“All patients suitable for home dialysis should do PD first”

2008 BC Nephrology Day Conference

October 2, 2008

Vancouver, British Columbia

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“All patients that are suitable for dialysis should do PD first prior to in center hemodialysis”

Why should all patients starting dialysis do PD first?

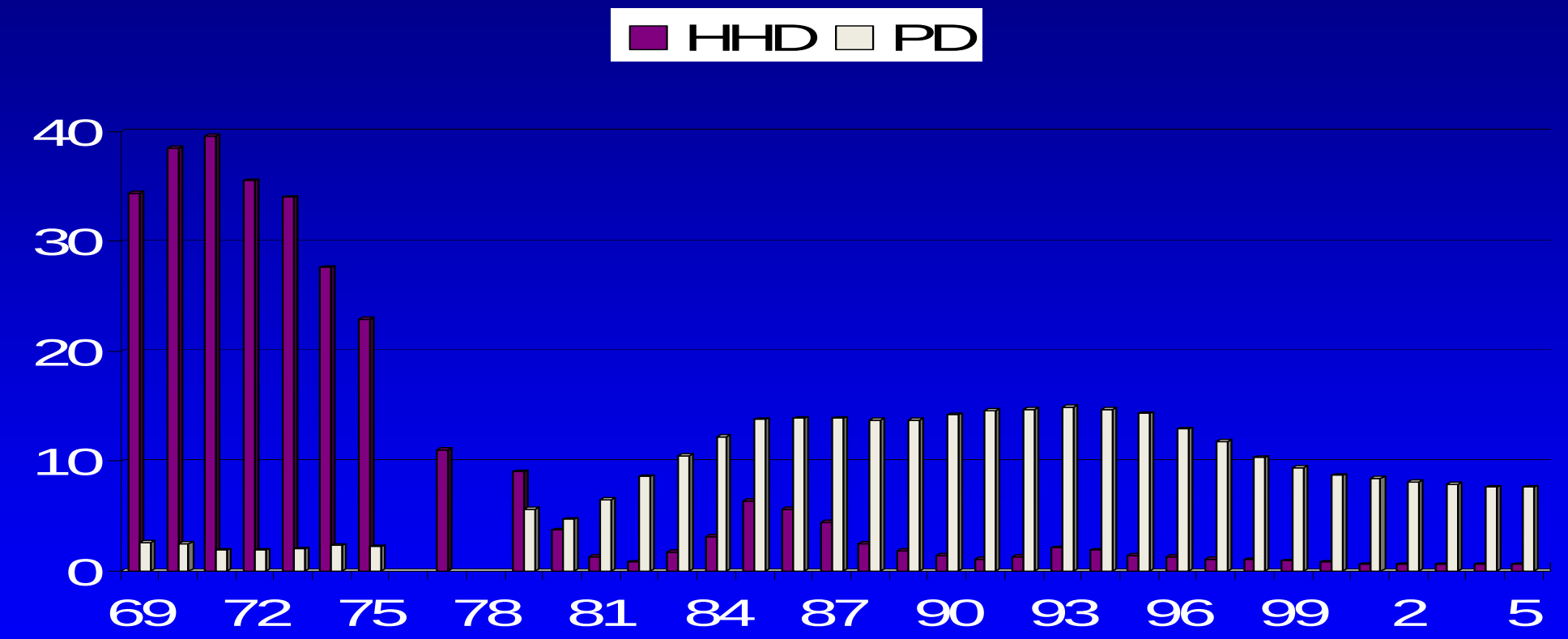
- Empowerment of patients to care for themselves at home
- Preserve residual renal function
- Preserve vascular access for later in center use if patient not transplanted
- Allow patients to travel
- Allow patients to continue to work

Why should all patients starting dialysis do PD first?

- Renal replacement bridge to transplant
- Gentle continuous renal replacement for aging patients with significant co-morbidy
- New connect technology that decreased infection rate
- Cycler technology improved supporting more dialysis during the night and pauses during the day

“What happened in the US in 1995 which changed the number of patients starting on peritoneal as their first choice of renal replacement therapy?

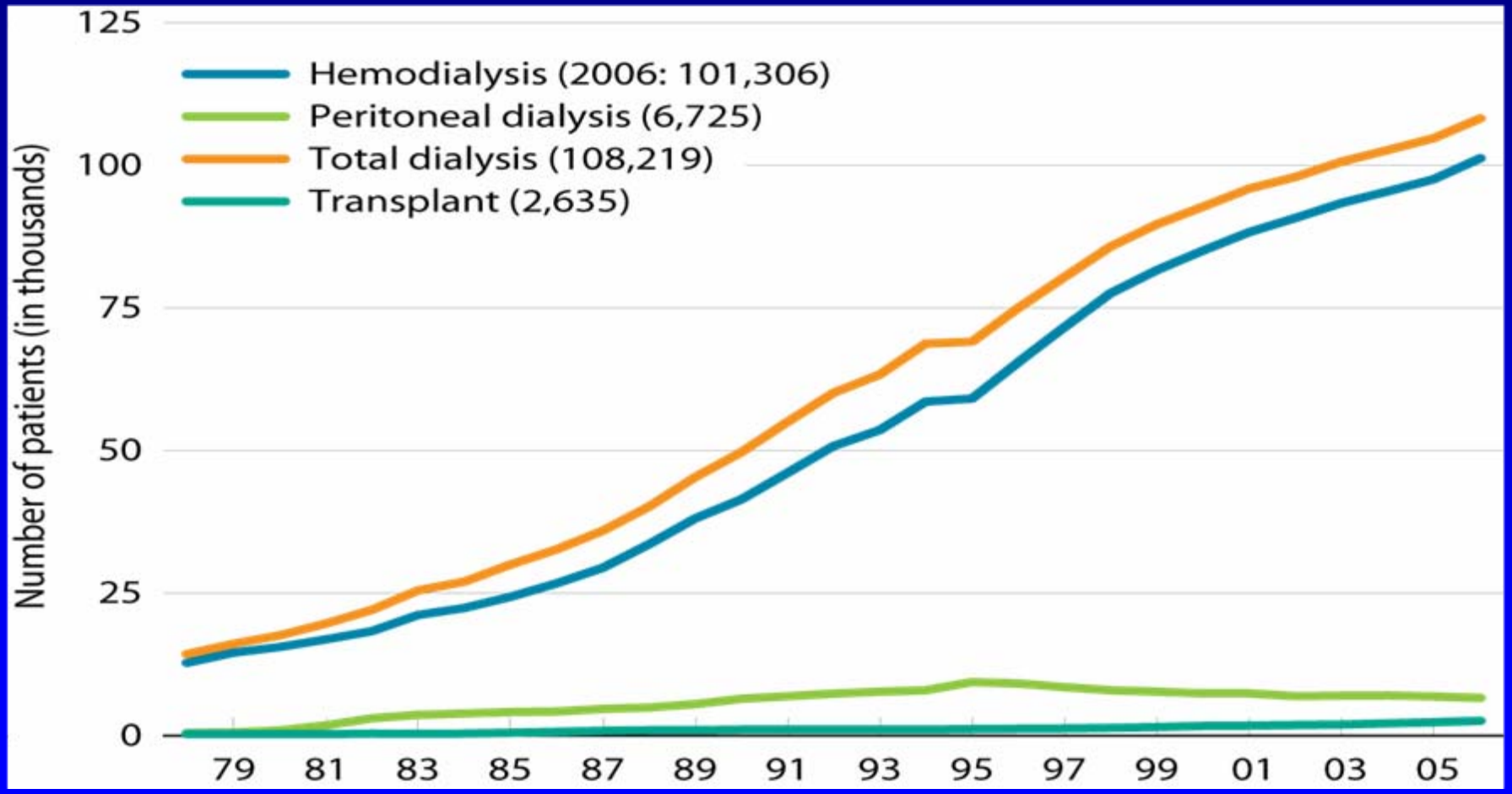
Percentage of dialysis patients on HHD and PD in the US – 1969-2006



Slide courtesy of Dr. Blagg

Incident patient counts by first modality

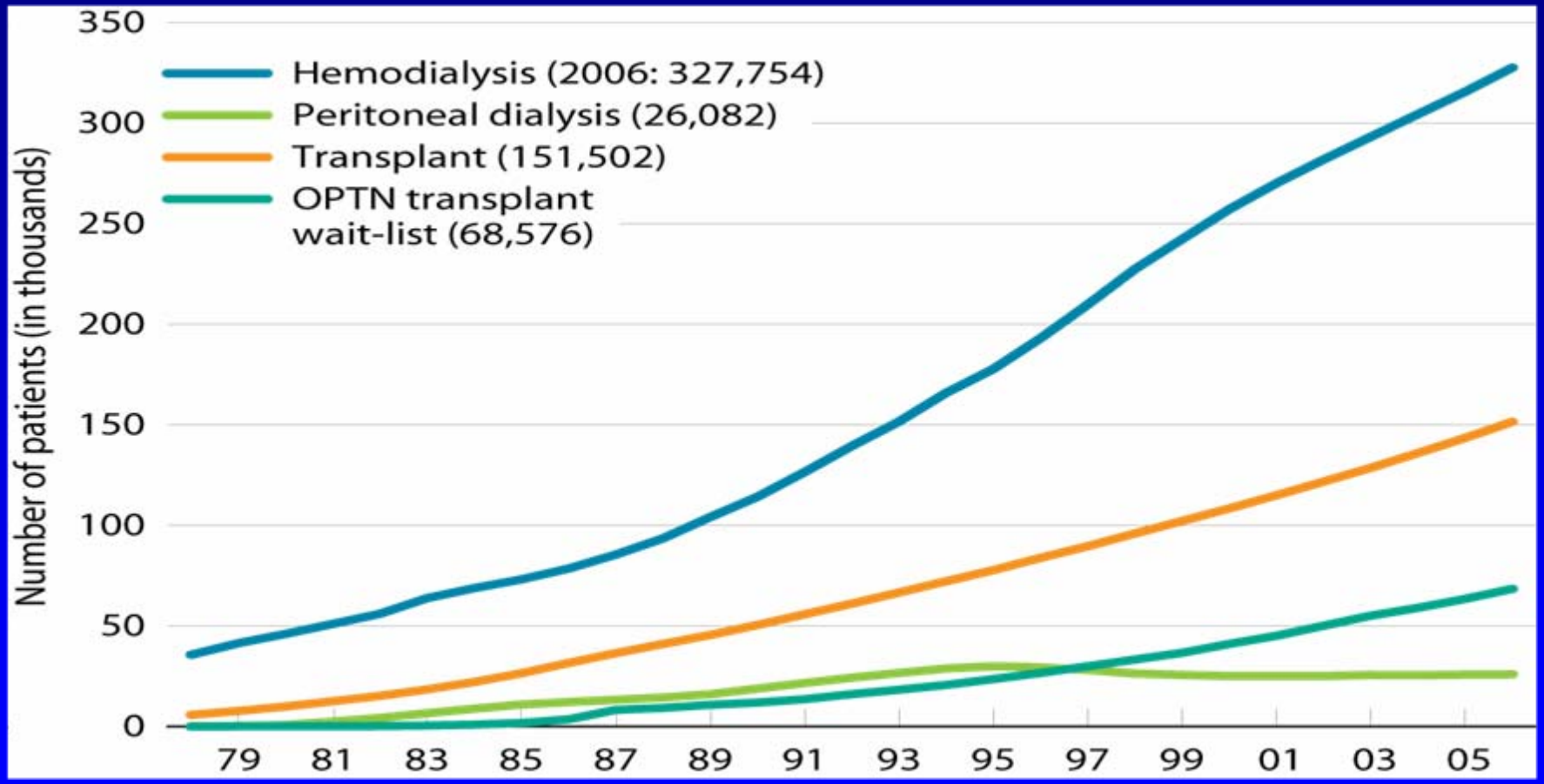
USRDS 2008 Annual Data Report Figure 4.1 (Volume 2)



Incident ESRD patients; peritoneal dialysis counts include CAPD & CCPD only.

Prevalent patient counts by modality

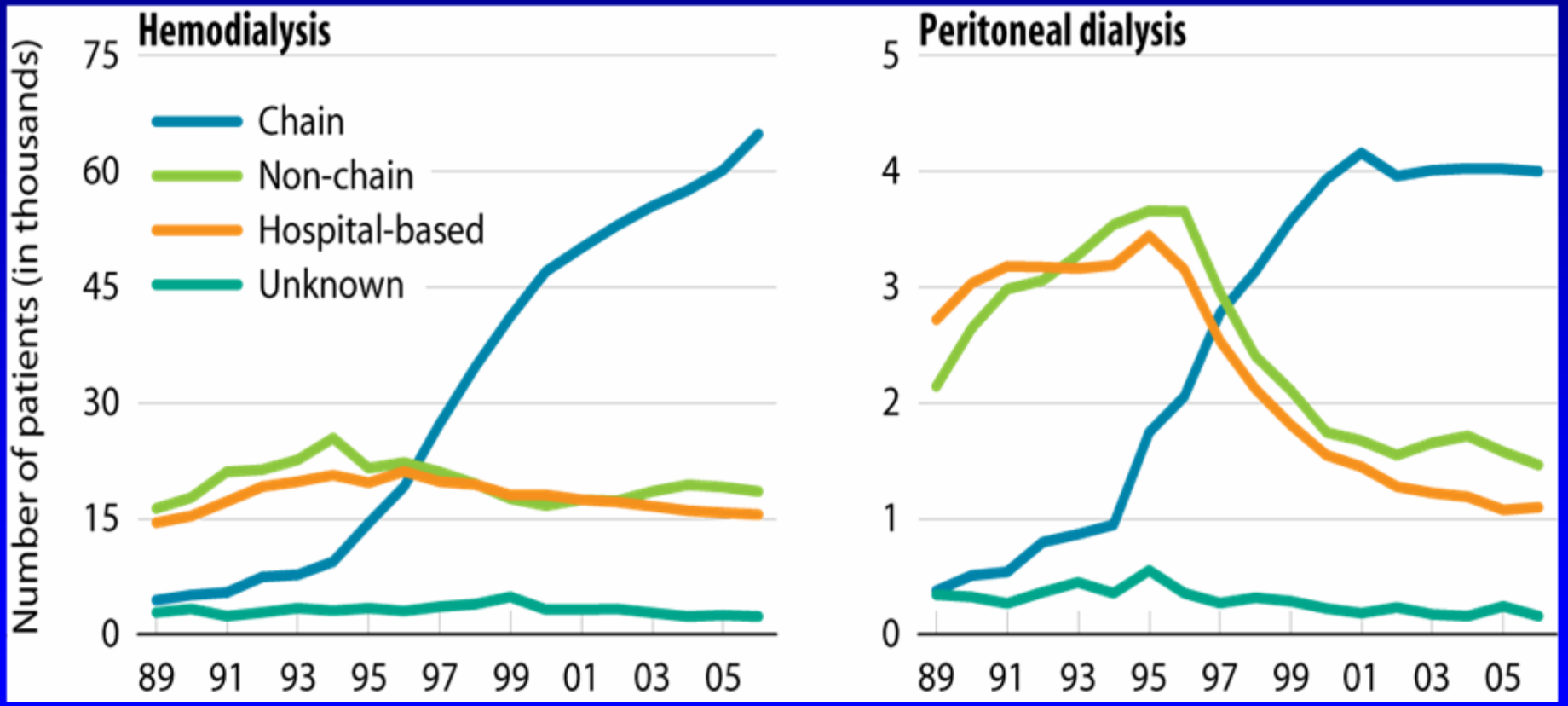
USRDS 2008 Annual Data Report Figure 4.2 (Volume 2)



December 31 point prevalent patients; peritoneal dialysis counts include CAPD & CCPD only. OPTN was created in 1986.

Incident patient counts by first modality and unit type

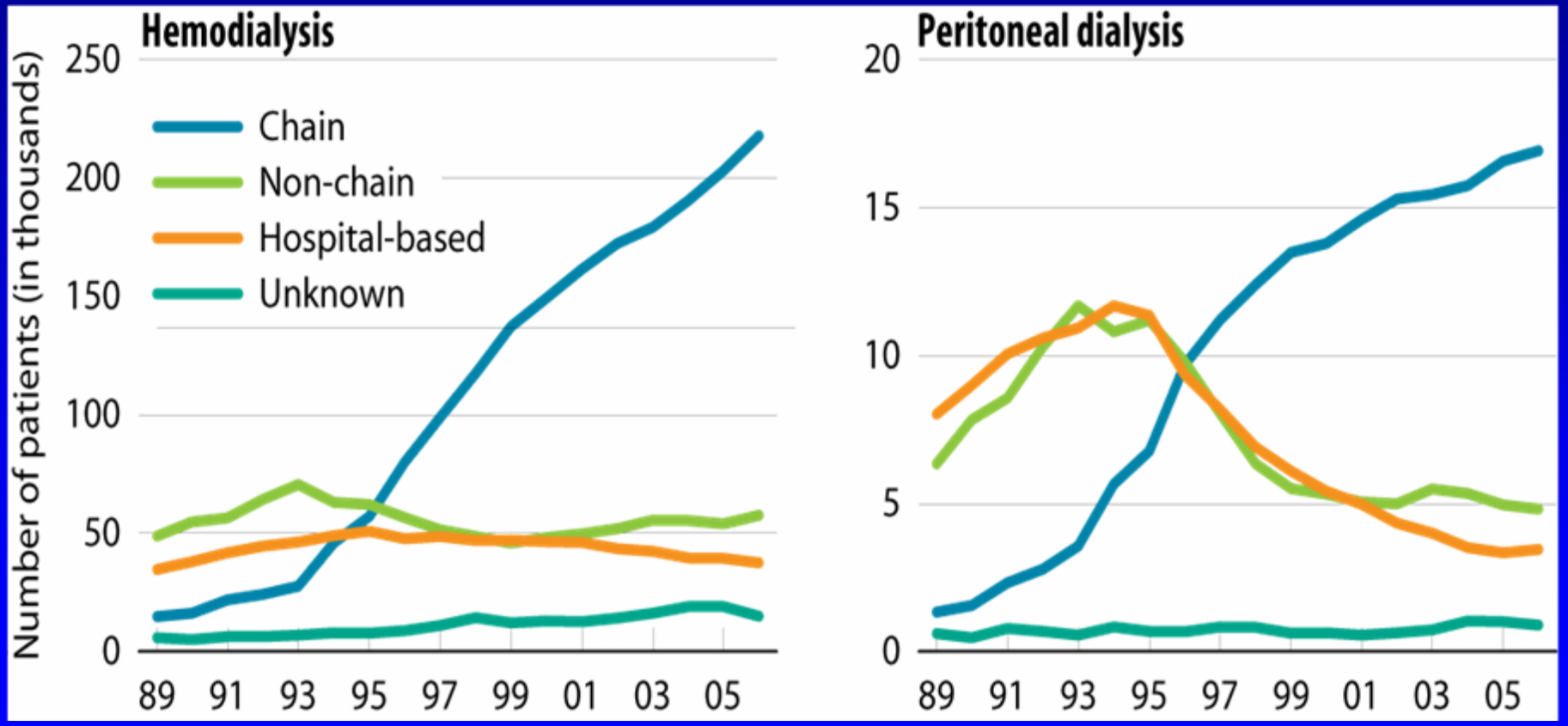
USRDS 2008 Annual Data Report Figure 4.3 (Volume 2)



Incident dialysis patients; peritoneal dialysis includes CAPD & CCPD only.

