

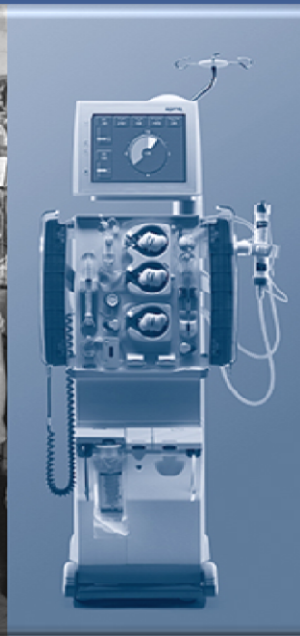
## **“In Touch – Leading & Succeeding In Renal Therapy”**

**Raymond M. Hakim, M.D., PhD., Chief Medical Officer  
Sr. Executive Vice President Clinical & Scientific Affairs FMCNA**

**Capital Markets Day  
Luton, September 1–2, 2010**



**Fresenius Medical Care**

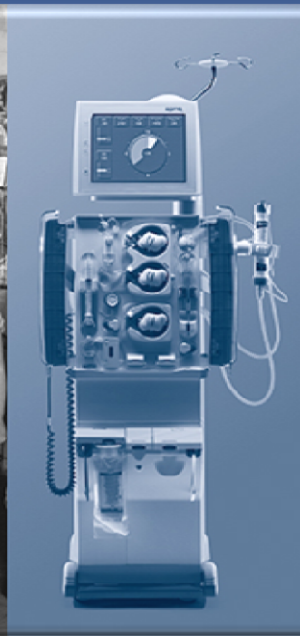


**Doing Well by Doing Good**



**Fresenius Medical Care**





# Improving Anemia Management & Outcomes



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# Optimization of Anemia Management



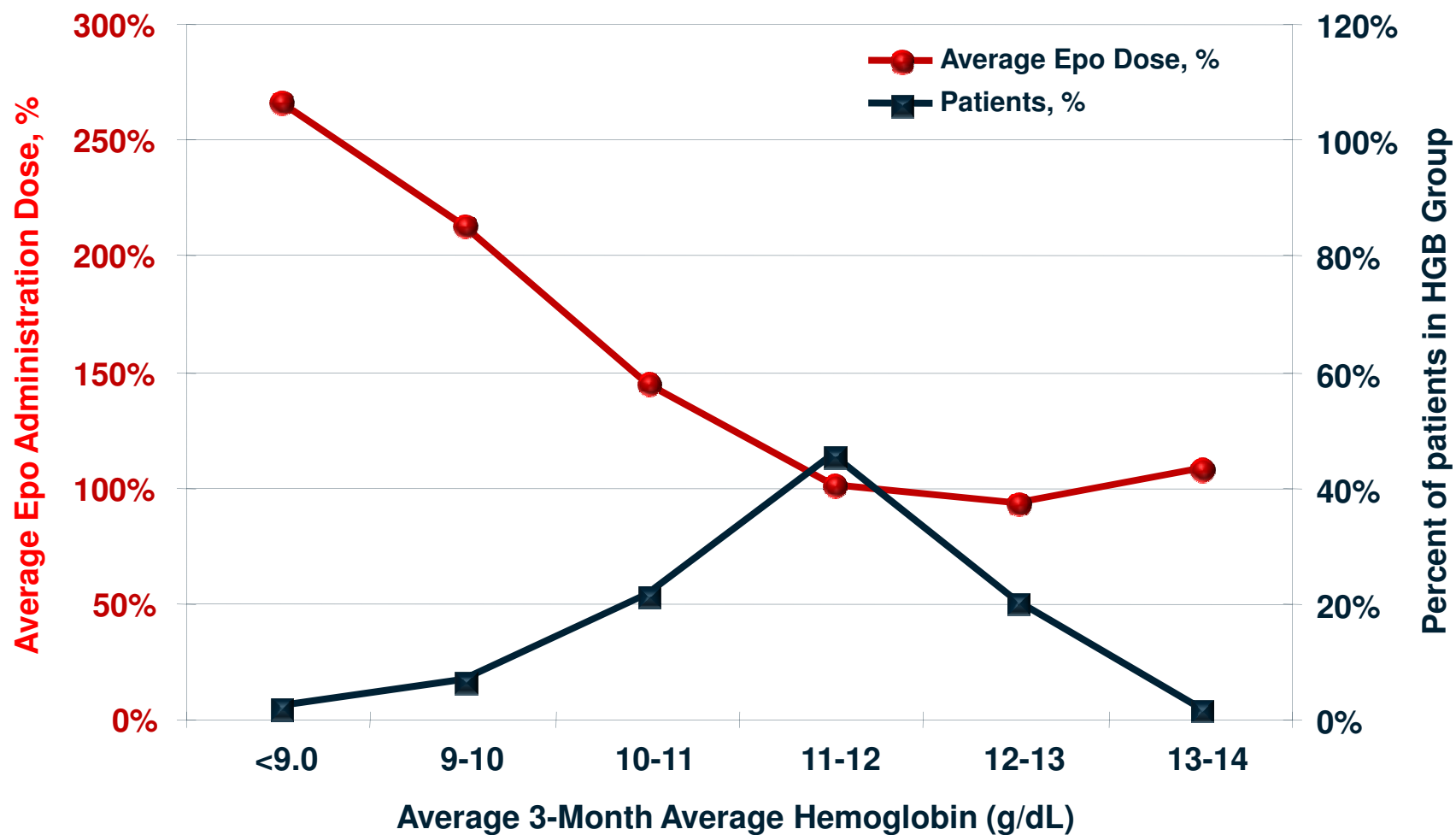
- 1. RightStart® at the initiation of dialysis**
- 2. RightReturn® after Hospitalization**
- 3. Catheter Reduction**
- 4. Clinical research to reduce inflammation:**
  - a. Investigate the use of anti-inflammatory agents and ultrapure dialysate to improve Epogen responsiveness**
- 5. Aim for an iron saturation (Tsat) of 30-50%**
- 6. Computerized anemia management algorithm**
- 7. Hemoglobin goal of 10.5 – 12.0 gm/dl (to avoid Hemoglobin <10 g/dl)**



# Optimization of Anemia Management



## Epo Dose vs. Hemoglobin (Q2 2010)



# Initiation Of Dialysis In The U.S.



- **57% had albumin concentration below lower limit of normal**
- **50% had no visit with dietitian (21% had one visit)**
- **80% of patients with Hgb<9 gm/dl were not receiving EPO**
- **82% initiated dialysis with a catheter**
- **18% had a permanent access 30 days before starting dialysis**
- **53% used temporary access 60 days after initiation**

# Co-Morbidities and Risk Factors Associated with Early Mortality



## Co-Morbidity

- Age
- Nutritional Status
- Diabetes
- Cardiovascular Disease
- LVH

## Risk Factors

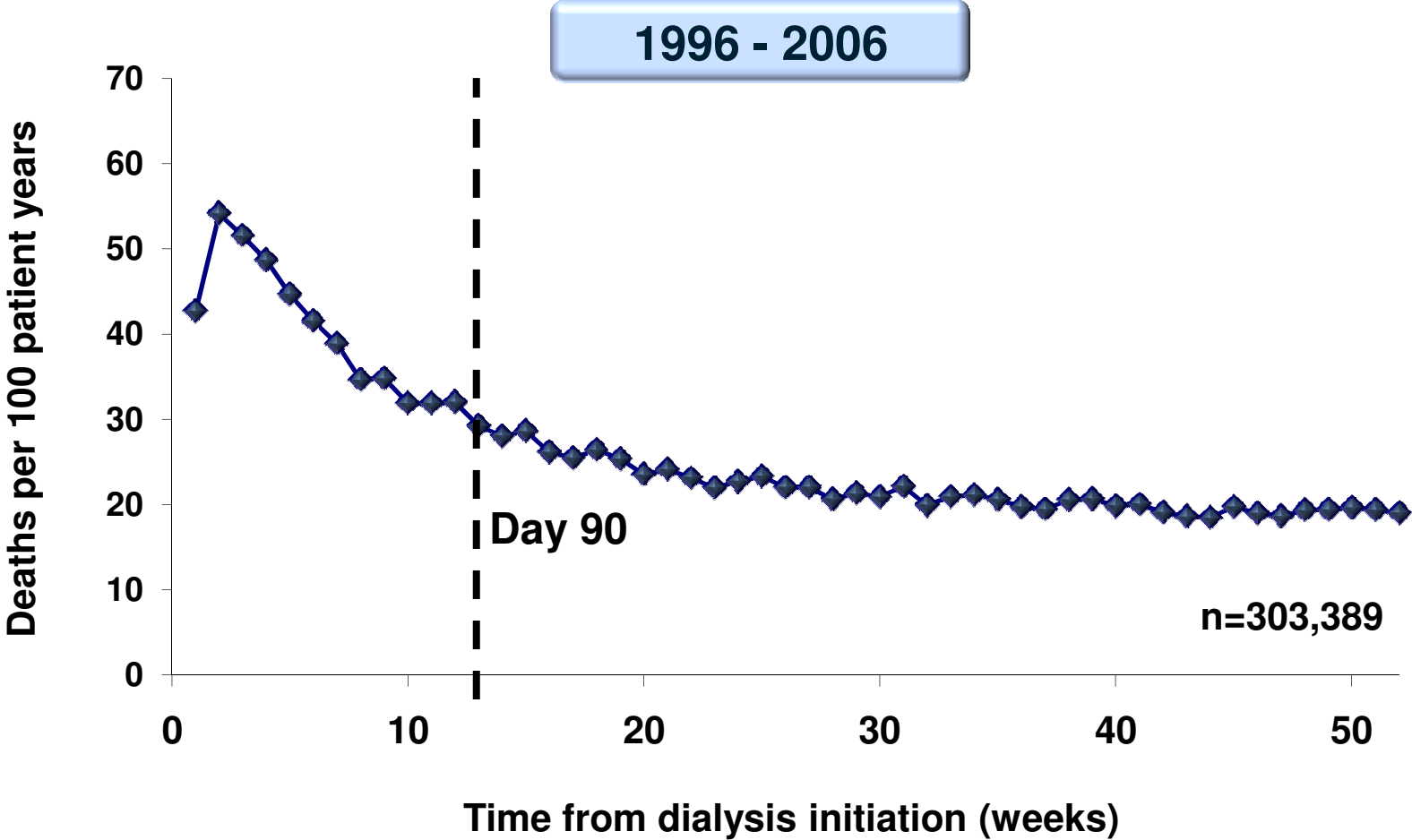
- Unplanned start (w/o permanent access)
- Short (<4 months) prior nephrological care
- Low residual renal output

## Reversible Risk Factors

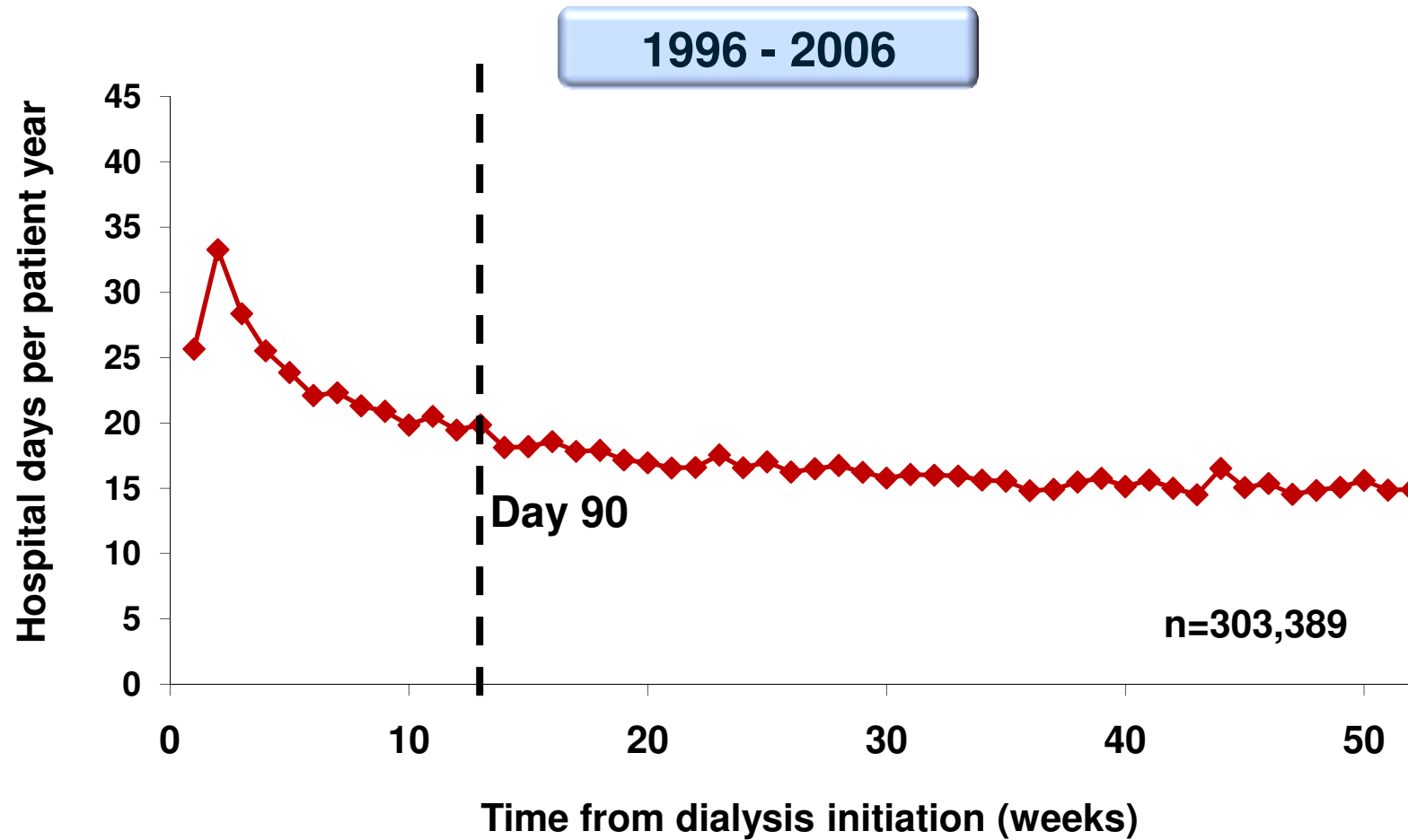
- High catheter rate
- Low albumin
- Anemia
- High Phosphorus
- Volume Overload

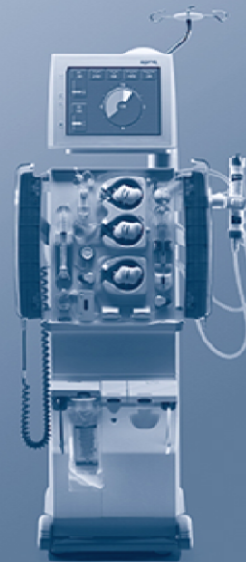


# Mortality in Year One of Dialysis



# Hospitalization in Year One of Dialysis





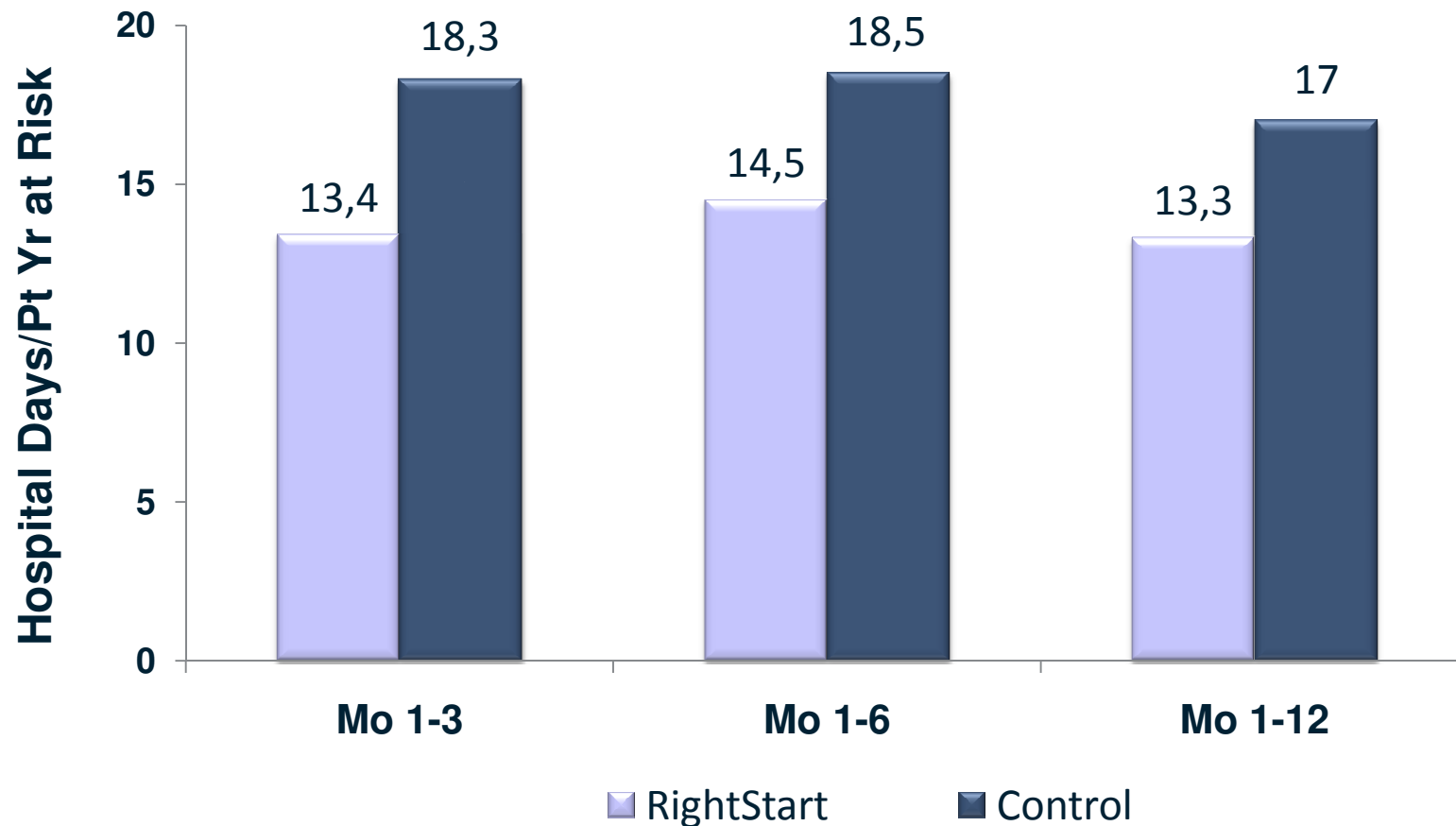
# RightStart® Program



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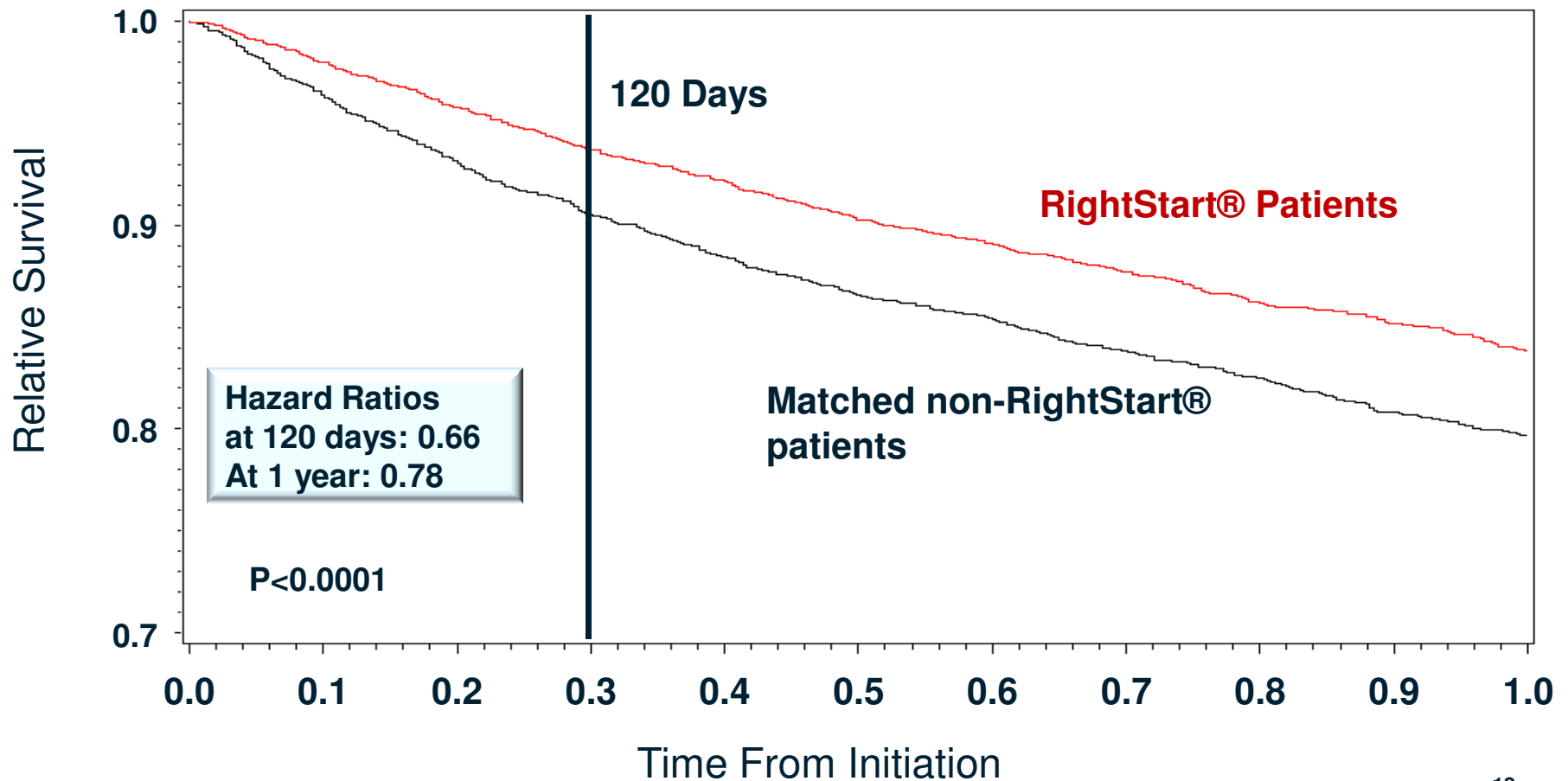
# Hospital Days Per Patient Year at Risk



