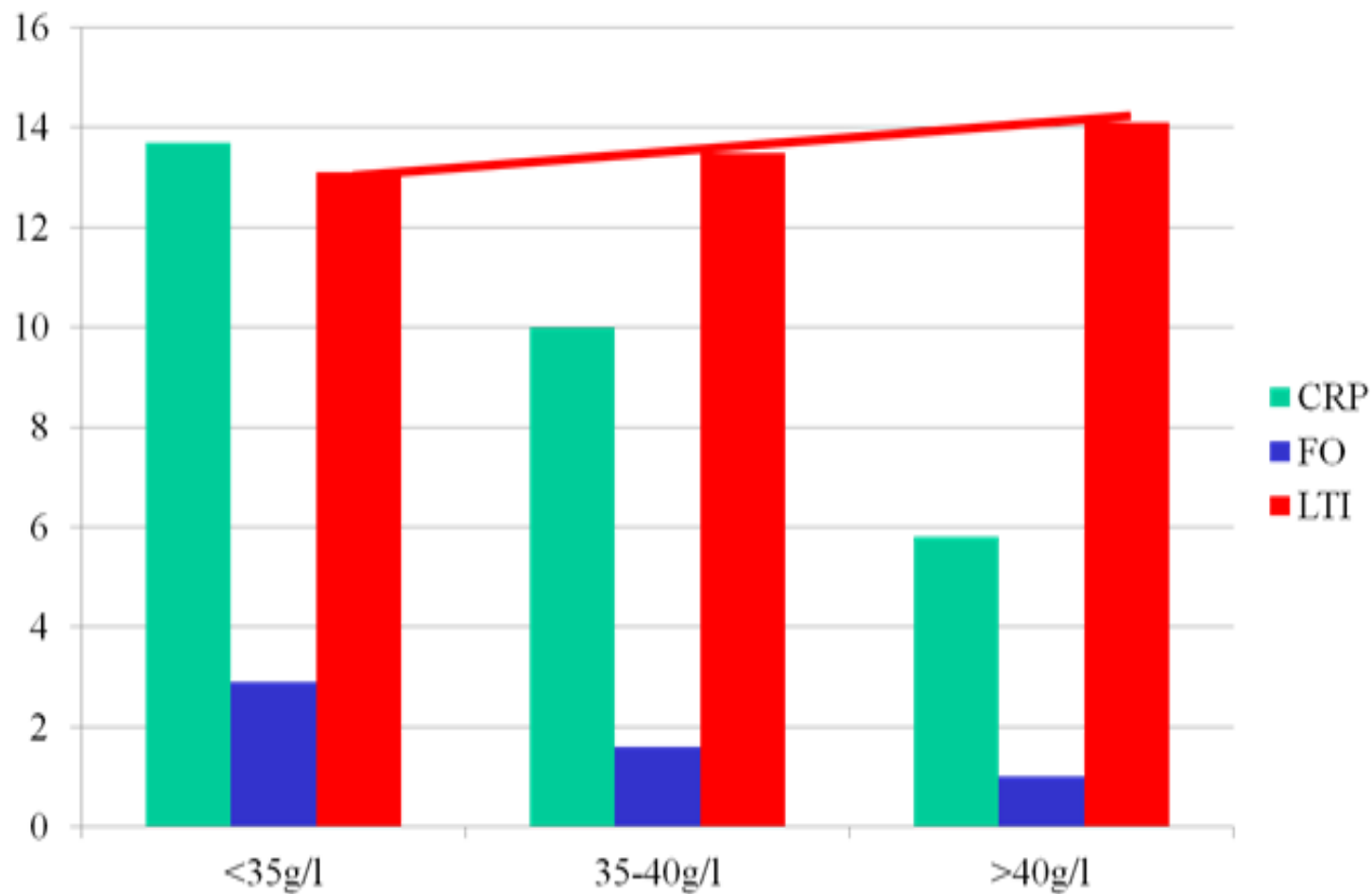


**Figure 1.** Consequences of fluid overload in PD patients. CHF, congestive heart failure; LVDD, left ventricular diastolic dysfunction; LVH, left ventricular hypertrophy; PAH, pulmonary arterial hypertension; intima media thickness (IMT).

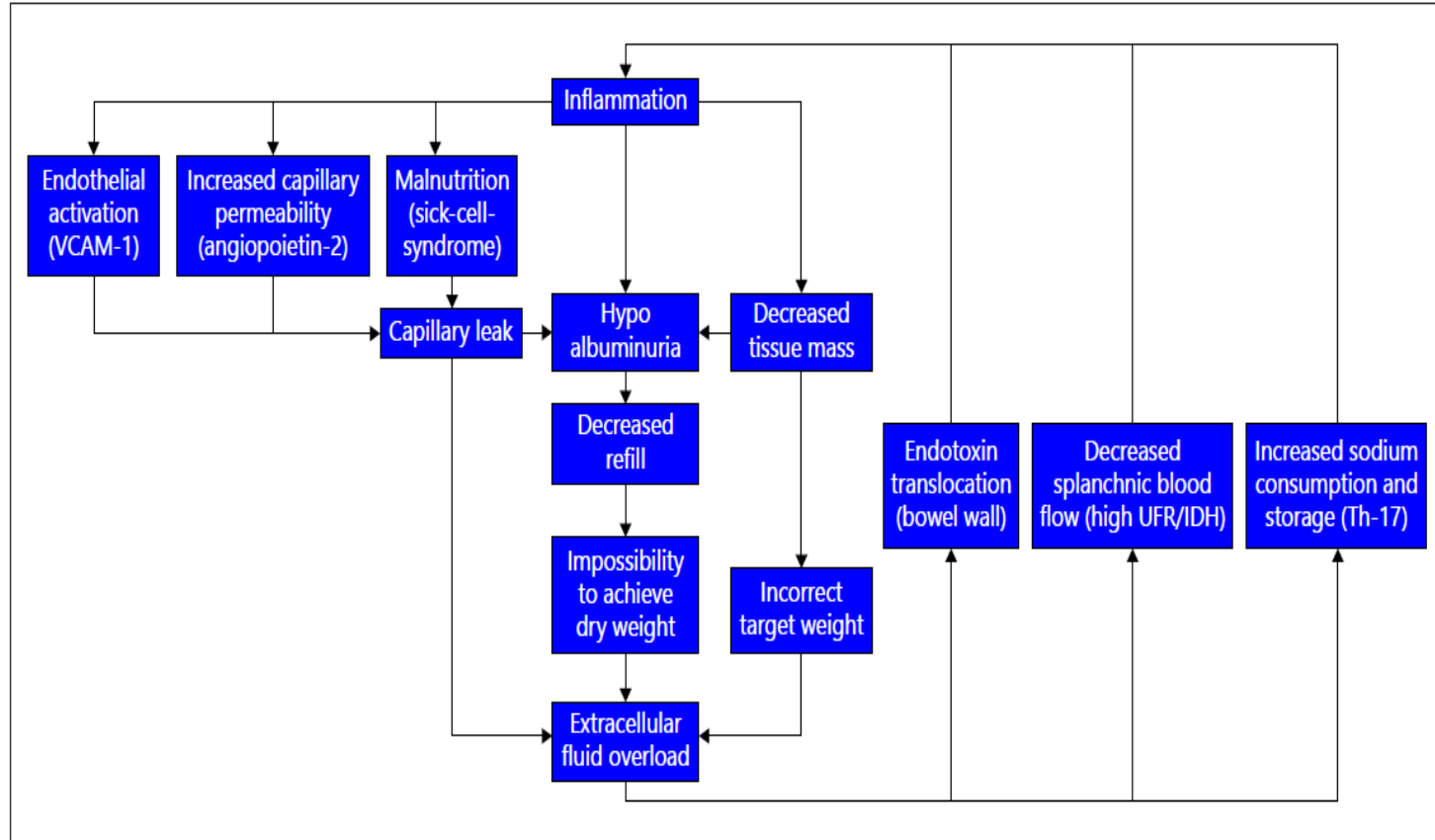
# Relation inflammation, nutrition, fluid overload

	Albumin [g/L]					
	<35.0		35.0-40.0		>40.0	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
BMI [kg/m <sup>2</sup> ]	314	25.0±4.6	333	26.3±4.9	302	26.5±4.8
LTI [kg/m <sup>2</sup> ]	311	13.1±3.1	329	13.5 ± 3.2	300	14.2±3.5
FTI [kg/m <sup>2</sup> ]	310	7.8±3.8	329	8.9±4.2	300	7.7±4.0
FO [L]	314	2.9±2.6	333	1.6±2.1	302	1.0±1.7
CRP [mg/L]	267	13.7±24.1	276	10.0±21.0	257	5.8 ±10.4

# Relation inflammation, nutrition, fluid overload

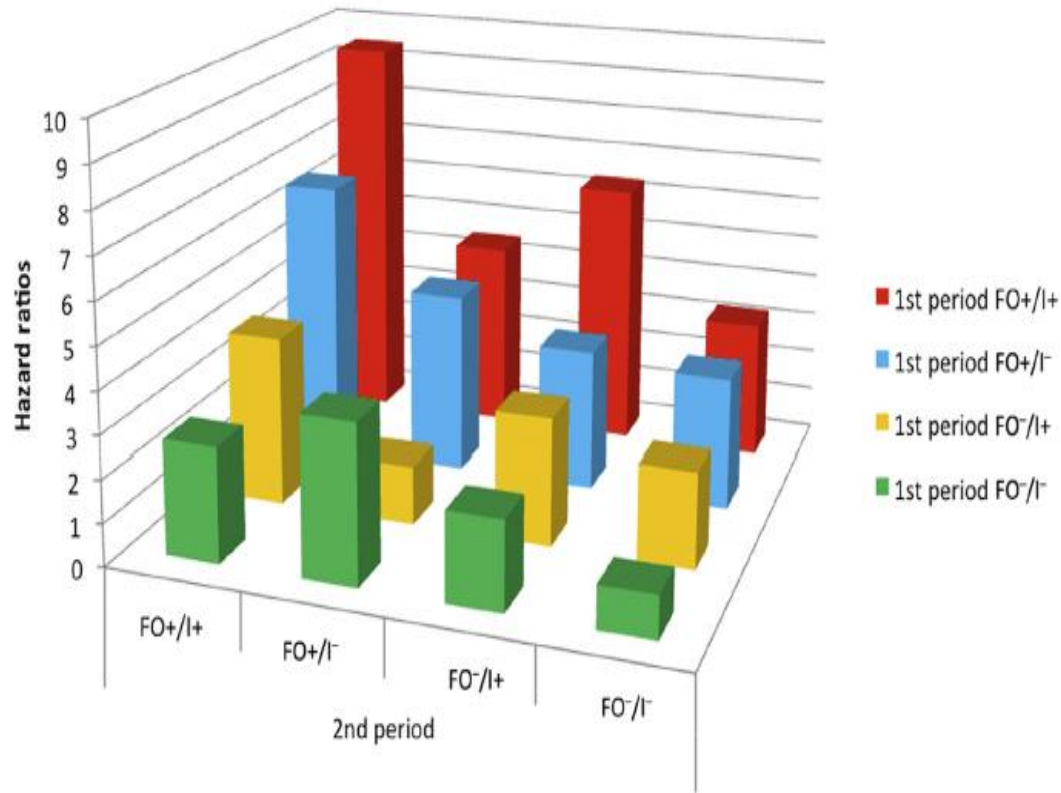


# Axe Hyperhydratation et Inflammation



**Fig. 3.** Potential pathophysiological explanations of the fluid overload and inflammation axis. VCAM, vascular cell adhesion protein; UFR, ultrafiltration rate; IDH, intradialytic hypotension; Th-17, T-helper 17 cells.

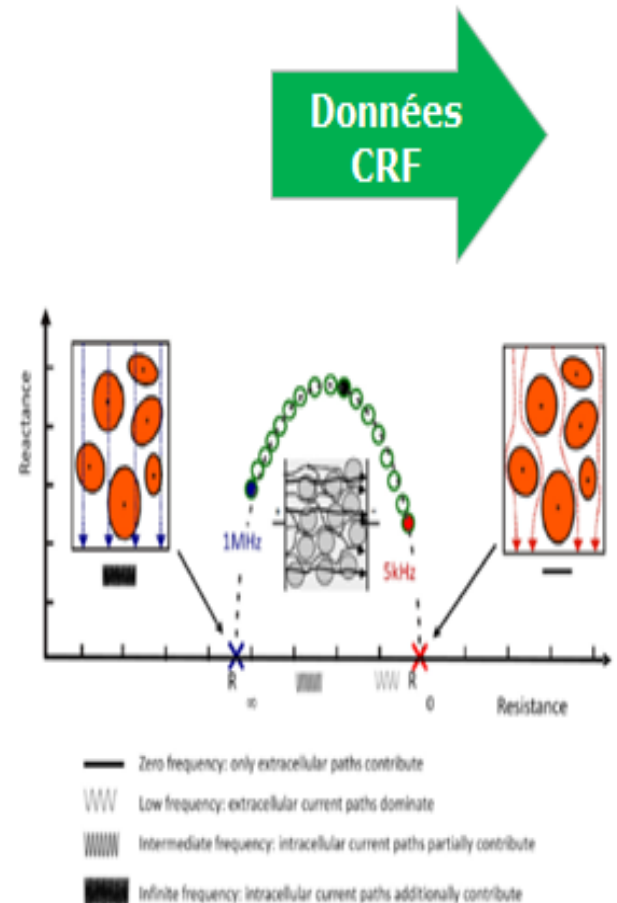




**Figure 5 | Dynamics of fluid status and inflammation and survival during 6-month follow-up.** Survival probabilities and hazard ratios from a Cox proportional hazards model adjusted for age, gender, dialysis vintage, access type (arteriovenous vs. catheter access), region, body mass index, normalized protein catabolic rate, ultrafiltration rate (<10 ml/h/kg, 10–13 ml/h/kg, or >13 ml/h/kg), diabetes mellitus, congestive heart failure, peripheral vascular disease, cerebrovascular disease, and present malignancy.