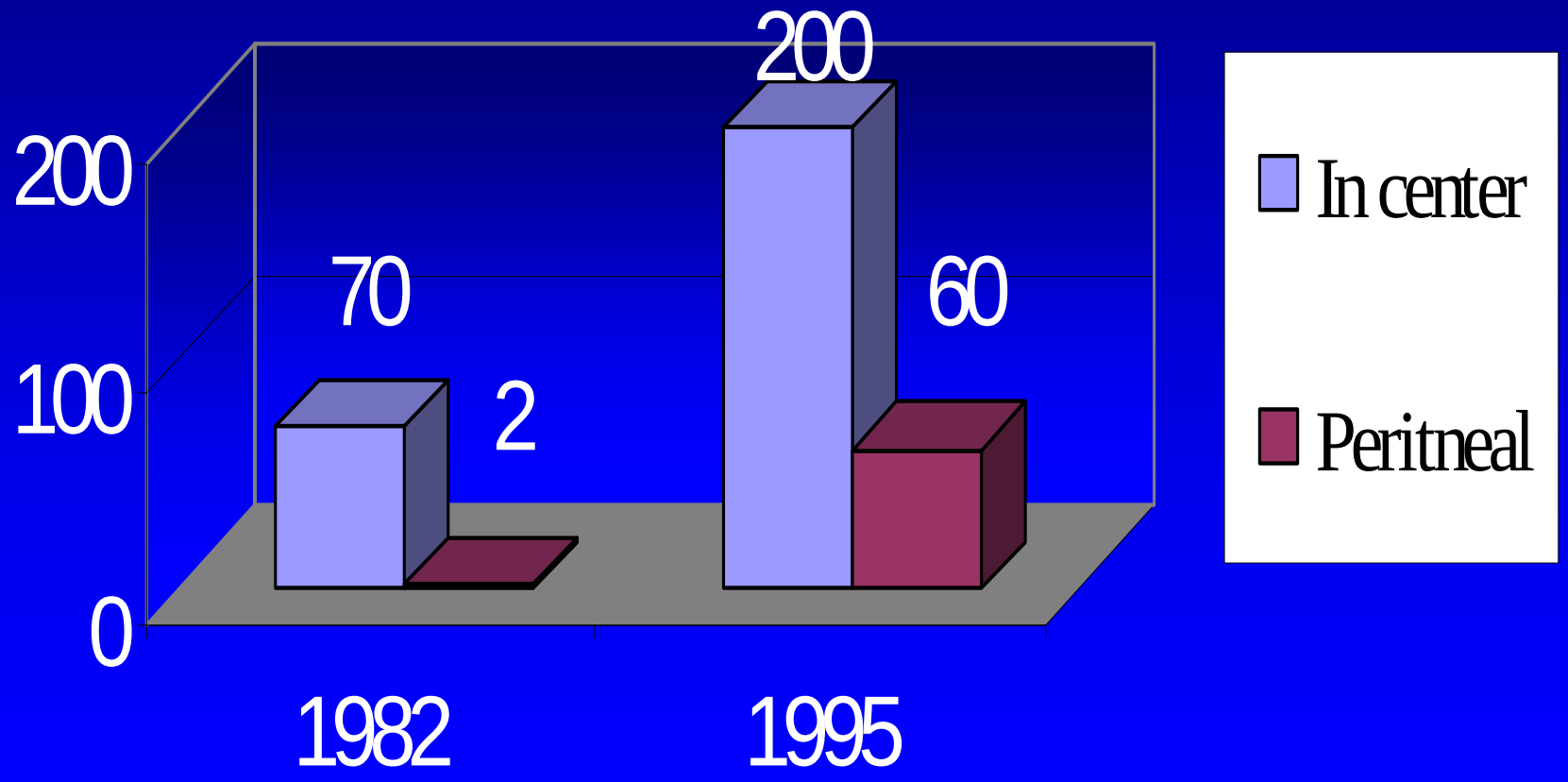
Prevalent patient counts by modality and unit type

USRDS 2008 Annual Data Report Figure 4.6 (Volume 2)



December 31 point prevalent dialysis patients.

PD Growth in Lynchburg



Results of increasing Peritoneal KT/V and Creatinine Clearance in PD patients

- Increasing hernias and pleural effusions from the increased intra abdominal pressure due to larger volumes per exchange
- Decrease in appetite resulting in lower albumin associated with increased exchange volumes
- Patient dissatisfaction because of the increased time needed to perform five or more exchanges per day

Results of increasing Peritoneal KT/V and Creatinine Clearance in PD patients

- Weight gain and other metabolic consequences from higher glucose exposure and absorption of glucose associated with more liters of exchange per day
- Increasing loss of protein with worsening nutritional status
- Inadequate ultrafiltration associated with falling albumins
- Increase in patient drop out

Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. Canada-USA (CANUSA) Peritoneal Dialysis Study Group

- A decrease of 0.1 unit in total (peritoneal and residual renal) Kt/Vurea was associated with a 5 percent increase in the relative risk of death
- A decrease in total (peritoneal and corrected residual renal) weekly creatinine clearance of 5 L/1.73 m2 body surface area was associated with a 7 percent increase in the relative risk of death

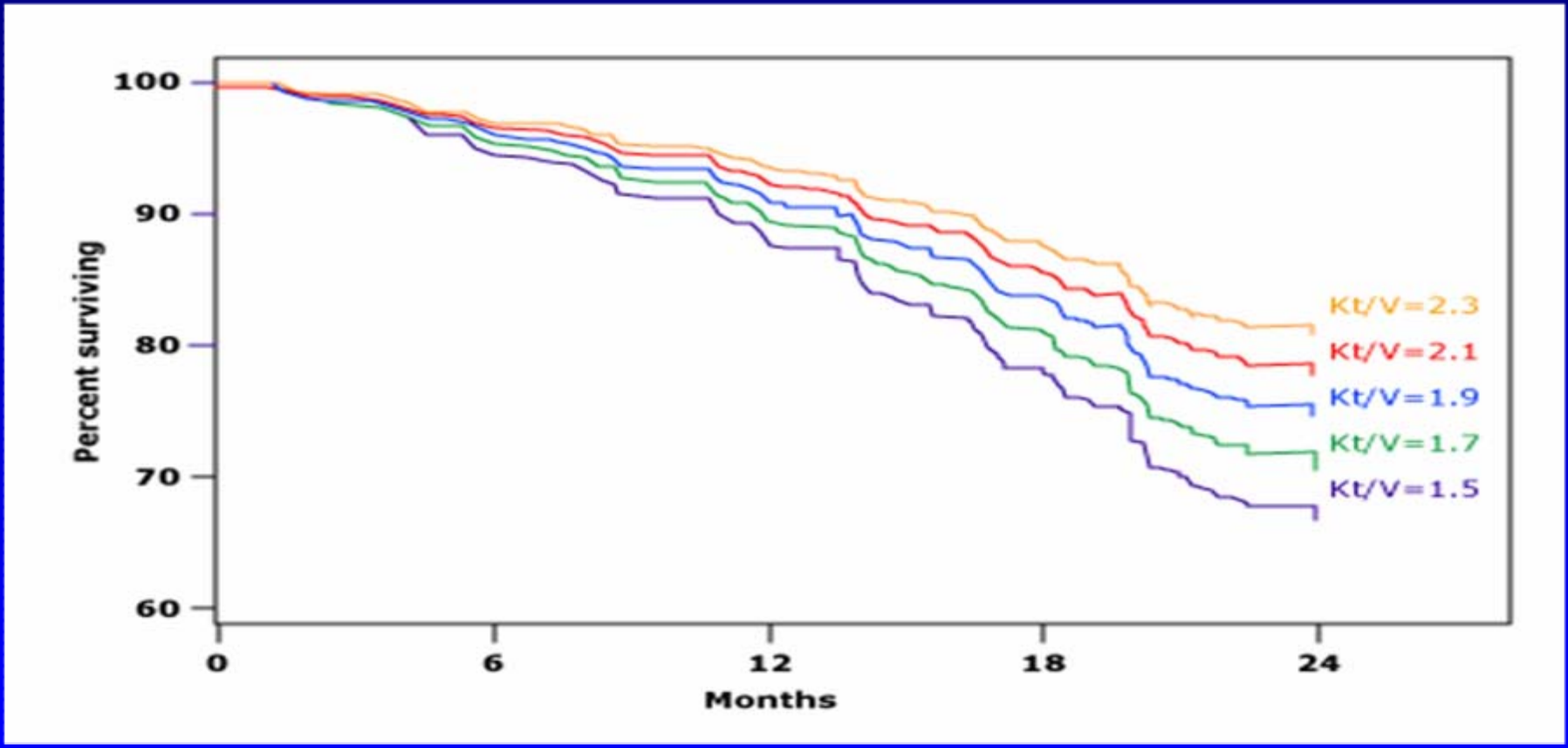
J Am Soc Nephrol 1996 Feb;7(2):198-207

Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. Canada-USA (CANUSA) Peritoneal Dialysis Study Group

- A decrease in creatinine clearance was associated with an increase in the relative risk of technique failure and incidence of hospitalization.
- A Kt/Vurea of 2.1 and a weekly creatinine clearance of 70 L/1.73 m2 body surface area were both associated with a 78 percent expected two year survival rate

J Am Soc Nephrol 1996 Feb;7(2):198-207

Kt/V predicts survival in continuous PD



Data from CANADA-USA (CANUSA) Peritoneal Dialysis Study Group, J Am Soc Nephrol 1996; 7:198.

Reanalysis of the CANUSA Study

- Survival was largely related to residual renal function (which changed over time) and not to peritoneal clearance alone (which did not change)
- That residual renal function predicted outcome not peritoneal clearance
- For a 250-ml increment in urine volume, there was a 36% decrease in the RR of death
- Neither net peritoneal ultrafiltration nor total fluid removal was associated with patient survival

J Am Soc Nephrol 2001 Oct;12(10):2158-62

What are the KDOQIs guidelines for providing minimum adequate Peritoneal Dialysis in 2006?

2006 KDOQI minimum Peritoneal Adequency Guidelines

- For patients with residual kidney function (RKF) (arbitrarily considered to be significant if urine volume is >100 mL/day):
  - The minimal delivered dose of small solute clearance should be a total (PD and RKF) Kt/V urea of at least 1.7/week. The total solute clearance (PD and RKF) in terms of Kt/V urea should be measured within the first month of PD and, subsequently, at least once every four months. A 24 hour urine collection for urine volume and solute clearance should be obtained, at a minimum, every 2 months.

2006 KDOQI Peritoneal Adequency Guidelines

- For patients without RKF (considered insignificant if urine volume is <100 mL/day):
  - The minimal delivered dose of small solute clearance should be a peritoneal Kt/V urea of at least 1.7/week. The dose should be measured within the first month of starting dialysis and, subsequently, at least every four months.

What options of renal replacement do our patients have today?

Estimated Urea Weekly stdKt/V Values

Treatment	Treatment Frequency	Weekly spKt/V	Weekly stdKt/V
CAPD	Continuous	-	1.7–2.0
HD (HEMO Study)	3×/wk	3.9-5.1	2.1-2.3
HD	4×/wk	4.0-4.8	2.6-2.9
Short Daily HD	6×/wk	4.0-5.0	2.7-3.2
Nocturnal HD	6×/wk	5.0-6.0	4.6-5.0
NxStage HD	6×/wk	3.0-3.6	2.1-2.5

Leypoldt et al, Semin Dial 2004

Estimated CKD Stages provided by each renal replacement modality

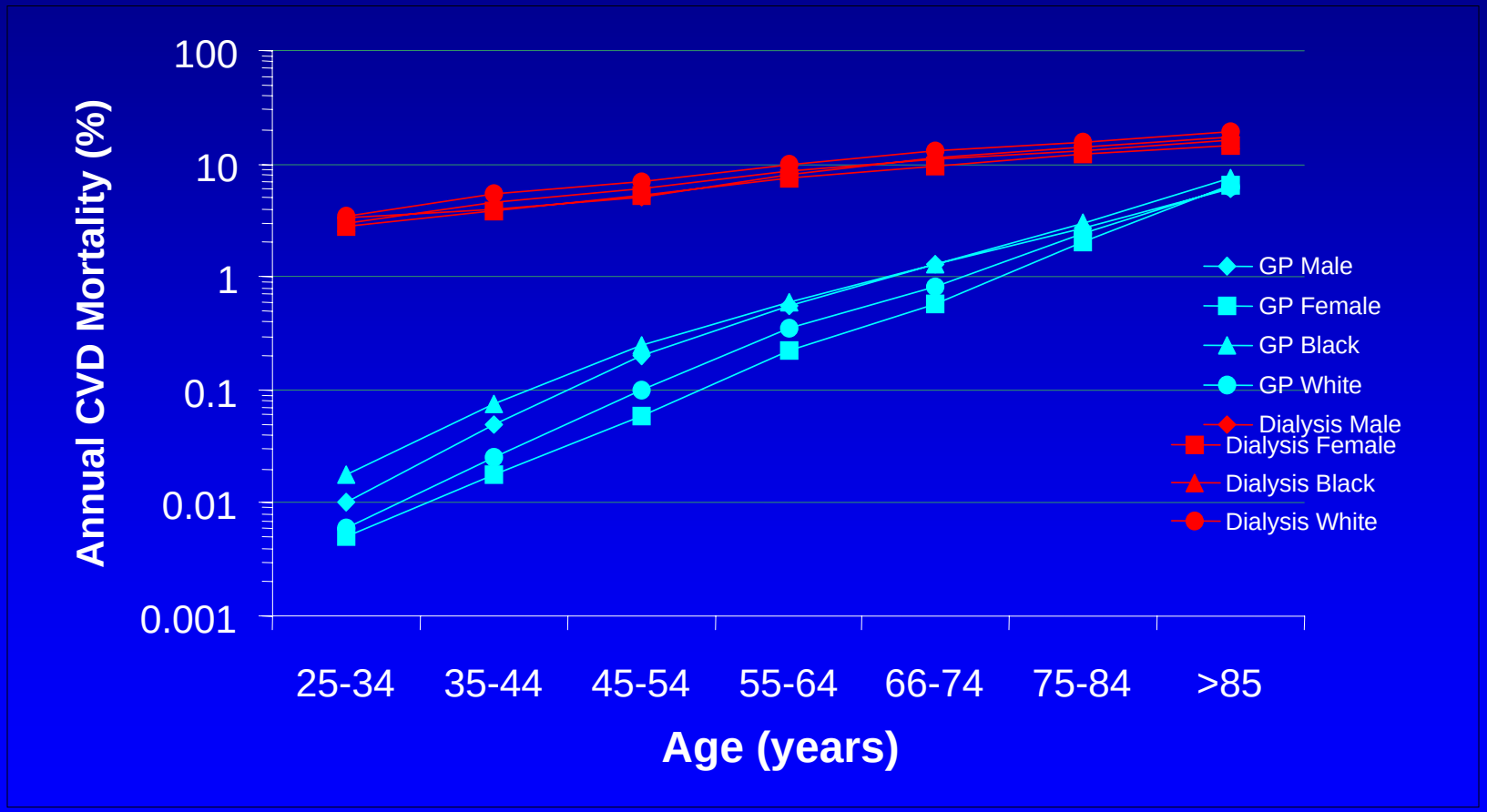
- We start patients on dialysis at CKD V
- In center hemodialysis provides CKD V renal replacement but does not control fluid and phosphorus
- CAPD provides CKD V renal replacement controlling fluid in some patients but not phosphorus
- Conventional home hemodialysis provides CKD V renal replacement but does not control fluid and phosphorus

Estimated CKD Stages provided by each renal replacement modality

- NxStage short daily provides CKD V renal replacement controlling fluid but not phosphorus
- Conventional short daily provides CKD IV renal replacement controlling fluid but not phosphorus
- Nocturnal hemodialysis $\geq$ five treatments per week provides CKD III renal replacement controlling fluid and phosphorus

Informed Consent!
What do we tell our patients?