# Survival of RightStart® Patients



**One Year Survival of RightStart® Pts vs. Case-Control matching, All Pts n=approx 8,000**



# Advantages of the RightStart® Program



<b>Number of new (incident) patients in US</b>	<b>100,000</b>
<b>Number of new (incident) patients in FMS</b>	<b>33,000</b>
<b>Current 1<sup>st</sup> Year Mortality (USRDS)</b>	<b>25.4%</b>
<b>Number incident pts at end of 1<sup>st</sup> year without RightStart®</b>	<b>24,618</b>
<b>Expected 1<sup>st</sup> Year Mortality with RightStart® (HR = 0.75)</b>	<b>19.0%</b>
<b>Number incident pts at end of 1<sup>st</sup> year with RightStart®</b>	<b>26,730</b>
<b>Lives Saved/Lives Extended from RightStart®</b>	<b>~ 2100 pts/Yr</b>



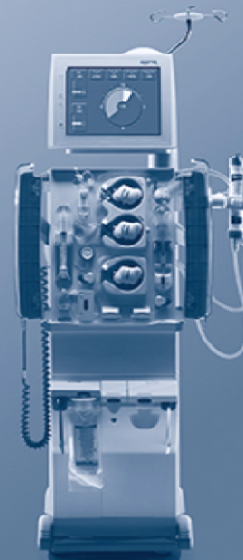
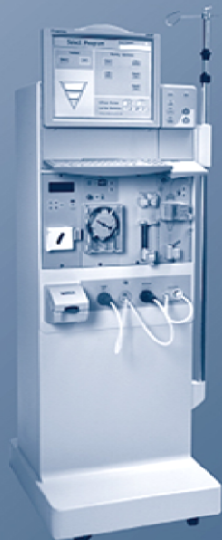
# RightStart® Program Summary



**Patients initiating dialysis present with several co-morbidities and risk factors, and knowledge deficits that are associated with a high initial 90-day mortality rate, (generally not reflected in published data).**

**Several of these risk factors can be attenuated or reversed more rapidly with an intensive team effort during the initial 90 days of therapy.**

**The RightStart® program, consisting of focused attention on reversible risk factors and patient education, resulted in a significant reduction in mortality and hospitalization during those initial 90 days, which extended up to 1 year following initiation of dialysis.**



# RightReturn® Program



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# Re-Hospitalization After Discharge from Hospital



## Medicare Fee-For-Service (N=3 million)

Medical Discharges	% Cumulative Re-Hospitalizations
0-30 days	21.1%
30-60 days	30.3%
61-90 days	36.6%
91-180 days	47.9%
181-365 days	59.4%



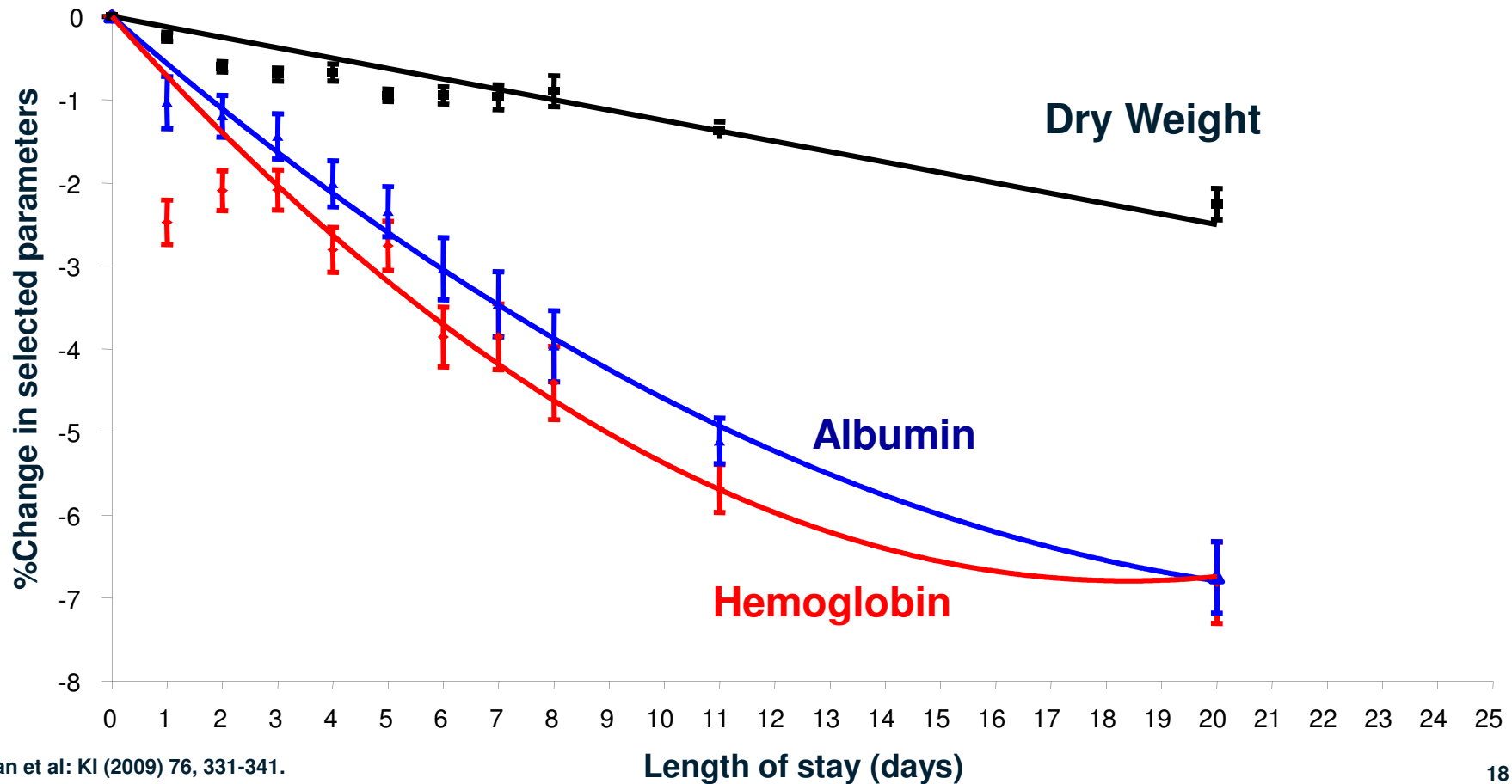
# Predictors of Re-Hospitalization



		<u>Relative Risk</u>
<b>Age</b>	<55 yr	1.0 (ref)
	55-69 yr	0.99
	70-79	1.07
<b>ESRD</b>		1.42
<b>No. of Re-Hospitalizations</b>	0	1.0
	1	1.37
	2	1.75
	≥3	2.5

# Pre- To Post-Hospitalization Outcomes

**% Change in Dry Weight, Albumin, & Hgb  
From Pre- to Post-Hospitalization  
N=126,000 HD pts at FMCNA in 2007**



# Medical Goals that are Synergistic with the “Bundle”



- 1. Reduce hospitalization and mortality in first 120 days**
- 2. Optimize iron, Epogen management**
- 3. Increase prevalence of home therapies**
- 4. Reduce catheter rates, the main cause of BSI and Epogen “resistance”**

# Treatment Options Program (TOPs) Overview



- **Initiated to educate patients with Stage 3 or 4 CKD prior to ESRD**
- **Consists of a two-hour education program provided at least every month in each FME “area”**
- **Patients are referred by their nephrologists or PCPs**
- **Non-biased presentation of available treatment modalities**
  - **In center**
  - **Home Therapy**
  - **Transplant**
  - **No therapy**
- **Patients are encouraged to attend with family members**
- **Advantages of Permanent Access are emphasized**

# Treatment Options

## September 2006 thru May 2010



- **35,521 pre-ESRD TOPS educations performed so far**
- **132,930 patients admitted to FMS**
  - **11,579 of this group had TOPS education**
  - **121,351 starts did not have TOPS education**
- **Only 8.7% of total starts were TOPS educated**

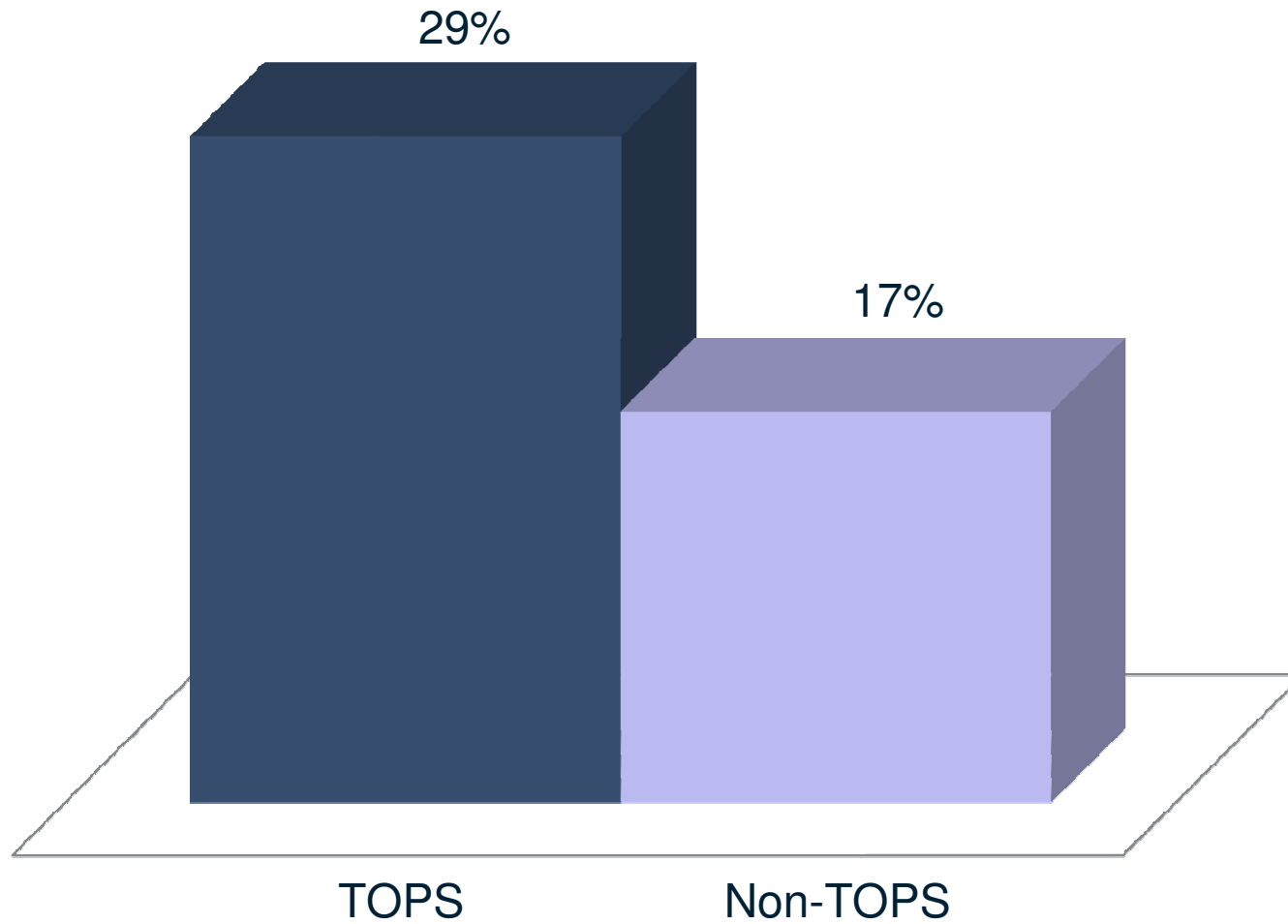


# Follow up

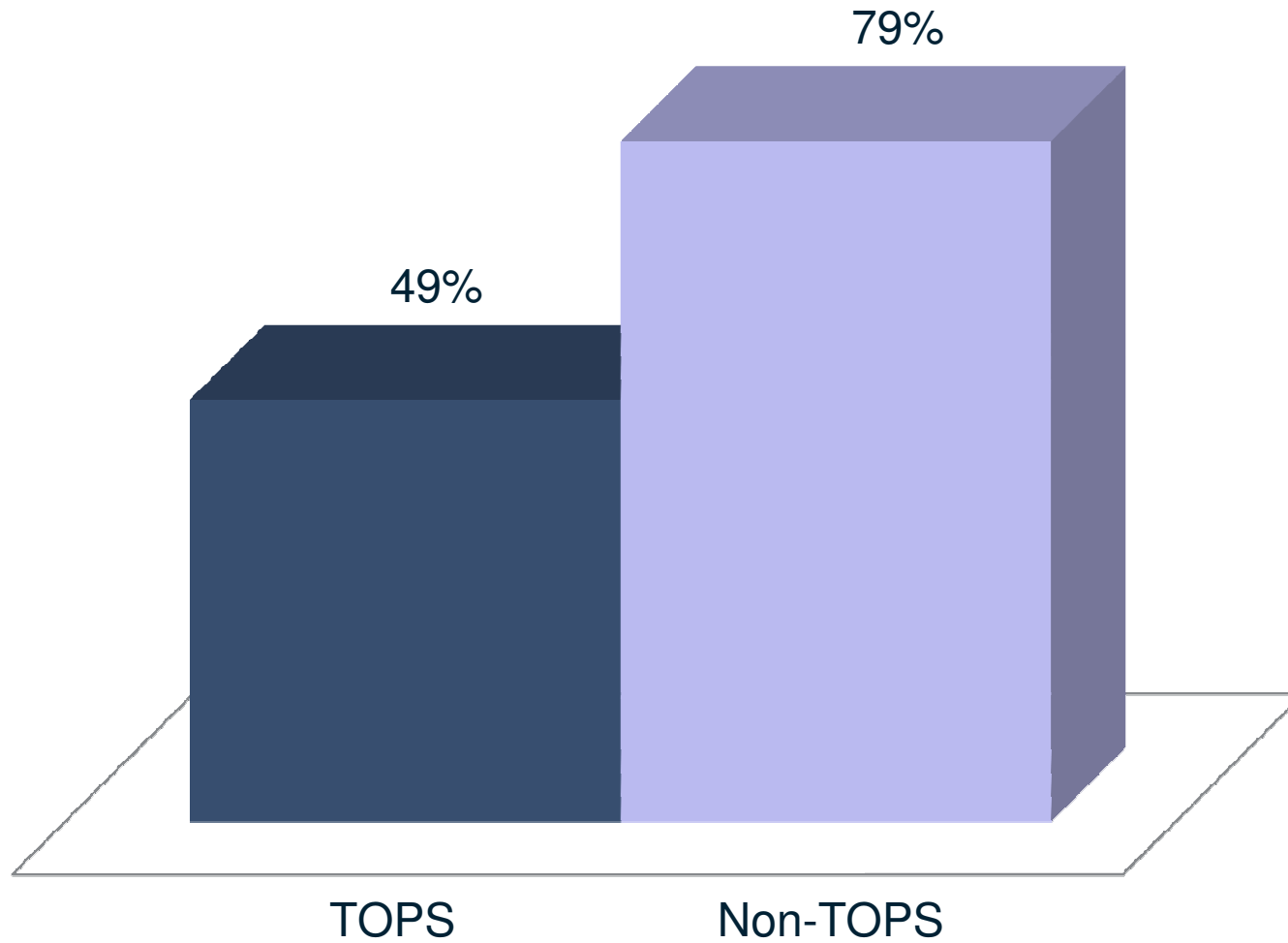


- **Goals**
  - **Improve home therapy awareness**
  - **Increased use of fistulas**
  - **Decrease catheter utilization**
  - **Early removal of catheters if necessary**
- **Follow up at 30, 90 and 180 days after TOPs education**
  - **Remind patient to go back to referring physician**
  - **Invite them and their families to return for another round of TOPs (prn)**

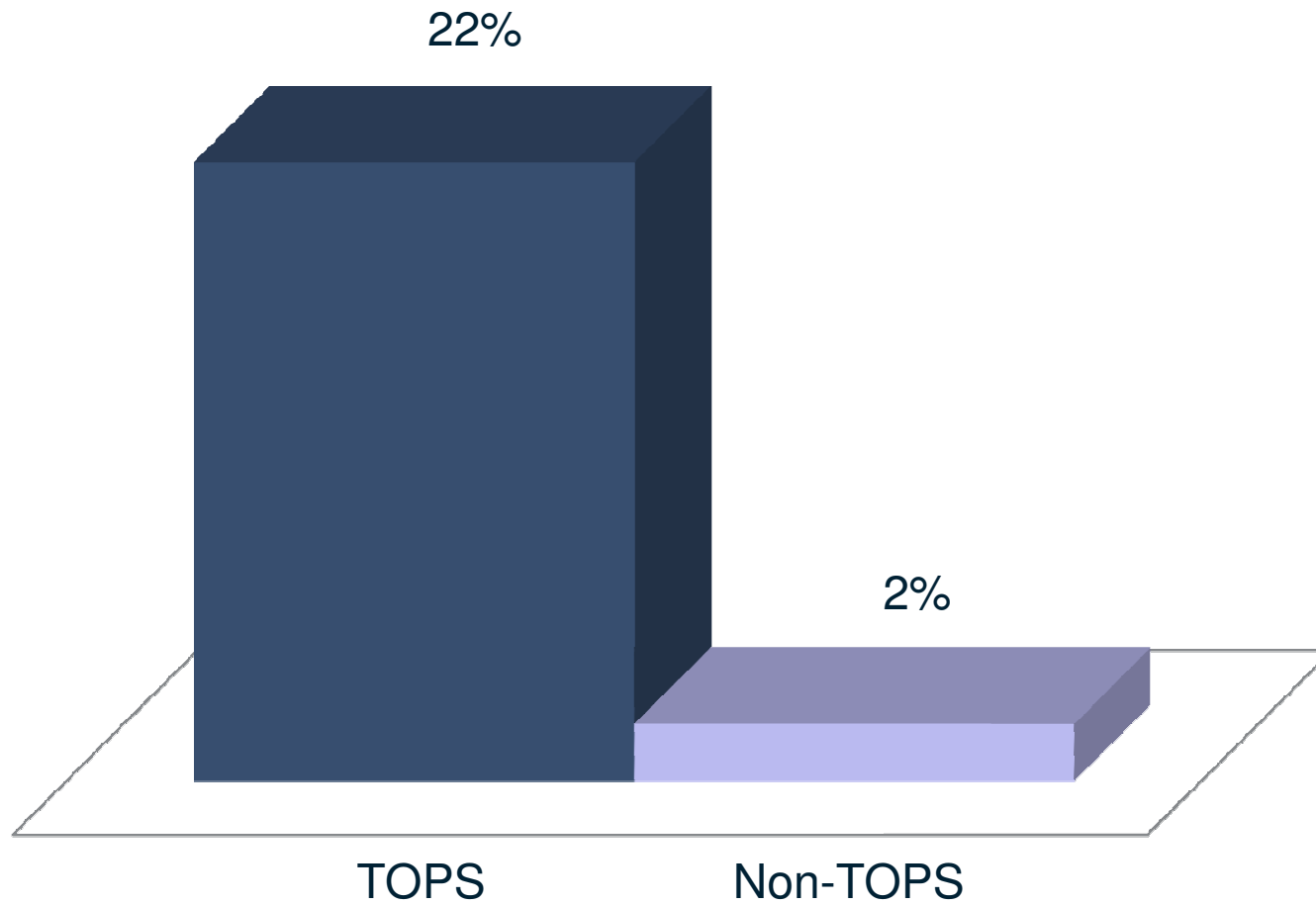
# Fistula/Grafts Start (Feb-May 2010)



# HD Catheter Starts (Feb-May 2010)



# Home Therapy Starts (Feb-May 2010)

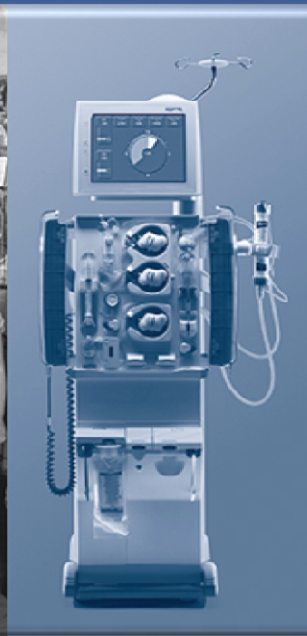


# Treatment Options Program (TOPs) Outcomes



## Participation in TOPS leads to:

- Increased knowledge about Home Therapies and rate of home therapy selection
- Decrease use of hemodialysis catheters
- Greater use of AVF at start of dialysis
- Improved survival rate at 90 days after initiation of dialysis



# Catheter Reduction Initiative



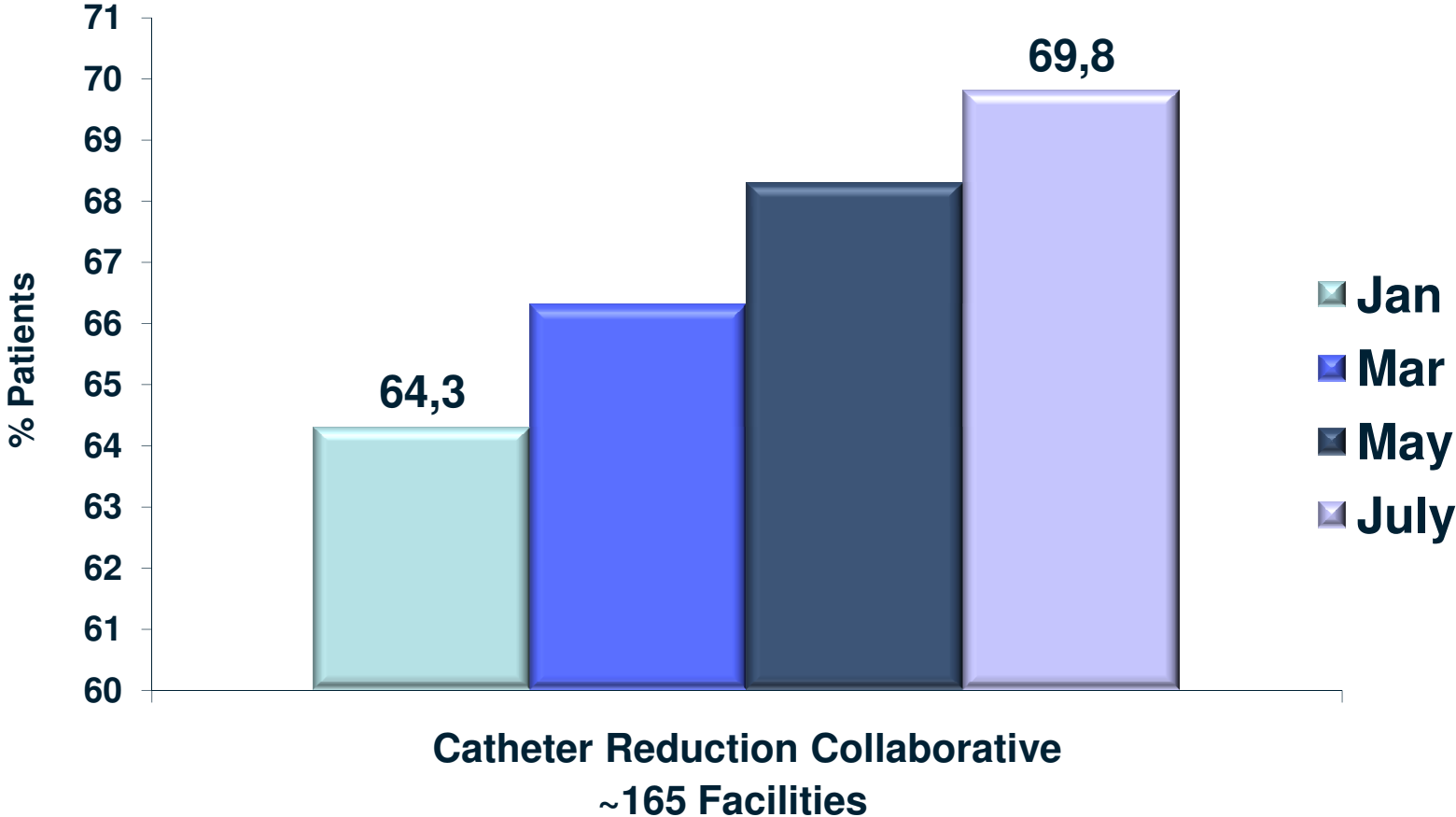
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# Catheter Maintenance Costs Per Patient