# Evaluation de la volémie

- Examen Clinique
- Pro-BNP (dysfunction et overload)
- Echo pulmonaire
- Echocardiographie
- **BIOIMPEDANCE MULTIFREQUENCY**
  - Extracellular water (ECW)
  - Intracellular water (ICW)
  - Body water (TBW)



Principles of bioimpedance and  
bioimpedance spectroscopy



# **Initiative for Patient Outcomes in Dialysis – PD: IPOD-PD Study**

**Final Results**



# Study Facts

## Study design

- ☞ observational, prospective
- ☞ 28 countries
- ☞ 135 centres
- ☞ 1092 incident PD patients
- ☞ up to 5 years follow-up

## Study objectives

- ☞ Assessment of hydration status at baseline and during follow-up
- ☞ RRF, transport status, prescription, technique failure

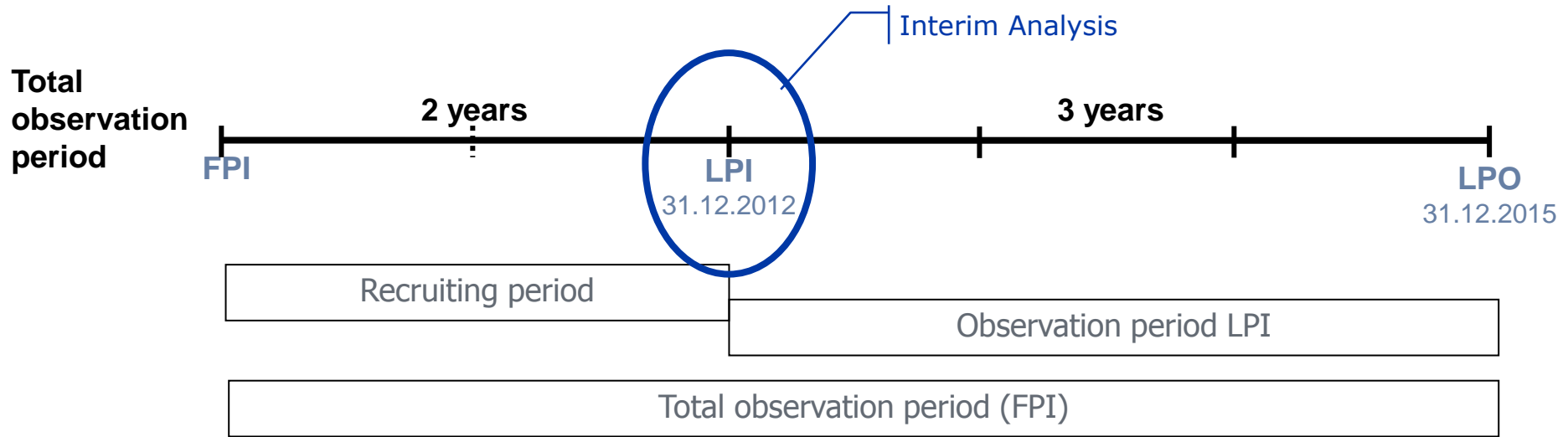
## Study treatment

- ☞ The patients were treated according to the practice of the clinics and received the peritoneal solutions according to physician's decision

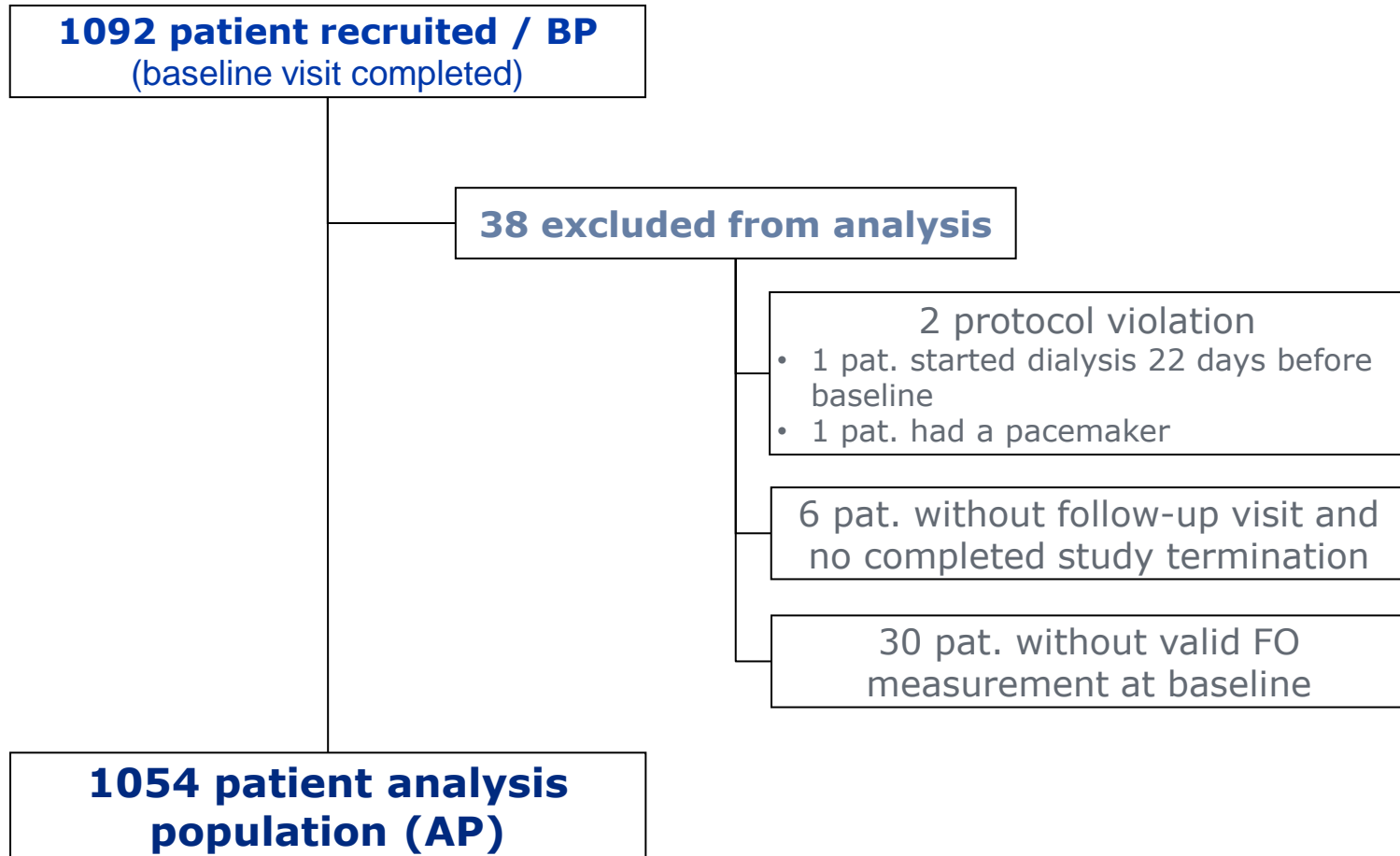
# Protocol

## Timelines

- ➡ Recruiting period end app. 2 years after inclusion of the first patient (FPI)
- ➡ After inclusion of the last patient (LPI) all patients were observed for 3 more years



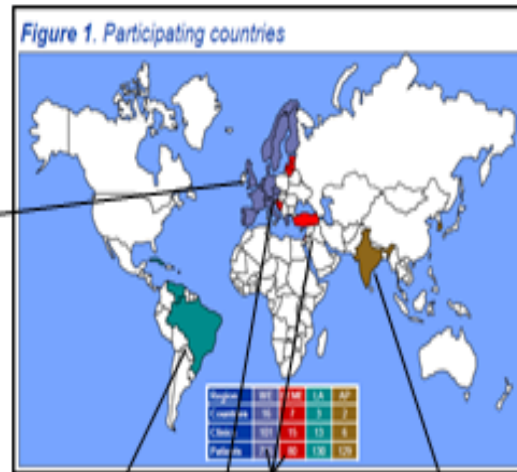
# Analysis population



BP = Baseline population

# IPOD-PD study = Répartition géographique des patients

Western Europe (WE)	
	n
Belgium	19
Czech Republic	30
Finland	28
<b>France</b>	<b>50</b>
Germany	57
Greece	38
Italy	31
Netherlands	13
Portugal	16
Spain	260
Sweden	29
Switzerland	1
UK	86
Norway	13
Denmark	41
Austria	3



## Eastern Europe & Middle East (EEME)

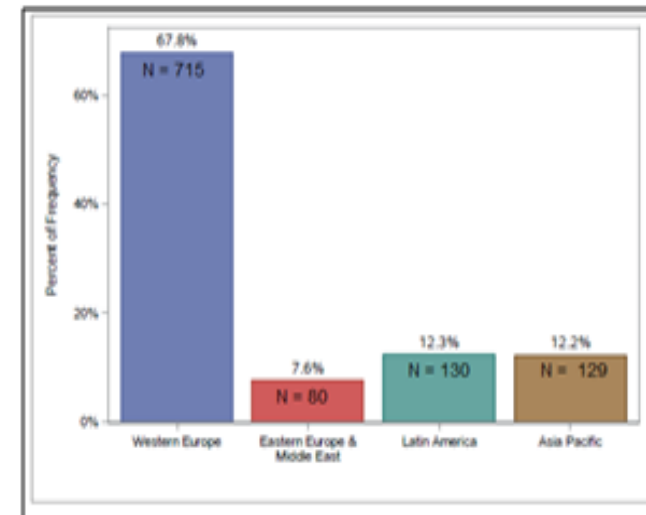
	n
Bosnia	16
Croatia	6
Israel	7
Estonia	17
Latvia	22
Lithuania	6
Turkey	6