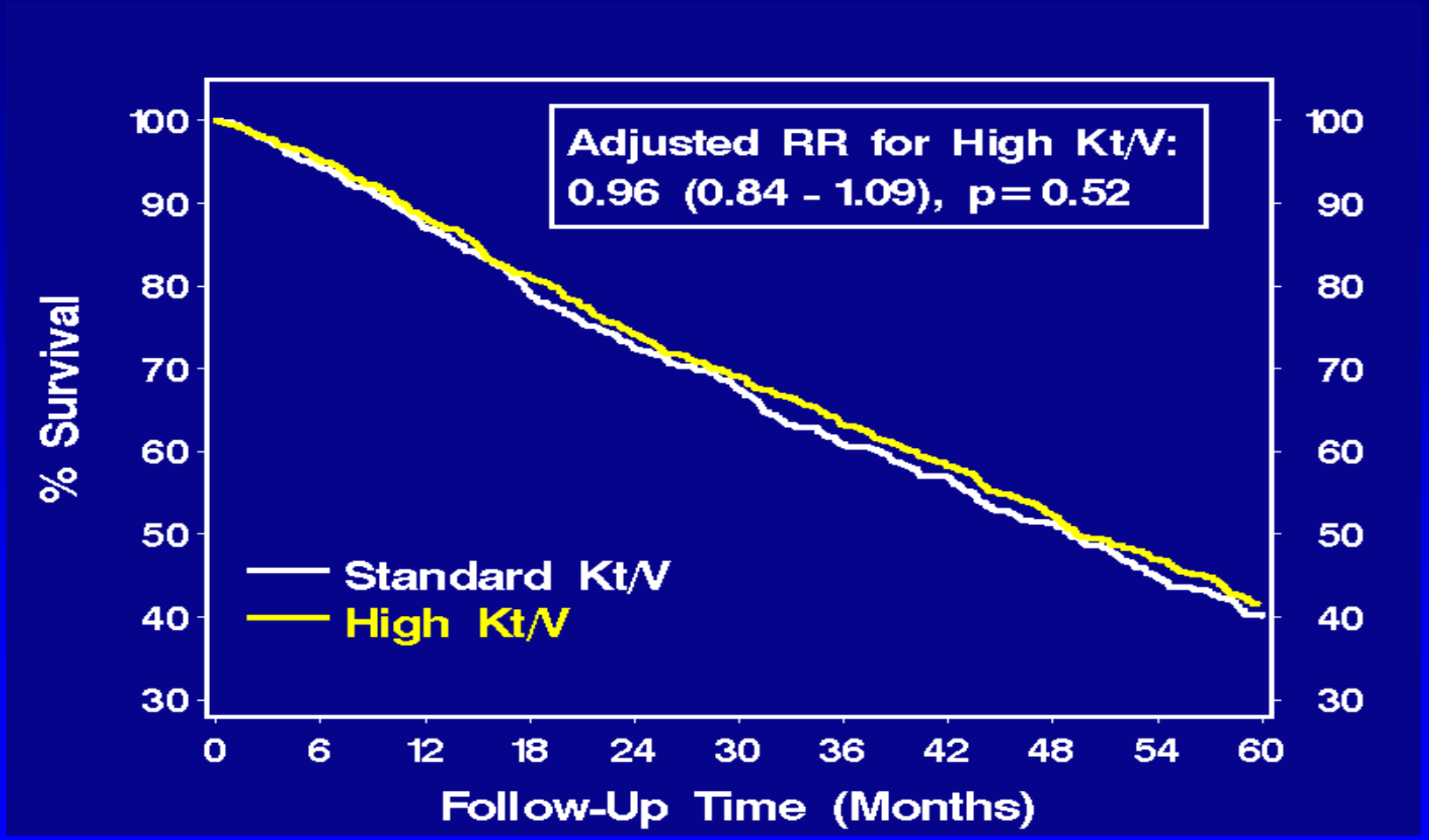
Cardiovascular disease mortality general population vs ESRD patients



GP = General Population.

Foley RN, et al. Am J Kidney Dis. 1998;32:S112-S119

HEMO Study: Survival by dose group



Eknoyan et al, N Eng J Med 2002

The ADEMEX Study

- Prospective, randomized, controlled trial
- Evaluated outcome of peritoneal patients looking at KT/V of 1.75 vs. 2
- Study showed that there was no significant improvement with outcomes of patients with a standard weekly KT/V of 1.75 vs. 2

J Am Soc Nephrol 13:1307-1320, 2002

All-cause mortality rates, 2006, by age

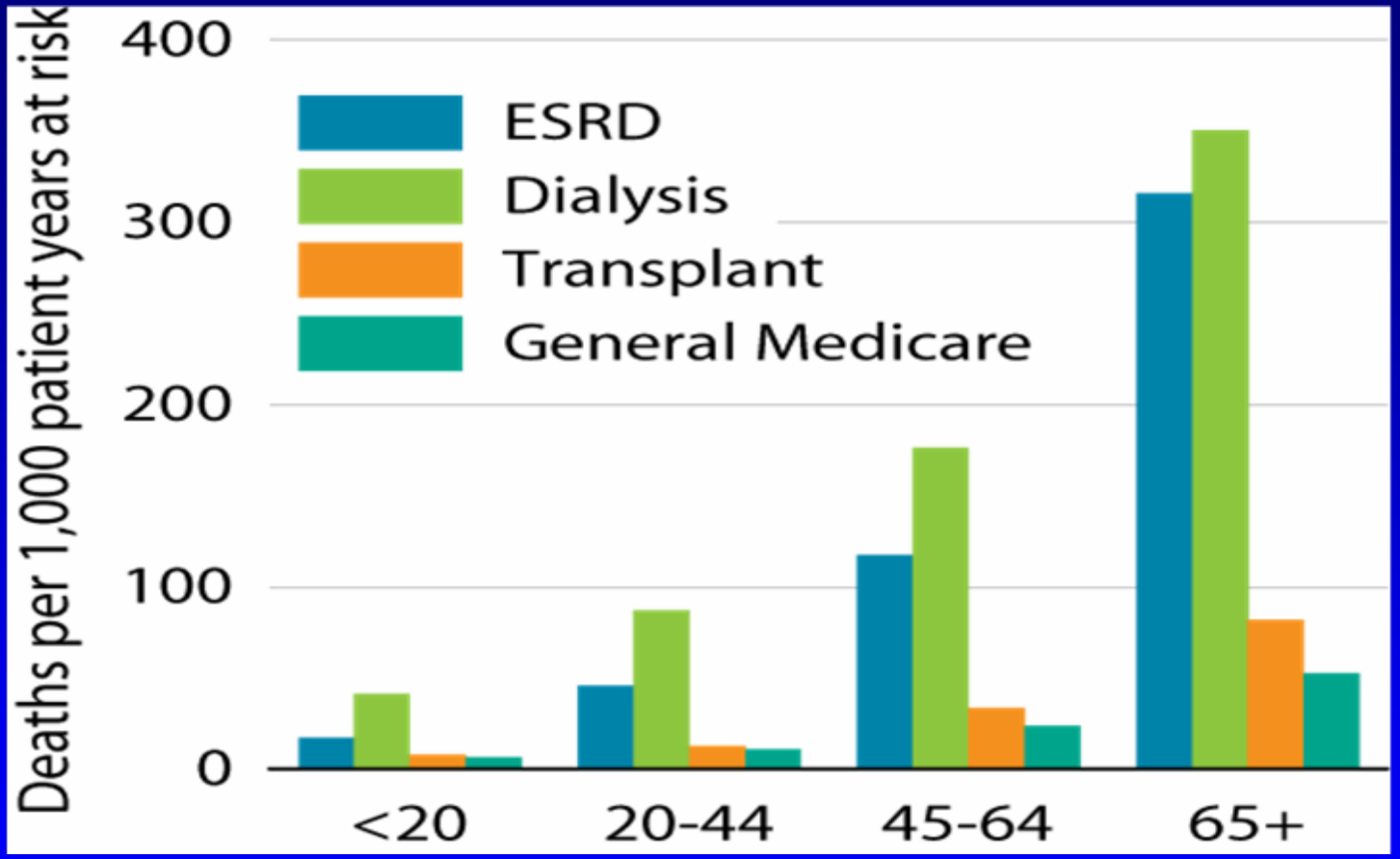


Figure 6.8 (Volume 2) ESRD: prevalent ESRD patients, 2006. General Medicare: non-ESRD patients with at least one month of Medicare eligibility in 2006. Adjusted for gender & race. Medicare patients, 2006, used as reference cohort.

The 2008 USRDS Annual Data Report

Adjusted mortality rates by vintage

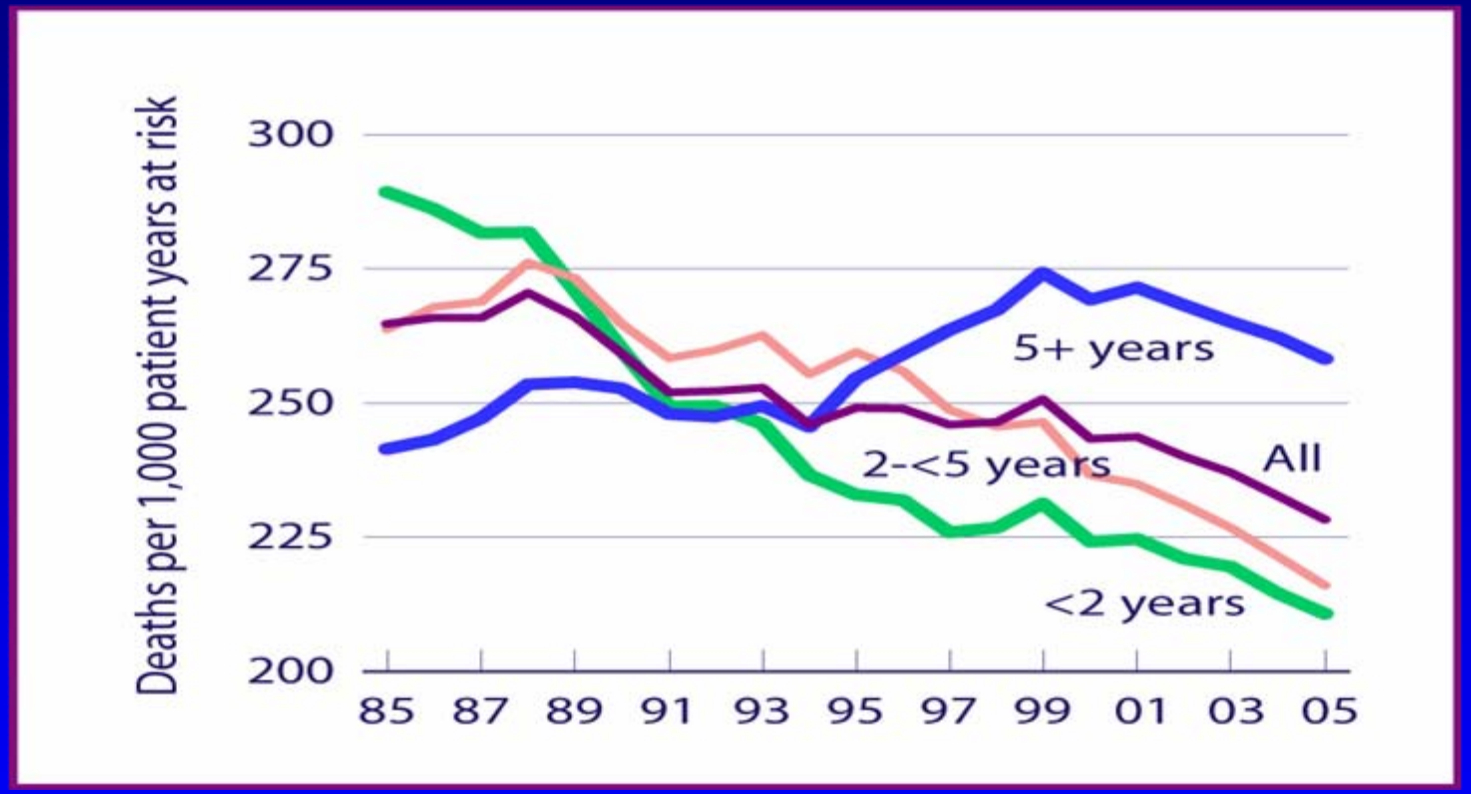


Figure 6.14: Period prevalent dialysis patients; adjusted for age, gender, race, & primary diagnosis. Dialysis patients, 2001, used as reference cohort

2007 Annual Data Repot Text Based Atlas of End-Stage Renal Disease in the United States

Mortality rates by modality

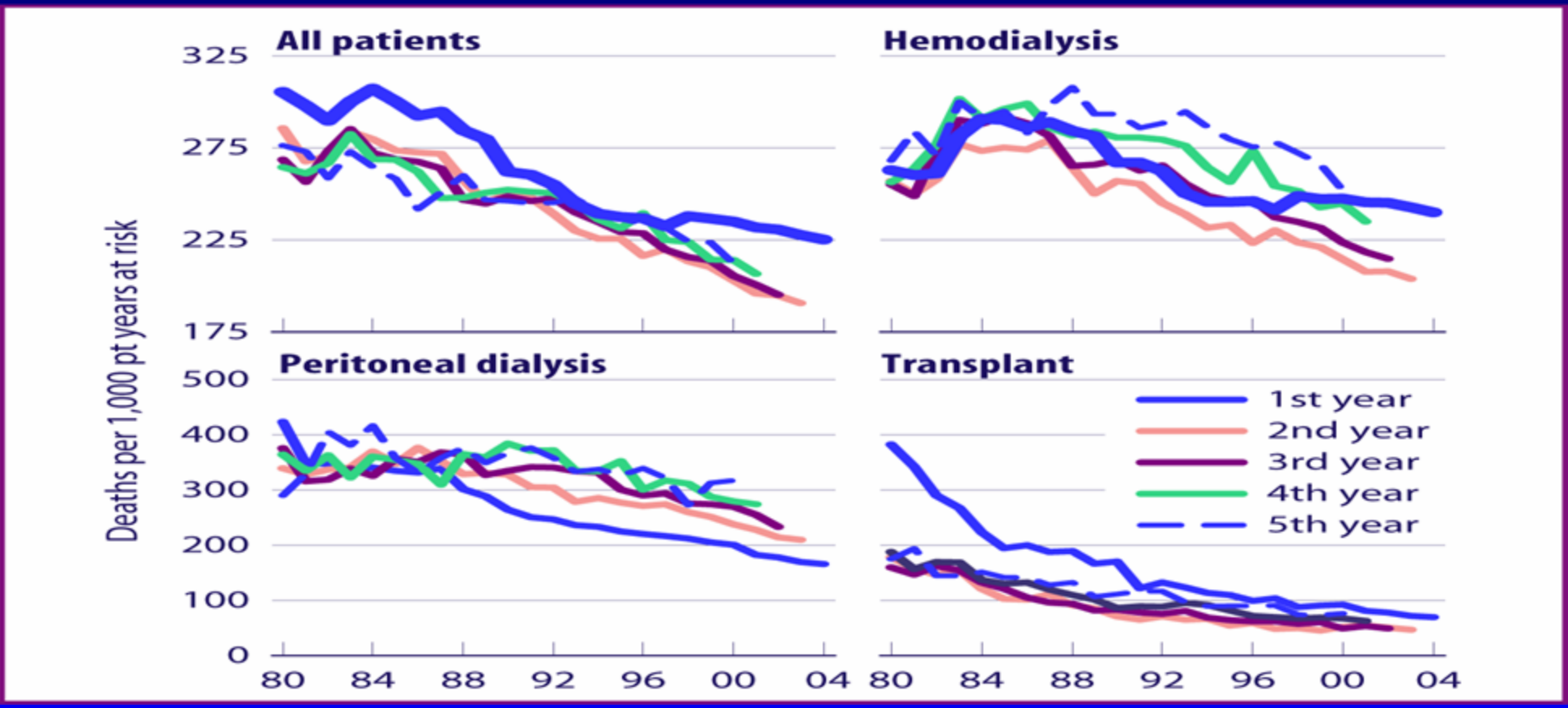


Figure 6.2: Incident ESRD patients; adjusted for age, gender, race, & primary diagnosis. Incident ESRD patients, 1996,used as reference cohort 2007 Annual Data Repot Text Based Atlas of End-Stage Renal Disease in the United States

Adjusted five-year survival, by modality & primary diagnosis: 1997-2001

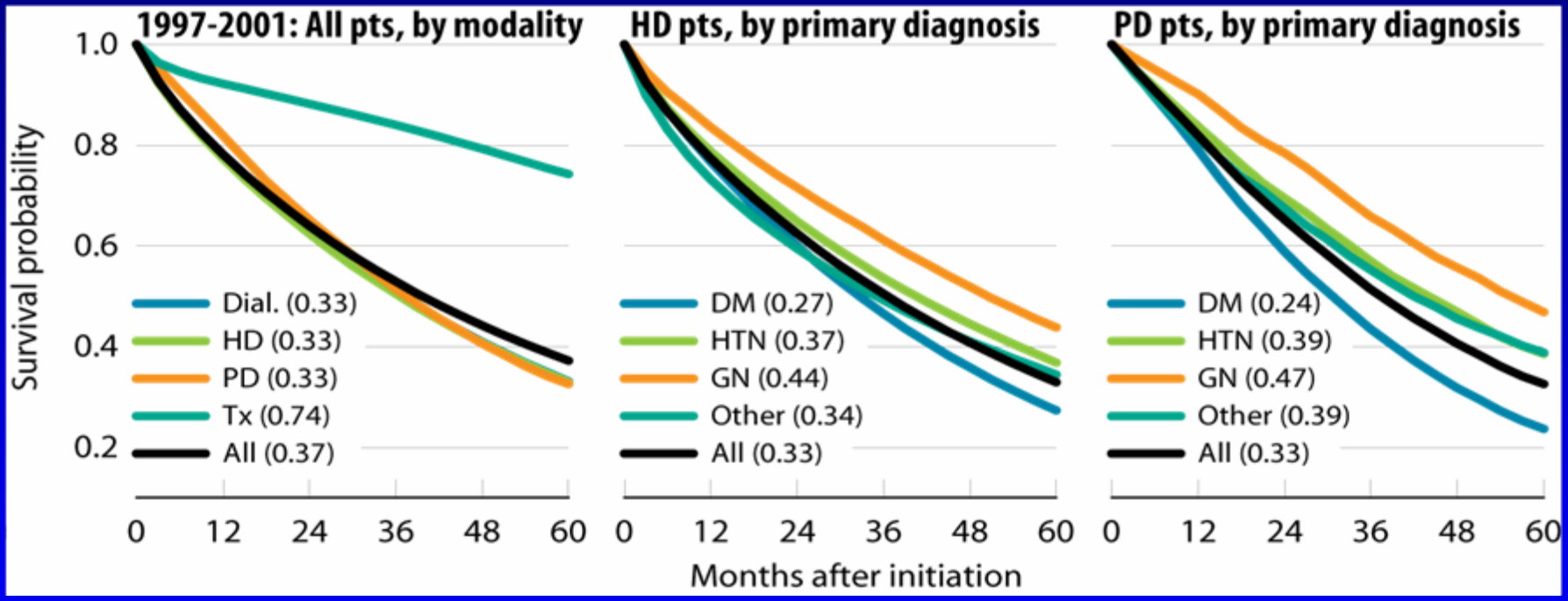


Figure 6.10 (Volume 2) incident dialysis patients & patients receiving a first transplant in the calendar year. All probabilities adjusted for age, gender, & race; overall probabilities also adjusted for primary diagnosis. All ESRD patients, 2005, used as reference cohort. Five-year survival probabilities noted in parentheses. Dialysis patients followed from day 90 after initiation; transplant patients followed from the transplant date.