“Out of pocket” catheter related costs in the Bundle environment ~ \$ 10,000 per patient per year



# Hydration Management



- **Hydration management is essential to:**
  - **Reduce hospitalization, ER visits, and “missed treatments.**
- **Increasing evidence that cardiovascular mortality (~50% of all deaths) is not “atherosclerotic” heart disease, but left ventricle failure.**

# Background and Medical Need

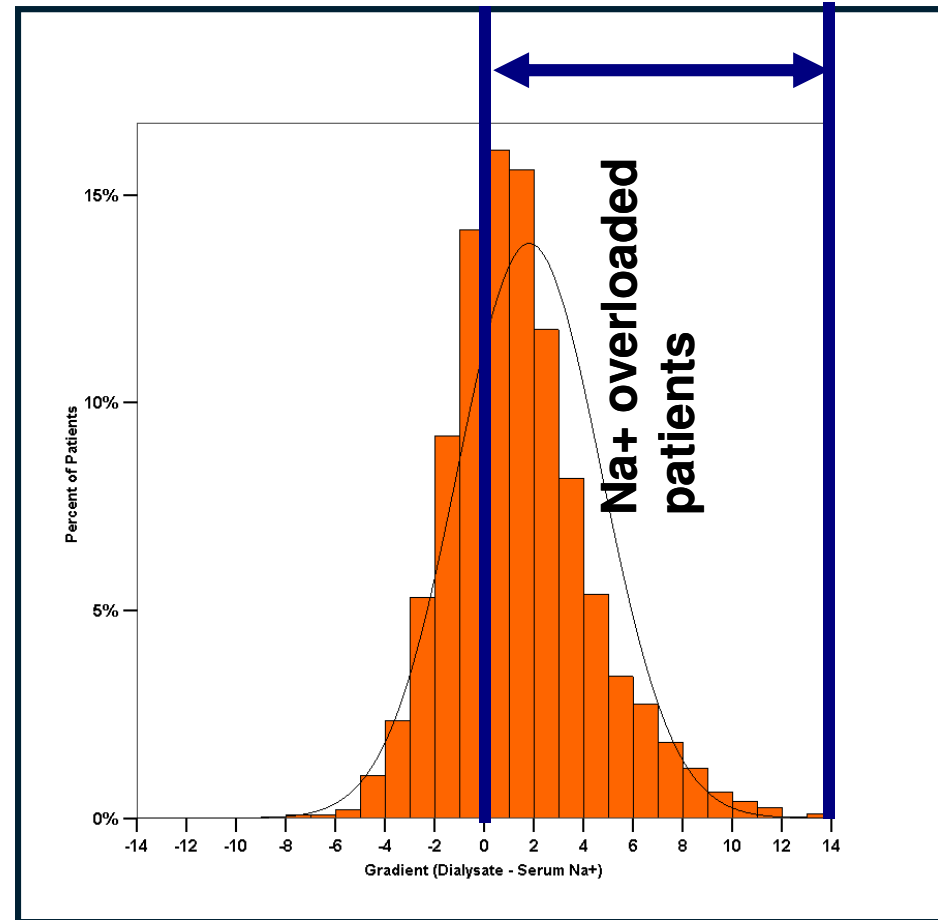


- The state of hydration depends on:
  - Salt and water intake by patient (dietary counseling)
  - Sodium “loading” during dialysis
- Sodium loading during dialysis is a major contributor to fluid overload
  - increased thirst
  - increased fluid intake
- Sources of sodium loading during HD:
  - **influx from dialysate (dialysate sodium higher than serum sodium)**
  - priming and rinsing of blood lines with saline
  - treatment of hypotensive episodes and cramps with saline infusions

# Na<sup>+</sup> Distribution – 2008 Data

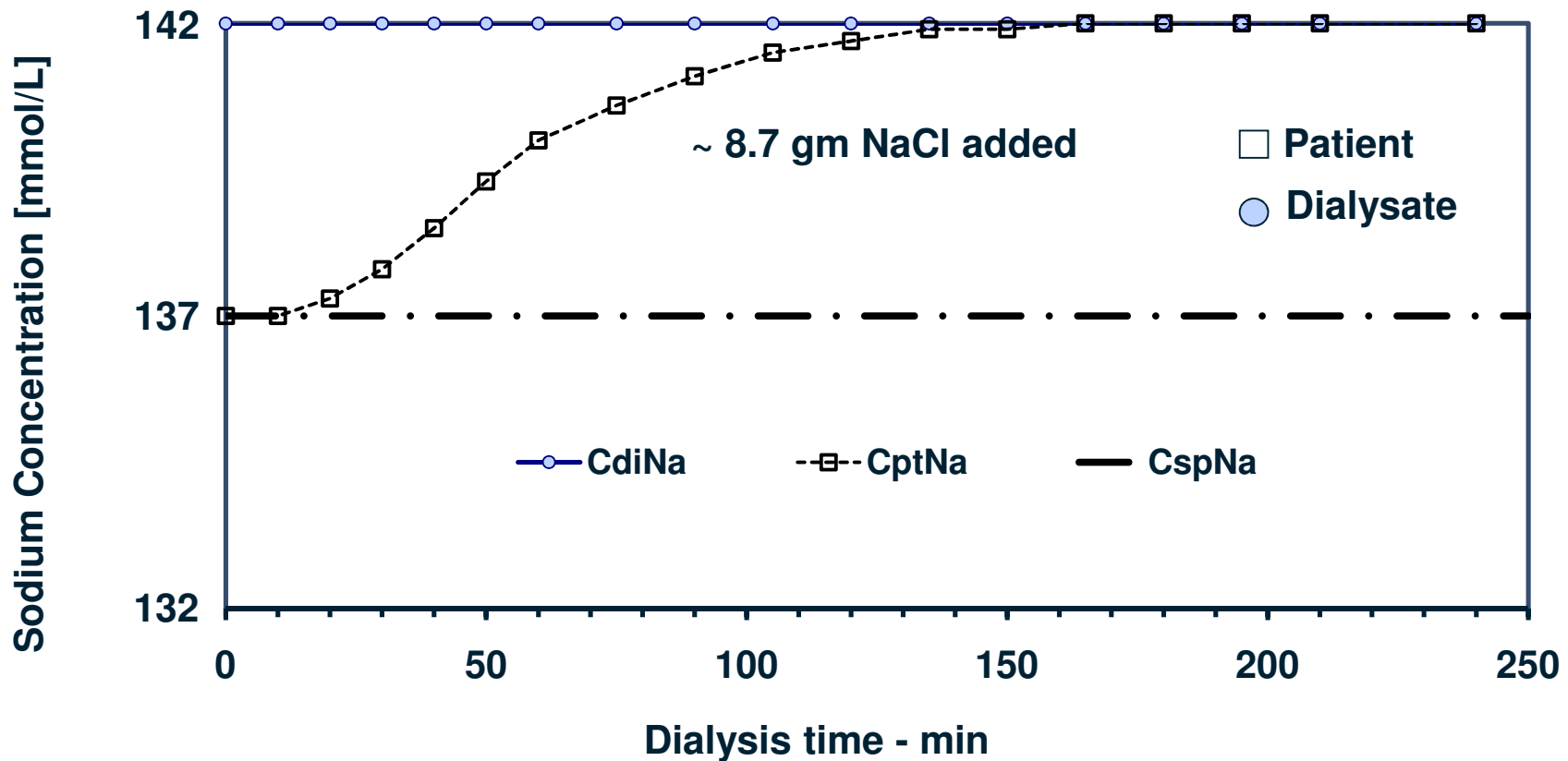
70% of patients dialyze with dialysate sodium levels in excess of their serum Na<sup>+</sup> levels

Na<sup>+</sup> Gradient



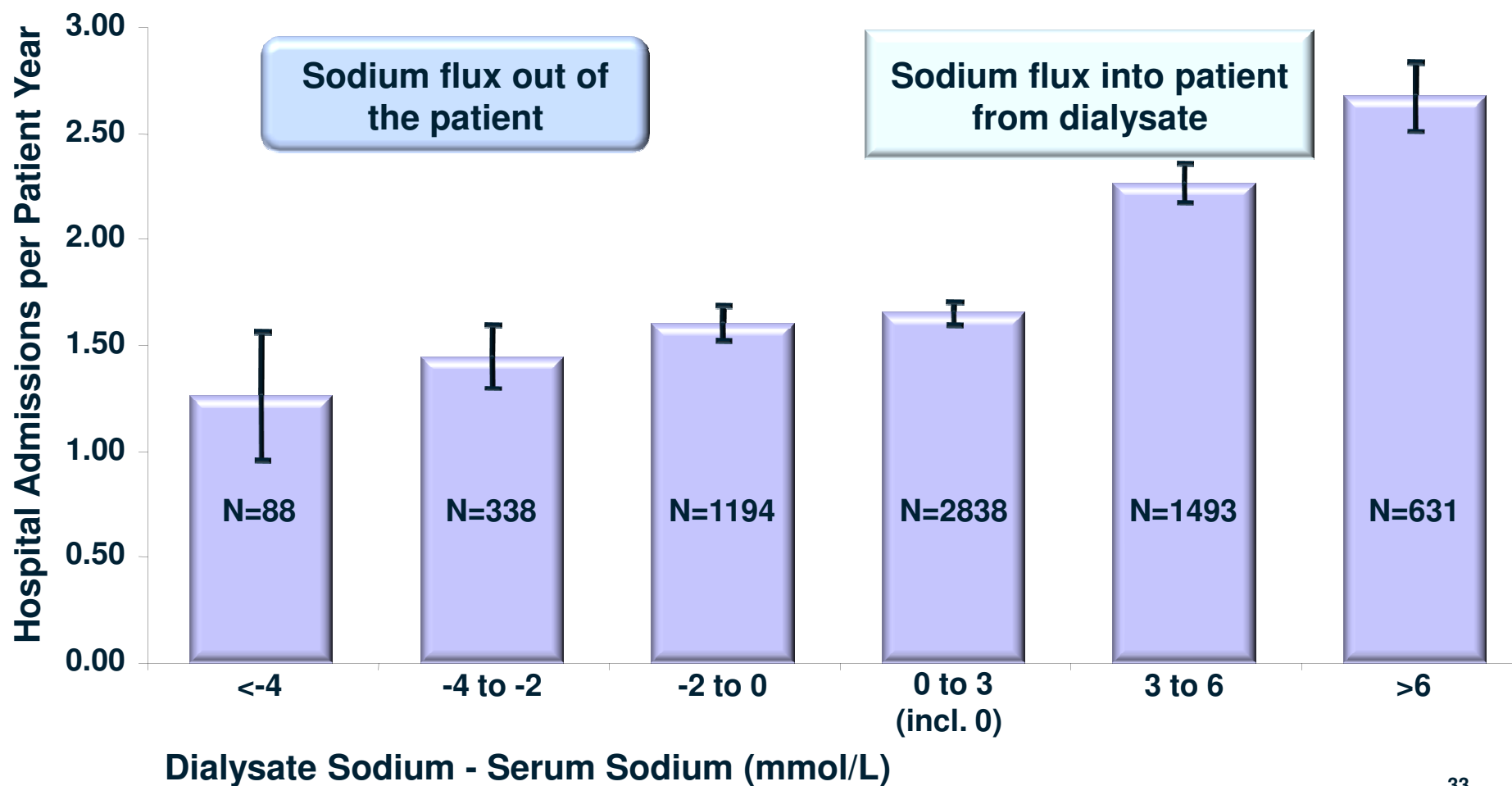
# Projected Sodium Transfer from Dialysate to Serum

A constant Dialysate Na<sup>+</sup> 5 mEq/L greater than Serum Na<sup>+</sup> will result in very marked positive Na balance during dialysis



# Hospital Admissions

Hospital Admissions per Patient Year ( with 95% CI)  
2007, RRI Patients, N=6852





# Economic Impact of Fluid Overload

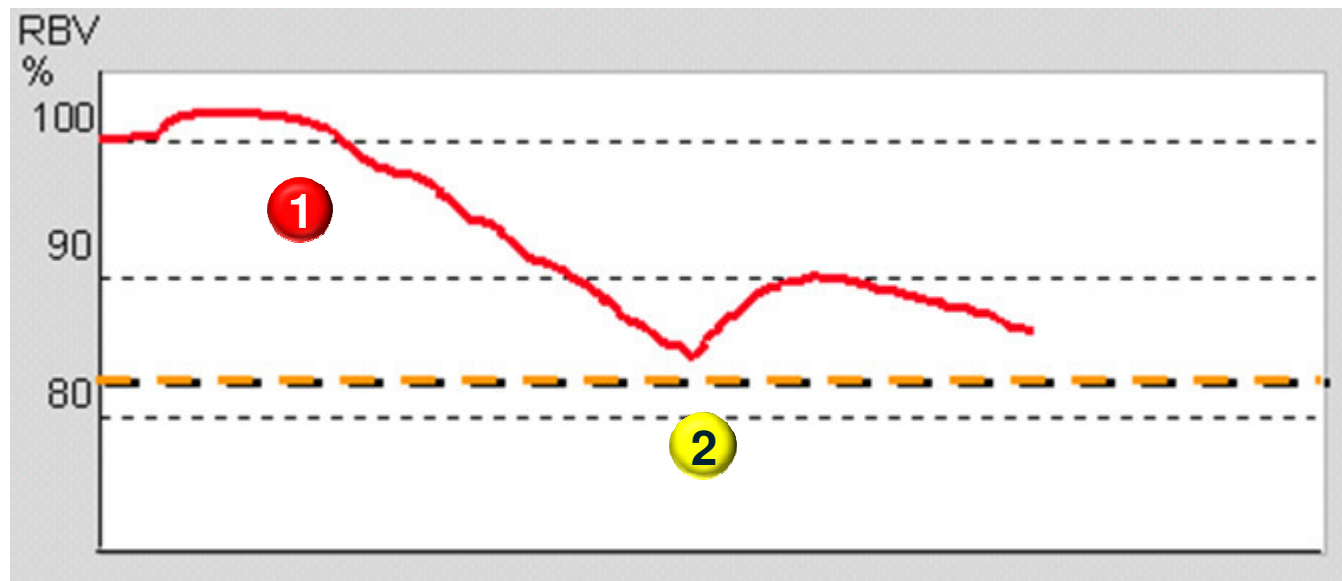


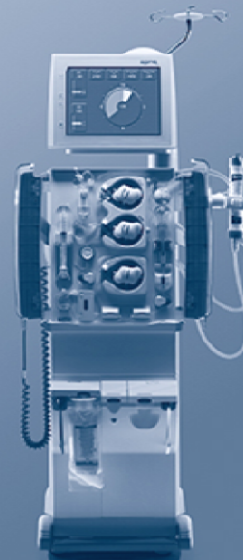
**Recent publication (CJASN, 2010) corroborated these estimates**

**Hospitalizations ( $\leq 5$  days) due to fluid overload in prevalent HD patients did cost Medicare / Medicaid a total of \$266 million (\$6,372 per episode) over a 2-year follow-up period in recent study**

# Blood Volume Monitor

- BVM tracks change of relative blood volume (RBV)
- If fluid removal exceeds plasma refilling RBV will drop **1**
- A rapid drop of RBV may lead to systematic hypotension
- A biofeedback control prevents RBV to drop below individual threshold **2**

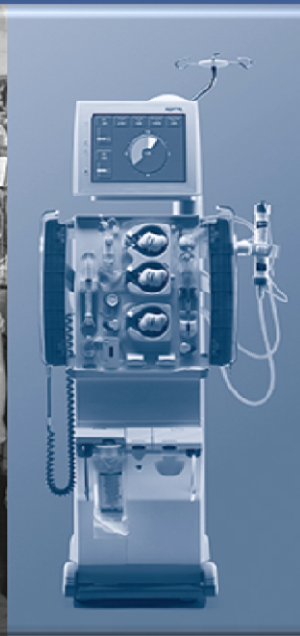




**Thank You!**



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## Solving Today's Medical Needs In Renal Replacement Therapy: Bone Mineral Metabolism

Jose A Diaz-Buxo, MD, FACP  
Chief Medical and Regulatory Officer  
SVP Renal Products Group



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# Overview



- **Bone and mineral metabolism (BMM) complications remain a major source of complications among patients with chronic kidney failure**
- **Despite significant advances in understanding the pathophysiology and treatment of these conditions achieved during the past 40 years, many problems remain to be solved**
- **The challenge we face in preventing and treating disorders of BMM is best appreciated by taking into account the many factors involved in its development**



# Chronic Kidney Disease - Factors Influencing Mineral and Bone Disorders



## CHRONIC KIDNEY DISEASE— MINERAL AND BONE DISORDER

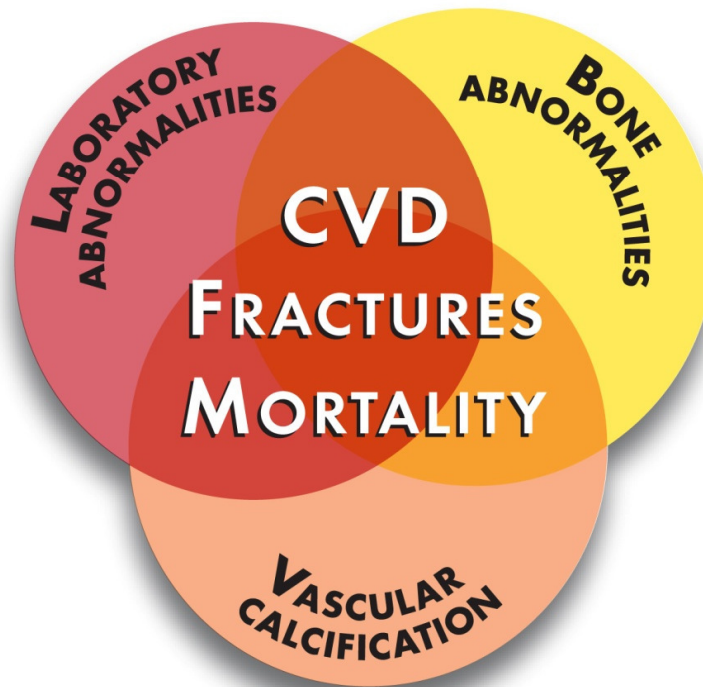
Dietary  
Ca, P, Vit D

GI absorption  
Ca, P, Vit D

25 OH vit D  
Skin/Liver

1,25 OH vit D  
Kidneys

PTH  
Secretion



Renal handling  
Ca, P, 1,25 Vit D

Bone reservoir  
handling Ca, P

Bone factors  
BMP, OPG, FGF

Drugs  
supplements

Metabolic acidosis

## CKD-MBD



# KDOQI Targets for BMM are not Achieved in Most HD Patients<sup>1,2</sup>



- **51-52 % of patients achieve the calcium target**
- **47-49 % the phosphate**
- **68-78 % the calcium-phosphate product**
- **24-31% the PTH**
- **Only 2.4-6.9% of patients meet all 4 targets**
- **Clinical trials show that adjustment of dialysis prescription has great potential to achieve better control of the bone mineral metabolism. For example, dialysate calcium concentration, duration of the dialysis session and hemodiafiltration all have an impact on calcium, phosphate and PTH.**

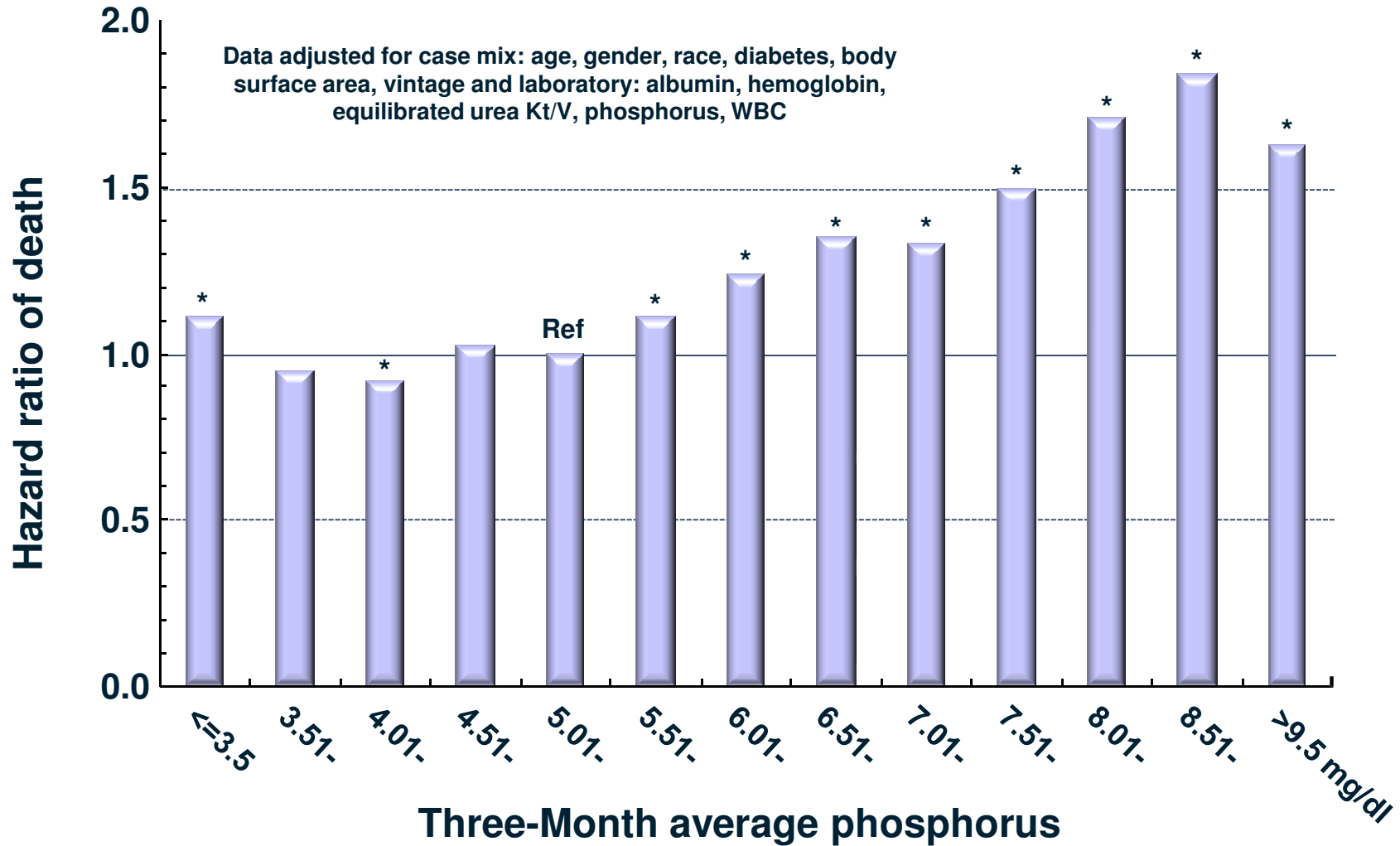
<sup>1</sup>Davenport A, et al. Blood Purif 30:111–117,2010 <sup>2</sup>Gotch F, et al. Blood Purif 29: 163-176 2010