## Latin America (LA)

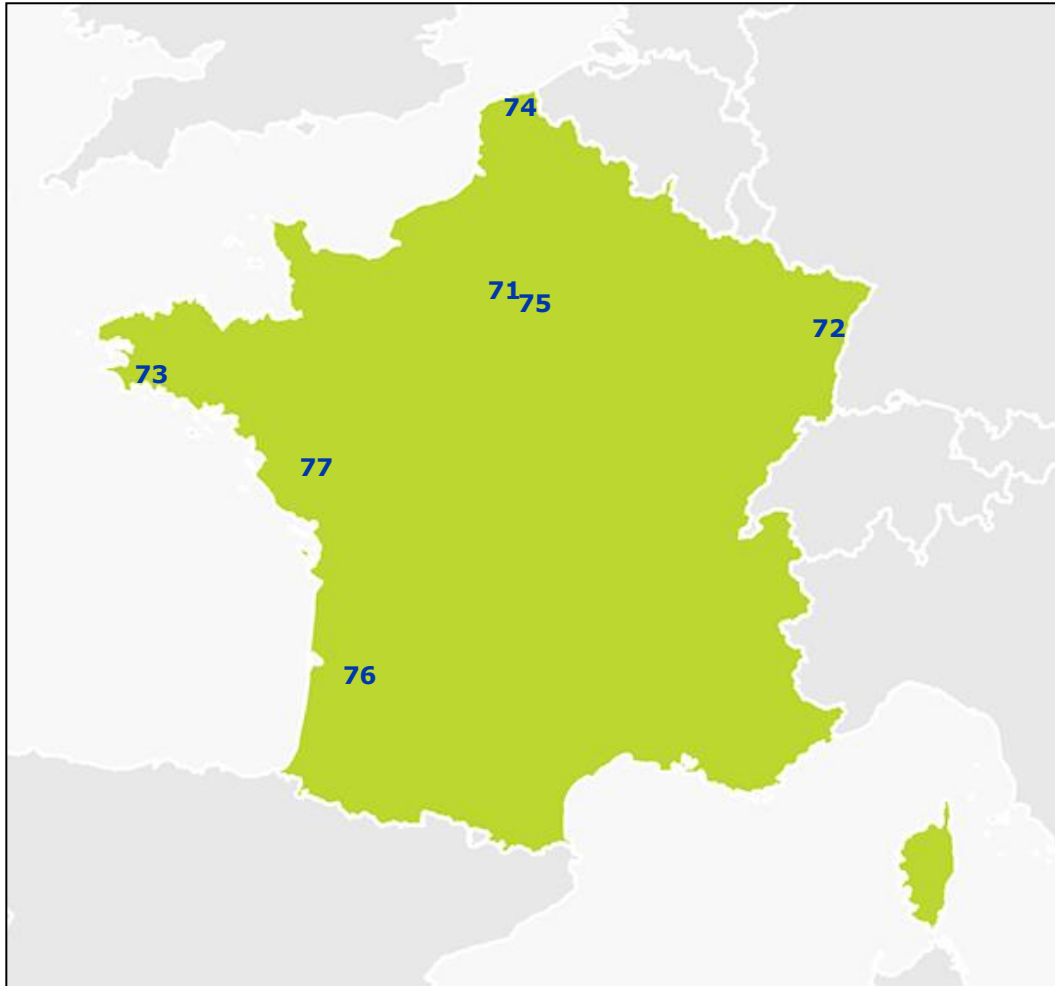
	n
Brazil	74
Cuba	6
Venezuela	50

## Asia Pacific (AP)

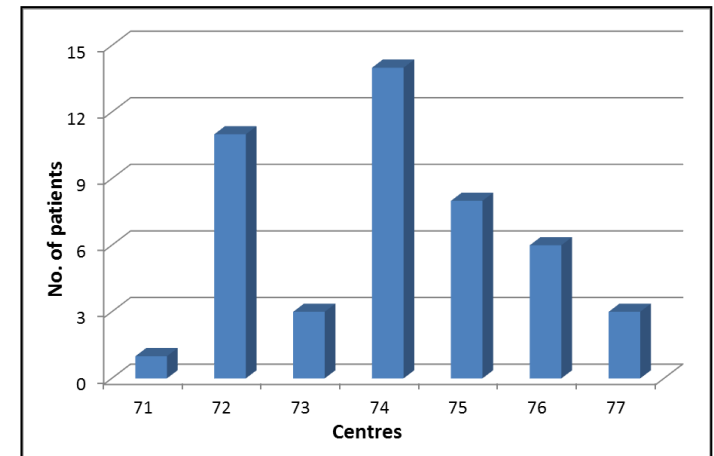
	n
Korea	127
India	2



# Participating Countries - France



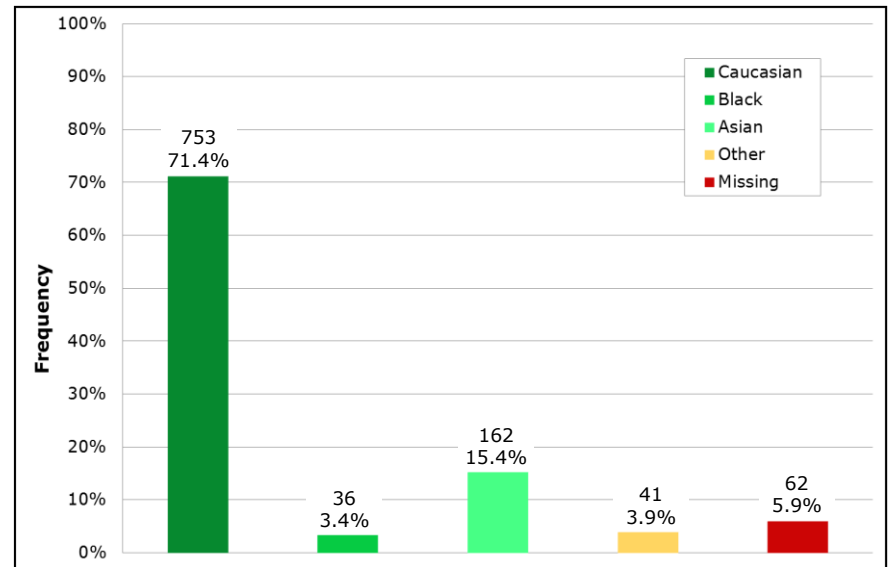
Centres included	7
Centres with at least 1 patient	7
Patient's included	46



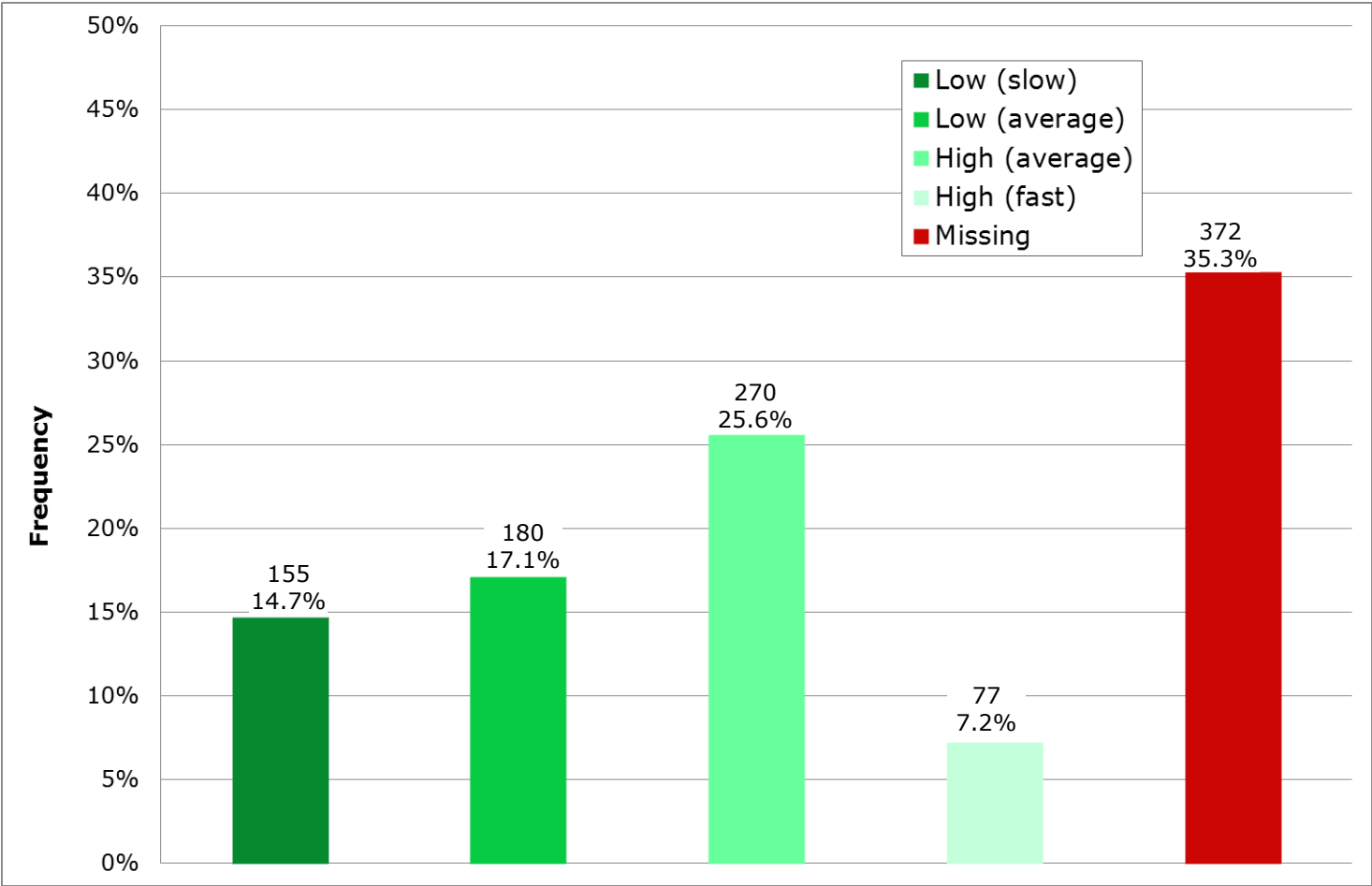
# Baseline characteristics

n	1054
Age [years]	58.1 ± 15.3
Sex (men) [%]	57.4
Height [cm]	166.0 ± 10.1
Weight [kg]	71.9 ± 16.2
Blood pressure (sys) [mmHg]	139.4 ± 21.7
Blood pressure (dias) [mmHg]	79.9 ± 12.8

## Ethnic origin



# Transport status at first assessment





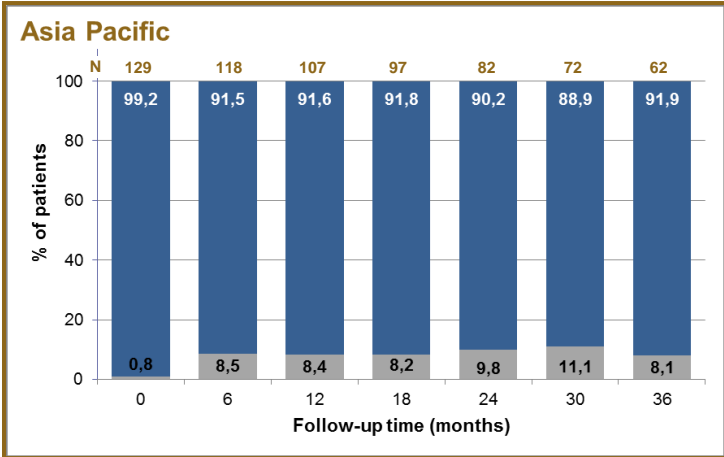
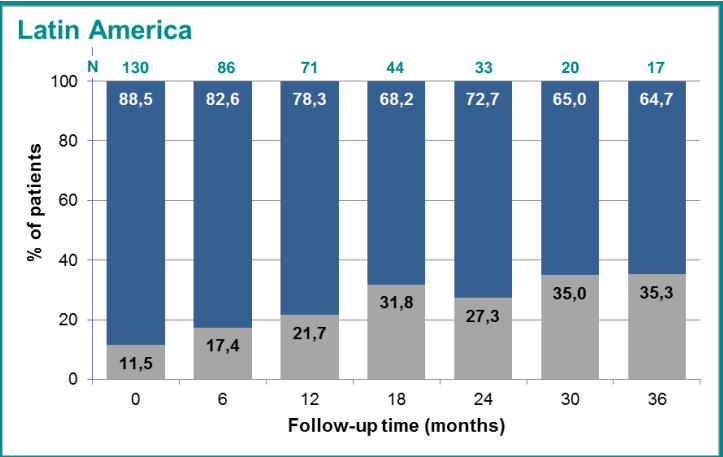
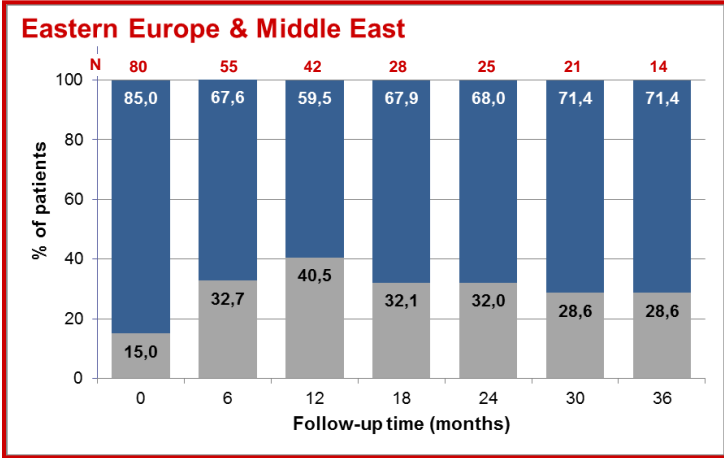
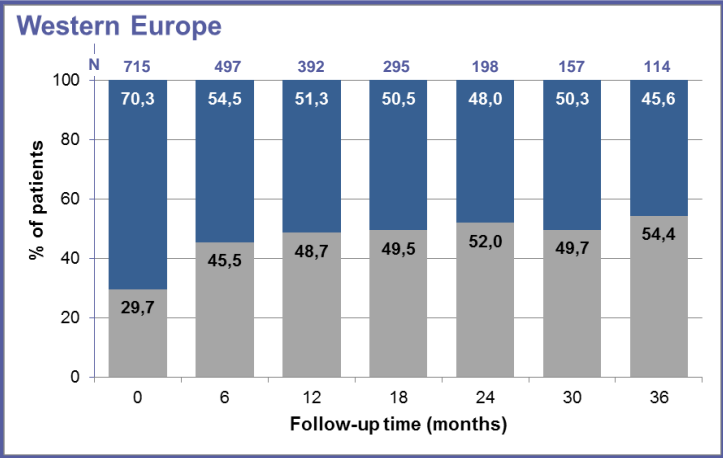
# Availability of transport status test by region

Region / Visit		At least 1 test is available		No test is available		Total
		n	%	n	%	N
Western Europe	Month 1	167	24.6	512	75.4	679
	Month 3	289	44.9	354	55.1	643
	Month 6	338	57.9	246	<b>42.1</b>	584
Eastern Europe & Middle East	Month 1	15	19.7	61	80.3	76
	Month 3	15	22.7	51	77.3	66
	Month 6	19	30.6	43	<b>69.4</b>	62
Latin America	Month 1	42	33.3	84	66.7	126
	Month 3	69	57.0	52	43.0	121
	Month 6	65	58.0	47	<b>42.0</b>	112
Asia Pacific	Month 1	109	84.5	20	15.5	129
	Month 3	112	88.9	14	11.1	126
	Month 6	120	97.6	3	<b>2.4</b>	123

➡ After 6 months transport status test is still not available for **2.4%** of the patients in Asia Pacific, **42%** in Western Europe and Latin America and **69%** in Eastern Europe!