The 2008 USRDS Annual Data Report (ADR) Reference Tables

Adjusted admissions & days by modality

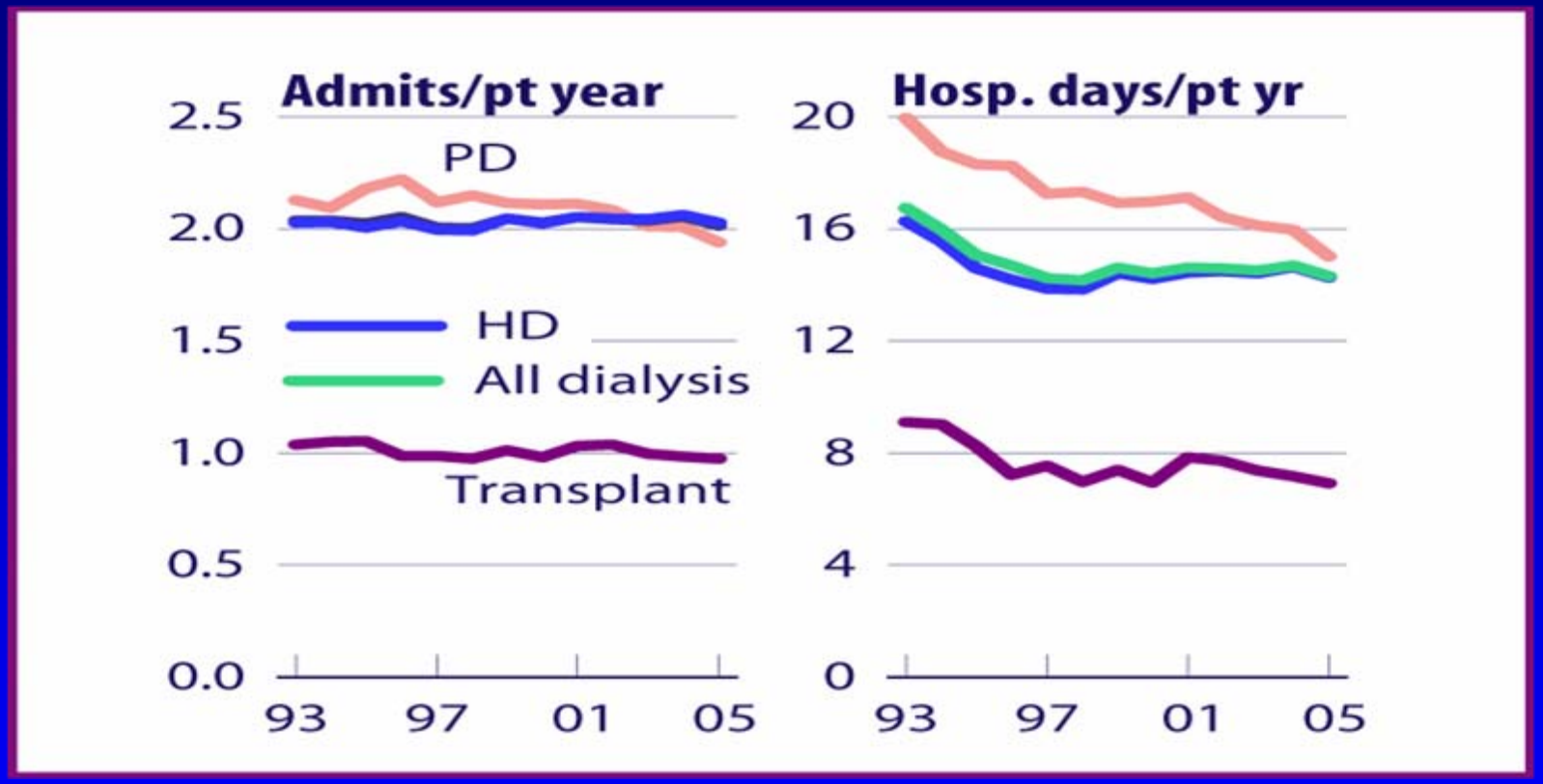
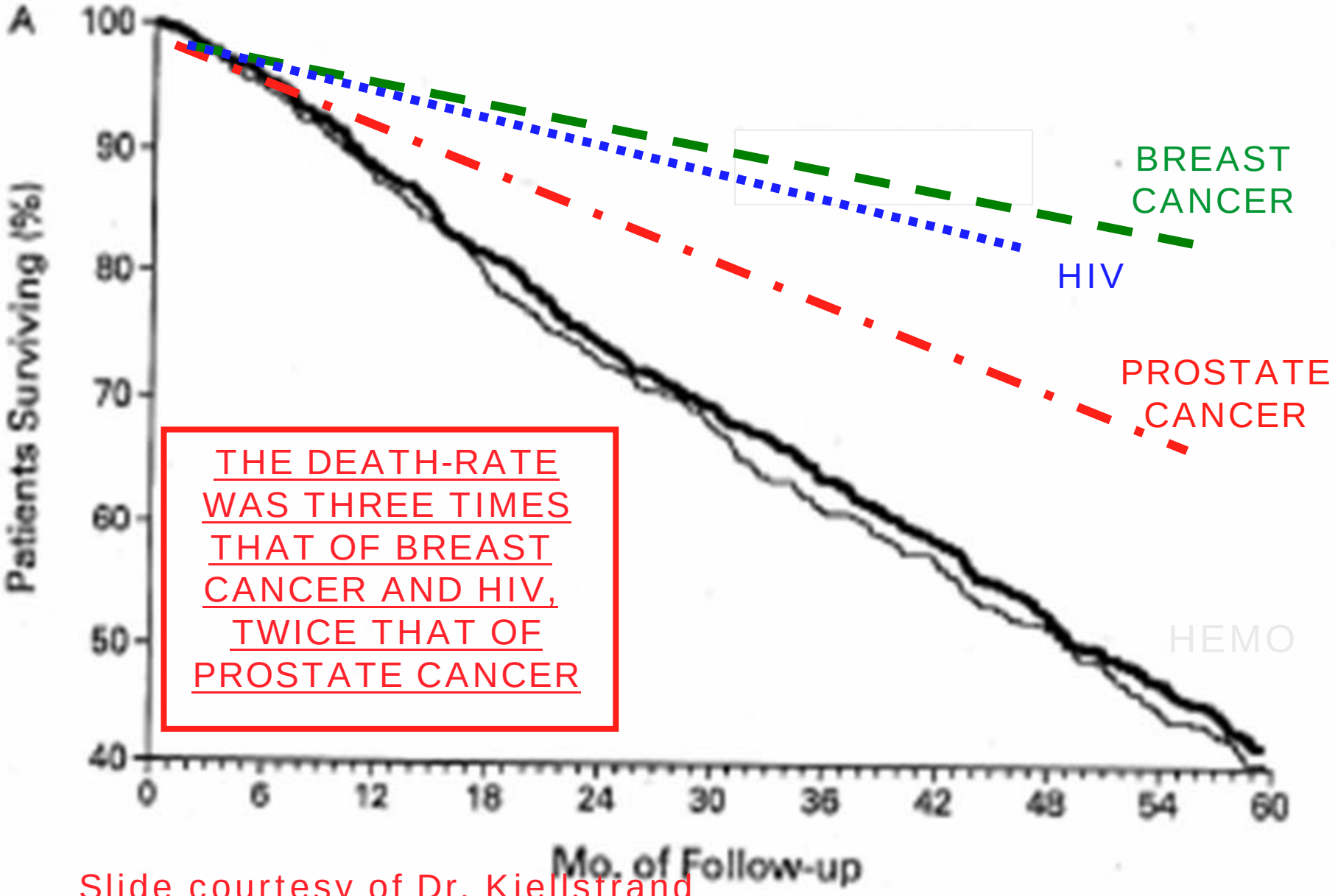


Figure 6.2: Period prevalent ESRD patients; rates adjusted for age, gender, race, & primary diagnosis. ESRD patients, 2005, used as reference cohort

2007 Annual Data Repot Text Based Atlas of End-Stage Renal Disease in the United States

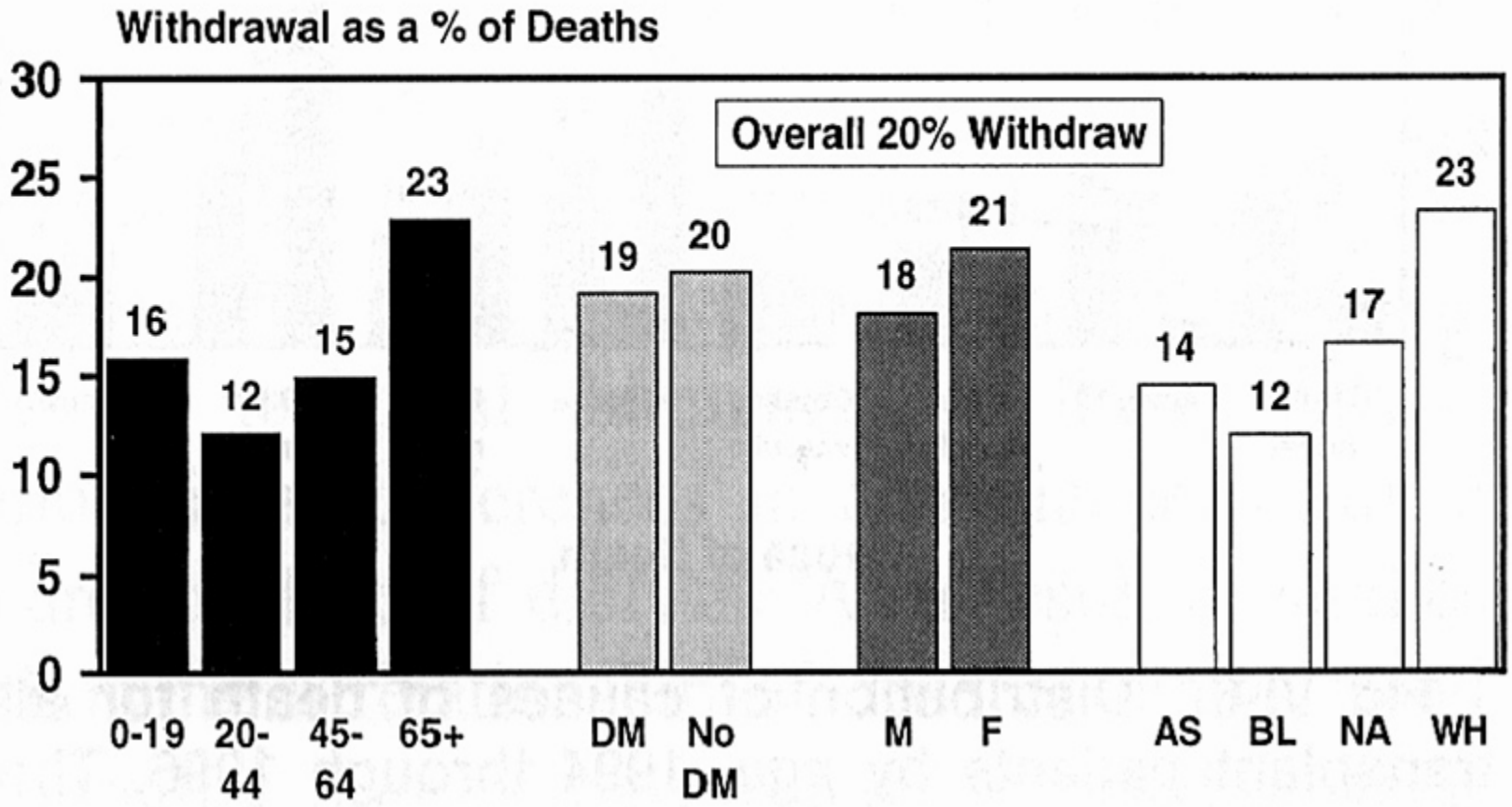


Slide courtesy of Dr. Kjellstrand

THE SECOND LEADING CAUSE OF DEATH OF PD AND IN-CENTER HEMODIALYSIS IS TO STOP:

USRDS AJKD 32: Suppl1: S86, 1998

Slide courtesy of Dr. Kjellstrand



Withdrawal & hospice status, by age

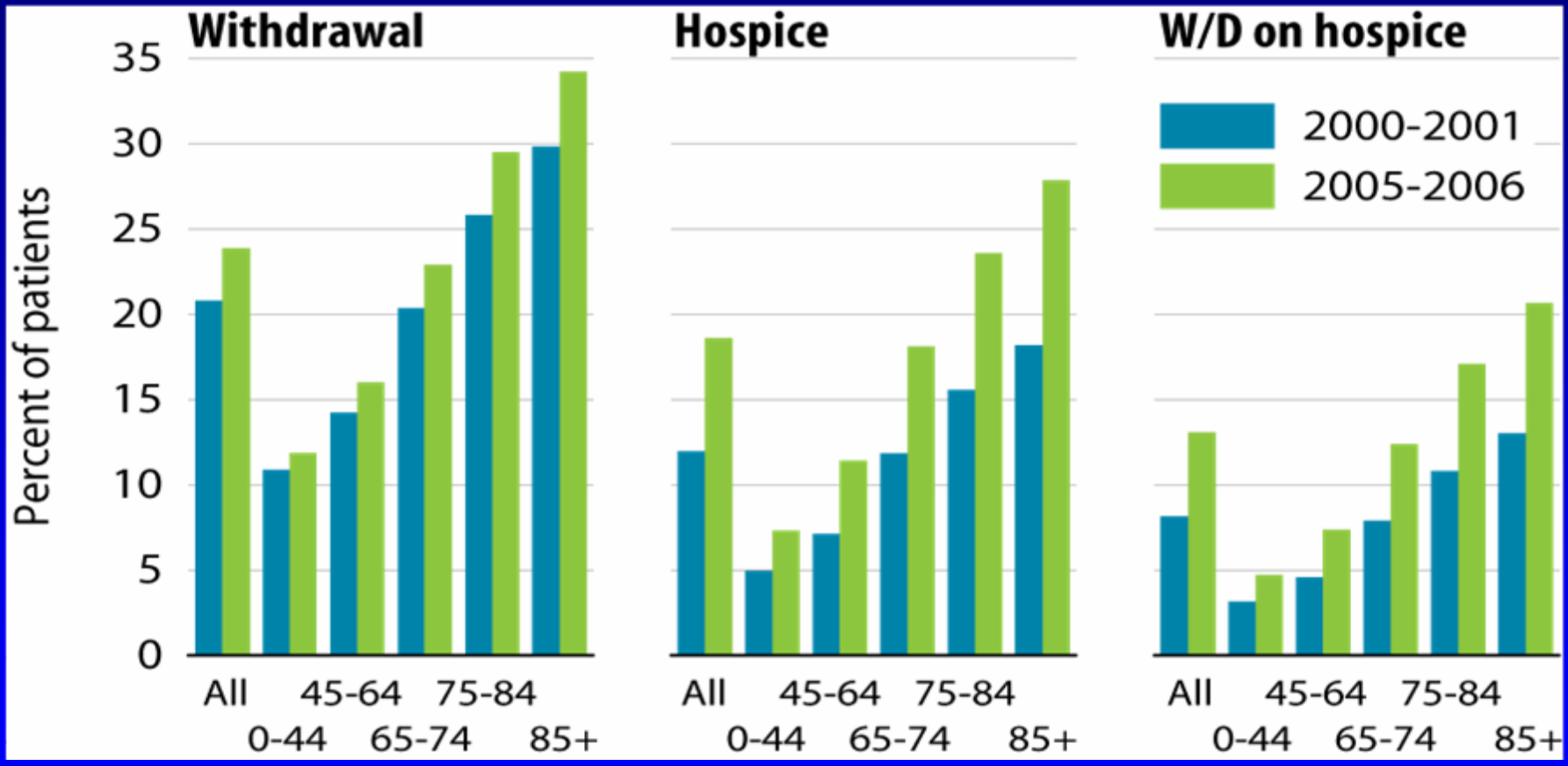


Figure 6.18 (Volume 2) incident & prevalent ESRD patients dying in 2000–2001 or 2005–2006. The 2008 USRDS Annual Data Report (ADR) Reference Tables

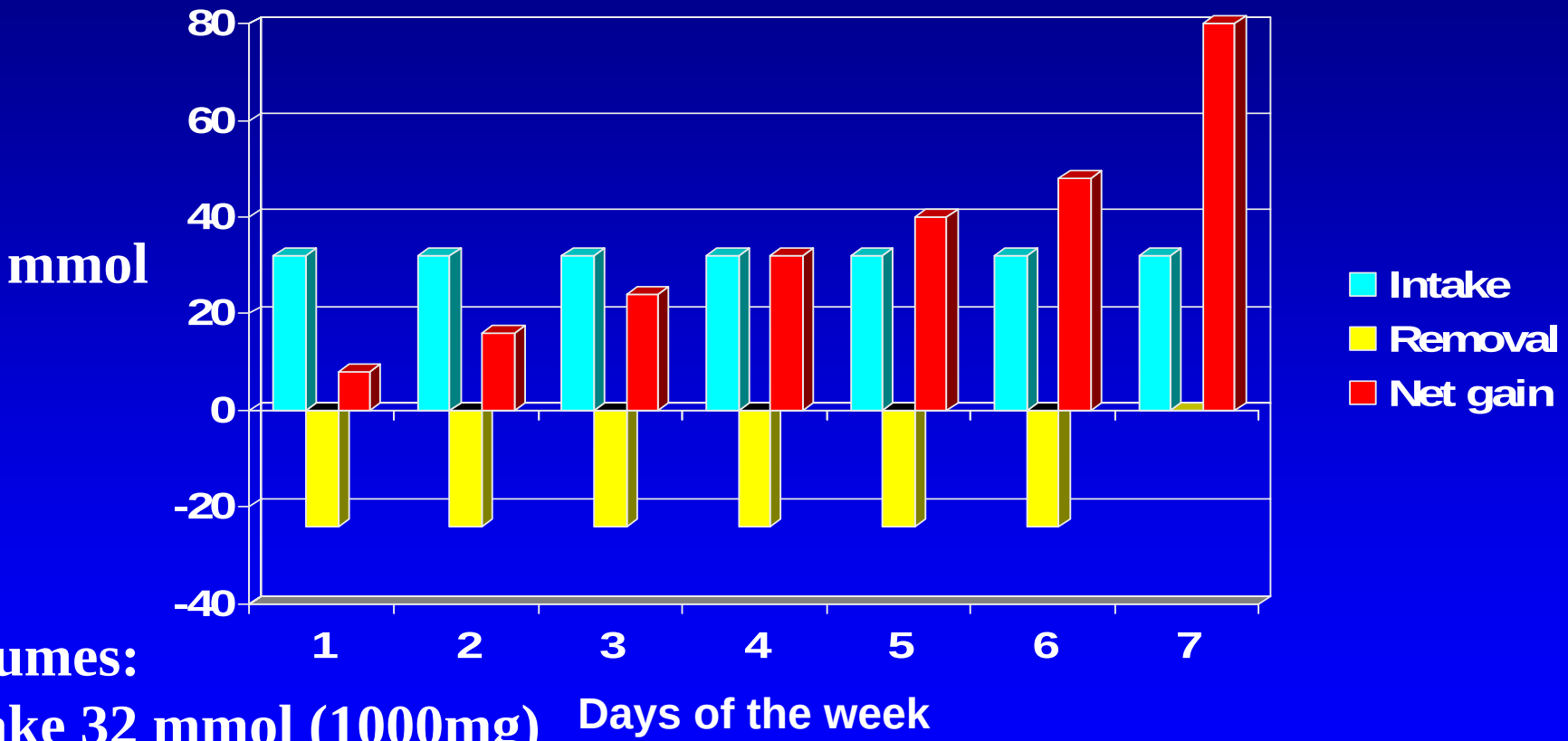
Annual Drop out Rate per 100 patient years for UVA Lynchburg in center program 2007