# FMC Approach to Bone and Mineral Metabolism



- **Use our extensive database to identify signals, trends, drugs and clinical practice effects on BMM**
- **Integrate clinical practices, dialysis prescription, nutrition and drugs into our therapeutic approach**
- **Construct theoretical models, test concept in pilot studies and validate them (Phosphorus Kinetic Modeling - PKM)**
- **Support development of drugs and devices to correct BMM abnormalities**

# Relative Risk of Mortality versus Phosphorus

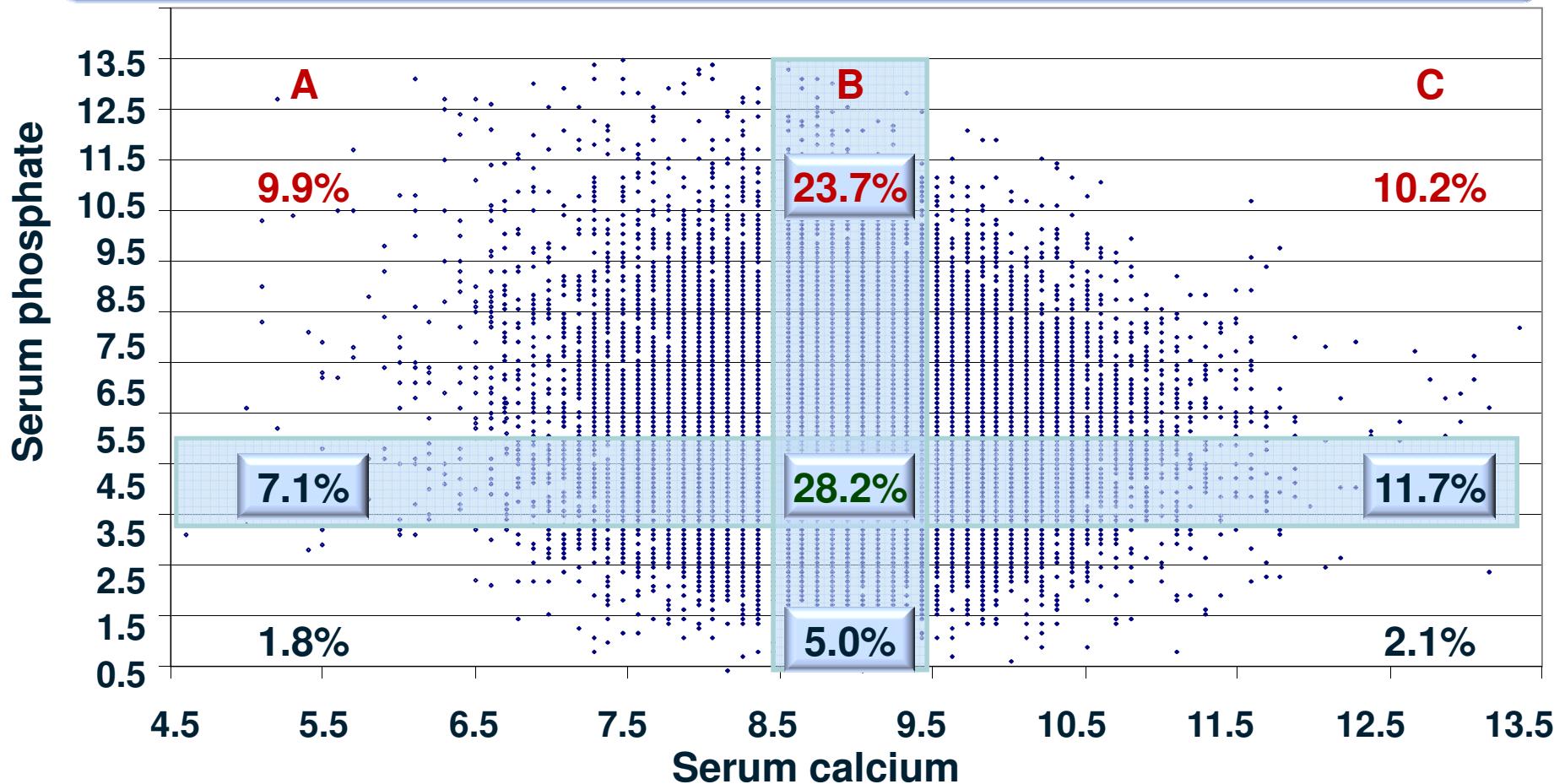


Data source: Fresenius Data Warehouse  
Baseline period: Q4 2005; Follow-up period: 2006

# Need for Improved Treatment Algorithm to Achieve Phosphate and Calcium Targets



Distribution of phosphate and calcium among patients receiving PhosLo®  
(n=31,712)



Data source: Fresenius Data Warehouse  
Latest lab results between 3/1/2007 and 5/31/2007 among patients with open order for PhosLo® at that time

# Introduction to Phosphorus Kinetic Modeling (PKM)



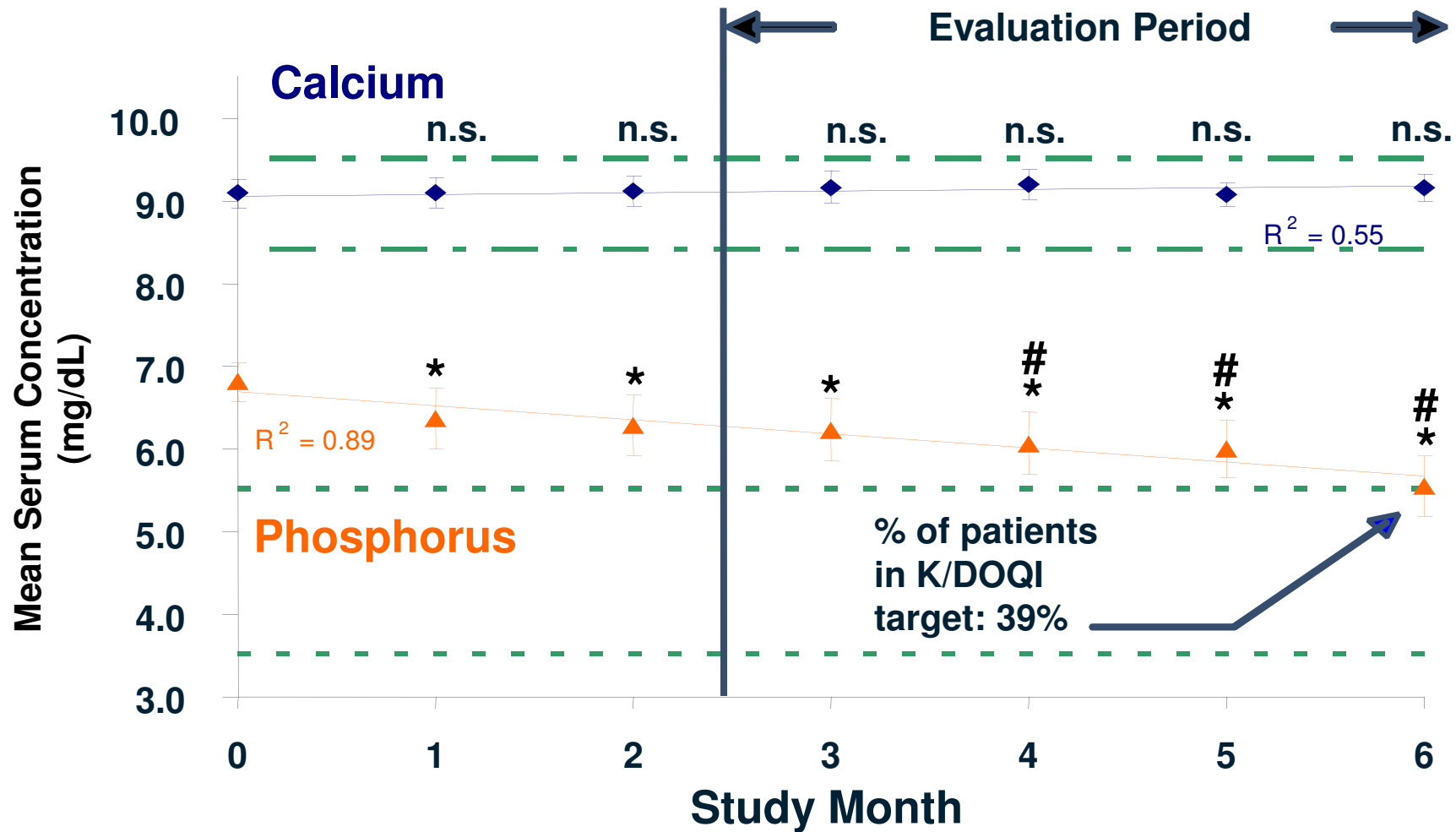
- **Hyperphosphatemia in dialysis patients is a major cause of:**
  - **Morbidity (Calcification, cardiovascular disease, bone disease)**
  - **Mortality**
- **Calcium acetate effectively binds phosphorus in the gut to prevent absorption, but may increase calcium load**
  - **Most dialysis patients are in positive calcium balance, regardless of phosphate binder**
- **Patient compliance with therapy is a strong determinant of phosphate and calcium balance**

# The Phosphorus Kinetic Model (PKM)



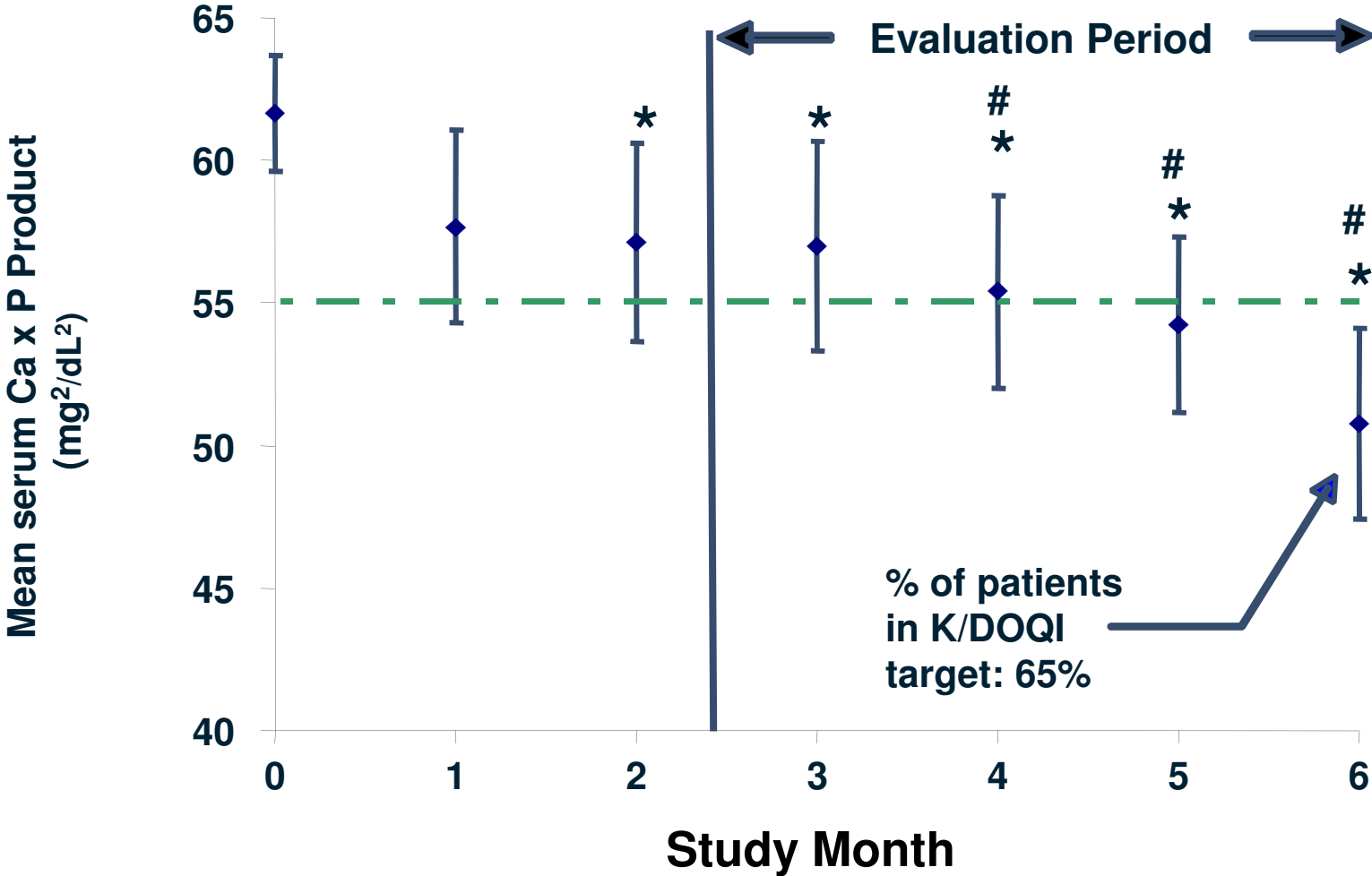
- **Definition:**
  - A kinetic model identifying the interacting effects of vitamin D analogues, phosphate binders and dialysate Ca on P and Ca mass balance in hemodialysis
- **Goal of PKM model:**
  - To help control a hemodialysis patient's serum P level through the use of Calcium Acetate and achieve K/DOQI guidelines for P and Ca without the need for additional blood draws and lab tests
  - Optimize phosphate binder therapy and patient compliance
  - Match Ca removal during dialysis to Ca accumulation between dialyses to prevent Ca overload or depletion
- **Seamless integration between central lab (Spectra), clinic and PKM report**
- **FMC has completed a pilot study and is conducting a second clinical trial to validate the model**

# Serum Phosphorus and Calcium



Error bars represent 95% confidence interval, \*  $p < 0.05$ , compared to month 0  
 #  $p < 0.01$ , compared to month 0

# Calcium Phosphorus Product



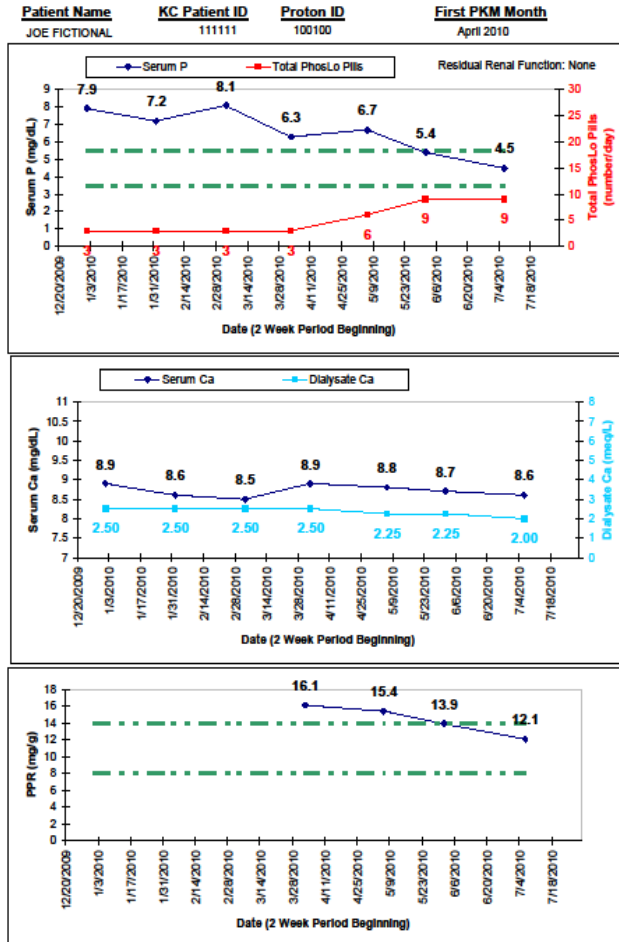
Error bars represent 95% confidence interval, \* p < 0.05, compared to month 0  
# p < 0.01, compared to month 0



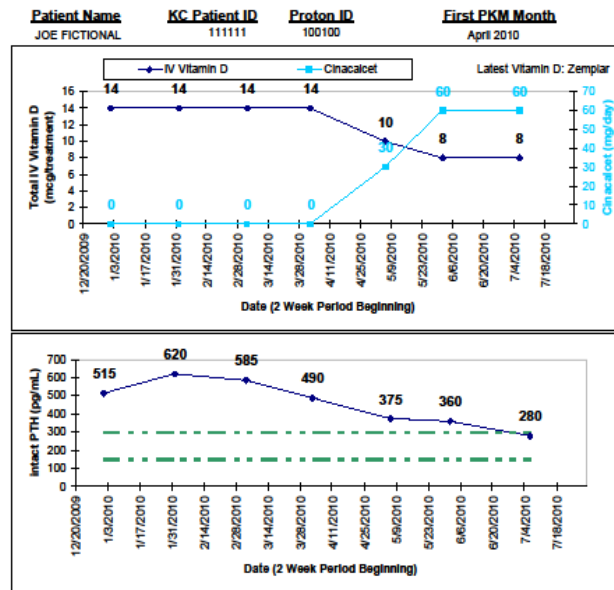
# Physician Report



Facility ID: 1234 **Monthly Patient PKM Report** Run Date: 7/2010



Facility ID: 1234 **Monthly Patient PKM Report** Run Date: 7/2010



Current Prescription/ Lab Values on PKM Date	PKM Model Recommendations
--	---------------------------

Serum phosphorus:	4.5 mg/dL	
Serum phosphorus (post):	1.8 mg/dL	
PhosLo prescription:	9 pills per day	Maintain pills per day
Serum calcium:	8.6 mg/dL	
Serum calcium (post):	8.2 mg/dL	
Dialysate calcium prescription	2.0 meq/L	2.0 meq/L
IV Vitamin D prescription:	8 mcg/treatment	8 mcg/treatment
Cinacalcet prescription:	60 mg/day	60 mg/day
Phosphorus Protein Ratio:	12.1 mg/g	Within recommended range
PPR Recommended Range:	8 - 14 mg/g	

- I agree with the recommendations in this report and would like any changes in prescription implemented.
- I have noted above those changes to be made or no changes in prescription should be made at this time.

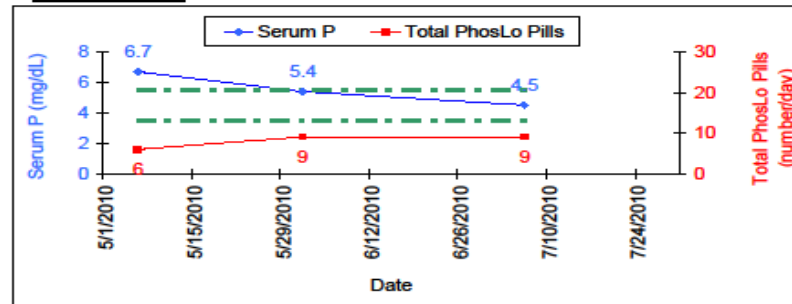
Physician Signature \_\_\_\_\_

Date \_\_\_\_\_

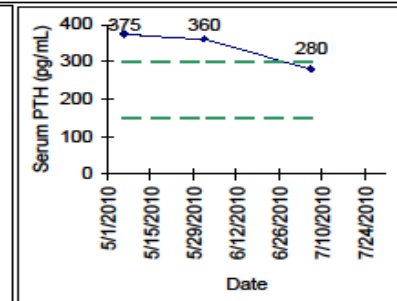
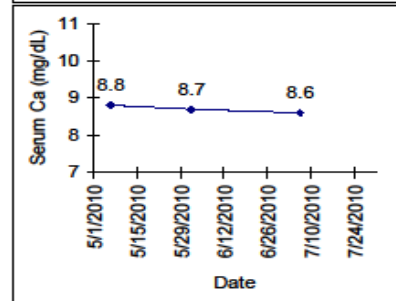
# Patient Report

**PKM Patient Report for July 2010**

**Patient Name:** JOE FICTIONAL



**Phosphorus Status**



**PTH Status**



**Protein Intake**

65 g each day

Comment about protein intake. E.g., Adequate protein intake; or Concentrate on better protein intake

**Phosphorus Intake**

787 mg each day

Comment about P intake. E.g., Adequate phosphorus intake; or Watch out for high phosphorus foods

**Protein Phosphorus Ratio**

12.1 mg P per g protein

Comment about PPR. E.g., Within recommended range; or Concentrate on compliance with PhosLo

**New PhosLo Prescription**

Total: 9 pills each day

Breakfast: \_\_\_\_\_

Lunch: \_\_\_\_\_

Dinner: \_\_\_\_\_

Snacks: \_\_\_\_\_

**New Sensipar Prescription**

60 mg each day

Time of day: \_\_\_\_\_

# PKM 2 Study Rationale



- **Validation of positive results from the pilot study**
  - The primary endpoint is the change in serum phosphorus between a baseline period and the latest value of the intervention period.
- **Addressing the changing clinical/ business paradigm**
  - PKM algorithm is patient-centric
  - Revised PKM algorithm helps manage multi-faceted BMM therapy
    - Efficient and effective calcium acetate binder therapy
    - Dialysate calcium concentration
    - Efficient Vitamin D use
    - Optimal use of Cinacalcet
  - **PKM 2 support quality of care metrics/ initiatives (Bundle)**

# PKM Clinical Application

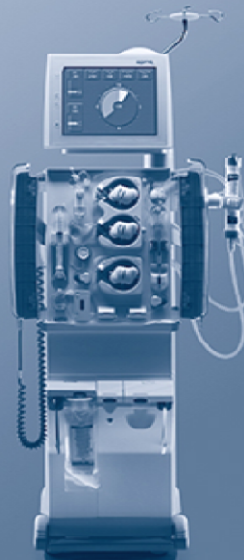


- **Prescribe patient-specific parameters:**
  - **Recommended dietary phosphorus intake**
  - **Vitamin D dose**
  - **Dialysate**
  - **Phosphate binder dose**
  - **Cinacalcet dose**
- **Assess patient compliance**
- **PKM will assist nephrologists in adjusting both phosphate binder dose, dialysis prescription and patient compliance to achieve desired phosphate and calcium values in support of BMM**