# PD treatment

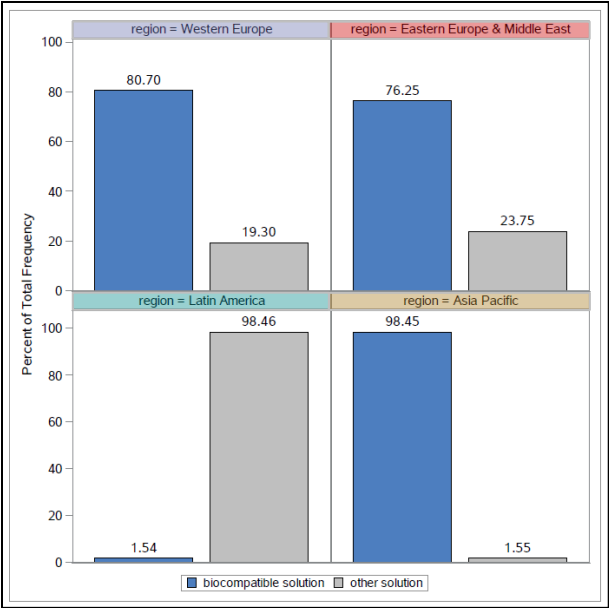
## Changes in PD modality during the study – by region



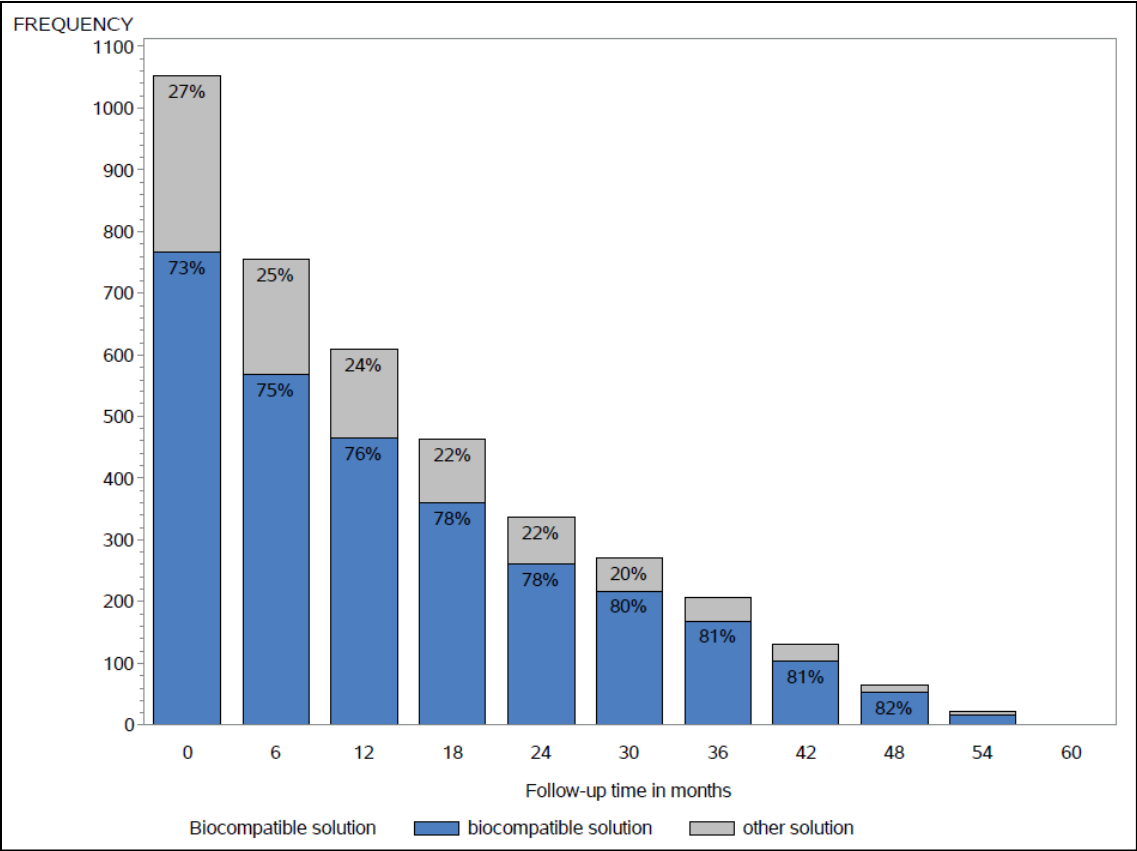
■ APD   ■ CAPD

# PD treatment

## Biocompatible solution at baseline by region

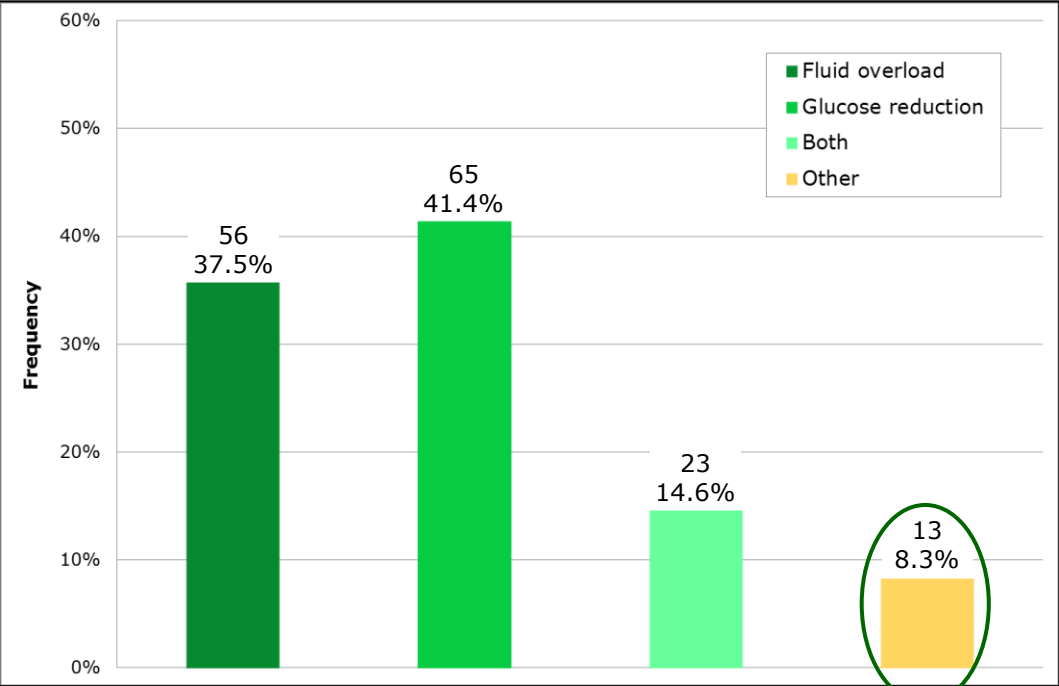


## Biocompatible solution during the study



# PD treatment

## Polyglucose use at baseline – Reason

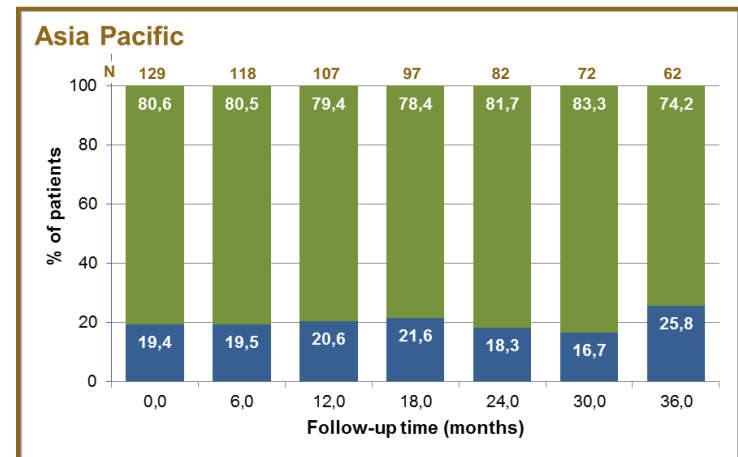
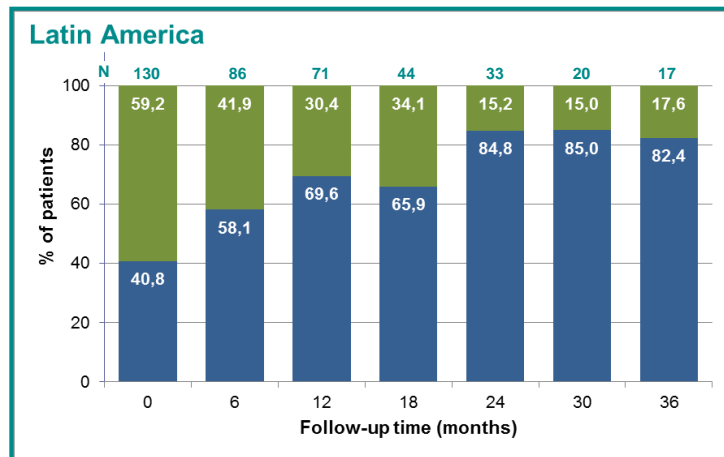
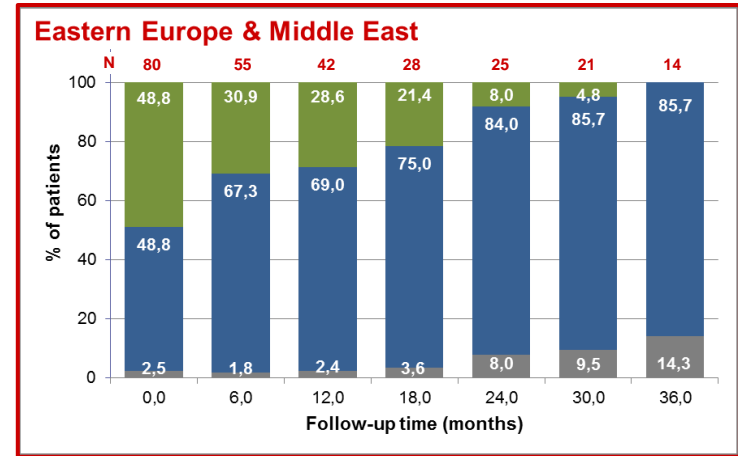
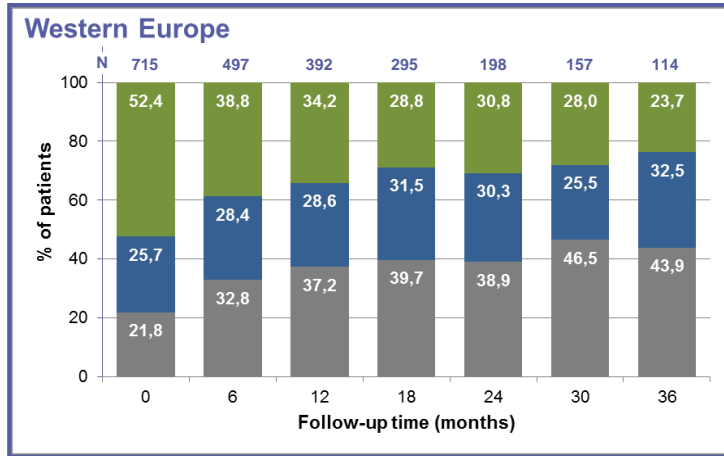


Polyglucose baseline **157** patients  
12 patients get **only Polyglucose**

- Standard care 3
- Achieve efficient dialysis 1
- Is better overnight exchange 1
- No necessary more than 1 exchange / day 1
- Dialysis dose 1