- UVA Lynchburg in center program census 239
  - In center transplant rate/100 patient years 4.1
  - In center death rate/100 patient years 21.2
  - In center total drop out rate/100 patient years 37.1

Annual Drop out Rate per 100 patient years for Wake Forest PD program 2006

- Wake Forest PD program 2006 169
  - PD transplant rate/100 patient years 18
  - PD death rate/100 patient years 22
  - PD total drop out rate/100 patient years 82

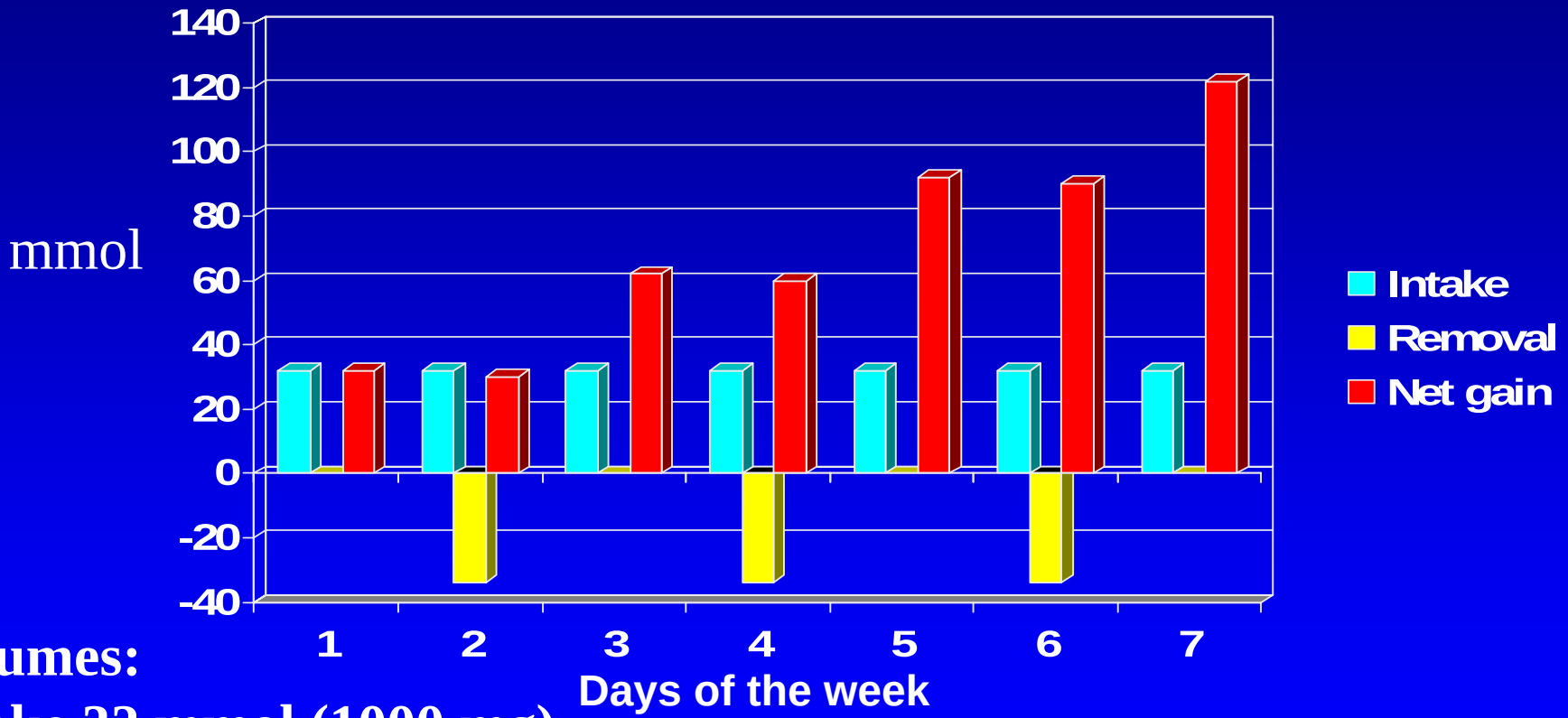
Phosphorous balance - SDHD



Assumes:
Intake 32 mmol (1000mg)
Removal 24 mmol
6 Days/wk x 2.5 hrs

Adapted: Kidney Int, 67 S95. 2005 pp 28-32
Slide courtesy of Dr. Glickman

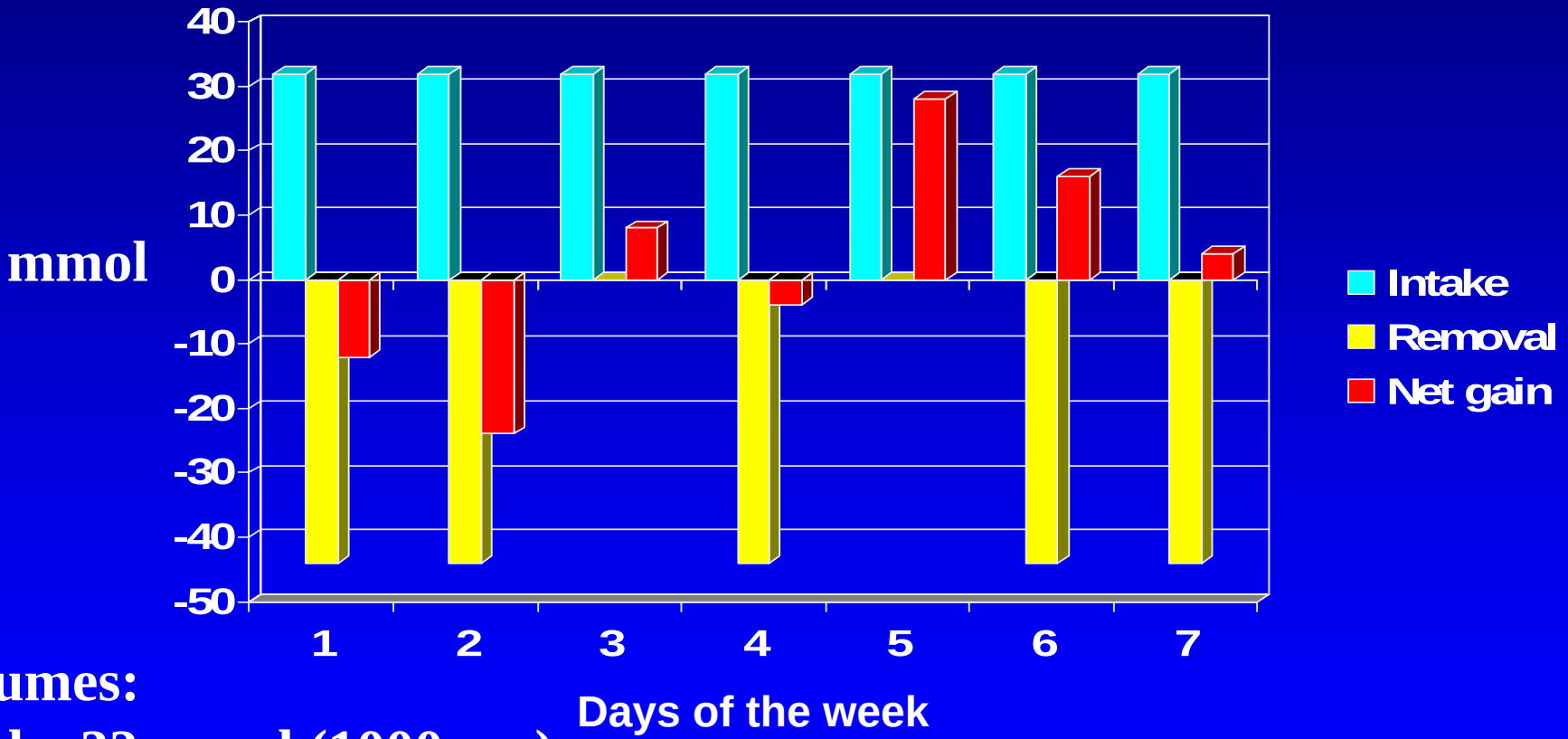
Phosphorous balance - CHD



Assumes:
Intake 32 mmol (1000 mg)
Removal 34 mmol
3 Day/wk x 4 hr

Adapted: Kidney Int, 67 S95. 2005 pp 28-32
Slide courtesy of Dr. Glickman

Phosphorous balance - NHD



Assumes:
Intake 32 mmol (1000 mg)
Removal 44 mmol
5 Days/wk x 8 hrs

Adapted: Kidney Int, 67 S95. 2005 pp 28-32
Slide courtesy of Dr. Glickman

Sudden deaths in dialysis patients

- Sudden and cardiac deaths are most common on Mondays and Tuesdays
- For Monday, Wednesday, Friday patients, 20.8% of sudden deaths occur on Monday compared to 14.3% expected ($P = 0.002$) - a 45% increase in mortality
- For Tuesday, Thursday, Saturday patients, 20.2% of cardiac deaths occur on Tuesday compared to 14.3% expected ($P = 0.0005$).
- There is an even distribution of sudden and cardiac deaths throughout the week in peritoneal dialysis patients

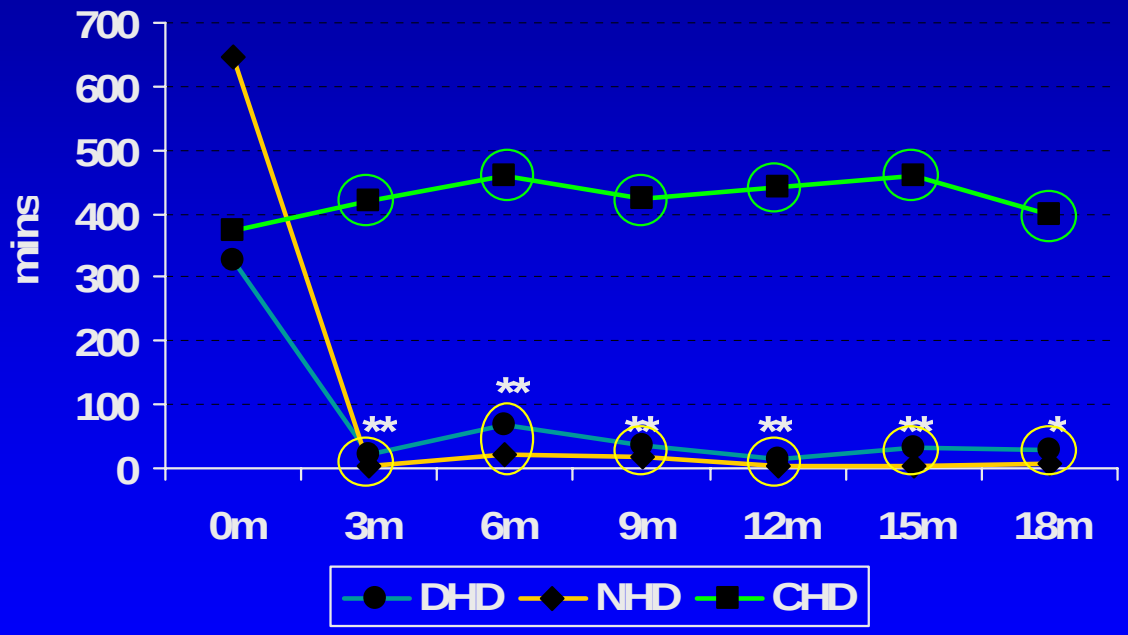
Bleyer AJ, Russell GB, Satko SG: Sudden and cardiac death rates in hemodialysis patients. Kidney Int. 1999;55:1553-1559

Side effects occur during and after conventional hemodialysis in 15 to 50% of treatments

- Hypotension
- Nausea and vomiting
- Headaches
- Cramping
- Washed out feeling after dialysis

Time to recover from dialysis

Heidenheim et al AJKD 2003



* Different from baseline @ p ≤ 0.05

Between-group difference @ p ≤ 0.05

Results of Three times per week In Center Hemodialysis and PD

- Greater than 60% death rate in five years for in center and PD patients
- Hospital admissions two per dialysis patient per year unchanged for 15 years
- Hospital days per dialysis patient per year down from 16 to 14 days over the last 15 years
- Patients on in center and PD die three faster than women with breast cancer and 2 times faster than men with prostate cancer

Results of Three times per week In Center Hemodialysis and PD

- Every fourth patient will choice to withdraw from dialysis
- High drop out rates for PD and in center hemodialysis 40 to 80 patients per 100 patient years
- Phosphorus and Calcium/Phorphorus product controlled in only 50% of patients on in center hemodialysis and PD

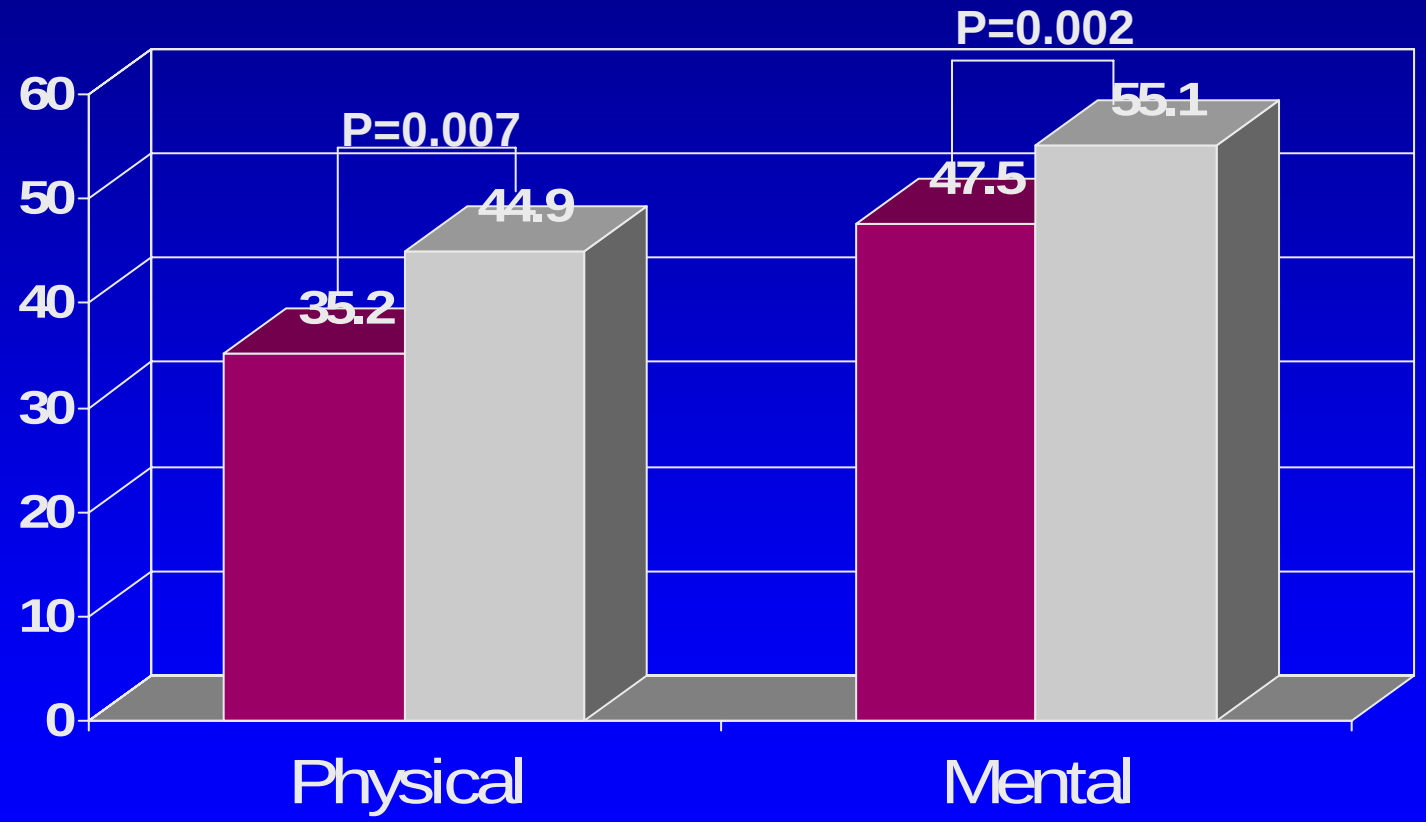
Results of Three times per week In Center Hemodialysis

- Sudden death 45% higher on Monday and Tuesday on in center hemodialysis
- Hypotension, nausea, vomiting, headaches and cramping occur 15 to 50% of every treatment
- Washed out feeling after dialysis
- Delayed recovery time

Does daily home hemodialysis provide better outcomes than three times per week in center hemodialysis and peritoneal dialysis?