# PKM Conclusions



- **Useful tool for helping chronically hyperphosphatemic patients meet phosphorus target without increasing serum calcium.**
- **PKM report provides valuable bone and mineral metabolism information to physicians and patients that can be used as formal prescription**
- **PKM provides cost effective optimization of BMM therapy**

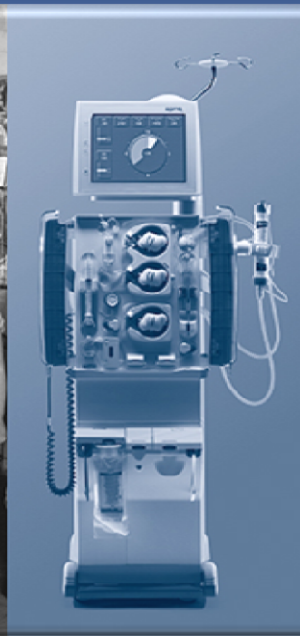


**Thank You!**



**Fresenius Medical Care**





# Dry Weight and Bone Mineral Metabolism Management in EMEALA

Wolfgang Wehmeyer  
Senior Vice President International Marketing & Medicine



Fresenius Medical Care

# Fresenius Medical Care Experience



**OnlineHDF and Body Composition Monitor (BCM) and Bone Mineral Metabolism Management (BMM) are as important as eating and drinking.**

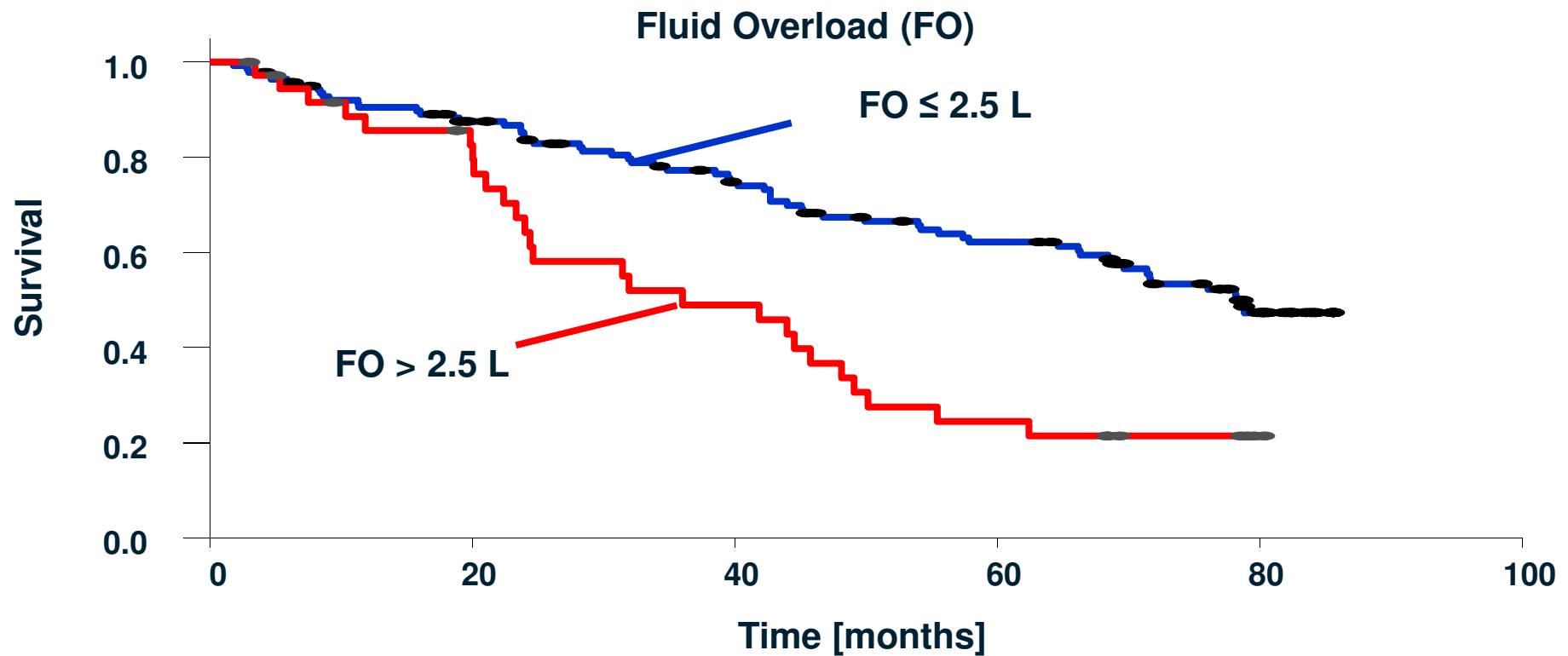


**An Affordable and User Friendly Product with Impressive Impact**

**Fluid Overload is as Serious as Diabetes**

# Fluid Overload is as Serious as Diabetes

## Kaplan Meyer comparison



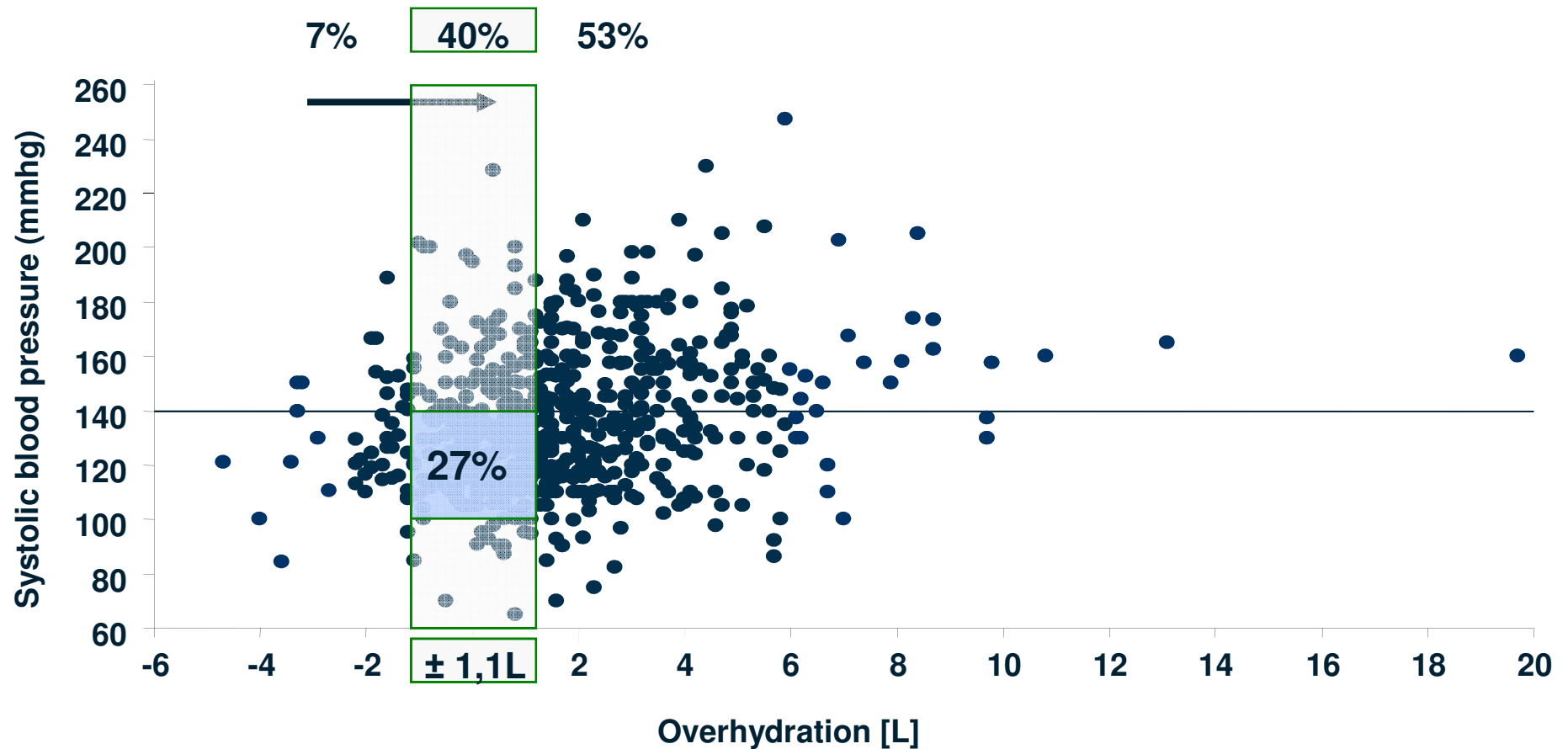
The mortality risk of overhydration in haemodialysis patients.  
Wizemann V, Wabel P, Chamney P, Zaluska W, Moissl U, Rode C,  
Malecka-Masalska T, Marcelli D.  
Nephrol Dial Transplant. 2009 May;24(5):1574-9.

**An Affordable and User Friendly Product with Impressive Impact**

**Fluid Overload is as Serious as Diabetes**

**50 - 60% of All PD Patients are “Out of Range” (30-40% in HD)**

# 50-60% of All PD Patients are “Out of Range”



Assessment of Fluid Status and Nutritional Status in European Peritoneal Dialysis Patients.  
Objective Measurement through Body Composition Monitoring  
1 Van Biesen W, 2Covic A, 3Fan S, 4Claes K, 5Lichodziejewska-Niemierko M, 6Verger C,  
7Steiger J, 8Wabel P, 8Gauly A, 8Schoder V, 8Himmele R

**An Affordable and User Friendly Product with Impressive Impact**

**Fluid Overload is as Serious as Diabetes**

**50 - 60% of All PD Patients are “Out of Range” (30-40% in HD)**

**We Can Do Something About It**

# We Can Do Something About It

## Prescription Intervention Pays Off

**Underhydrated**

**Normal Range**

**Overhydrated**

- **Less interdialytic symptoms**
- **No side effects**



- **better blood pressure**
- **less antihypertensive drugs**
- **No side effects**

# BCM

# Outstanding Clinical Documentation



More than 50 publications in the past 3 years

## BCM in pre-ESRD patients:

Essig M, Escoubet B, de Zuttere D et al. Cardiovascular remodelling and extracellular fluid excess in early stages of chronic kidney disease. *Nephrol Dial Transplant* 2008; 23: 239-248

→ EDTA 2010: Bioimpedance Utility in the Evaluation of Hydration Status in non-dialysis CKD patients; Simona Stancu,1,2 Ligia Petrescu,1,2 Adrian Zugravu,1,2 Gabriel Mircescu,1,2; Date: Sunday, June 27, 2010

## BCM in PD:

Devolder I, Verleysen A, Vijt D, Vanholder R, Van Biesen W. Body composition, hydration, and related parameters in hemodialysis versus peritoneal dialysis patients. *Perit. Dial Int* 2010; 30: 208-214

→ EDTA 2010: MULTIFREQUENCY BIOIMPEDANCE ASSESSMENT OF HYDRATION STATUS IN PERITONEAL DIALYSIS AND FACTORS ASSOCIATED WITH FLUID OVERLOAD; F. Ferrer,1 M.J. Carvalho,1 L. Oliveira,1 O. Santos,1 A. Rodrigues,1 A. Cabrita 1 Sunday, June 27, 2010 - 12:00 AM; Session Info: Oral Session: Peritoneal dialysis

## BCM in HD:

Machek P, Jirka T, Moissl U, Chamney P, Wabel P. Guided optimization of fluid status in haemodialysis patients. *Nephrol Dial Transplant* 2010; 25: 538-544

Wizemann V, Rode C, Wabel P. Whole-body spectroscopy (BCM) in the assessment of normovolemia in hemodialysis patients. *Contrib Nephrol*, 161: 115-118, 2008

→ EDTA 2010: DETERMINATION OF DIALYSIS DOSE: A CLINICAL COMPARISON OF METHODS; Peter Ahrenholz,1 Petr Taborsky,2 Margot Bohling,3 Peter Rawer,4 Nouredin Ibrahim,5 Martin Gajdos,6 Petr Machek,7 Michaela Sagova,8 Hans Gruber,9 Pavel Moucka,10 Ivan Rychlik,11 Gerd Leimenstoll,12 Pavel Vyskocil,13 Gunter Toenne,14 Jindriska Possnickerova,15 Joerg Woggan,16 Werner Riegel,17 Helmut Schneider,18 Ralf Wojke,19; Date: Sunday, June 27, 2010 - 12:00 AM

→ EDTA 2010: PREVALENCE OF FLUID OVERLOAD IN EUROPEAN HD PATIENTS; Peter Wabel,1 Tomas Jirka,2 Volker Wizemann,3 Wojciech Zaluska,4 Pedro Ponce,5 Ulrich Moissl,1 Sebastian Wieskotten,1 Paul Chamney,1 MEDOS Study Group Saturday June 26, 2010 - 12:00 AM

## BCM and outcome:

Wizemann V, Wabel P, Chamney P, Zaluska W, Moissl U, Rode C, Malecka-Masalska T, Marcelli D: The mortality risk of overhydration in haemodialysis patients. *Nephrol Dial Transplant* 24: 1574-1579, 2009

## BCM: hypertension and fluid management

Wabel P, Moissl U, Chamney P, Jirka T, Machek P, Ponce P, Taborsky P, Tetta C, Velasco N, Vlasak J, Zaluska W, Wizemann V: Towards improved cardiovascular management: The necessity of combining blood pressure and fluid overload. *Nephrol Dial Transplant* 23: 2965-2971, 2008

→ EDTA 2010: HYPERTENSION MANAGEMENT-THE NECESSITY TO STRATIFY PATIENTS BY FLUID STATUS; Peter Wabel,1 Petr Machek,2 Paul Chamney,1 Ulrich Moissl,1 Tomas Jirka,2 Date: Saturday, June 26, 2010 - 12:00 AM

## BCM and nutrition:

Wieskotten S, Heinke S, Wabel P et al. Bioimpedance-based identification of malnutrition using fuzzy logic. *Physiol Meas*, 29: 639-654, 2008

EDTA 2008: Wizemann V, Rode C, Chamney PW et al. Fluid overload and malnutrition assessed with bioimpedance spectroscopy (BIS) are strong predictors of mortality in hemodialysis patients. *Nephrol Dial Transplant Plus*, 1(Suppl 2): ii16-ii17, 2008

## BCM: patented body composition model

Chamney PW, Wabel P, Moissl UM et al. A whole-body model to distinguish excess fluid from the hydration of major body tissues. *Am J Clin Nutr*, 85: 80-89, 2007

## BCM validation against gold standard

Wabel P, Chamney P, Moissl U, Jirka T: Importance of Whole-Body Bioimpedance Spectroscopy for the Management of Fluid Balance. *Blood Purif*, 27:75-80, 2009

Passauer J, Miller H, Schleser A et al. Evaluation of clinical dryweight assessment in haemodialysis patients by bioimpedance-spectroscopy. *J Am Soc Nephrol*, 18: 256A, 2009

Lindley E, Chamney P, Wuepper A, Ingles H, Tattersall J and Will E: A comparison of methods for determining urea distribution volume for routine use in on-line monitoring of haemodialysis adequacy. *Nephrol Dial Transplant* 24: 211-216, 2009

Moissl UM, Wabel P, Chamney PW et al. Body fluid volume determination via body composition spectroscopy in health and disease. *Physiol Meas*, 27: 921-933, 2006

→ EDTA 2010: ASSESSING BODY COMPOSITION IN HEMODIALYSIS PATIENTS WITH A MULTIFREQUENCY BIO-IMPEDANCE DEVICE: A MULTICENTRIC EVALUATION OF REPRODUCIBILITY; Wim Van Biesen,1 J.C. Stolar,2 Y. Philips,3 S. Treille,4 R. Vanholder,1; Sunday, June 27, 2010 - 12:00 AM

EDTA 2008: Moissl U, Wabel P, Chamney PW et al. Validation of a bioimpedance spectroscopy method for the assessment of fat free mass. *NDT Plus*, 1(Suppl 2): ii215, 2008

ASN 2007: Moissl U, Bosaeus I, Lemmey A et al. Validation of a 3C model for determination of body fat mass. *J Am Soc Nephrol*, 18: 257A, 2007

EDTA 2007: Wabel P, Rode C, Moissl U et al. Accuracy of bioimpedance spectroscopy (BIS) to detect fluid status changes in hemodialysis patients (abstract). *Nephrol Dial Transplant*, 22(Suppl 6):VI 129, 2007

ASN 2007: Wabel P, Chamney PW, Moissl U et al. Reproducibility of bioimpedance spectroscopy (BIS) for the assessment of body composition and dry weight. *J Am Soc Nephrol*, 18: 255A, 2007

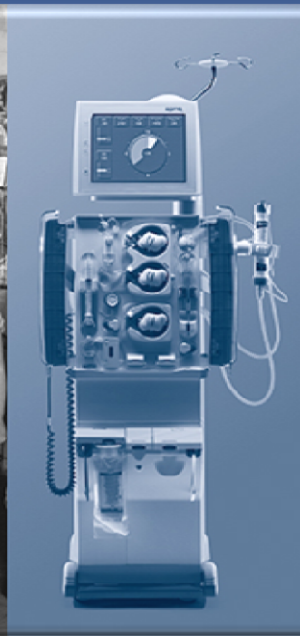
# Achieving Benefits for Patients Requires a Change in Clinical Procedures



- **Guiding Rules for NephroCare Centers**
- **Prescription Strategy of PD Solutions**
- **Scientific Marketing**







**Bone Mineral Metabolism**  
**FME Online HDF and Osvaren®**

**A Superior Treatment Proposition**

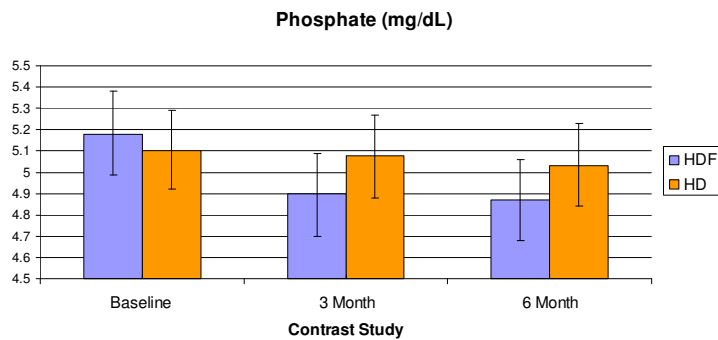


**Fresenius Medical Care**

# Fresenius Medical Care HDF / Online HDF



## Improved Phosphate Control over HF Dialysis



Penne et al. 2010 (CONTRAST study)

- Decreased pre-dialysis phosphate levels after 6 months of treatment with online HDF
- Phosphate treatment targets were satisfied more often, whereas the use of phosphate-binding agents was reduced.
- Increased phosphate removal using HDF potentially may improve clinical outcomes

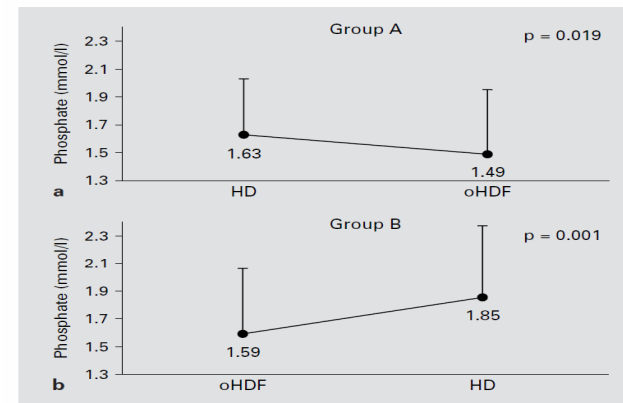
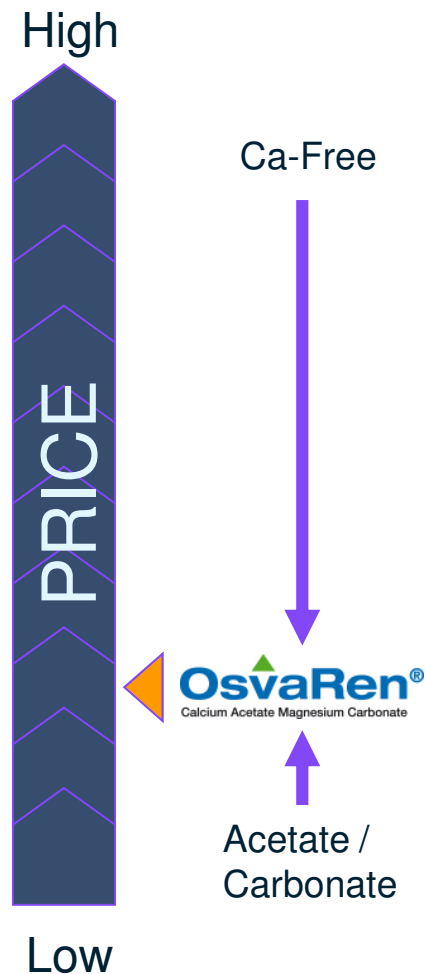


Fig. 3. Serum phosphate levels (a in group A, b in group B): mean  $\pm$  SD.