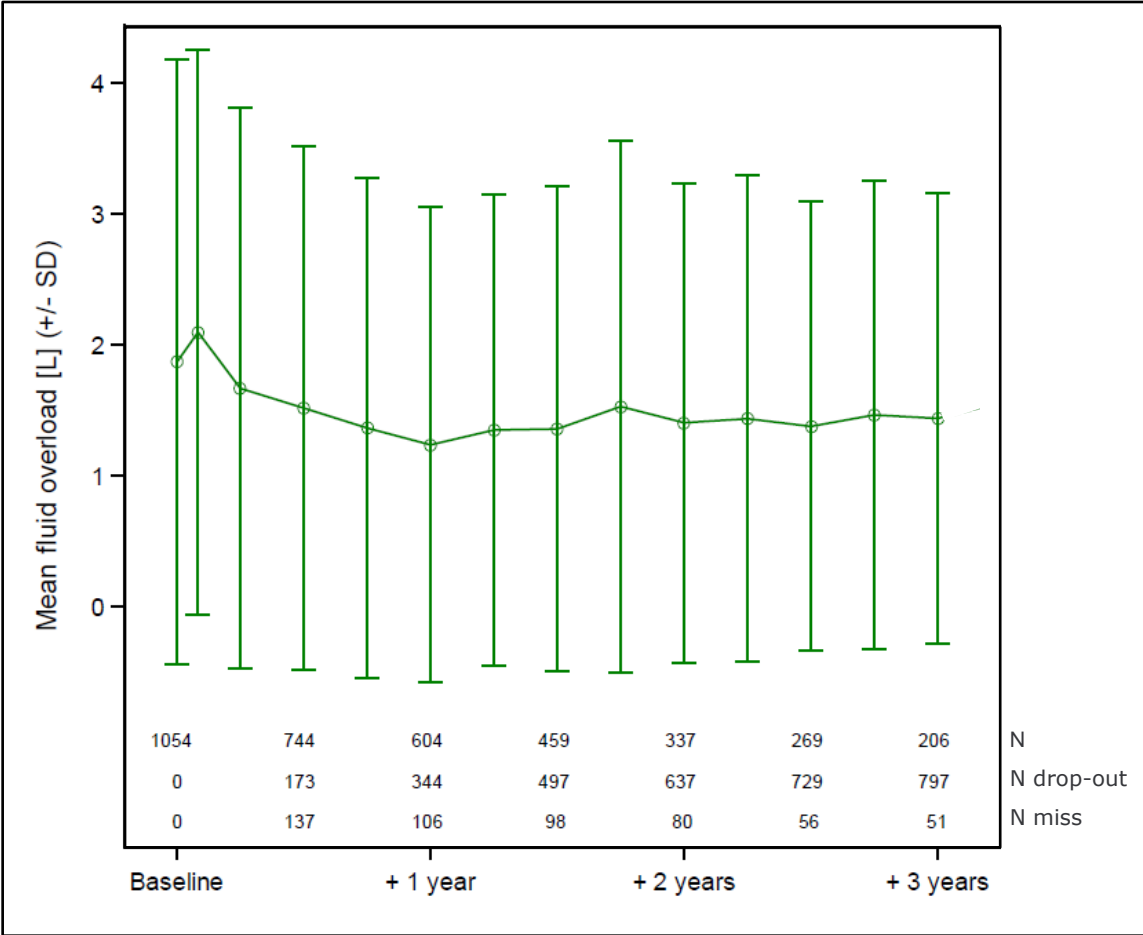
# PD treatment

## Changes in use of polyglucose and hypertonic solution – by region



Polyglucose
  Hypertonic
  No hypertonic

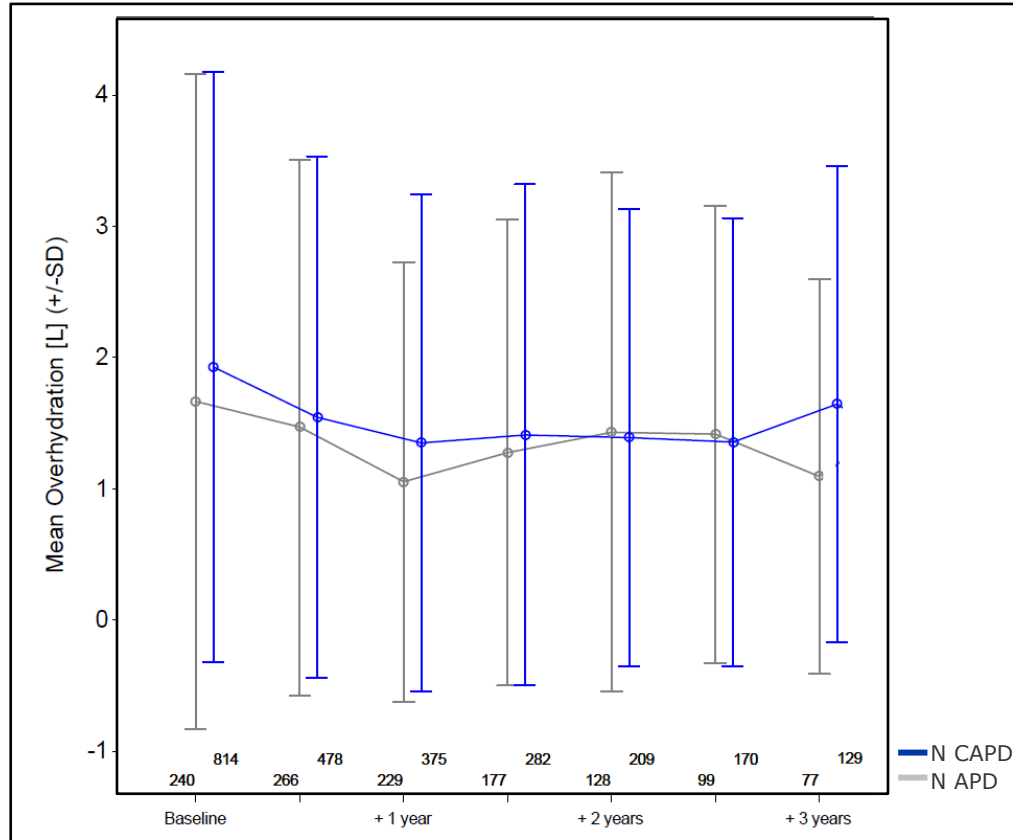
# Course of fluid overload [L]



FO at Baseline	N	Mean	STD	Min	Median	Max
	1054	1.9	2.3	-3.3	1.5	17.7

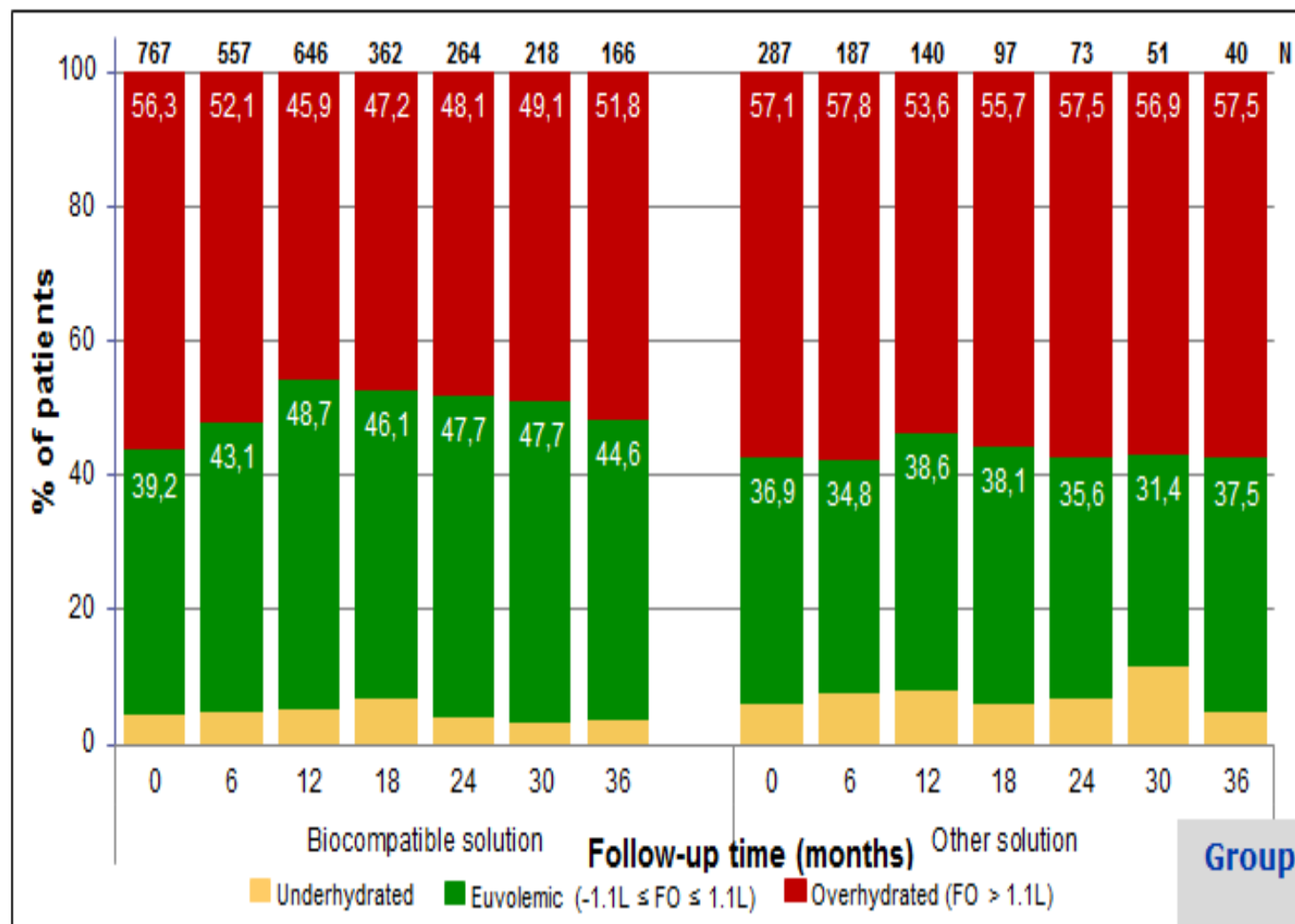
# Course of fluid overload by PD modality

Time dependent group allocation



FO at baseline		N	Mean	STD	Median
	CAPD	814	1.9	2.3	1.6
	APD	240	1.7	2.5	1.2

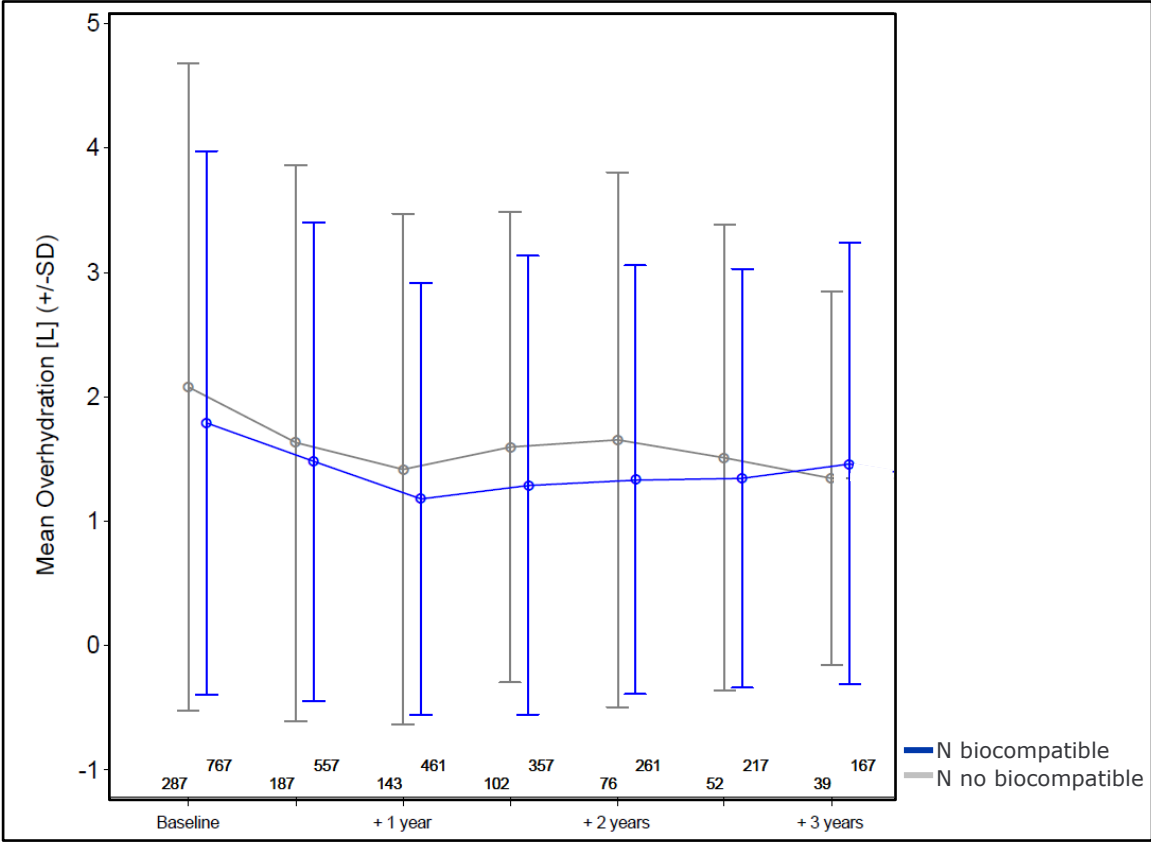
# IPOD-PD study = Evolution de l'hydratation selon la biocompatibilité des solutions





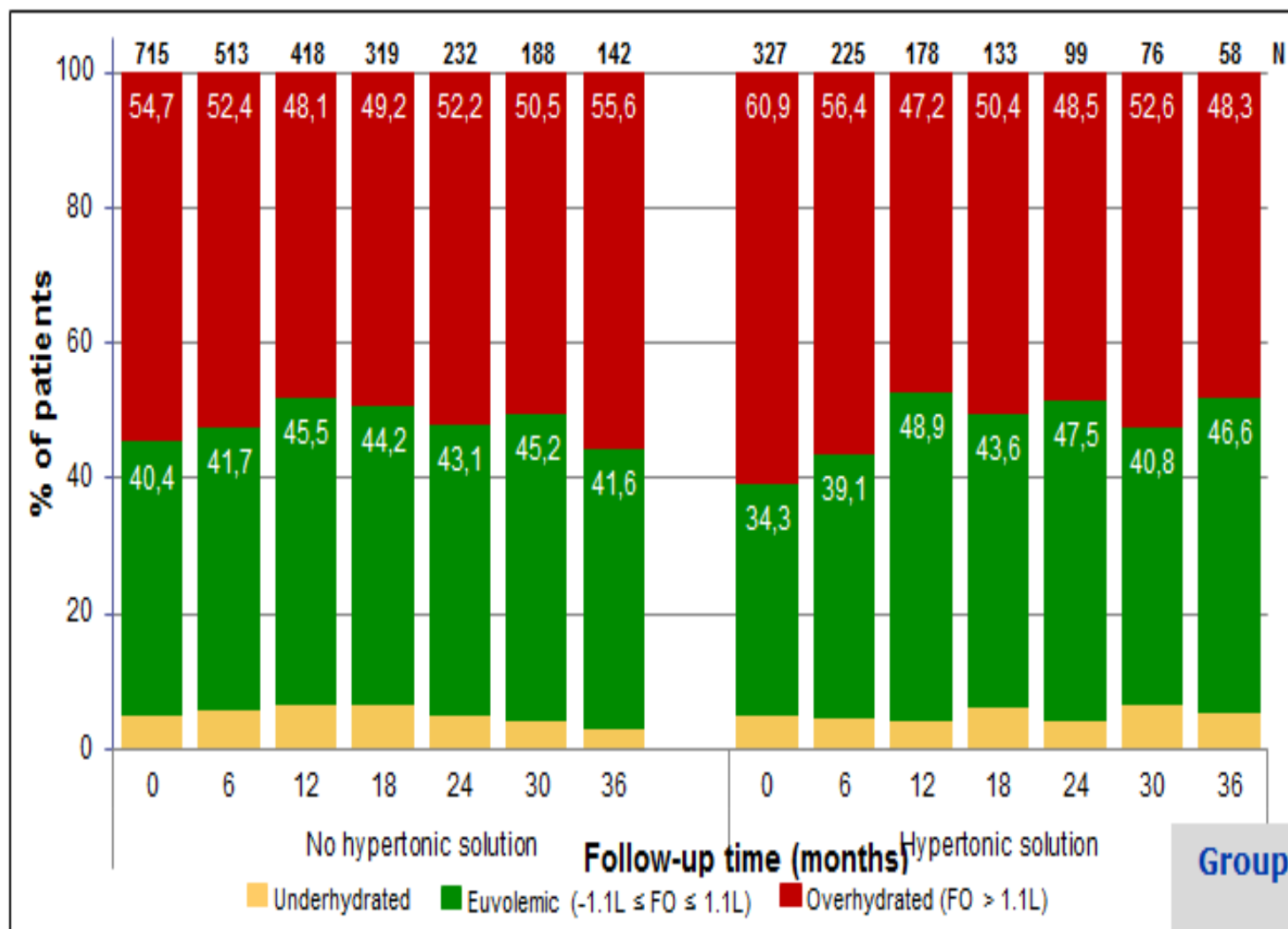
# Course of fluid overload by biocompatible solution