Quality of Life Improvements
SF 36 Scores

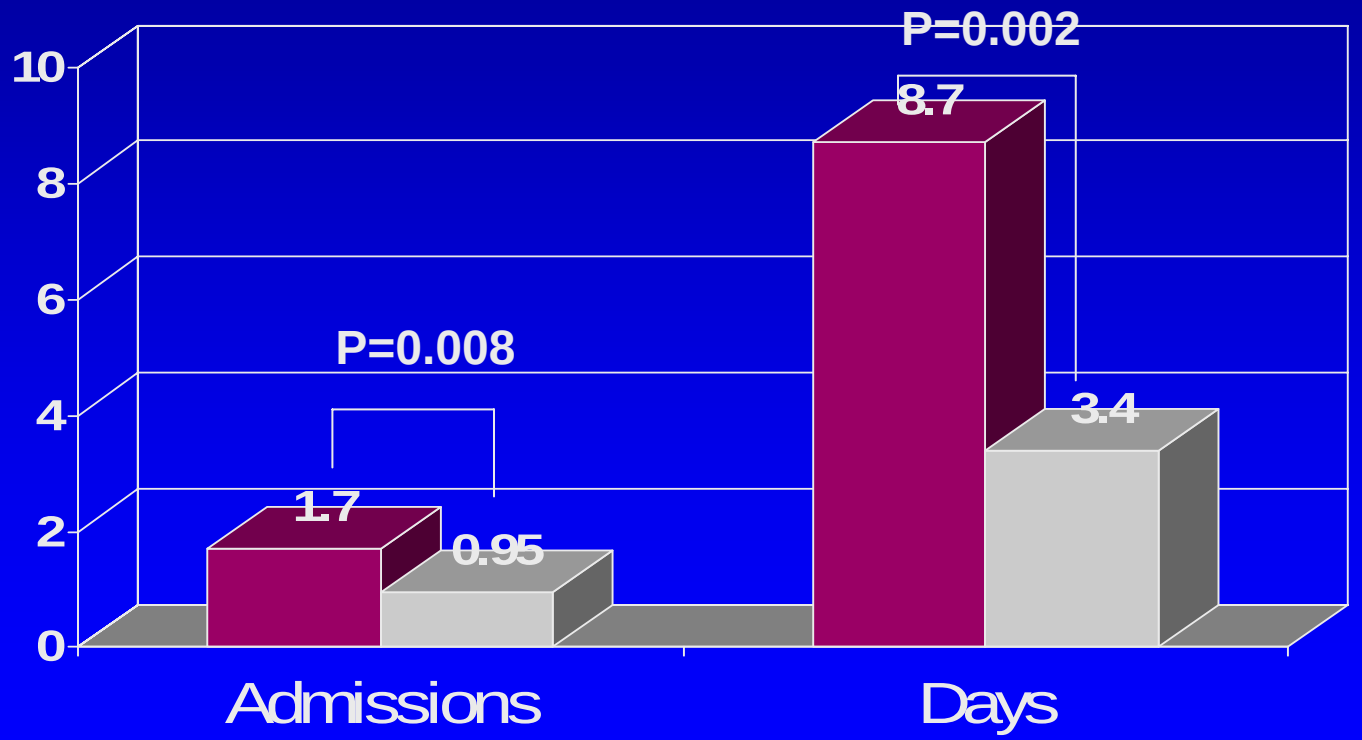
Daily
Nocturnal



Lockridge, et al, Hemodialysis International 8:61, 2004

60% Reduction in Hospital Days
42% Reduction in Hospital Admissions

Daily
Nocturnal

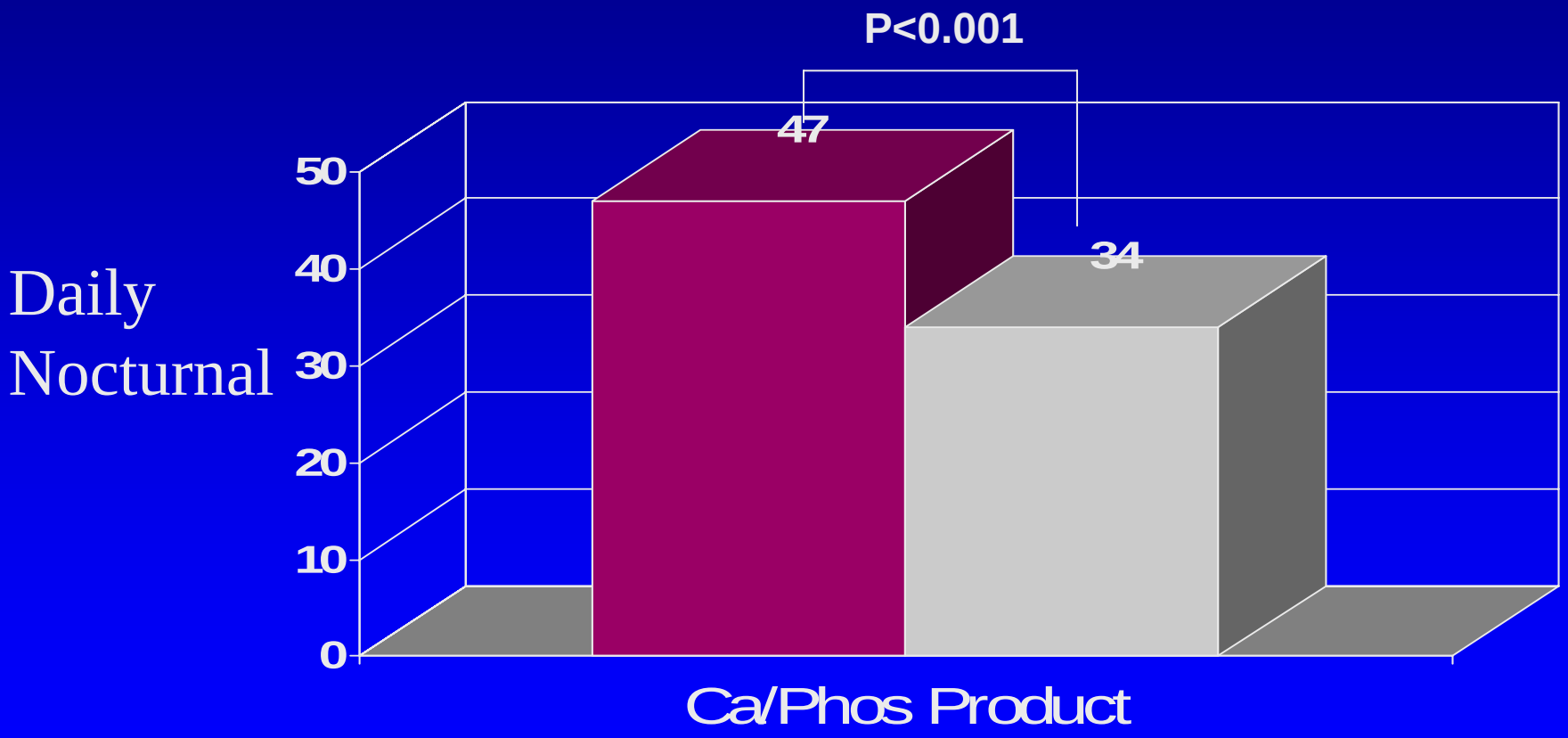


Lockridge, et al, Hemodialysis International 8:61, 2004

Improved Phosphorous Control Short Daily Hemodialysis

- 17% to 31% reduction in phosphorous levels
- 15% reduction in Ca x P product
- 24% to 75% reduction in phosphate binders

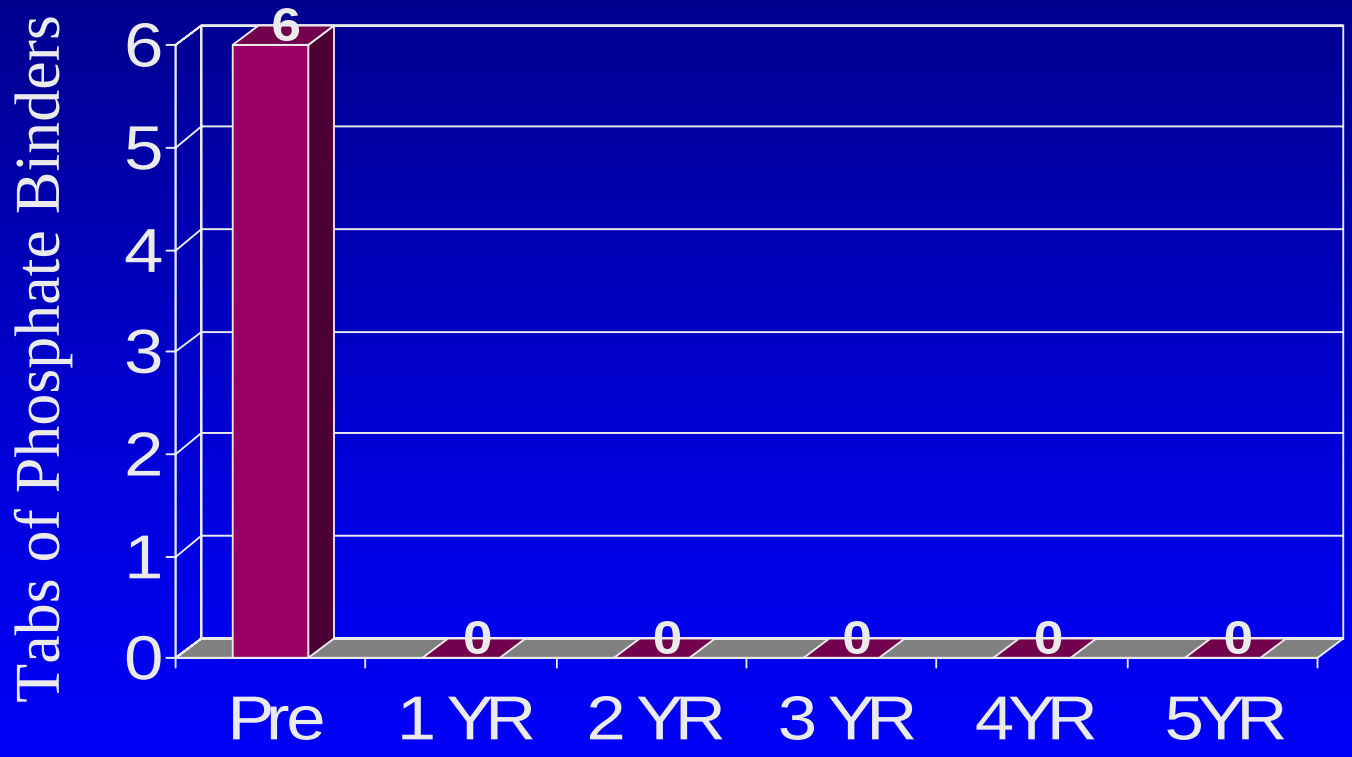
Ca/PO_4 Product on Daily Nocturnal Hemodialysis



Lockridge, et al, Hemodialysis International 8:61, 2004

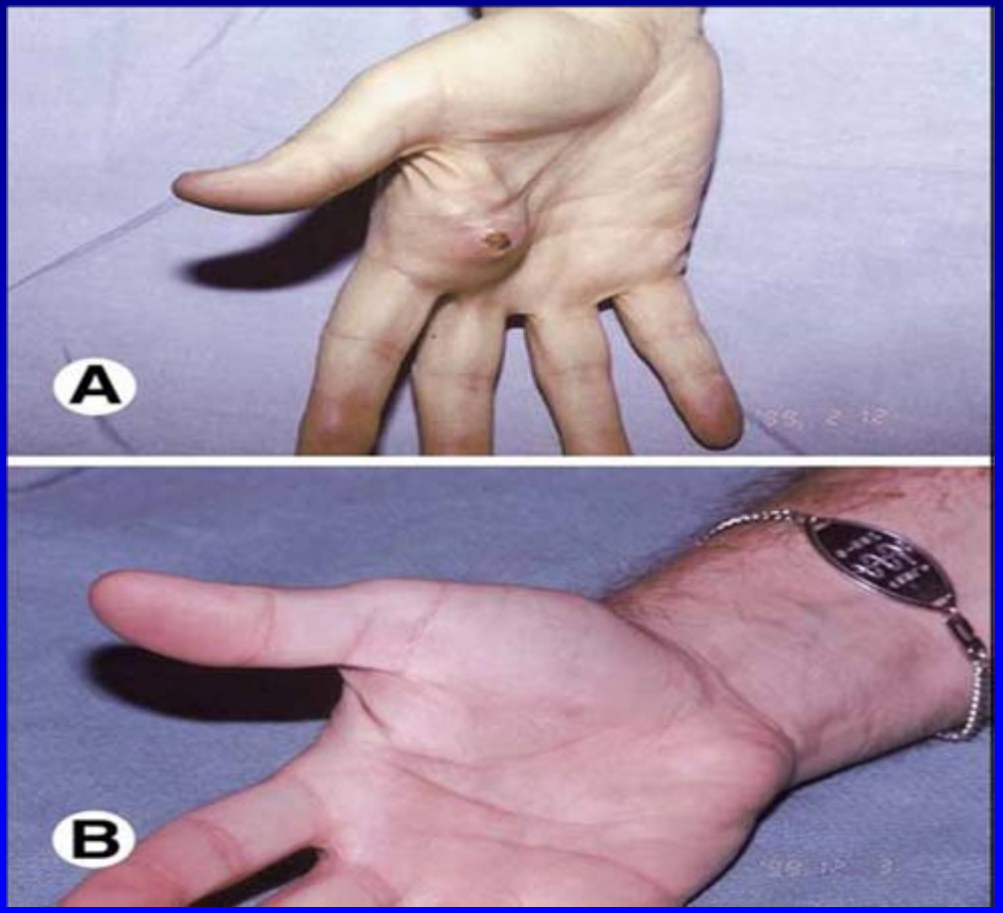
Phosphate Binder Usage

Daily
Nocturnal



Lockridge, et al, Hemodialysis International 8:61, 2004

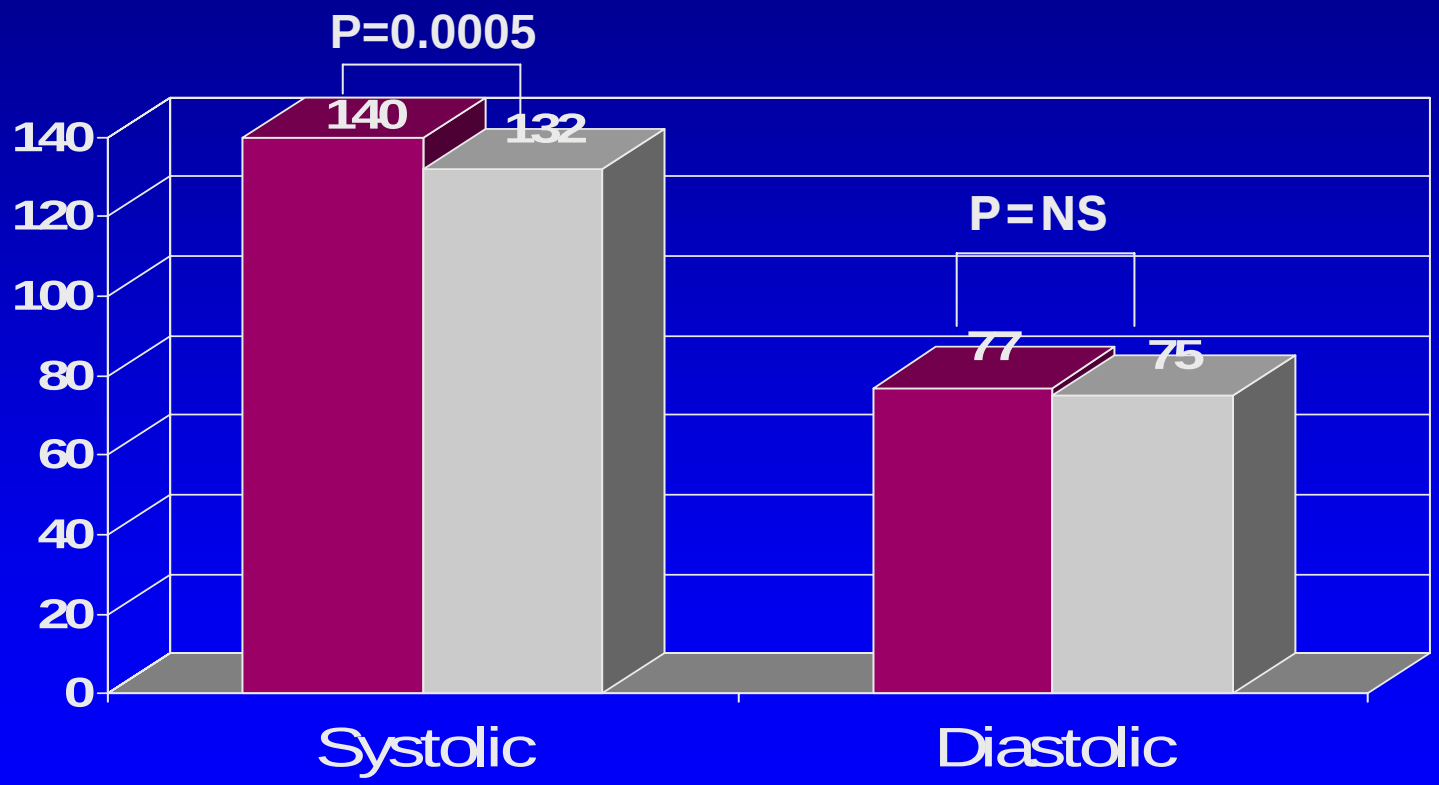
Resolution of Calcium –Phosphate Deposits