Vaslaki et al. 2006

- Convective solute transport in oHDF improved the elimination of phosphate
- A constant lowering of serum phosphate levels was possible, which has been not described before to our knowledge

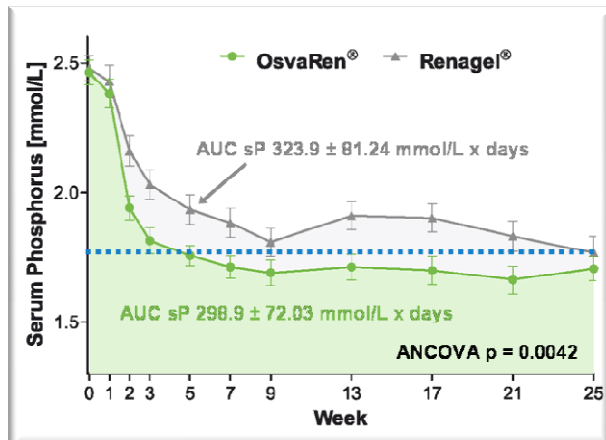


- **A new combination drug for Hyper-phosphatemia**
- **Strong data from prospective, randomized trial (CALMAG)**
  - **Effective Phosphate control, faster to target than Sevelamer**
  - **Full Calcium Control through reduction of Ca++ component**
- **Addition of anti-calcification potential through benefit of Mg++**
- **Premium Priced over Calcium based binders**
- **Economically attractive through excellent value compared to Ca-free binders**



# Convincing Data

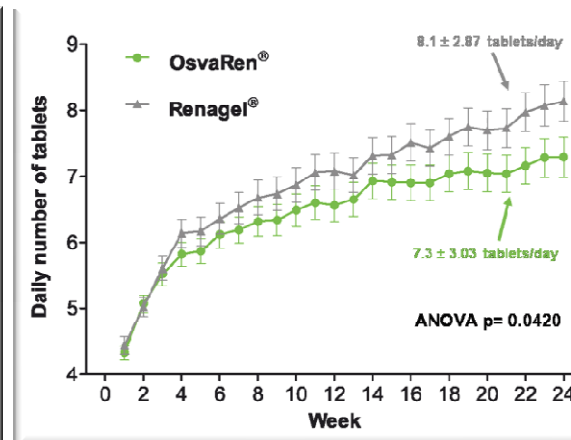
## Serum Phosphorous



Time course of serum phosphorus: Fast decline with Osvaren

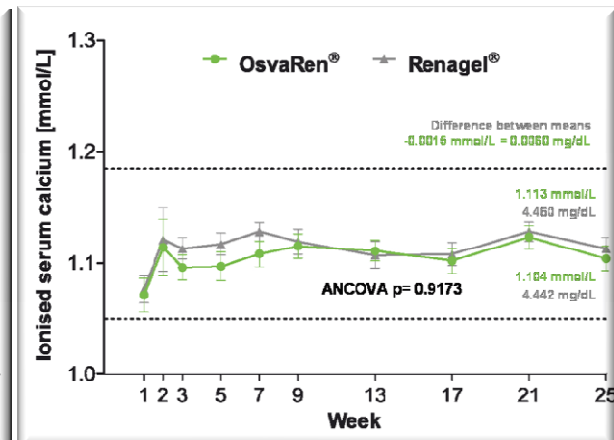
Area under the curve (AUC, [=total exposure]) for serum phosphorus significantly lower with Osvaren

## Pills per patient per day



Study medication intake/day significantly lower at week 25 with Osvaren

## Ionized Serum Calcium

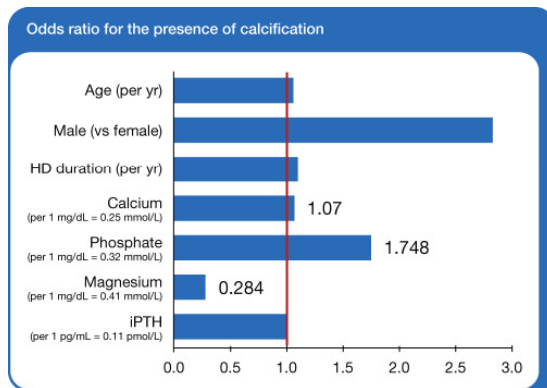


No significant difference in ionised serum calcium between groups

# Sufficient Serum Magnesium: Benefits

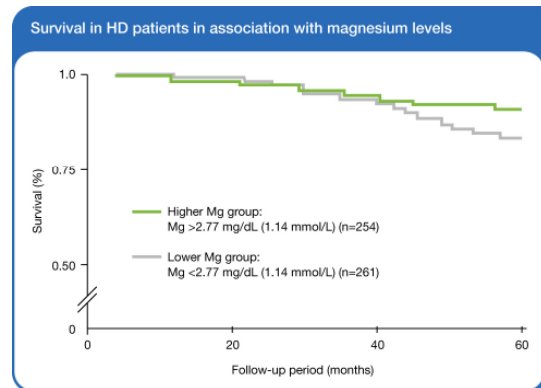
## Serum Magnesium Is A Significant Predictor For Survival In Dialysis Patients

### Ishimura 2007



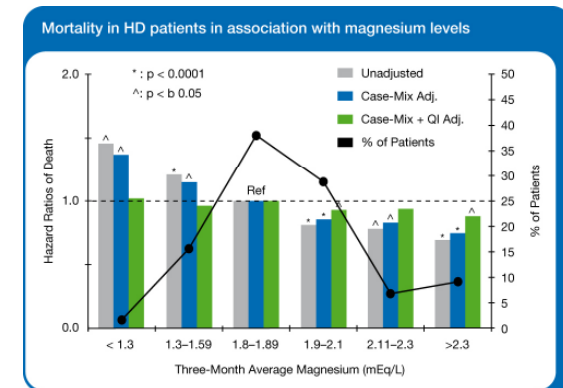
Lower serum magnesium levels are an independent factor of vascular calcification in patients with CKD

### Ishimura 2007



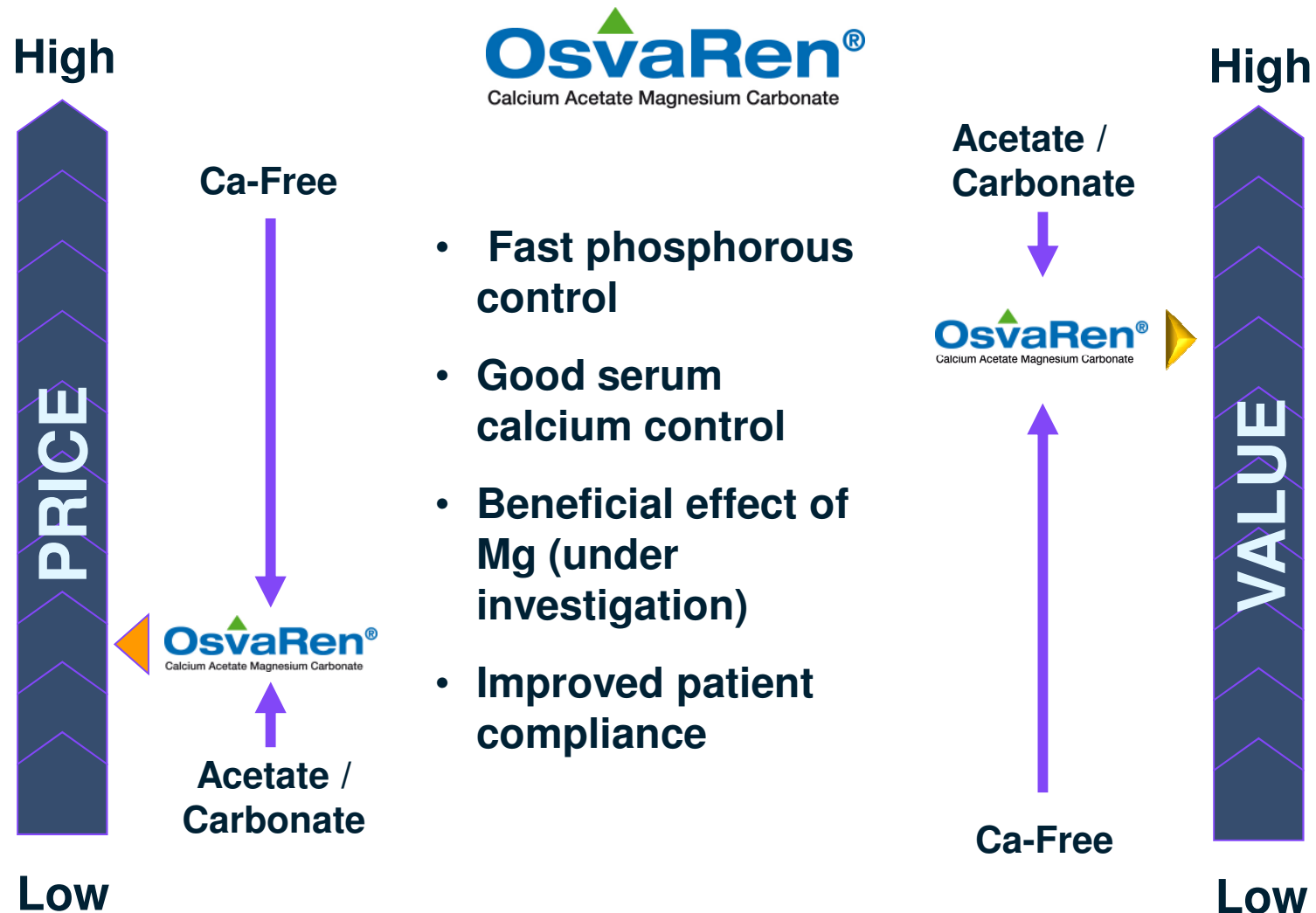
Study of 515 dialysis patients: Elevated magnesium levels are associated with improved survival

### Lacsson 2009

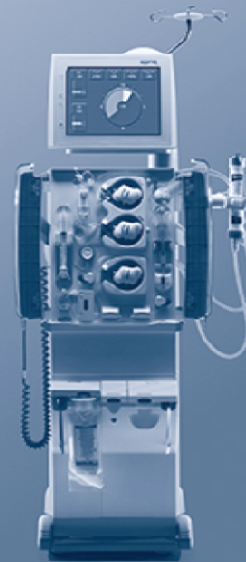


27,544 dialysis patients (FMCNA): Elevated magnesium levels are associated with lower risk of mortality

# Summary



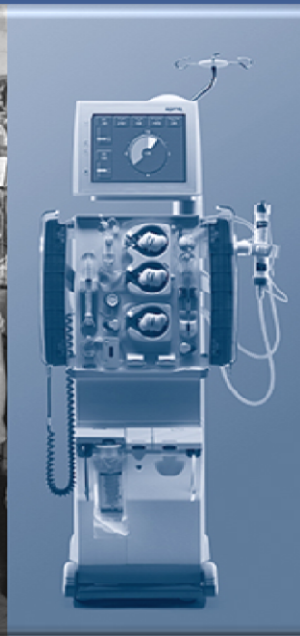




**Thank You!**



**Fresenius Medical Care**



# Hydration Management North American Strategies for Commercialization

Mark Costanzo, President  
Renal Therapies Group of FMCNA



Fresenius Medical Care



# Fluid Management Components Under Study At Fresenius Medical Care

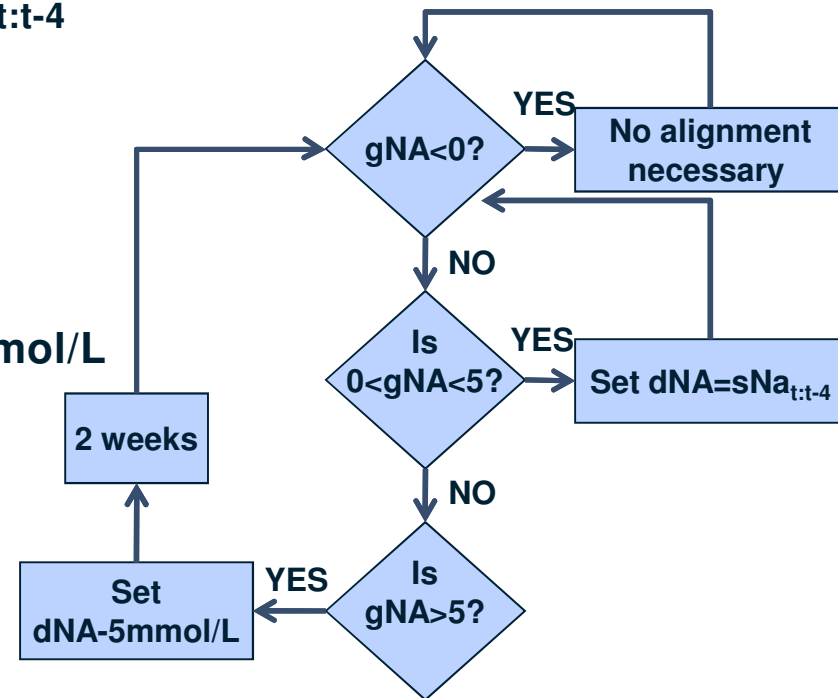


**Sodium (salt) management**  
**Alignment of serum and dialysate sodium**

**Determination of the target weight/dry weight**  
**Application of bioimpedance and plasma-refilling rate**

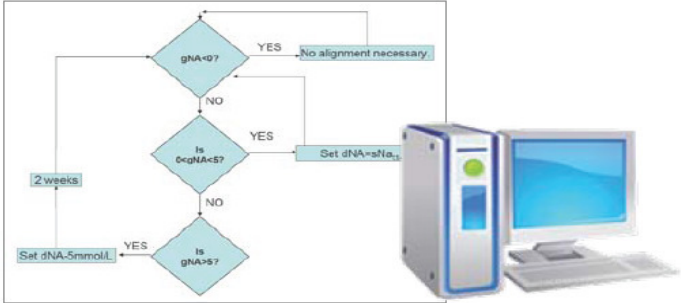
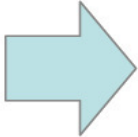
# Method to Correct Simplified Na<sup>+</sup> Alignment Algorithm

- Calculate mean of patient-specific serum Na<sup>+</sup> for the past four months ( $sNa_{t:t-4}$ )
- Calculate Na<sup>+</sup> gradient ( $gNa$ ) =  
$$\text{dialysate Na (dNa)} - sNa_{t:t-4}$$
- Na<sup>+</sup> Alignment
  - If  $gNa < 0$  → no alignment is necessary
  - If  $0 < gNa < 5$  → set  $dNa = sNa_{t:t-4}$
  - If  $gNa > 5$  → set  $dNa = \text{current dNa} - 5\text{mmol/L}$   
(and reassess in two weeks)



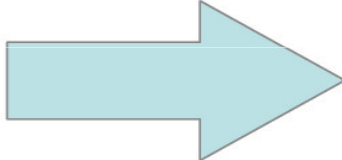
# Hydration Management Flow Diagram

Spectra Labs  
Na<sup>+</sup> Serum



Algorithm generates Dialysate Na<sup>+</sup> recommendations.

Physician receives report and generate order for Dialysate Na<sup>+</sup>.



2008T administers treatment prescribed Dialysate Na<sup>+</sup>



# Dry Weight: A Problematic Measure, in Practice



- **Dry Weight - the weight below which patients develop intradialytic hypotension (IDH) on HD**
- **Hypotension may occur in overhydrated patients when ultra filtration exceeds plasma refilling rate**
- **Physicians prescribe a target weight (TW) based on clinical assessment of the patient**
- **Currently, there are no routine methods available to objectively assess DW**

# Current Dry Weight Methodologies Technology for Volume Management



## Blood Volume Monitoring

Volume management with biofeedback technology



## Blood Temperature Monitoring

Achieving target dry weight while maintaining cardiovascular stability



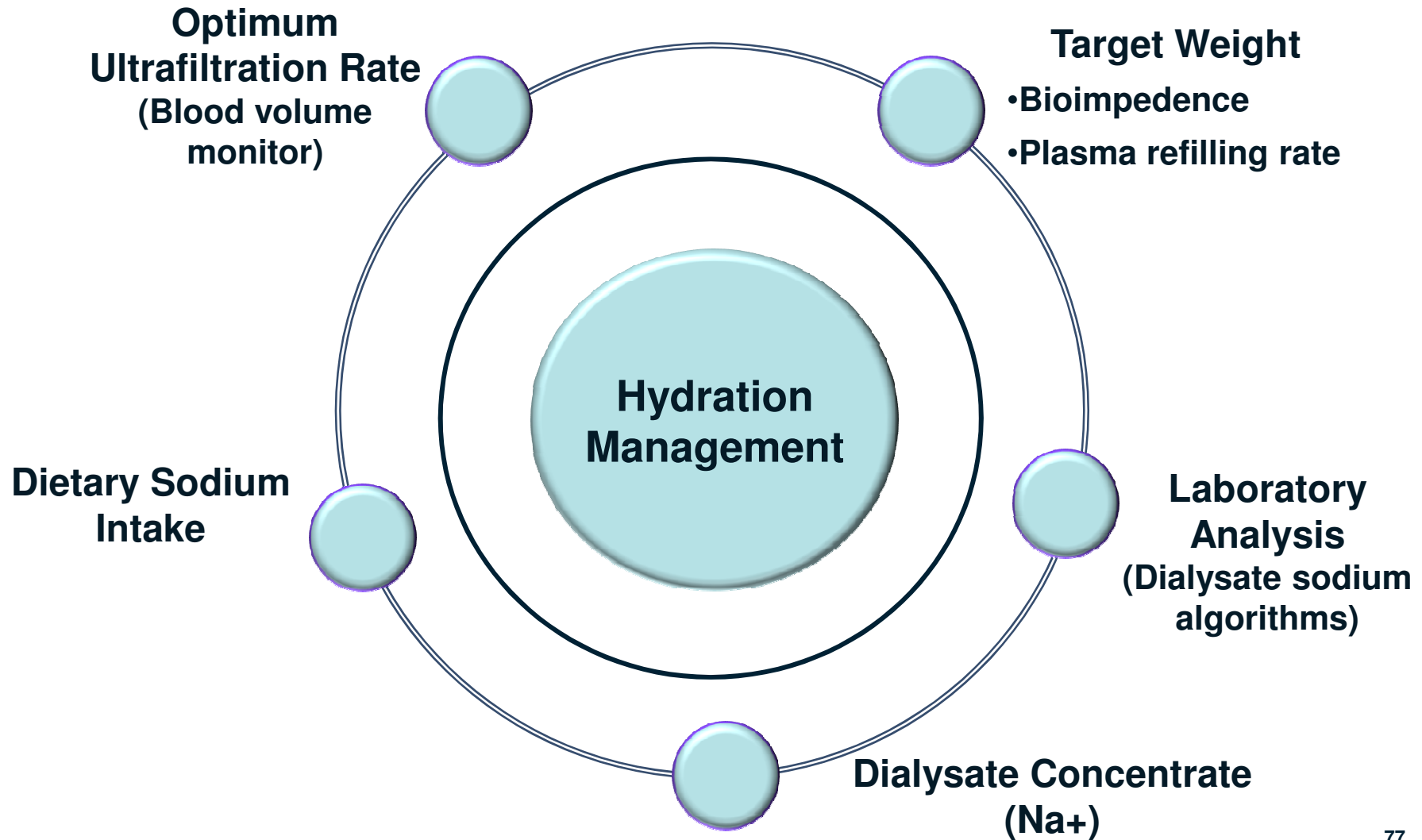
## Bioimpedance

Determining target dry weight



\* not 510k cleared

# Global Strategy – Renal Pharma/Therapy – Hydration Management



# 2008T with CDX

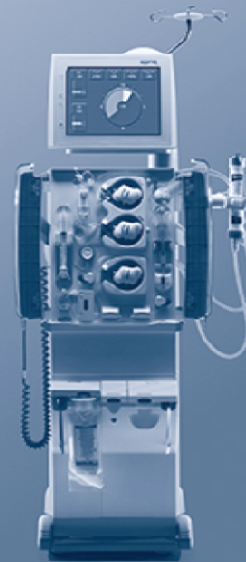
## Access to Data is Essential for Hydration Management



- **Fresenius Clinical Data Exchange™ (CDX) - provides access to clinic MIS system and dialysis treatment data on the 2008T platform**
- **Lab data and other key MIS content displayed on 2008T for comprehensive prescription decision making**
- **Online data from blood volume monitor/ bioimpedence measurements used for feedback control**
- **2008T allows chair side documentation for adjustment of prescription**







# Anemia Management



Fresenius Medical Care



# Anemia Management



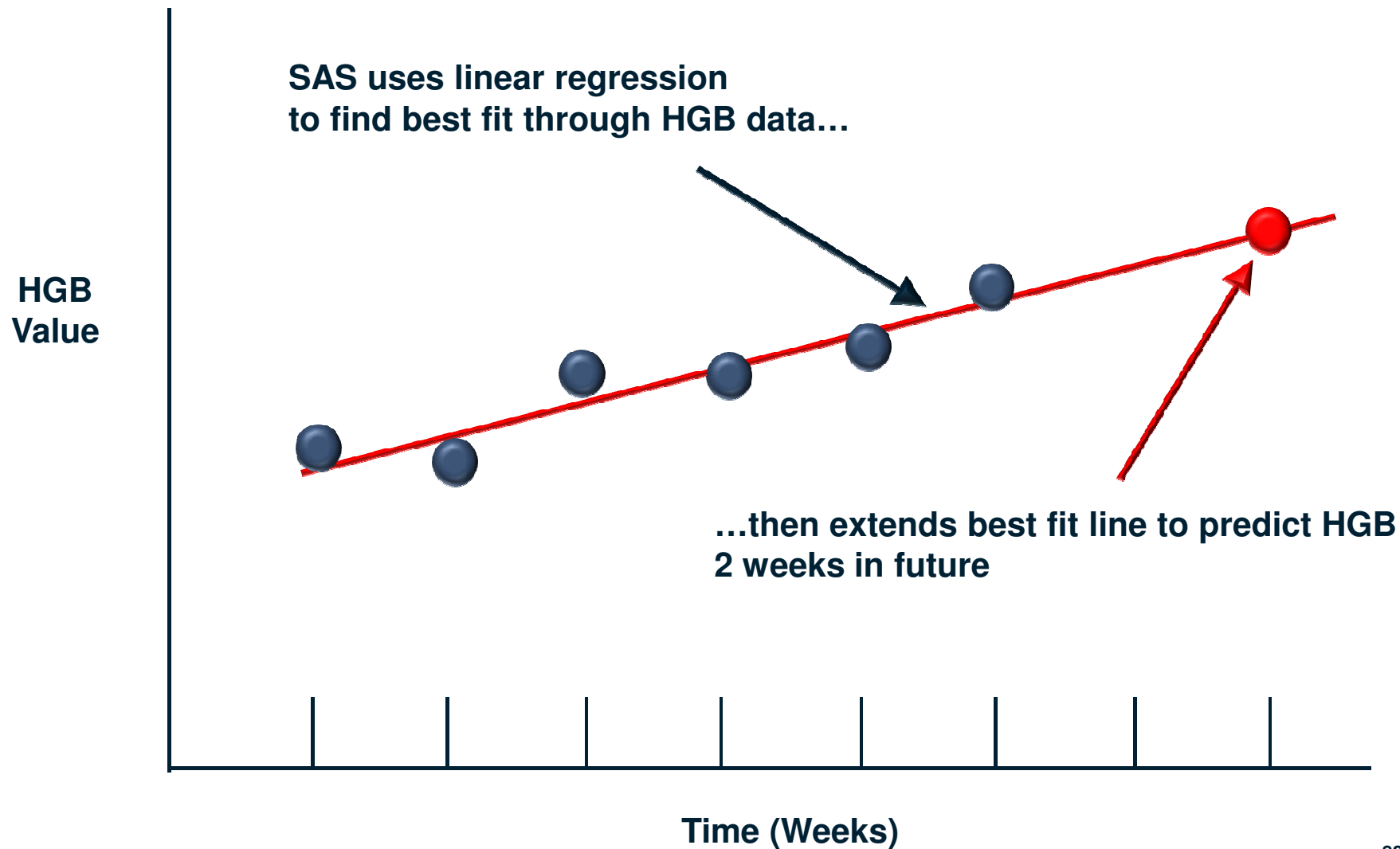
- **Improving Anemia Management and Outcomes**
- **Impact of Bundle**
- **Narrowing the Distribution to 10 -12 g/dl**
- **Improving IV Iron Management**
- **Reduced Inflammation**