Time dependent group allocation



FO at baseline		N	Mean	STD	Median
	Bio solution	767	1.8	2.2	1.5
	No bio solution	287	2.1	2.6	1.7

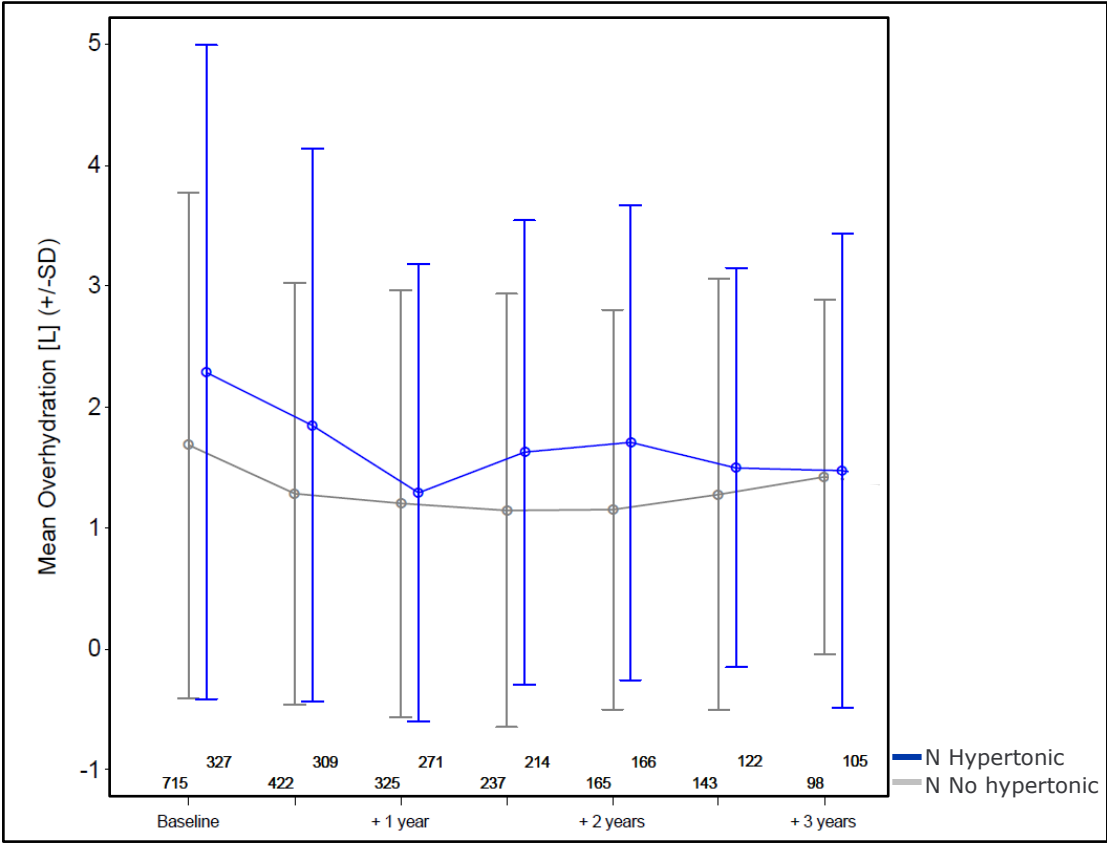
# IPOD-PD study = Hydratation selon le type de dialysat au Glucose



Group allocation at baseline

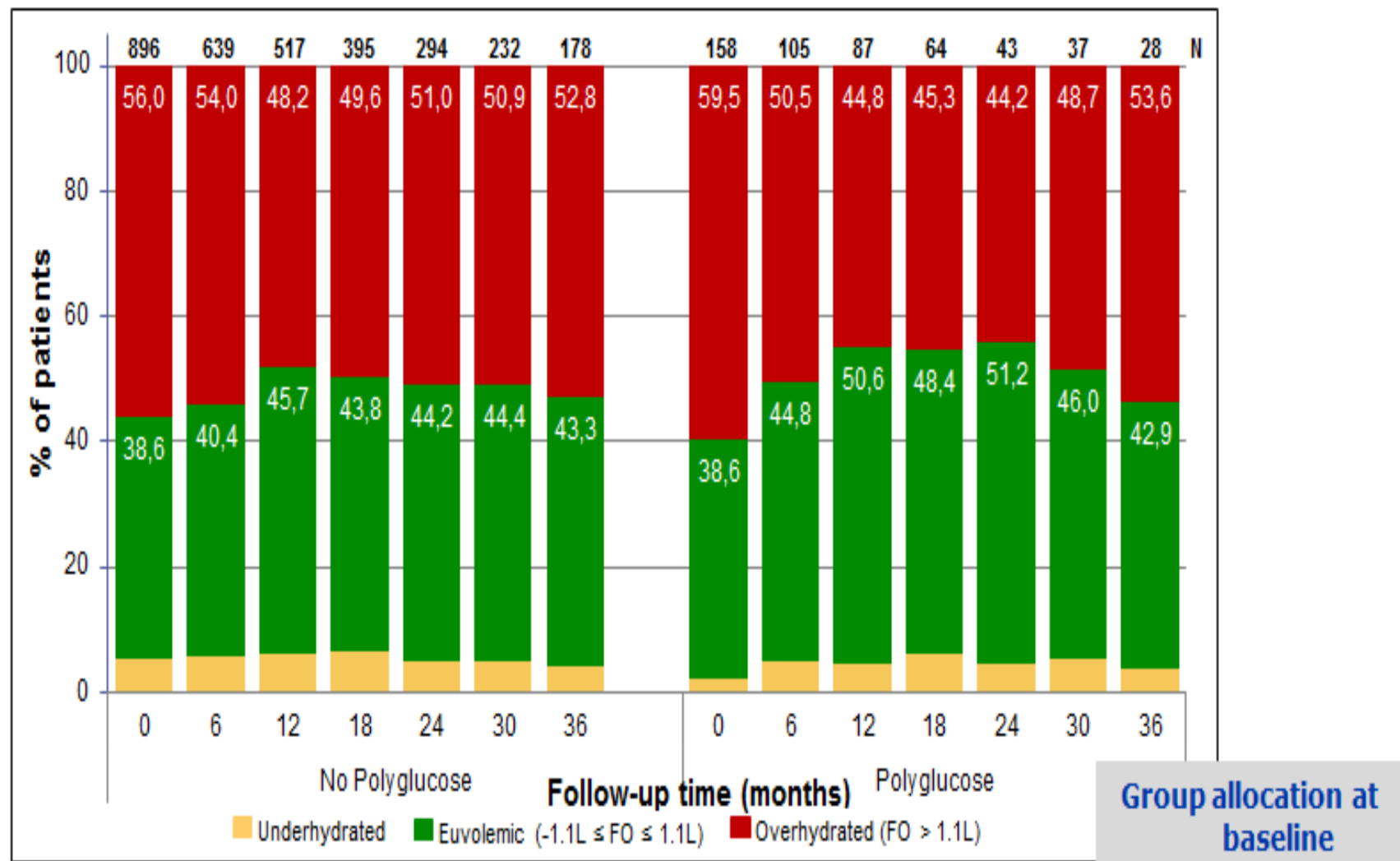
# Course of fluid overload by hypertonic agent

Time dependent group allocation



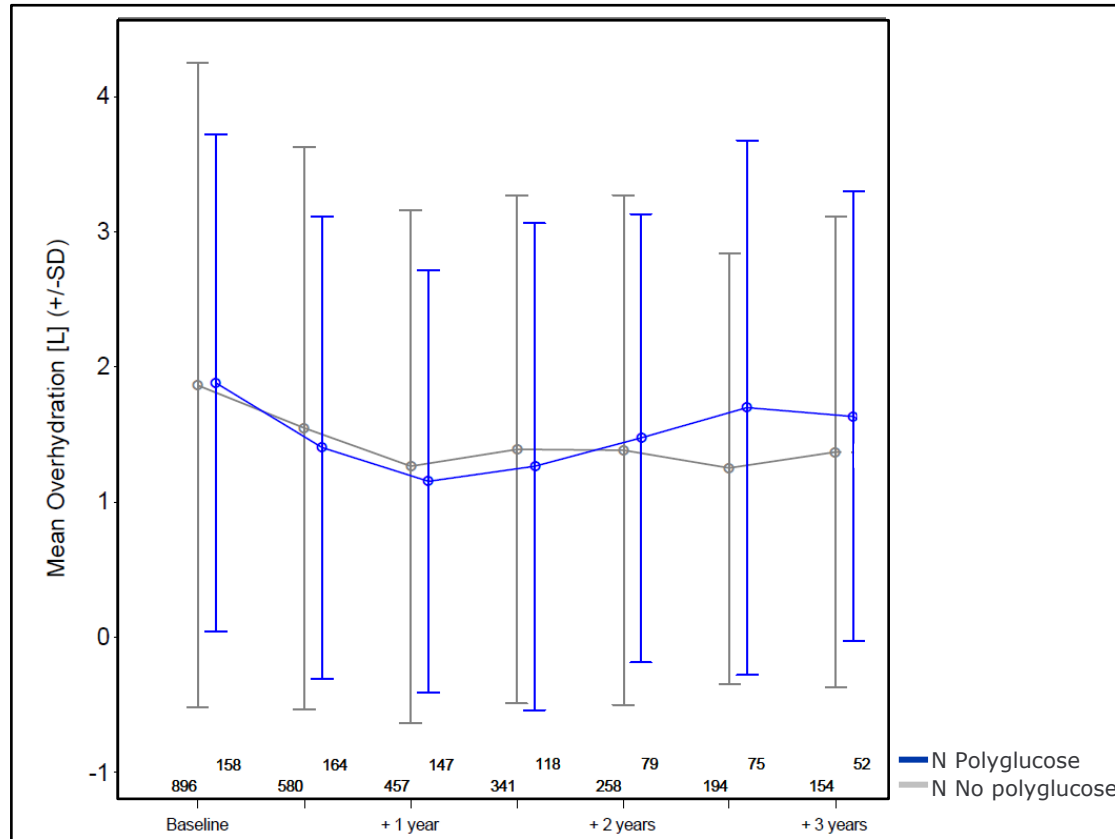
FO at baseline		N	Mean	STD	Median
	Hypertonic	327	2.3	2.7	1.8
No hypertonic	715	1.7	2.1	1.3	

# IPOD-PD study = Hydratation selon la prescription de dialysat au polyglucose



# Course of fluid overload by polyglucose use

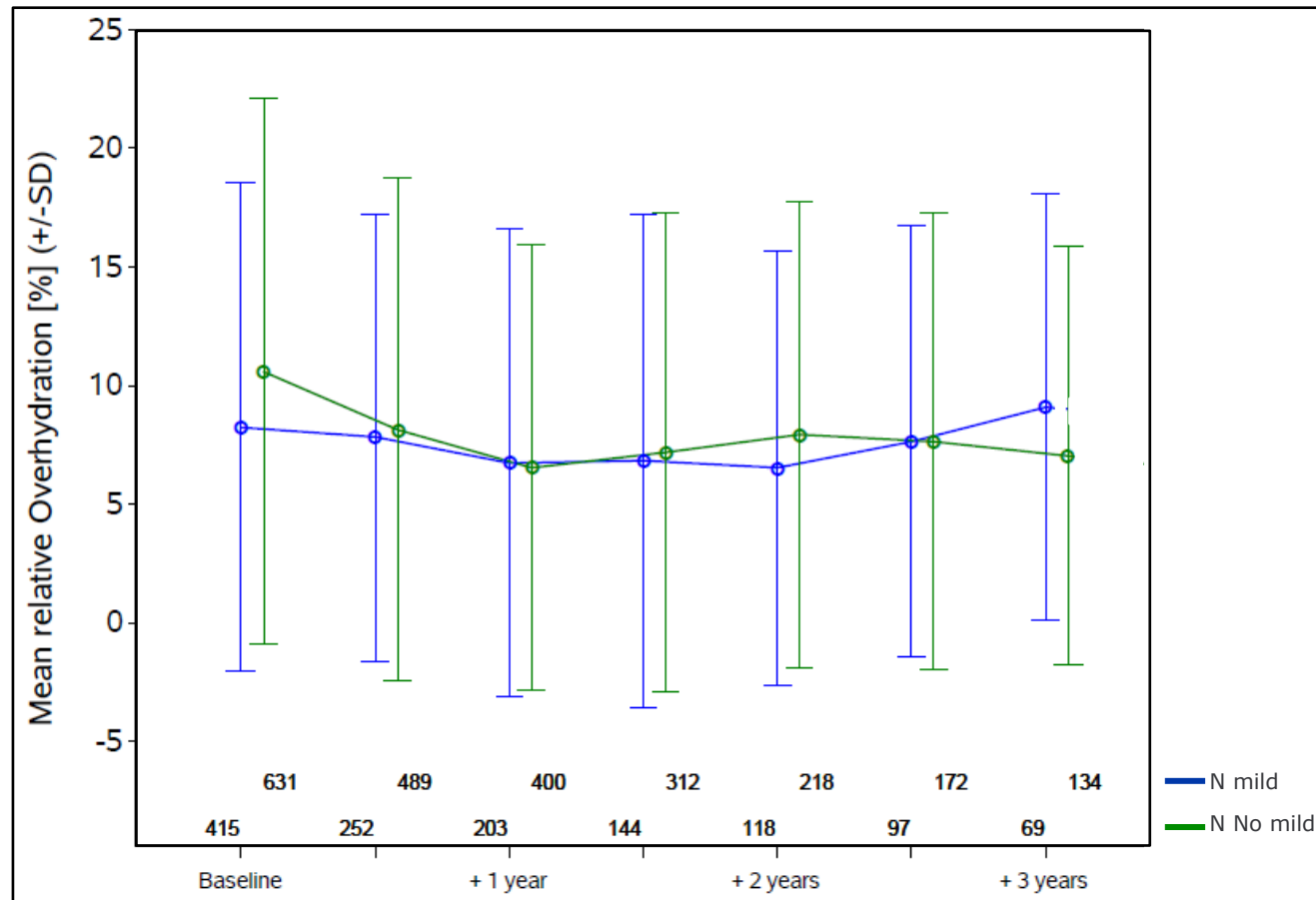
Time dependent group allocation



FO at baseline		N	Mean	STD	Median
	Polyglucose	158	1.9	1.8	1.7
No polyglucose	896	1.9	2.4	1.4	