Pierratos A, Kidney Int 65:1975-1986, 2004

Improved BP Control

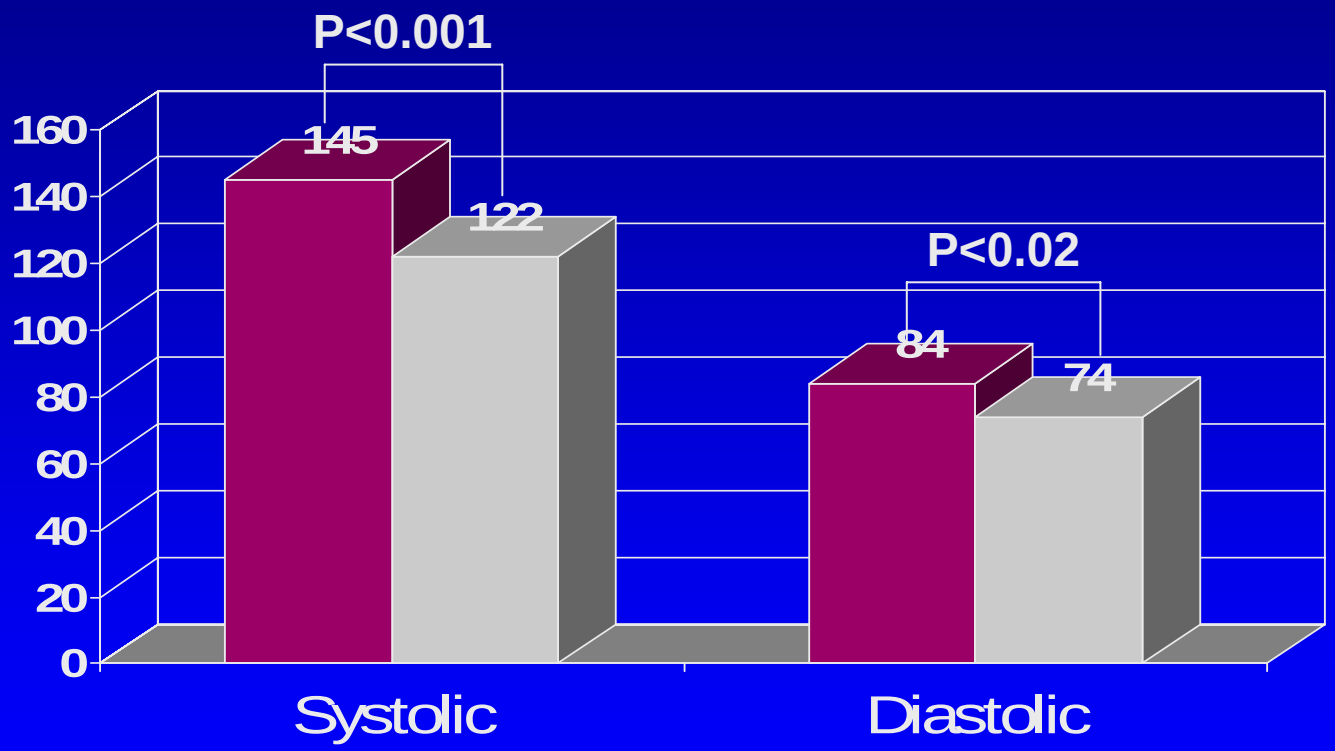
Short Daily Hemodialysis



Williams, Am J Kidney Dis, 43:90-102, 2004

Improved BP control

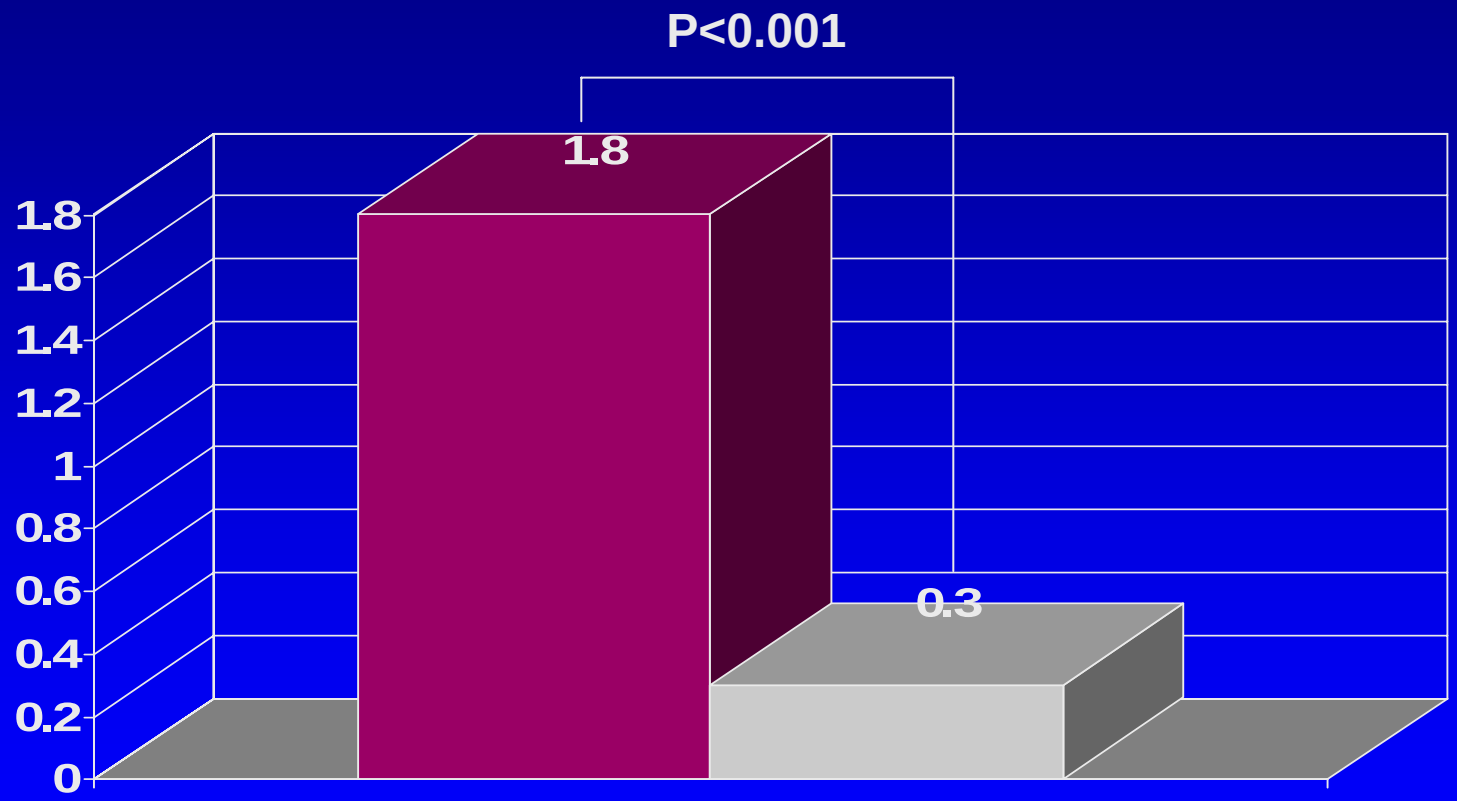
Daily
Nocturnal
N=28



Chan CT, Kidney Int 61:2235-39, 2002

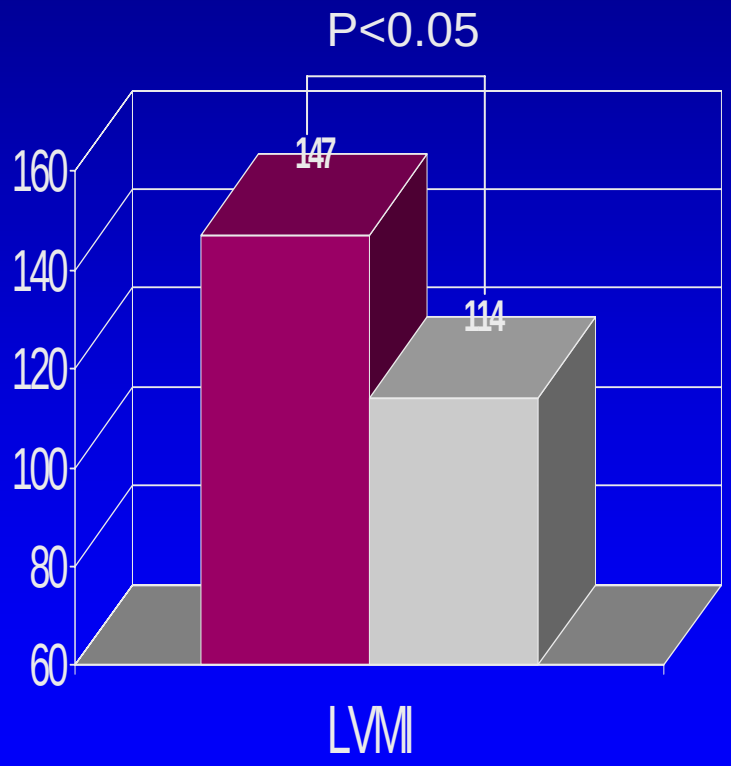
BP Medications

Daily Nocturnal



Chan CT, Kidney Int 61:2235-39, 2002

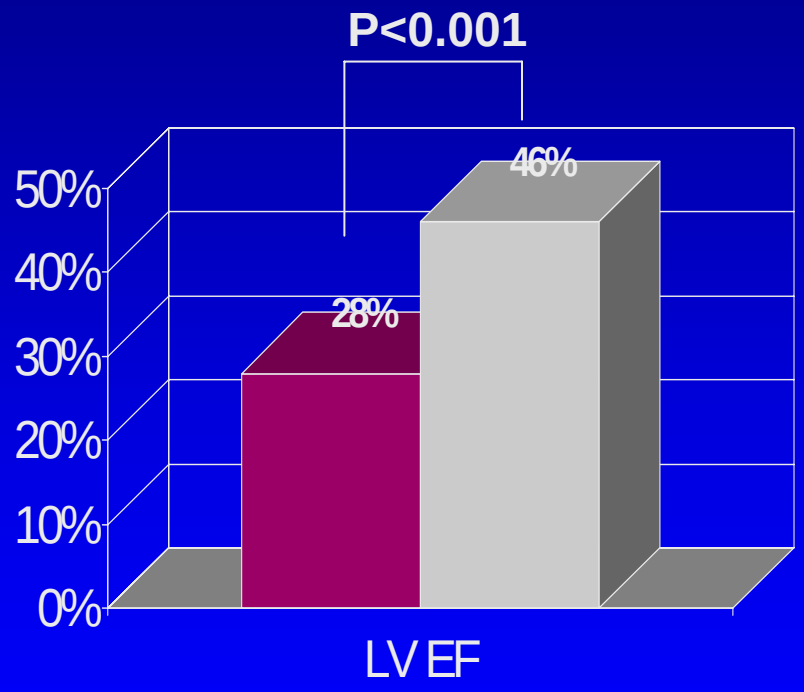
Reduction in LVMI in Daily Nocturnal



- 70% achieved normal LVMI (25% at start)
- LVMI correlates with final SBP
- Decrease in EDD, SWT and PWT

Chan CT, Kidney Int 61:2235-39, 2002

Improved LV Function in Daily Nocturnal



	CHD	NHD
SBP	139	120*
DBP	80	69
LVMI	180	143
CV Meds	2.2	0.7*

* P <0.05

N = 6

Chan, CT, NDT 17:1518, 2002

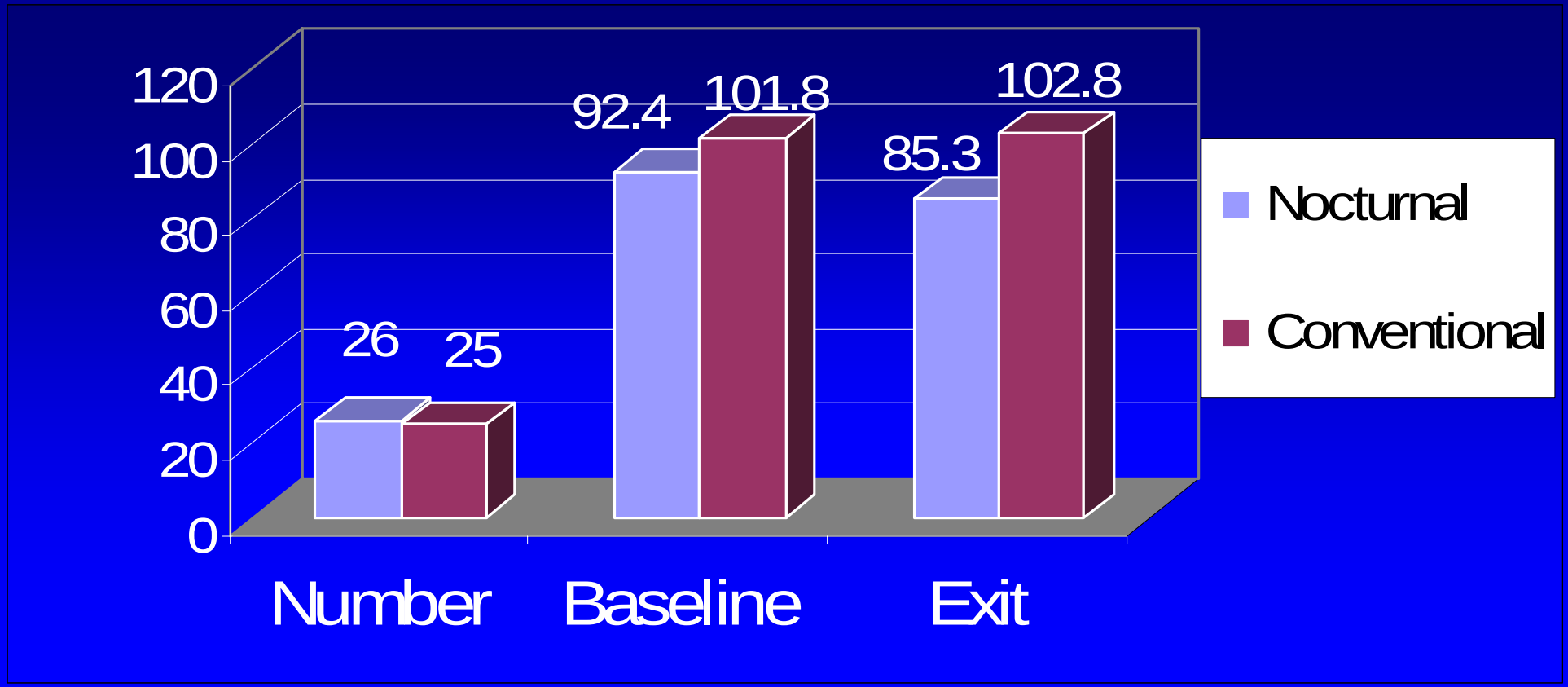
Cardiovascular Effects of NHD

	CHD	NHD – 1	NHD - 2
SBP	140	124 *	119 *
DBP	82	75 *	71 *
C.O.	4.9	5.3	5.5
S.V.	63	64	68
HR	78	75	80
TPR	1967	1647*	1499*

N = 18

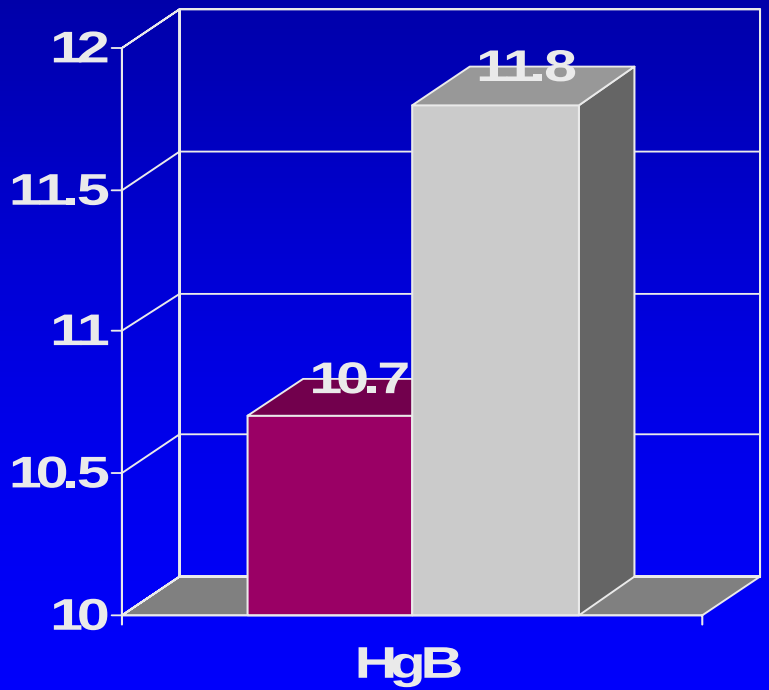
Chan, Hypertension 42:925, 2003

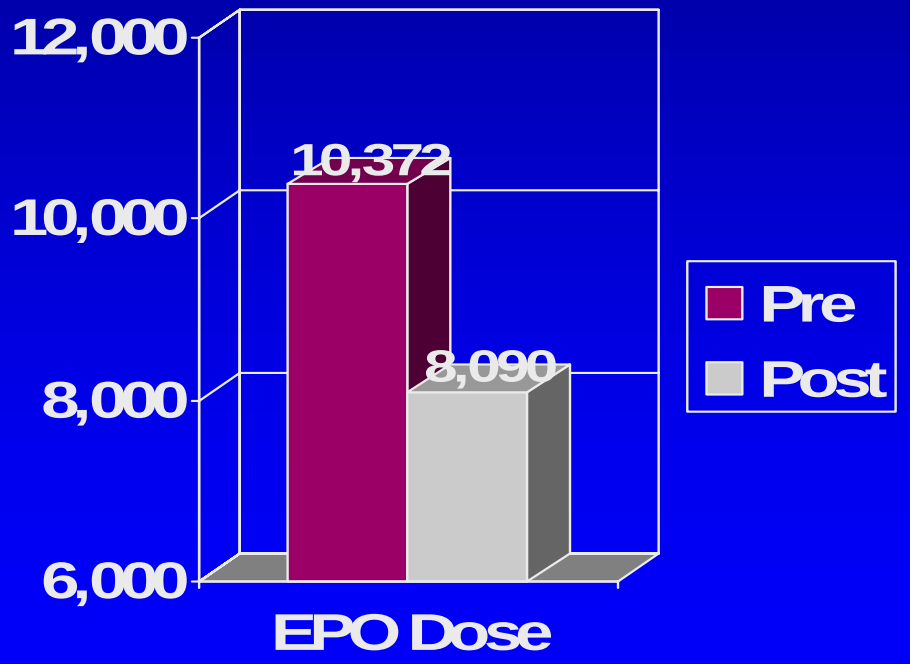
Effect of Frequent Nocturnal Hemodialysis vs Conventional Hemodialysis on Left Ventricular Mass and Quality of Life