# Narrowing the Distribution to 10–12 g/dL with Recommended Epogen Dose (RED) Algorithms

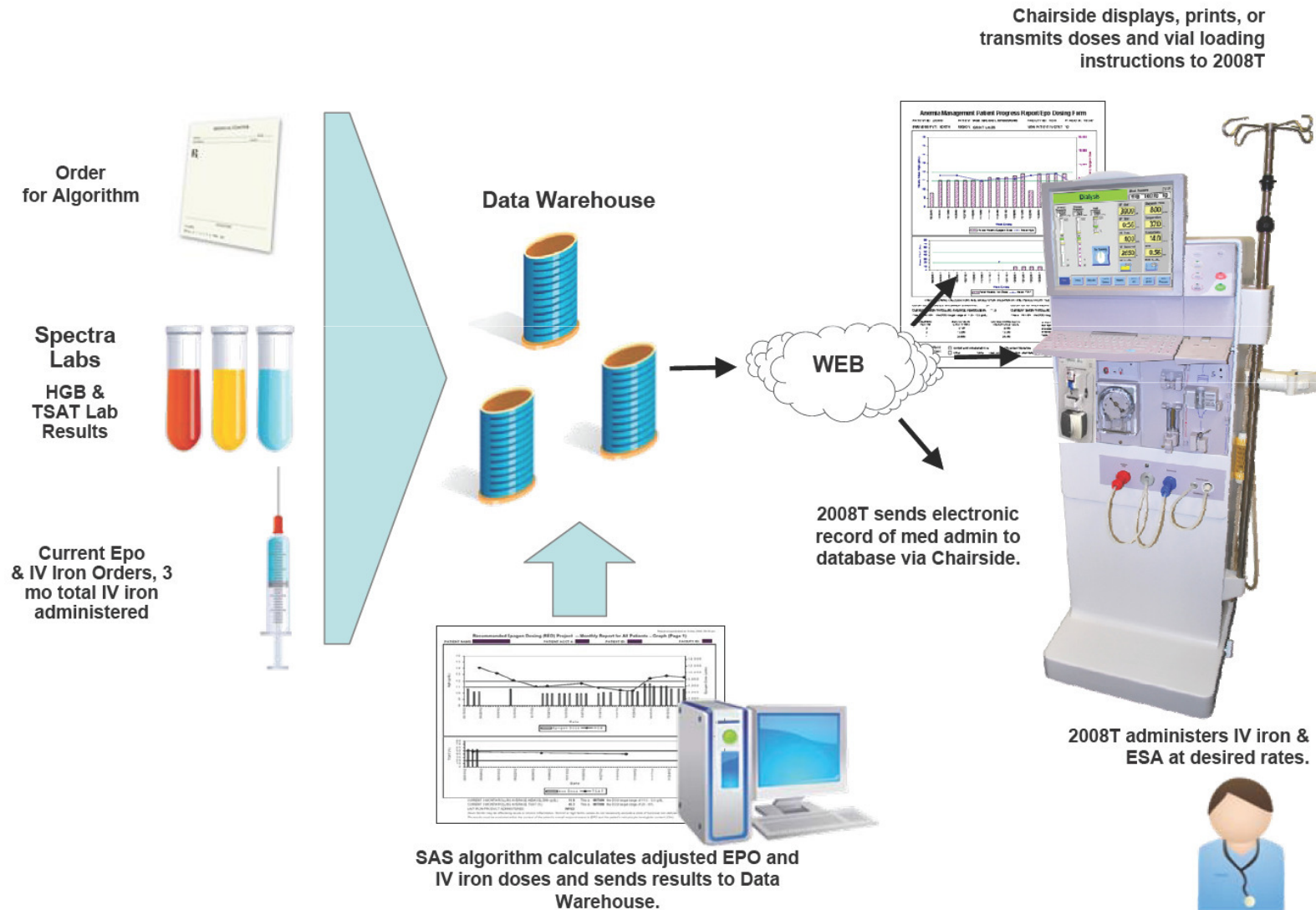


- **Spectra Lab Results:**
  - Weekly HGB values (up to 4 mo data)
  - Monthly TSAT values (up to 4 mo data)
  - Possibly latest ferritin value in past 4 mo (max value for IV iron)
  - Optional other lab values relevant to hyporesponse, such as albumin, CRP, aluminum, etc.
- **Clinical Data:**
  - Current Epogen prescription (dose and frequency)
  - Current IV iron prescription (dose, frequency)
  - Total IV iron administered in past 3 months prior to first run of algorithm. (Later, the HD machine or computer running the algorithm can accumulate this information.)

# Diagram of HGB Extrapolation



# Fresenius Medical Care Implementation of Anemia Management Algorithm



# Venofer - Iron Sucrose For Effective Iron Management



*Remarkable* **body of evidence**

**Safety**  
**Efficacy**  
**Tolerability**

**9 million patients**  
**180 million units**

**Venofer**<sup>®</sup>  
iron sucrose injection, USP

*Millions prescribed. Millions treated.™*

A large red 'V' shape is on the left. A doctor in a white coat stands next to it. The background is white with a grey reflection at the bottom.

# PharmaTech Venofer Pump Features/Benefits



- **Ease of use – Set dose and rate**
- **Accurate delivery - Precise dose and rate delivery**
- **Reduces set-up time – eliminates syringe fill and labeling**
- **Cost effective delivery**



# PharmaTech Anemia Management Module Concept



## Features/Benefits:

- Ability to tailor ESA and iron dosing to actual doses administered and optimized with the FMC algorithm.
- Doses entire deliverable volume of ESA from vial
- Documentation displayed for the dose administered
- Simplifies RN's task of measuring out exact ESA doses into the syringes

# **Water Purity: Does it Make a Difference in Reducing Inflammation?**



- **Bacteria, endotoxin and DNA fragments in the dialysate may pass into the blood with highly permeable dialysis membranes.**
  - **Monocytes activated by bacteria-derived substances secrete a variety of pro-inflammatory cytokines (IL-1 $\beta$ , IL-6 and TNF)**
  - **This inflammatory state is associated with malnutrition, accelerated atherosclerosis and a reduced erythropoietin responsiveness**
- **Ultrapure dialysis fluid is associated with:**
  - **improved nutritional status**
  - **an increased responsiveness to administration of iron and erythropoietin**



# Ultrapure Dialysate



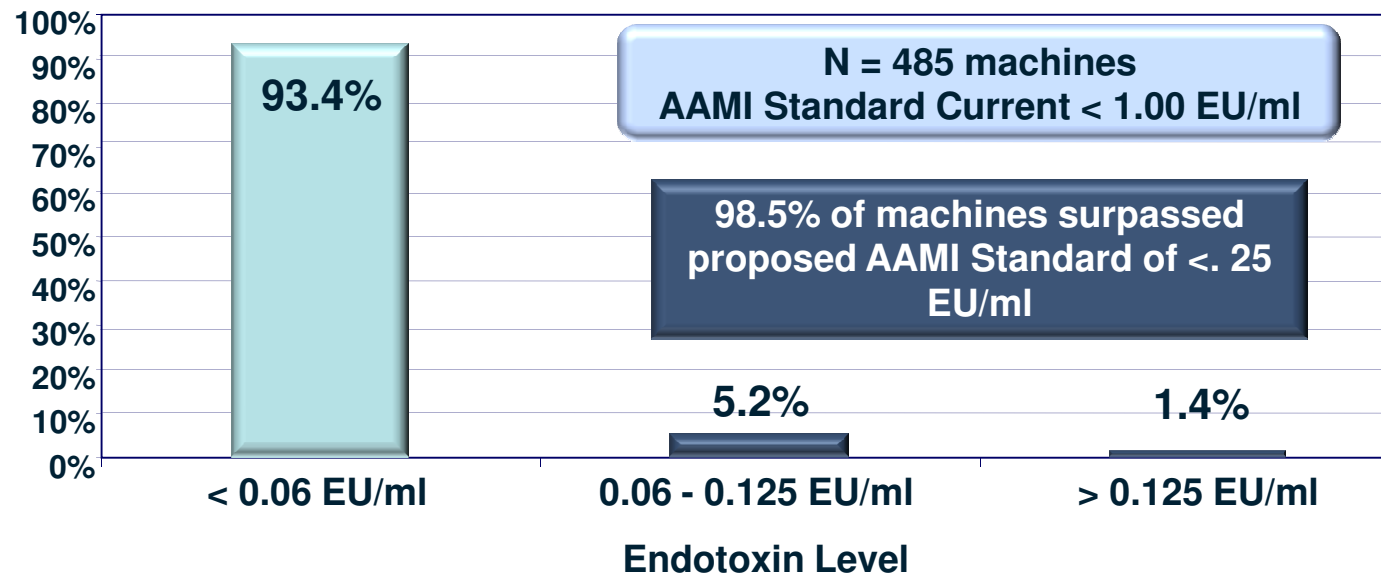
## Corrective Measures

- **Controlled ultrafiltration by placing Diasafe® Plus filters in the fluid path of standard HD machines**
- **Improve Water Quality**
  - **Reduce bioburden**
  - **Reduce dead space in centralized RO system**

# Diasafe® Plus Exceeding Proposed AAMI Standards



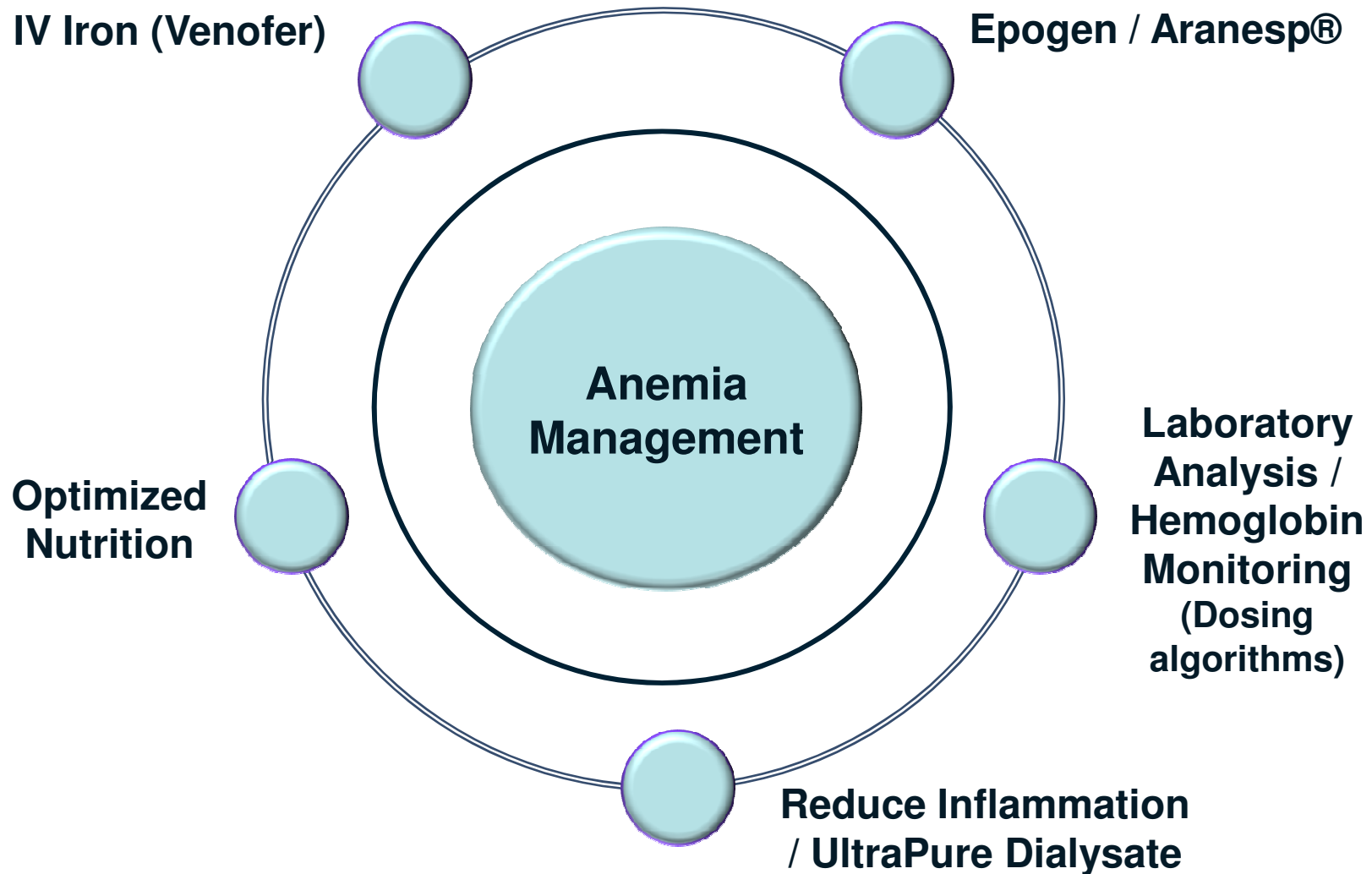
## Dialysate Endotoxin Levels Using Diasafe Filters and Conventional Facility Water Treatment



Sands J, Stano M., Li Z., Bryant R., Ofsthun N., Updyke D., Lazarus J. (2004). Diasafe® decreases endotoxin Levels 16 fold below new AAMI standard. (Abstract submitted for ASN)

AAMI = Association for the Advancement of Medical Instrumentation

# Global Strategy – Renal Pharma/Therapy – Anemia Management

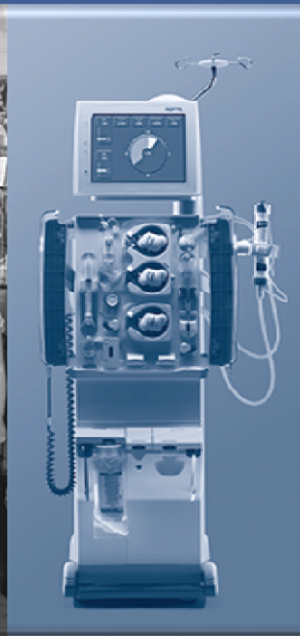


# 2008T with CDX Access to Data is Essential for Anemia Management



- **Fresenius Clinical Data Exchange™(CDX) - provides access to clinic MIS system and dialysis treatment data on the 2008T platform**
- **Lab data and other key MIS content displayed on 2008T for comprehensive prescription decision making**
- **Online data from Venofer® or AMM module used for feedback control**
- **2008T allows chair side documentation for adjustment of prescription**





# Bone Mineral Metabolism



Fresenius Medical Care

# Bone Mineral Metabolism



- **Compelling Need**
- **Phosphate and Bone Mineral Management – PharmaTech**
- **Pharmaceutical Delivery System – FMCRx**

# Compelling Need to Improve Phosphate & Bone Mineral Management



**Overall strong quality performance**

% of patients	North America (USA)		EMEA	
	Q2 2009	Q2 2010	Q2 2009	Q2 2010
Kt/V ≥ 1.2	96%	96%	95%	95%
Hemoglobin = 10-12 g/dl	64%	68%	54%	54%
Albumin ≥ 3.5 g/dl	82%	81%	88%	86%
<b>Phosphate 3.5-5.5 mg/dl</b>	<b>52%</b>	<b>55%</b>	<b>61%</b>	<b>61%</b>
Hospitalization days	10.1	9.9	8.5	9.2

\* The hospitalization rates for the US reflects adoption of CMS policy



# PharmaTech - Implementation of Phosphorus Kinetic Modeling



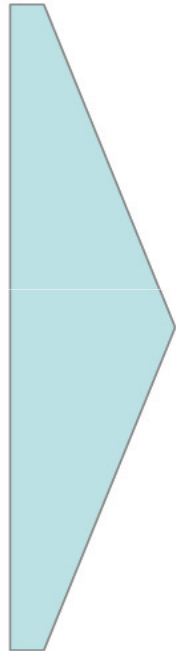
Algorithm order including post Ca/P labs



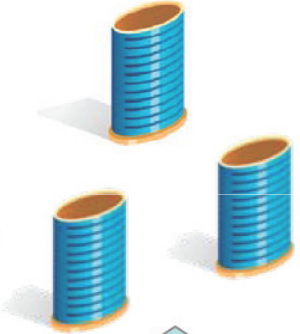
Spectra Labs  
P, Ca, & PTH Lab Results



Current Orders for PhosLo, Vitamin D, Cinacalcet, and Dialysis Ca



Data Warehouse



Physician receives report and signs prescriptions for PhosLo, Vit D and Cinacalcet



Cinacalcet/PhosLo prescription filled through FMCRx and delivered to patient's home



SAS algorithm calculates adjusted EPO and IV iron doses and sends results to Data Warehouse



# Phosphate Binder Portfolio



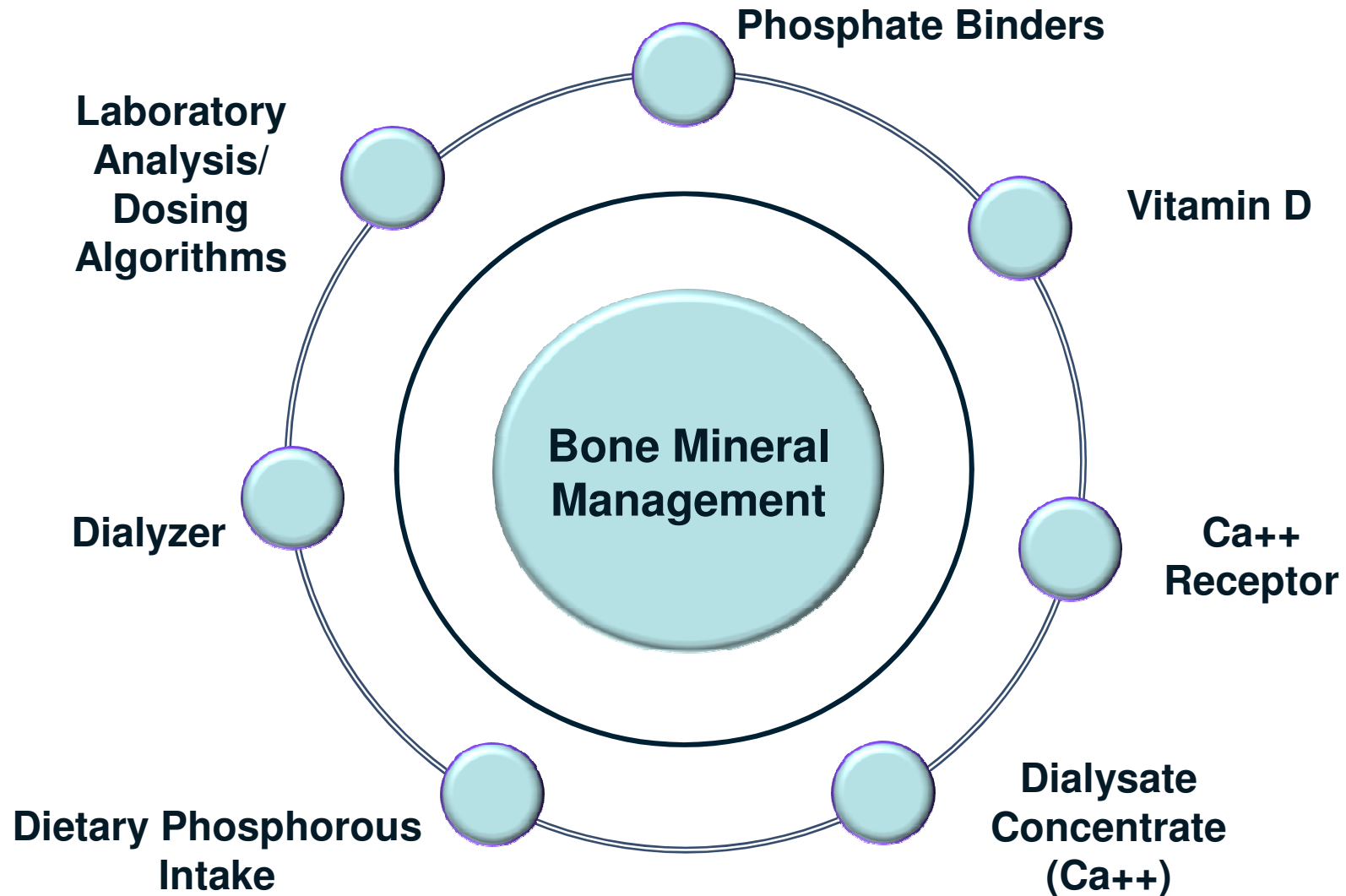
- **PhosLo (calcium acetate gelcap)**
- **PhosLo authorized generic**
- **Phoslyra (liquid calcium acetate formulation)**
  - **Clinical trials have proven safety and efficacy. Waiting for FDA to complete upstream reviews**
  - **Aim is to enhance patient adherence and thus serum P management by reducing pill burden, reduce fluid ingestion and providing an alternative for patients with swallowing difficulties**
- **Interest in licensing of branded or non-calcium based P binder: PA-21**

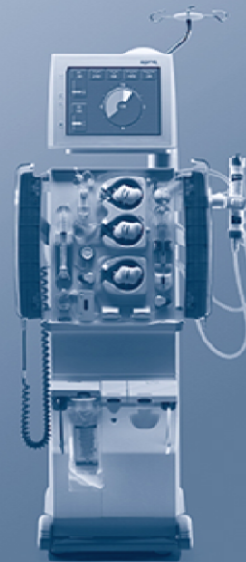
**FMCRx is a renal - focused specialty pharmacy with pharmacists who are trained on the special needs and medications of CKD and ESRD patients**

**Benefits to FMCNA include:**

- **Medication management improves compliance to drug regimen**
- **Improved adherence leads to improved quality of life for patients**
- **Convenience, shipped to the patient's home**
- **Medication summary report of all drugs prescribed and filled sent to clinics each month**
- **Control costs under the bundle**

# Global Strategy – Renal Pharma/Therapy – Bone Mineral Management

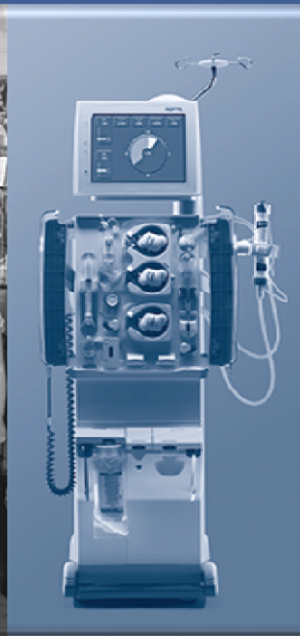




Thank you!