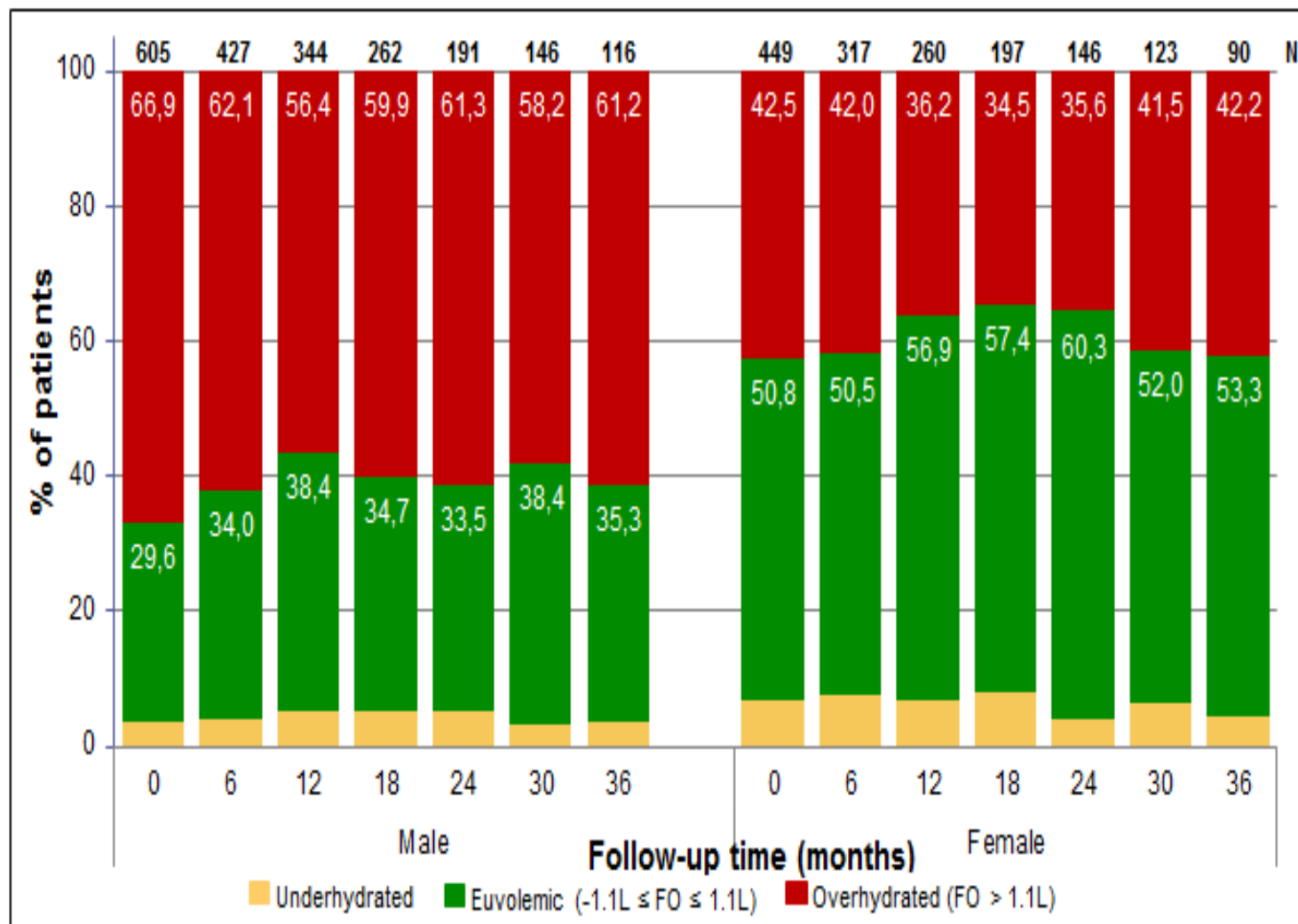
# Course of relative FO by mild/ not mild treatment

## Time dependent group allocation

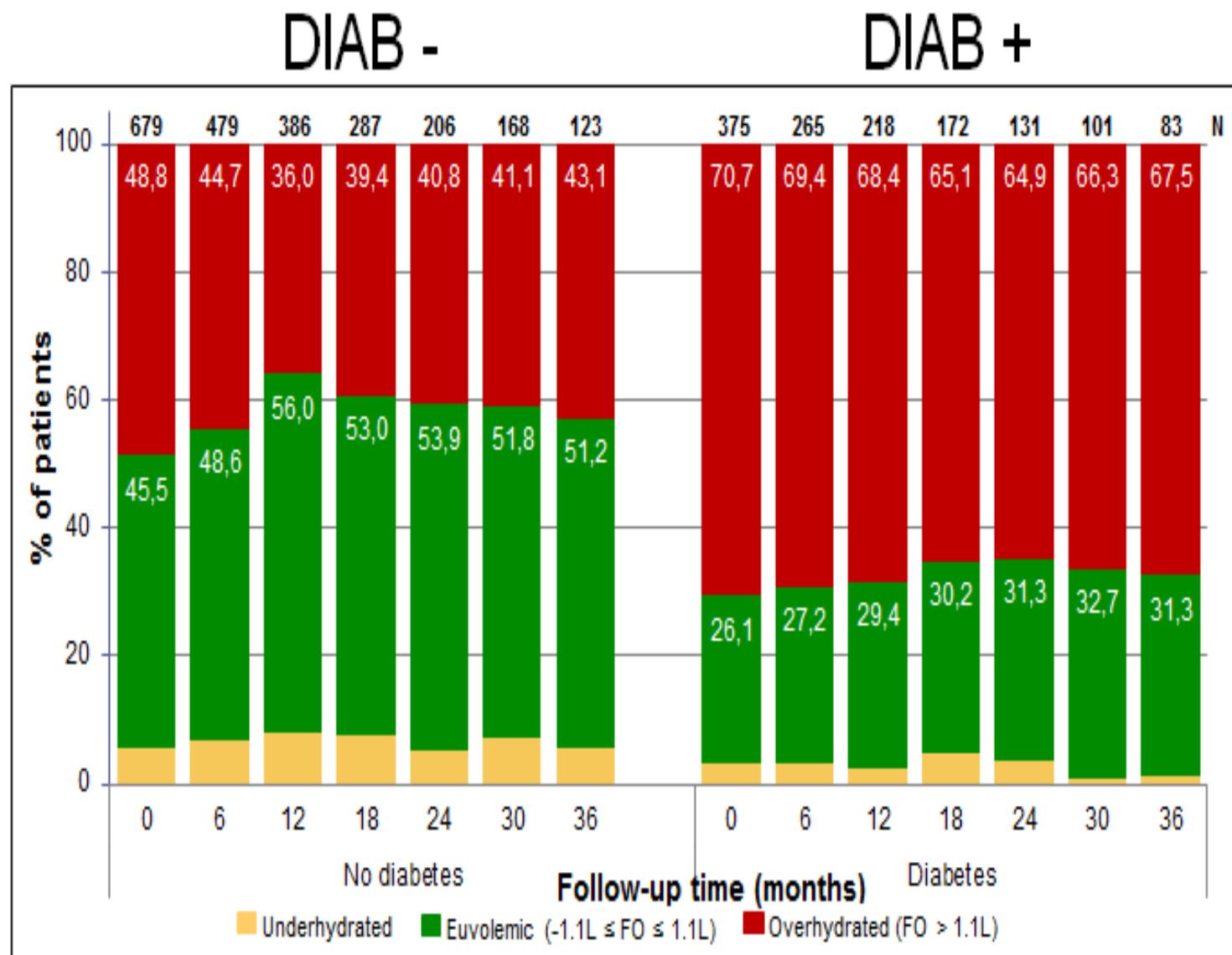


mild: only biocompatible, isotonic (glucose  $\leq 1.5$ ) fluids used, no polyglucose  
not mild: all other prescriptions