Fresenius Medical Care



## **“In Touch – Leading & Succeeding In Renal Therapy Worldwide”**

**Michael Brosnan, Chief Financial Officer**

**Capital Markets Day  
Luton, September 1–2, 2010**



**Fresenius Medical Care**

# Agenda



**1. Historical Highlights**

2. 2010 Financial Guidance

3. Goal 13 – Strategic Financial Objectives

4. Goal 13 – Strategic Financial Objectives - Capital Structure

5. Summary



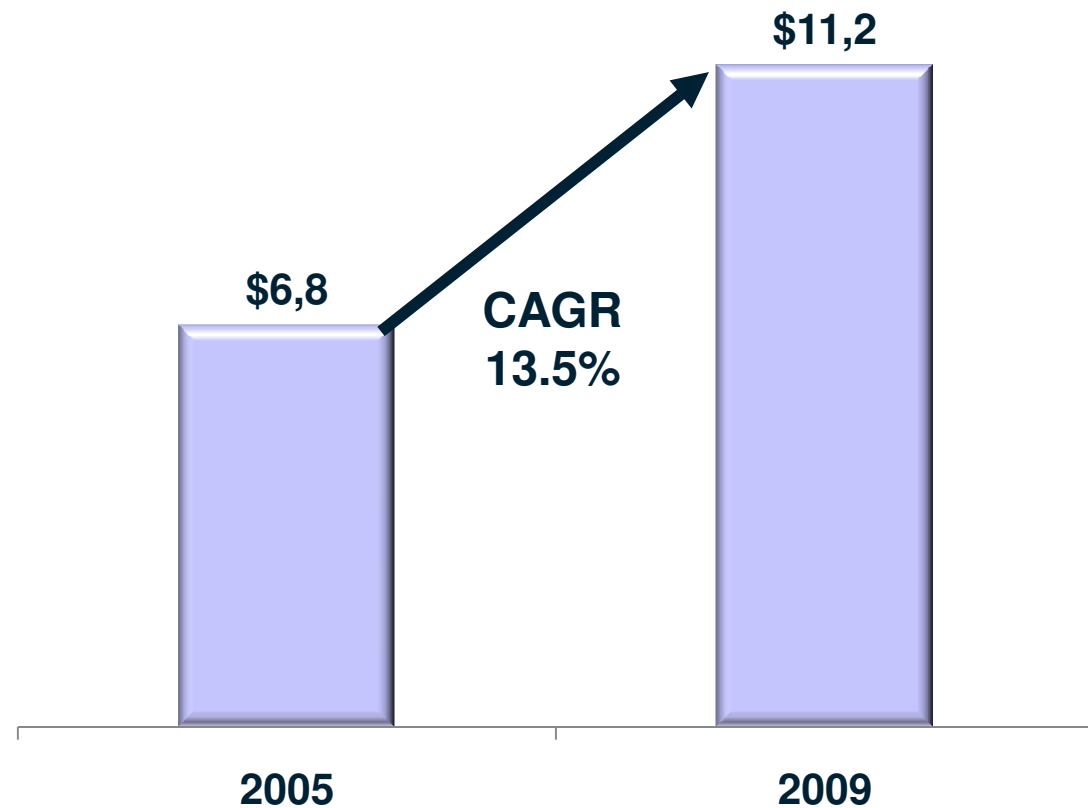
# Historical Highlights Topline Growth Drivers



## Topline Growth Drivers

- Geographic Expansion
- Market Share Gains
- Revenue Per Treatment Increases
- Geographical Mix Management
- Successful Execution of Acquisitions and Integration Strategy

## Revenue



# Historical Highlights

## Earnings Growth Drivers

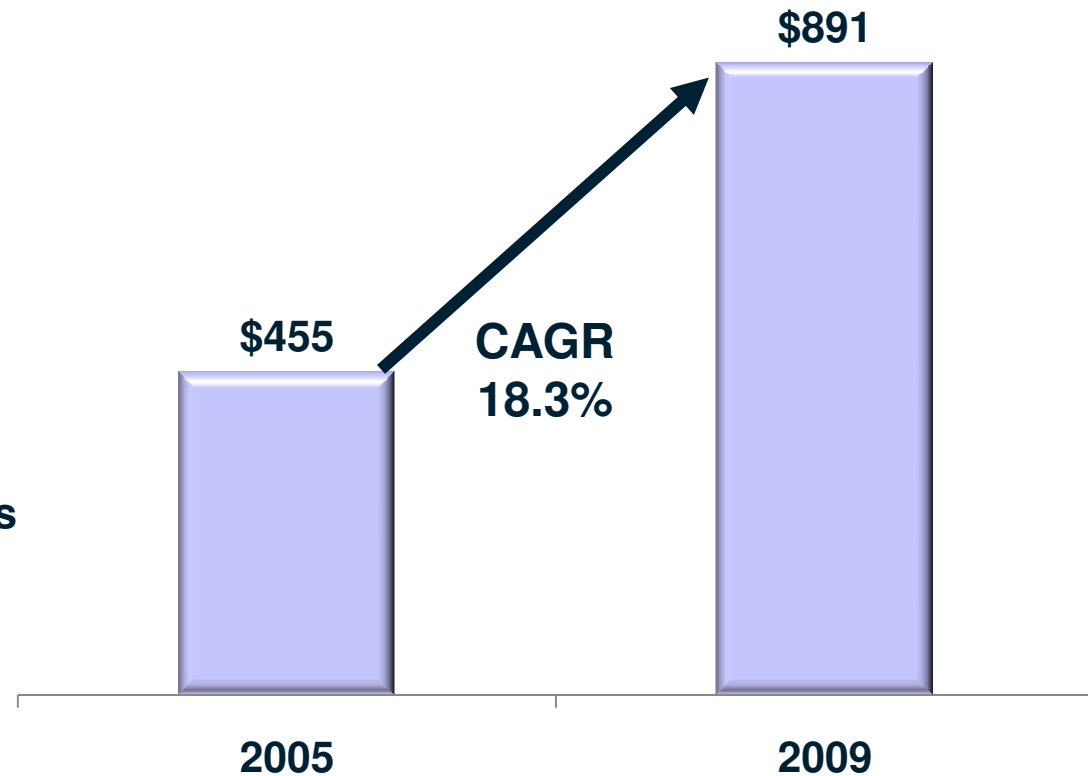


### Earnings Growth Drivers

- Scale Effects
- Revenue Per Treatment Increases
- Manufacturing Performance
- Product Mix
- Clinic Cost Control
- Favorable Financing Conditions
- Slightly Lower Tax Rate

### Net Income

attributable to FMC AG & Co. KGaA





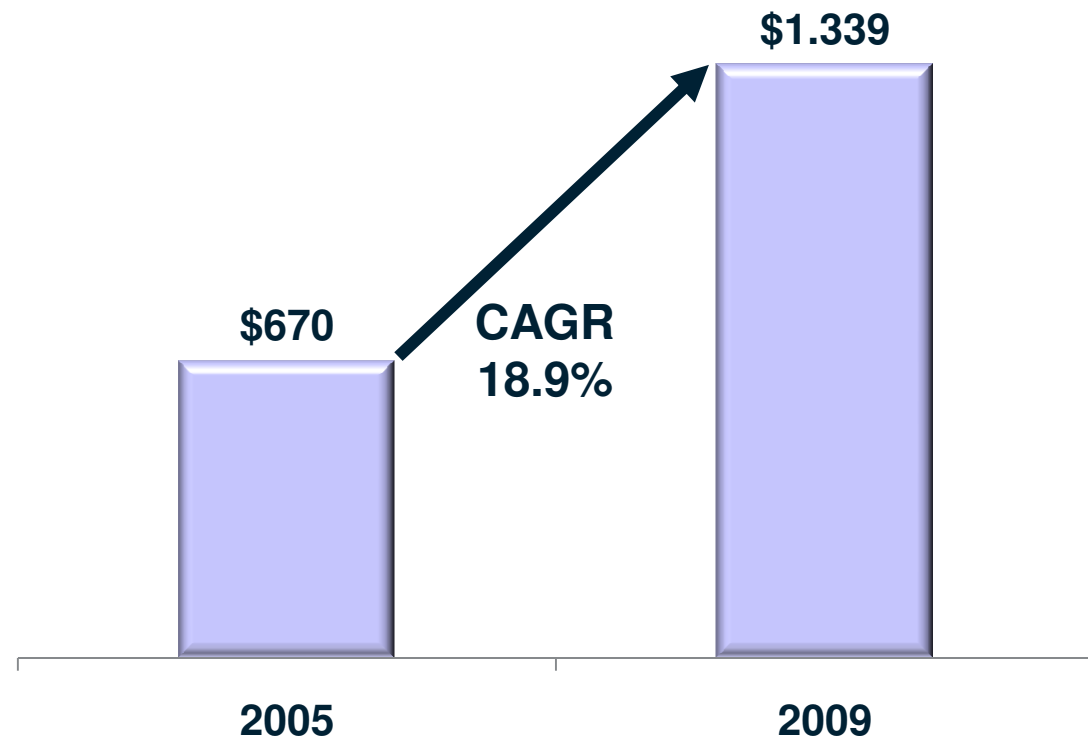
# Historical Highlights - Balance Sheet And Cash Flow Growth Drivers



## Balance Sheet and Cash Flow - Growth Drivers:

- Strong Operating and Free Cash Flow
- Increasing Net Income Levels
- Excellent Working Capital Management

## Operating Cash Flow



# Historical Highlights - Our Credibility With The Capital Markets



## Meeting Guidance and Investor Expectations

	2005	2006	2007	2008	2009
<b>Revenue</b>					
<b>Net Income</b> <small>attributable to FMC AG &amp; Co. KGaA</small>					
<b>Leverage</b>					
<b>Investments</b>					
<b>Operating Cash Flow</b>					

# Agenda



1. Historical Highlights

**2. 2010 Financial Guidance**

3. Goal 13 – Strategic Financial Objectives

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5. Summary

# Financial Guidance Outlook 2010



**Fully on Track for 2010 Targets**

US\$ millions	Guidance
<b>Net revenue</b>	<b>&gt; \$12,000</b>
<b>Net income</b> <small>attributable to FMC AG &amp; Co. KGaA</small>	<b>\$950 - 980</b>
<b>Leverage ratio (Debt/EBITDA)</b>	<b>&lt; 2.5</b>
<b>Capital expenditures</b>	<b>~ \$550 - 650</b>
<b>Acquisitions</b>	<b>up to \$500</b>

Updated

# Financial Guidance

## Goal 10 - Achievements



	<u>Goal 10</u>	<u>2010 - Guidance</u>
<b>Revenues</b>	> \$ 11.5 bn	> \$12.0 bn
<b><i>thereof: Pharma Sales</i></b> incl. internal sales	\$ 400 million	~ \$ 400 million
<b>EBIT Margin</b>	~ 20 bps (incremental increases p.a.)	~ 15.6 %
<b>Interest Expense</b>	< 6.5%	< 5.5%
<b>Tax Rate</b>	< 38 %	34.5% - 35.5 %
<b>Net Income / EPS</b> <small>attributable to FMC AG &amp; Co. KGaA</small>	Low to mid-teen (growth p.a.)	\$ 950 - \$ 980 million
<b>Operating Cash Flow</b>	Maintain to slightly improve current level of 10% of Revenue	> 10 % of Revenue
<b>CapEx &amp; Acquisitions</b>	~7 % of Revenue	~9 % of Revenue

# Agenda



1. Historical Highlights

2. 2010 Financial Guidance

**3. Goal 13 – Strategic Financial Objectives**

4. Goal 13 – Strategic Financial Objectives - Capital Structure

5. Summary

# Goal 2013 Strategic Financial Objectives

## Revenue Growth

(Average Annual, Constant Currency)



	Global Growth	Price/Mix Increase	Market Share & Acquisitions	Total
Services	5 – 6%	up to 2%	1 – 2%	6 – 9%
Products	4 – 5%	up to 1%	1 – 2%	5 – 7%
Total Objective				6 – 8%

# Goal 2013 Strategic Financial Objectives

## EBIT Margin



Current
~ 15.6%

2013
Average incremental increase of approximately 10 to 20 basis points per year

- **Scale effects**
- **Cost control**
- **Strategic investment / placement**
  - **US:** Bundle / De novos / Payor mix
  - **International:** Leveraging the existing organizational structure through expansions
- **Manufacturing capacity / demand management and efficiencies**



# Goal 2013 Strategic Financial Objectives

## Net Interest Expense

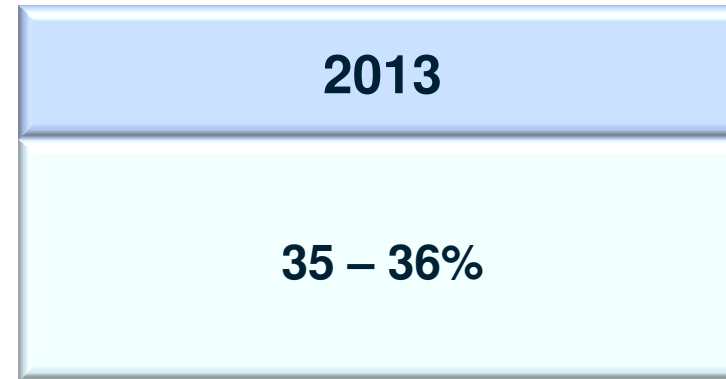
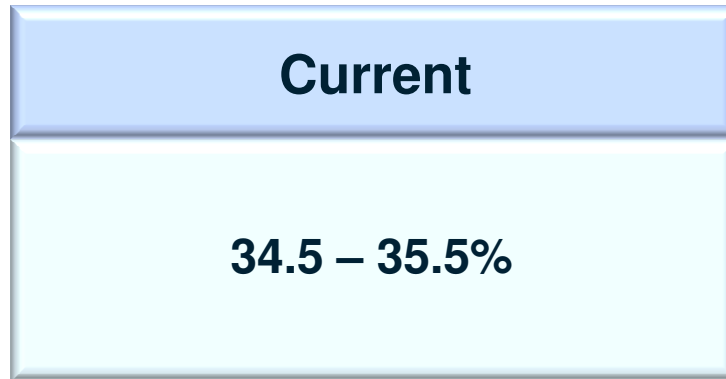


Current	2013
< 5.5%	~ 6 to 6.5%

- Amend & extend the existing Senior Credit Agreement by two years (Term Loan A and Revolving Facility)
- Issuance of Senior Bond early 2011 to refinance subordinated Trust Preferred Securities
- Issuance of Senior Bond to refinance Term Loan B of the Credit Agreement in mid 2012

# Goal 2013 Strategic Financial Objectives

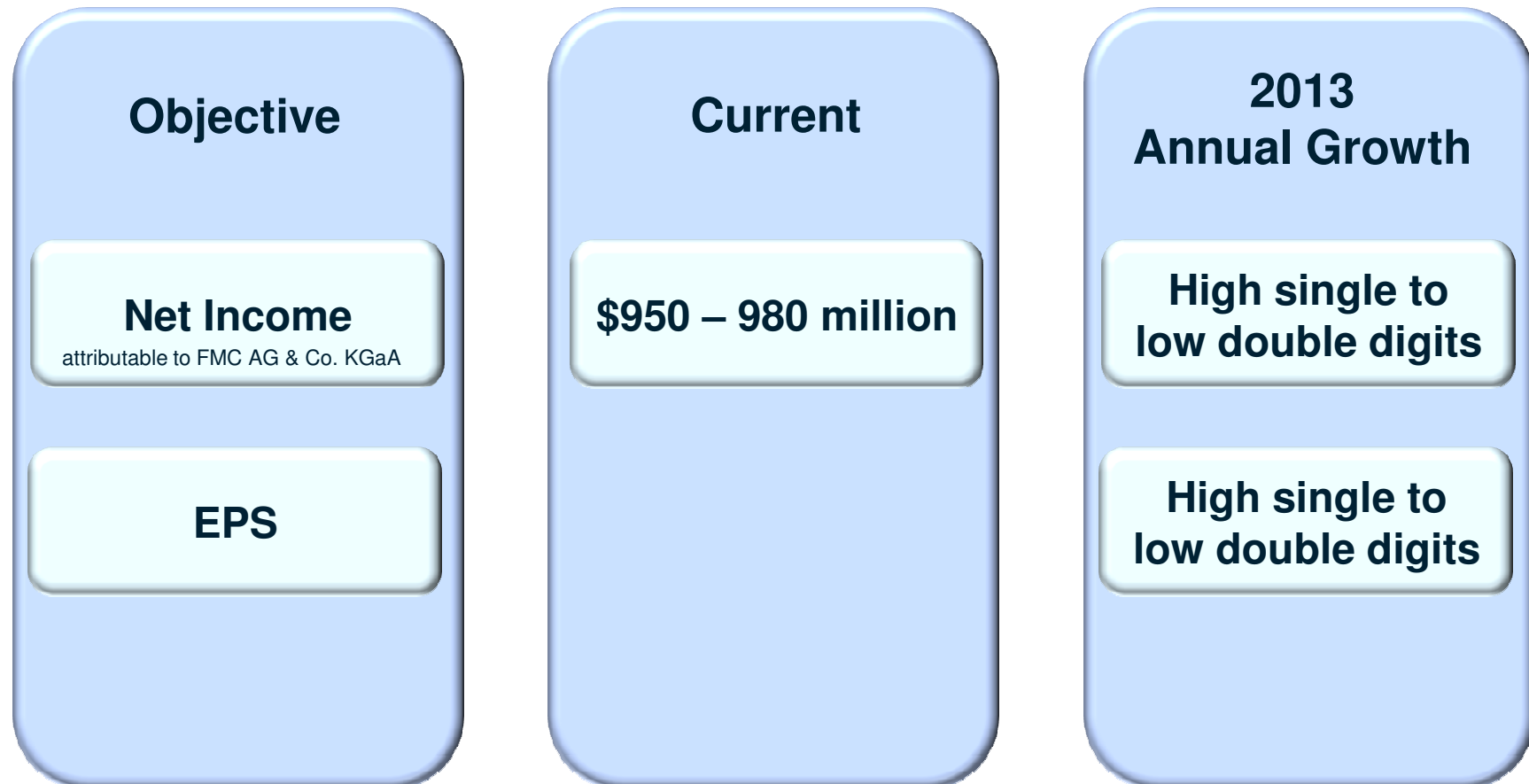
## Effective Tax rate



- Continue on a sustainable basis

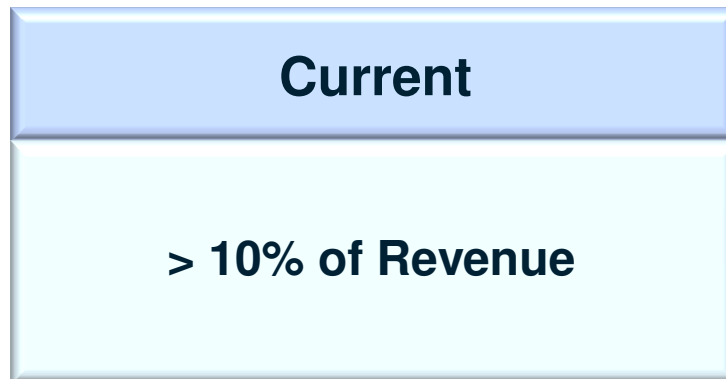
# Goal 2013 Strategic Financial Objectives

## Net Income / EPS



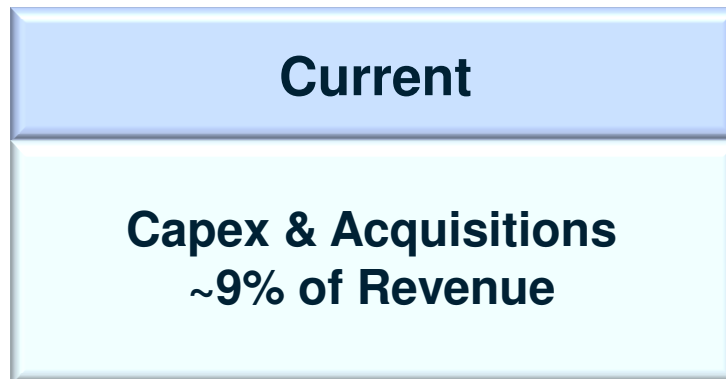
# Goal 2013 Strategic Financial Objectives

## Cash from Operations



- **Improve profitability**
- **Continue with effective working capital management**
  - **Strong collection process**
  - **Maintain effective inventory management**

# Goal 2013 Financial Objectives – Capital Expenditures and Acquisitions



- **Take advantage of existing growth opportunities**
- **Prudent investment to avoid dilution of return on invested capital**

# Goal 2013 Strategic Financial Objectives



	2010 - Guidance	Goal 13
<b>Revenues</b>	> \$12bn	6-8% Growth*
<b>EBIT Margins</b>	~ 15.6%	10 - 20 bps (incremental increases p.a.)
<b>Interest Expense</b>	< 5.5%	6.0 to 6.5%
<b>Tax Rate</b>	34.5 – 35.5%	35 – 36%
<b>Net Income</b> <small>attributable to FMC AG &amp; Co. KGaA</small>	\$950 - 980	High single to low double digits
<b>Operating Cash Flow</b>	> 10% of Revenue	> 10% of Revenue
<b>CapEx + Acquisitions</b>	~9% of Revenue	~7% of Revenue

\*Constant Currency

# Agenda



1. Historical Highlights

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**4. Goal 13 – Strategic Financial Objectives - Capital Structure**

5. Summary

# Goal 13 – Strategic Financial Objectives

## Capital Structure



- **FME has current guidance Debt/EBITDA ratio of < 2.5x**
- **Strategically our franchise can operate effectively with ~ 2.5x leverage**
- **Equivalent to a credit rating of BB to BBB-**
  - **Industry well suited to “reasonable” leverage**
    - **Non-cyclical**
    - **Predictable cash flow**
    - **Attractive profitability**
    - **Foreseeable investment needs**
- **This provides the flexibility to seek further investment opportunities and finance them with debt**



# Goal 13 – Strategic Financial Objectives

## Capital Structure



### Debt Portfolio

- **Amend & extend Senior Credit Agreement**
- **Transition to single tier**
- **Lengthen average maturity**
- **Target committed and unutilized facilities at \$300 – 500 million**

# Agenda



1. Historical Highlights

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**5. Summary**

# Summary

## Leadership

- Maintain our global leadership position
- Continue to shape the future of the dialysis industry

## Quality

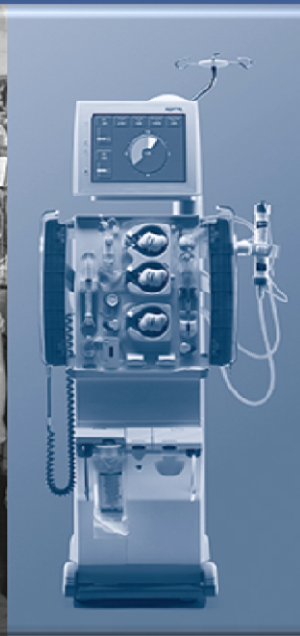
- Maintain superior quality in products and services

## Growth

- Benefit from product innovations
- Take opportunity of international growth potential
- Introduce new therapy offerings
- Continue horizontal expansion of service and product range

## Financial

- Control cost and spending
- Seek attractive investment opportunities
- Continue profitable growth momentum
  - Revenue to grow 6-8% per annum, constant currency
  - Earnings After Tax – high single to low double digits



Thank You for Your Interest in Fresenius  
Medical Care!



Fresenius Medical Care