# IPOD-PD study = Evolution de l'hydratation selon le Sexe

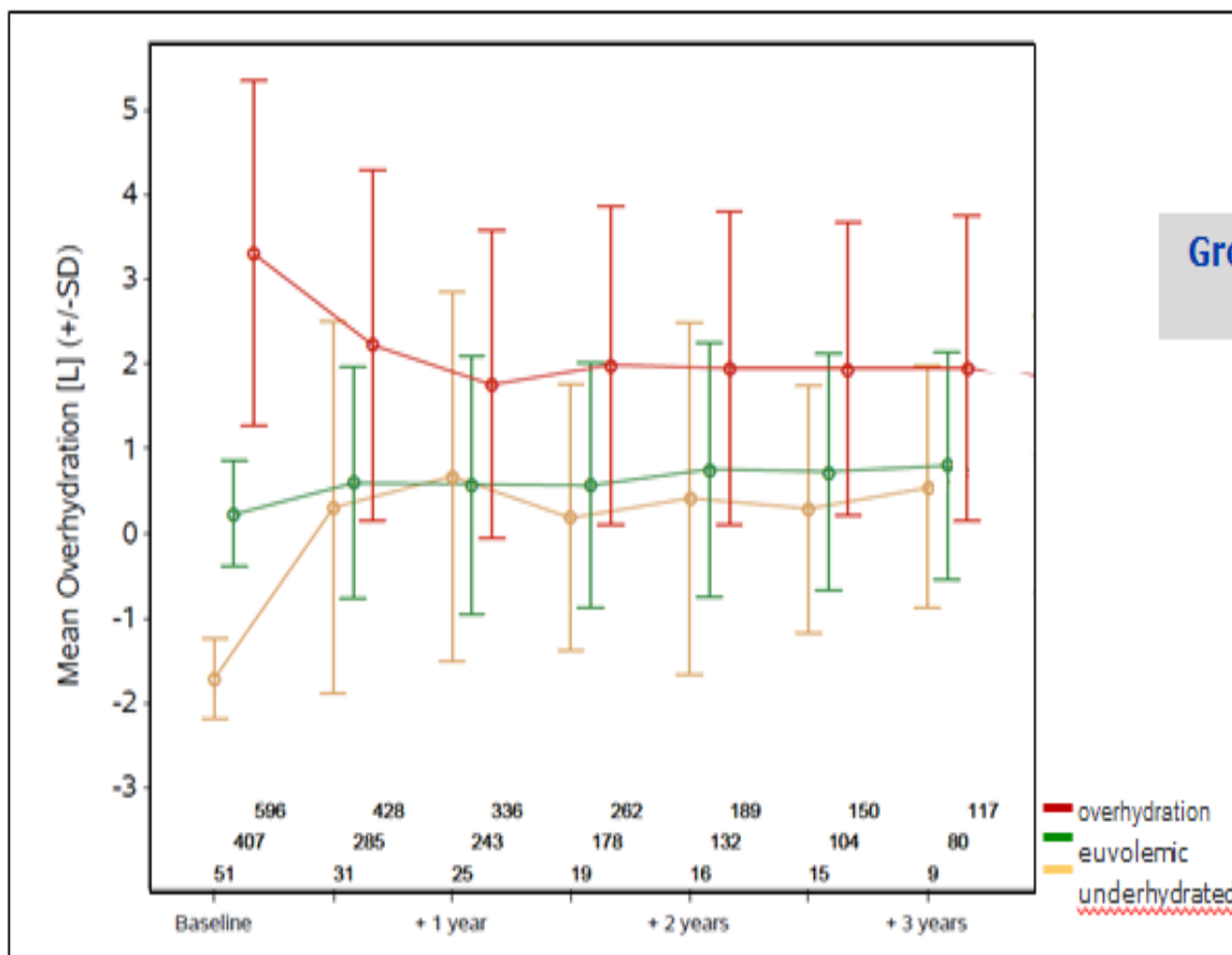


# IPOD-PD study = Evolution de l'hydratation selon le statut diabetique

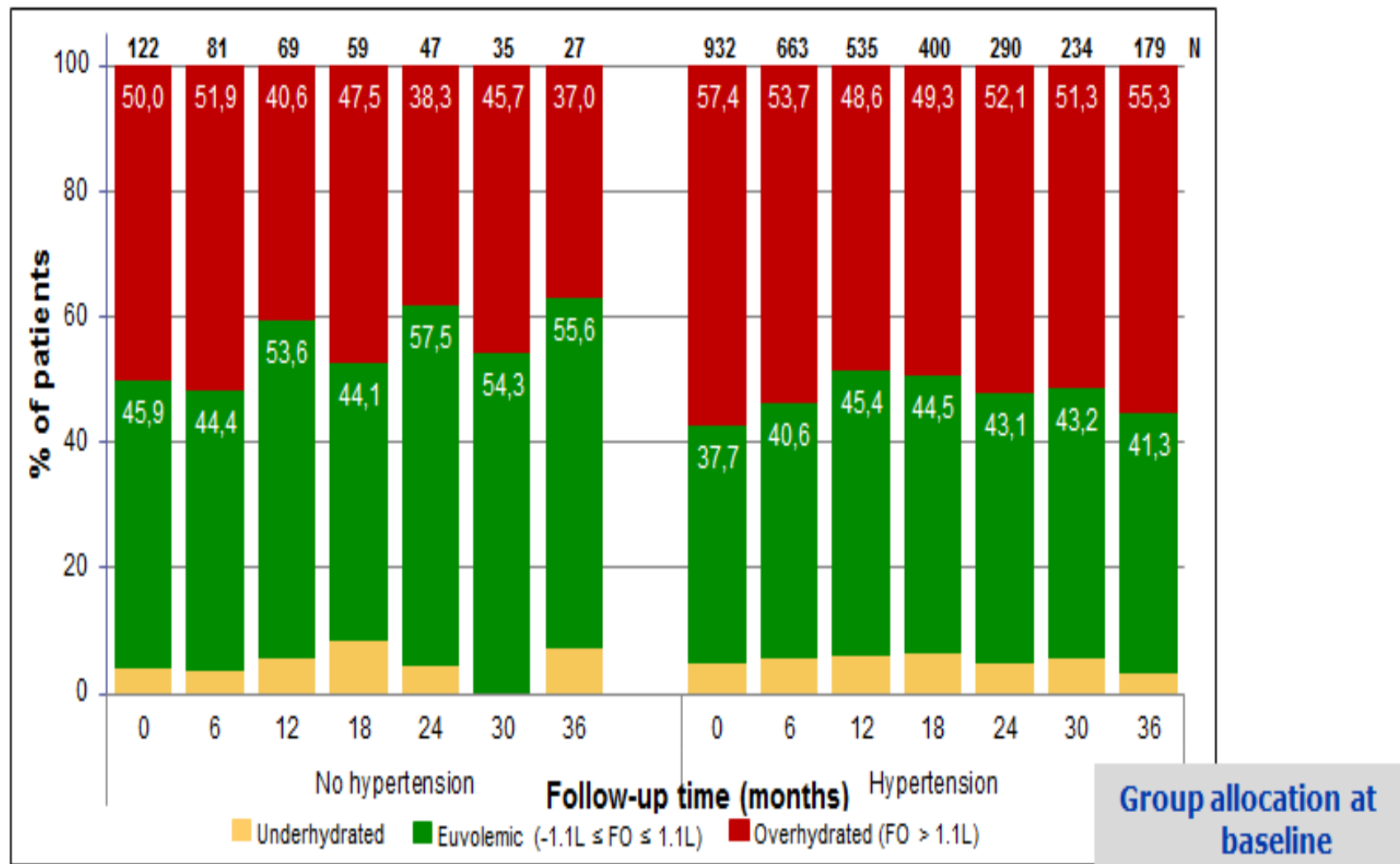




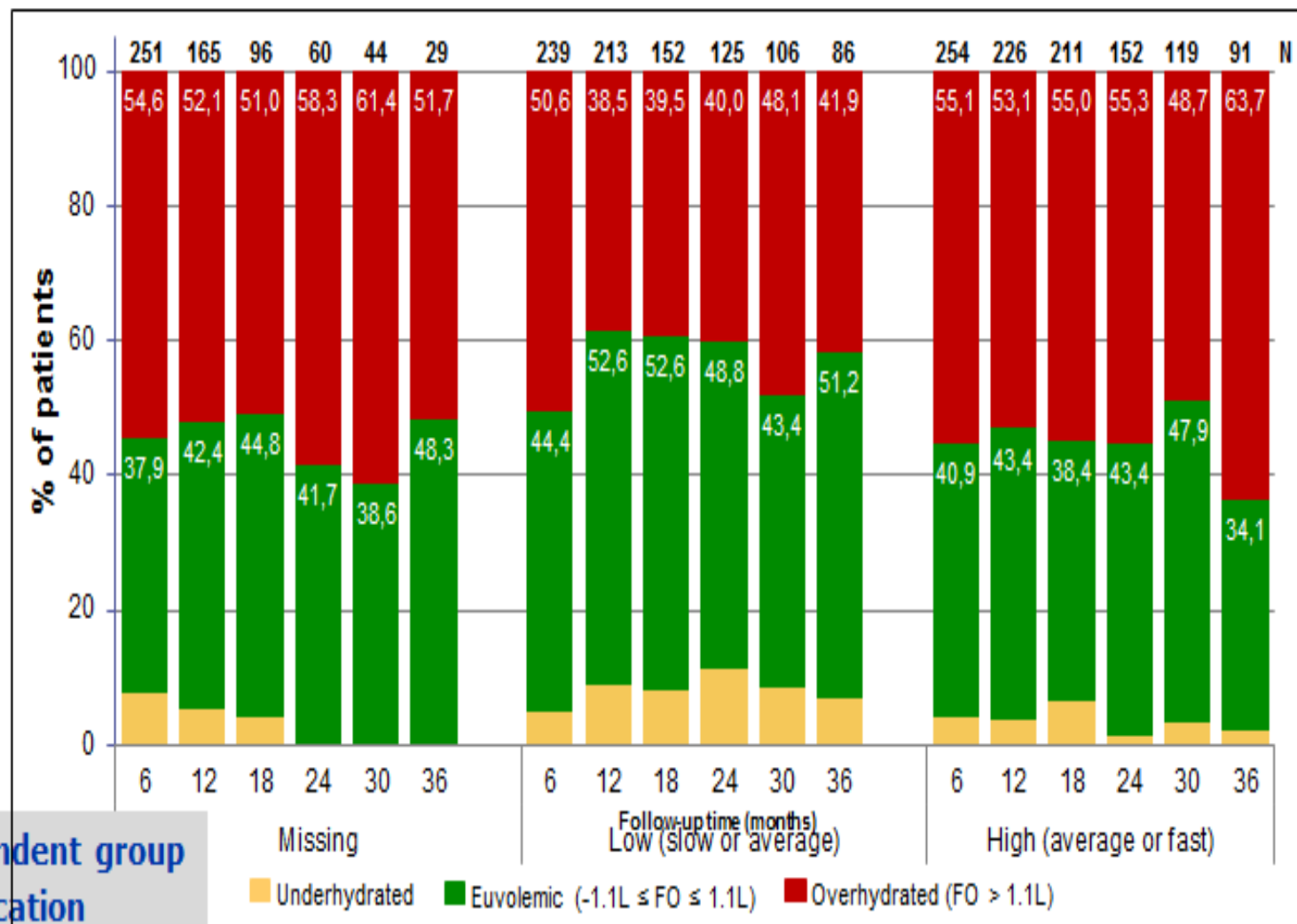
# IPOD-PD study = Evolution de la l'OH selon "l'hydratation" initiale



# IPOD-PD study = Evolution de l'hydratation selon la PA

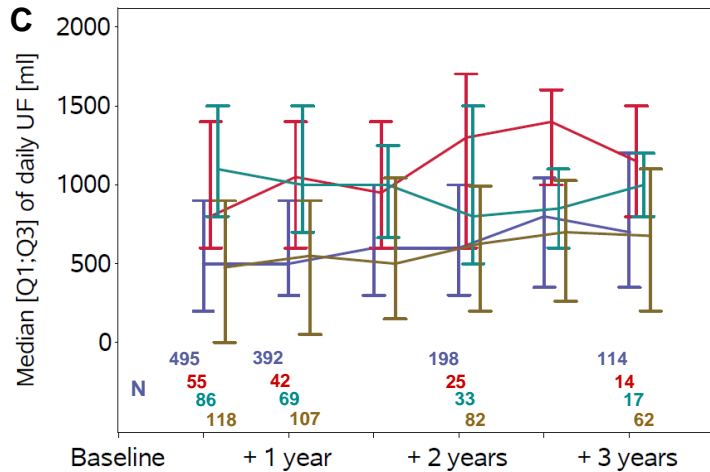
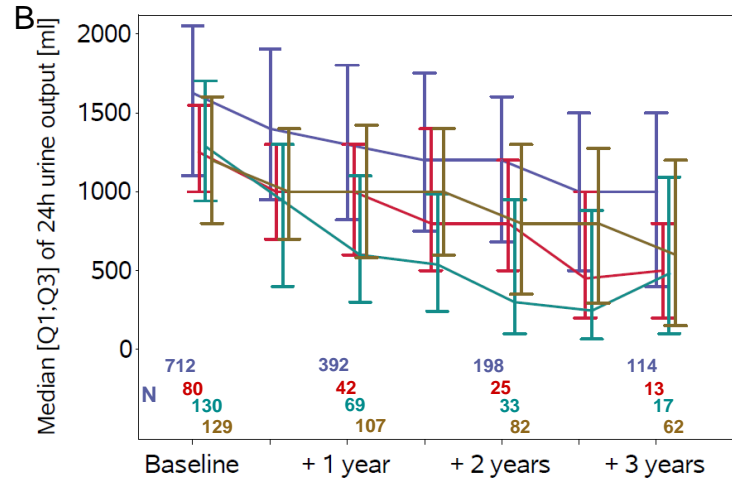
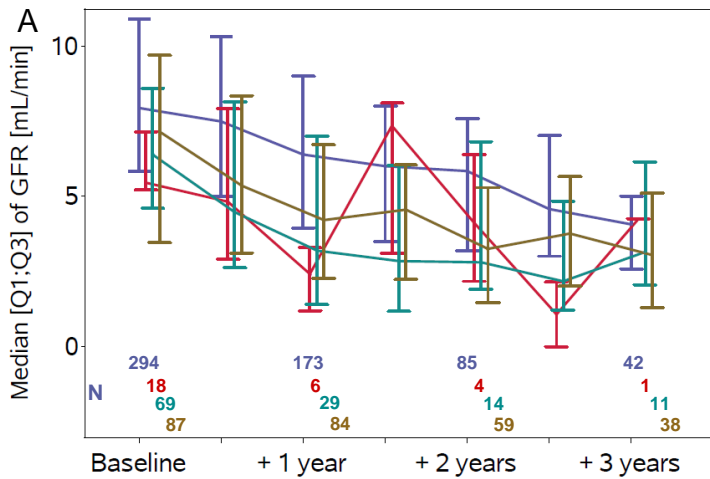


# IPOD-PD study = Evolution de l'hydratation selon le transport péritonéal



# Residual renal function

## Course of GFR(A), 24h urine output (B) and UF (C) – by region



# Final model

Summary of Failure Outcomes			
Total	Event of Interest	Competing Event	Censored
719	115	79	525

factor	category	reference	Subdistribution HR	Lower 95% Wald CL	Upper 95% Wald CL	Pr > ChiSq
region	Asia Pacific/ Korea (AP)	Western Europe (WE)	<b>0.40</b>	<b>0.20</b>	<b>0.82</b>	<b>0.013</b>
	Eastern Europe & Middle East (EE & ME)		0.81	0.38	1.70	0.57
	Latin America (LA)		0.78	0.43	1.41	0.40
Overhydrated at m0 and m6	overhydrated at m0; not overhydrated at m6	not overhydrated	<b>1.85</b>	<b>1.12</b>	<b>3.06</b>	<b>0.016</b>
	not overhydrated at m0; overhydrated at m6	at both time	<b>2.13</b>	<b>1.13</b>	<b>3.99</b>	<b>0.019</b>
	overhydrated at both time points	points	<b>3.17</b>	<b>1.93</b>	<b>5.22</b>	<b>&lt;.0001</b>
changes in hypertonic agent between m0 and m6	hypertonic agent at m0 & m6	no usage of	1.03	0.66	1.61	0.91
	start hypertonic agent	hypertonic agent	1.33	0.82	2.16	0.25
	stop hypertonic agent	at m0 & m6	0.74	0.25	2.23	0.59
changes in polyglucose between m0 and m6	polyglucose at m0 & m6	No usage of	1.11	0.62	1.97	0.73
	start polyglucose	polyglucose at	1.10	0.59	2.03	0.77
	stop polyglucose	m0 & m6	1.05	0.23	4.74	0.95
diabetes	yes	no	0.87	0.59	1.30	0.54
gender	male	female	0.97	0.66	1.42	0.86
age		per 10 years increase	<b>1.19</b>	<b>1.04</b>	<b>1.36</b>	<b>0.01</b>

- **Effect of overhydrated:** for all groups with at least 1 time point overhydrated HR>1
  - ➔ **In average technique failures occur faster for patients who are overhydrated (at 1 or both time points) than for patients who are not overhydrated.**
  - ➔ **Patients with both time points overhydrated have the highest HR, followed by patients who are not overhydrated at m0, but overhydrated at m6**
- **Effect of region:** HR of Asia Pacific <1 → in average technique failure occurs **slower in AP than in WE**
- **Effect of age:** HR > 1 → **The older the patient the faster technique failures occur** in average
- **No effect of hypertonic agent, polyglucose, diabetes and gender could be found**

# Conclusions

- ➡ **Fluid overload is frequent in incident PD patients**
- ➡ **Improvement in fluid overload during the first year treatment**
- ➡ **Fluid overload is associated with technique failure**
- ➡ **Use of hypertonic bags is not associated with better fluid status**
- ➡ **Use of icodextrin is not associated with better fluid status**
- ➡ **Suggestion that fluid balance is of importance in the prognostic of PD patients**