Culleton BF JAMA, Vol 298, No. 11, 2007

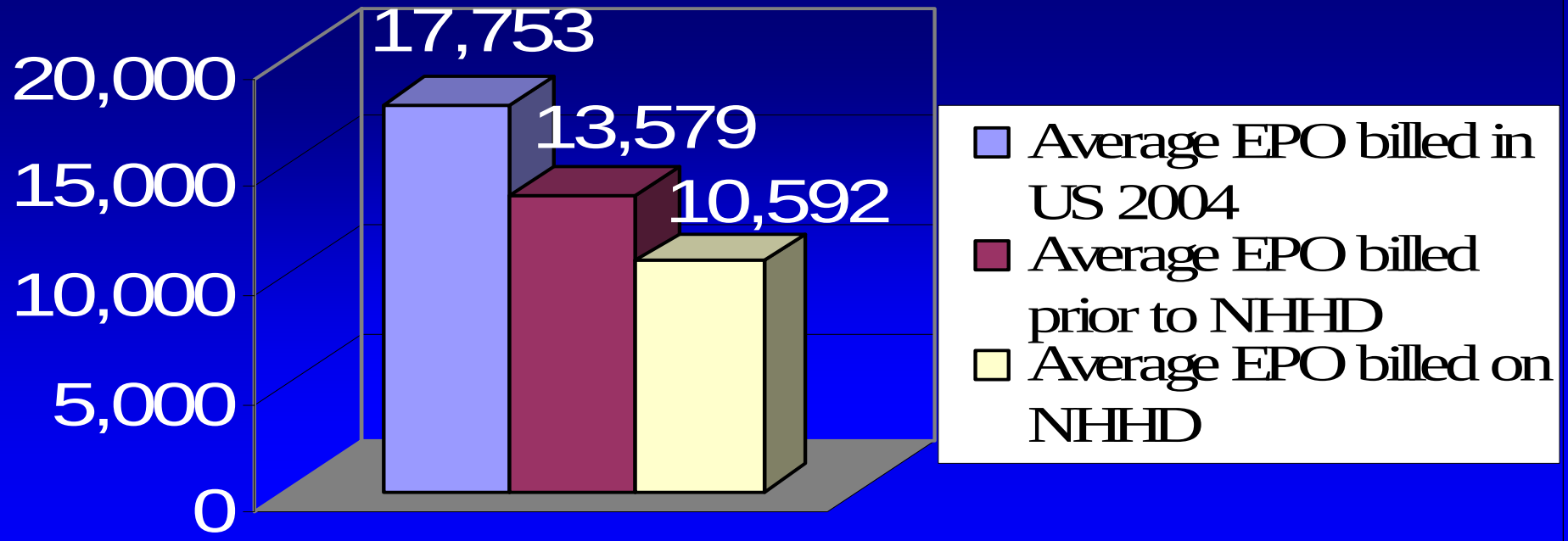
Improved anemia at lower Epo Dose





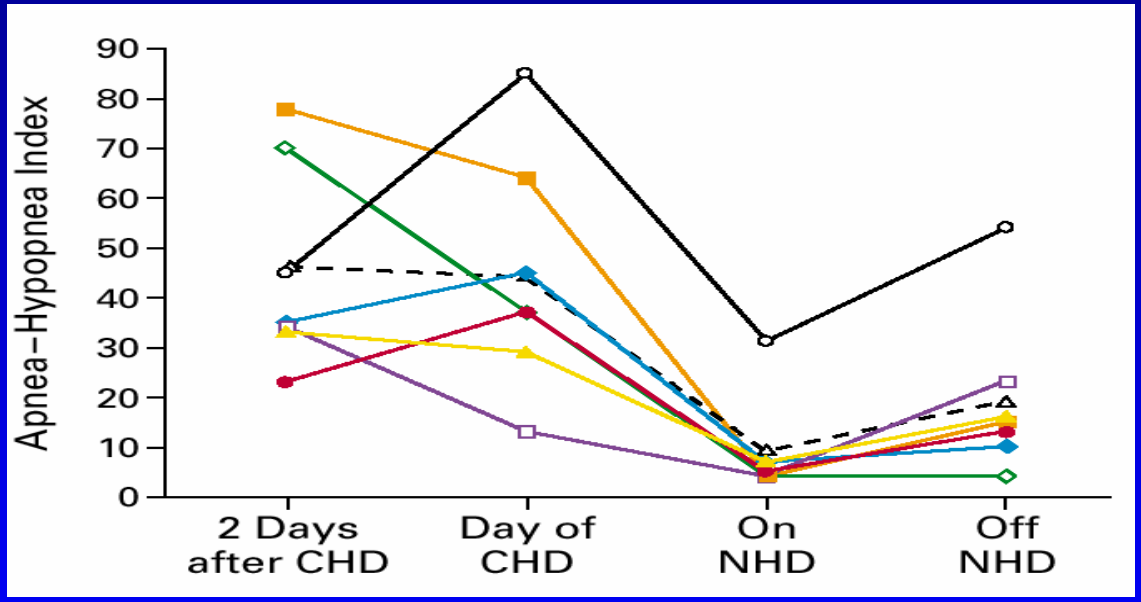
Chan CT, Kidney Int 61:2235-39, 2002

UVA Lynchburg NHHD program
Usage of EPO over nine years



Correction of Sleep Apnea with NHD

The first 14 patients of the Nocturnal Hemodialysis project in Toronto. 8 patients had sleep apnea (AHI>15/hr)

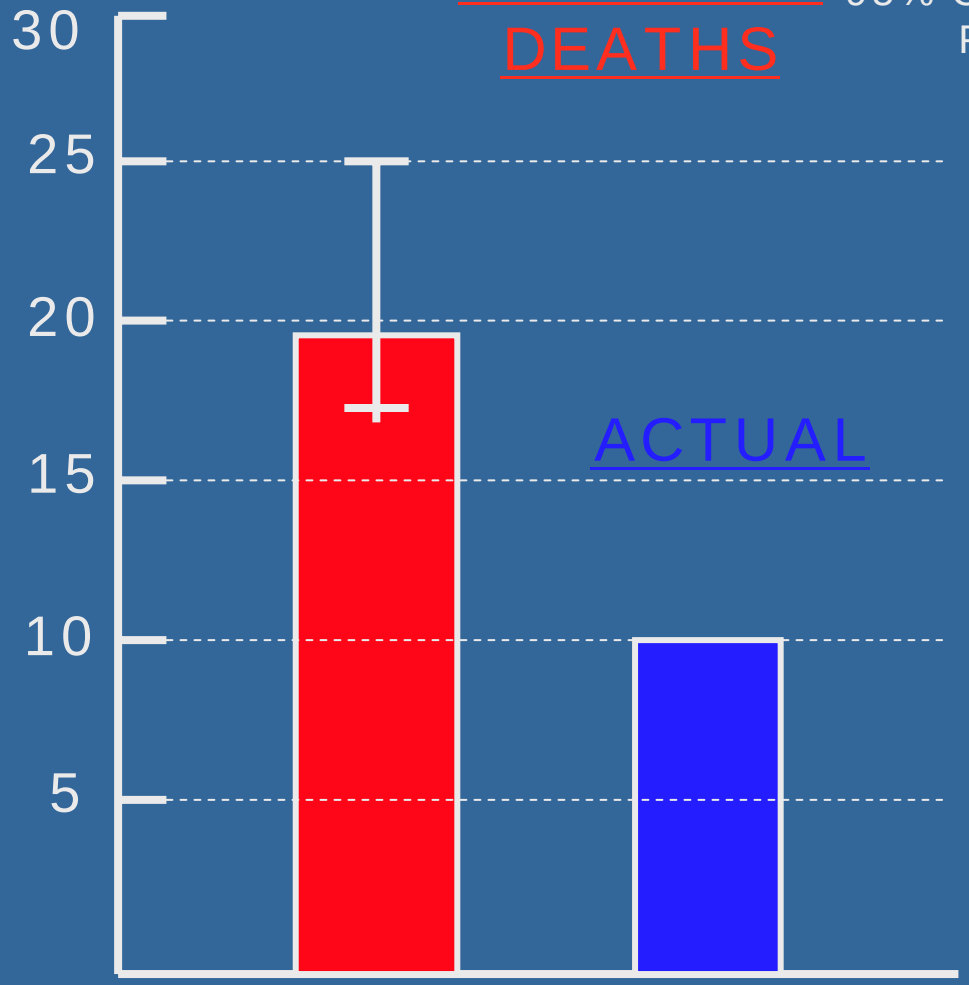


AHI Decreased from 46±19 to 9±9, p=0.06

Minimum O2 sat increased from 89.2±1.8 to 94.1± 1.6, p=0.005

Hanly P, Pierratos A. NEJM 2001

STANDARDIZED MORTALITY OF 117 DHD USA PATIENTS VS. USRDS 2003 - 4 DATA



WHEN COMPARING BY SMR USA DAILY HEMODIALYSIS HAS ONLY 40% THE DEATHRATE OF USRDS PATIENTS

SMR = 0.39

95% CONF = 0.19 - 0.51
P < 0.005

USRDS 2004
pp 560 -563
Blagg et al. Short Daily Hemodialysis Standardized Mortality Ratios, Hemodialysis Internat 2006 10:371-4

Slide courtesy of Dr. Kjellstrand

Survival in 415 patients treated by Short Daily Hemodialysis for 1006 patient years

- Pooled 23 years of patients doing Short Daily Hemodialysis – 1006 patient years – 415 patients
- Dialysis centers involved in study
  - HS Silvestrini, Perugia, Italy
  - El Camino Hospital, Mountain View, CA, USA
  - Claude Bernard University, Lyon, France
  - AURAL-Lyon, France
  - Northwest Kidney Centers and the University of Washington, Seattle, WA, USA
  - University Hospital of Turin, Italy

Kjellstrand et al. NDT May 2008

Survival in 415 patients treated by Short Daily Hemodialysis for 1006 patient years

- 150 patients treated in center, most because of medical compications
- 265 patients treated at home or in self care units
- On daily hemodialysis 29 ± 31 (0-272) months
- Treatment time 136 ± 35 min
- Frequency 5.8 ± 0.5 times per week
- Weekly stdKt/V 2.7 ± 0.55

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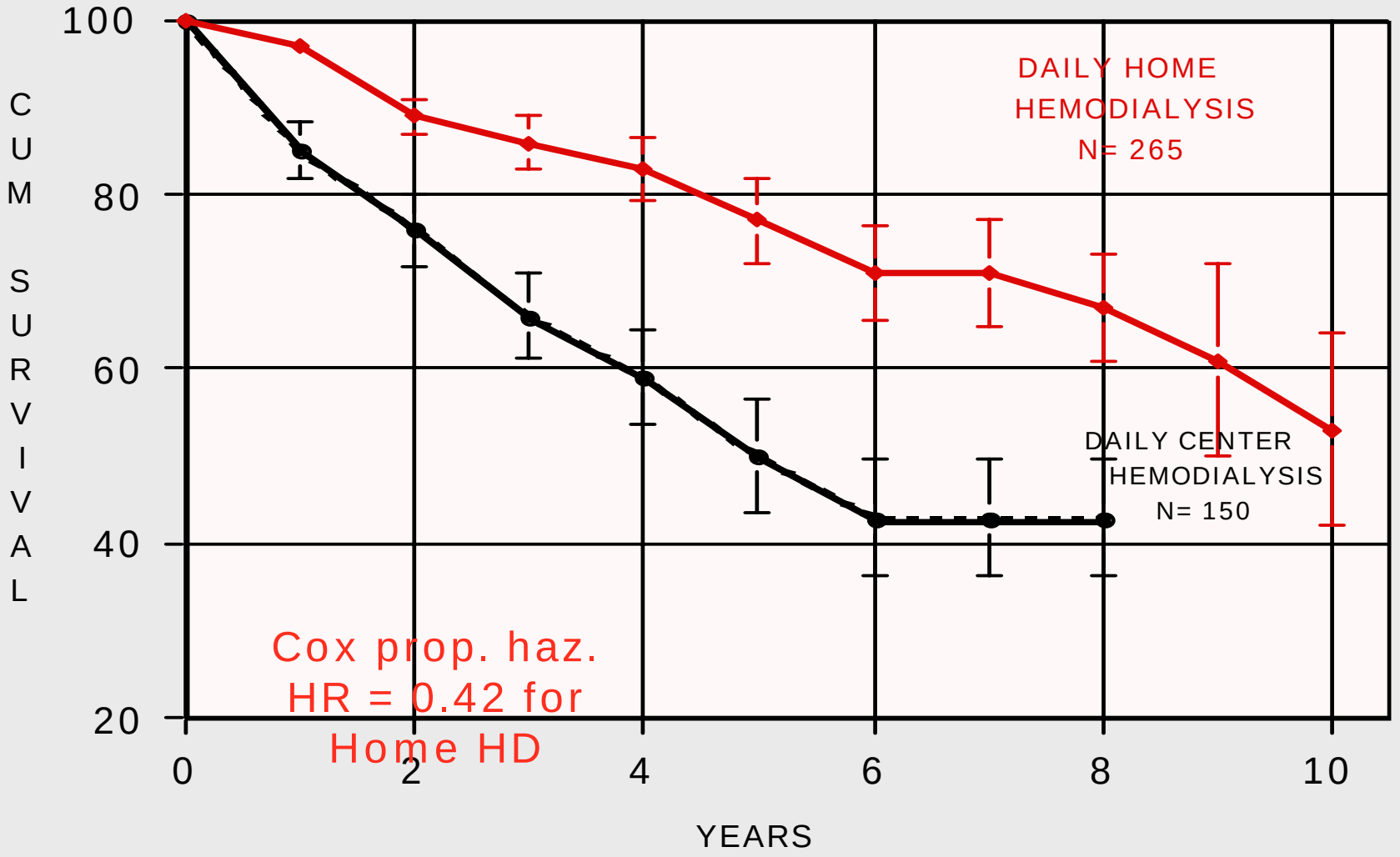
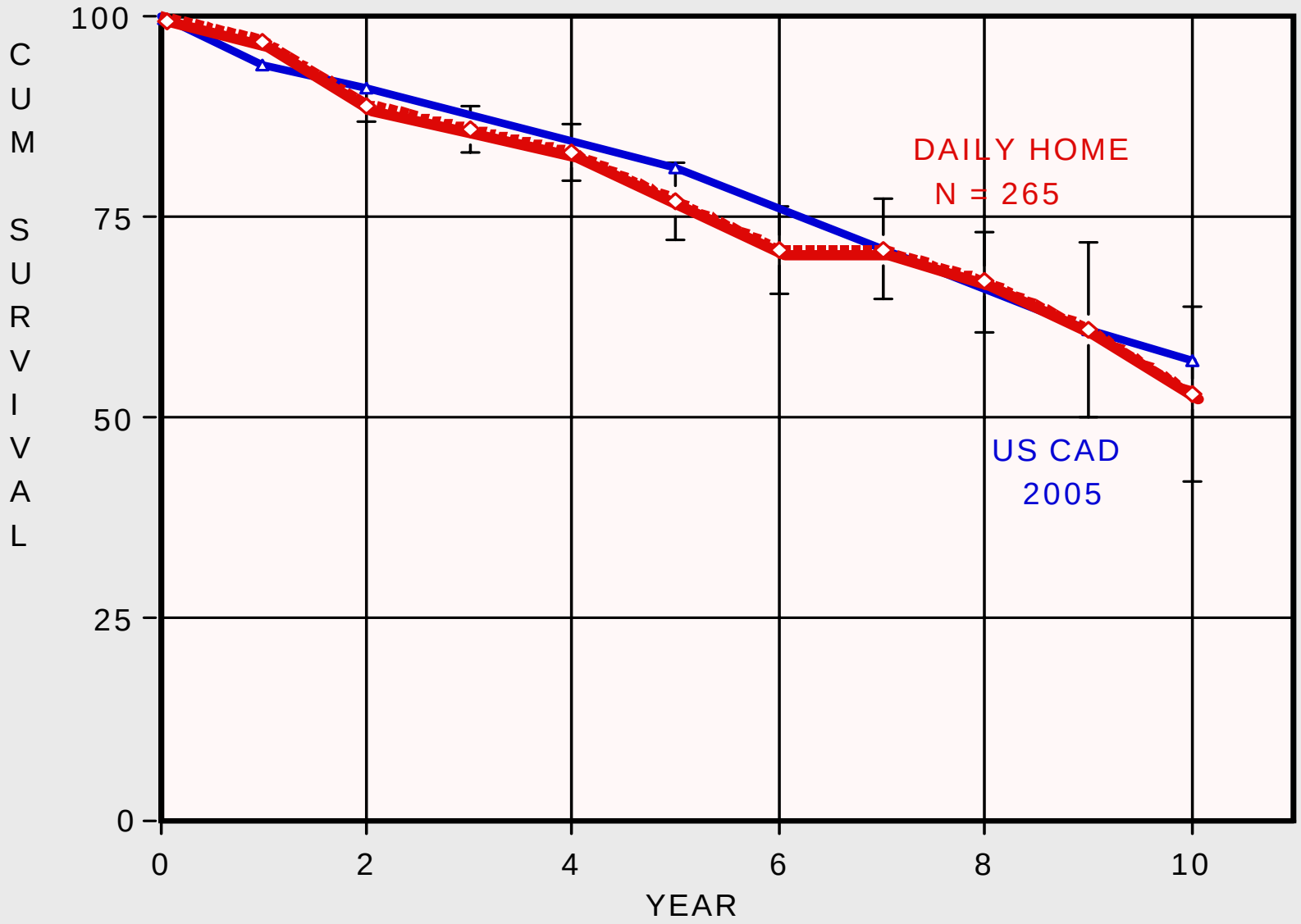
Survival in 415 patients treated by Short Daily Hemodialysis for 1006 patient years

- Eighty-five patients (20%) died
- 5-year cumulative survival 68 ± 4.1 %
- 10-year cumulative survival 42 ± 9 %
- Survival was compared with match patients from the USRDS 2005 Data Report using the standardized mortality ratio and the cumulative survival curves
- Both comparisons showed that the survival of the daily hemodialysis patients was 2-3 times higher and the predicated 50% survival time 2.3 -10.9 years longer than that of the matched US hemodialysis control

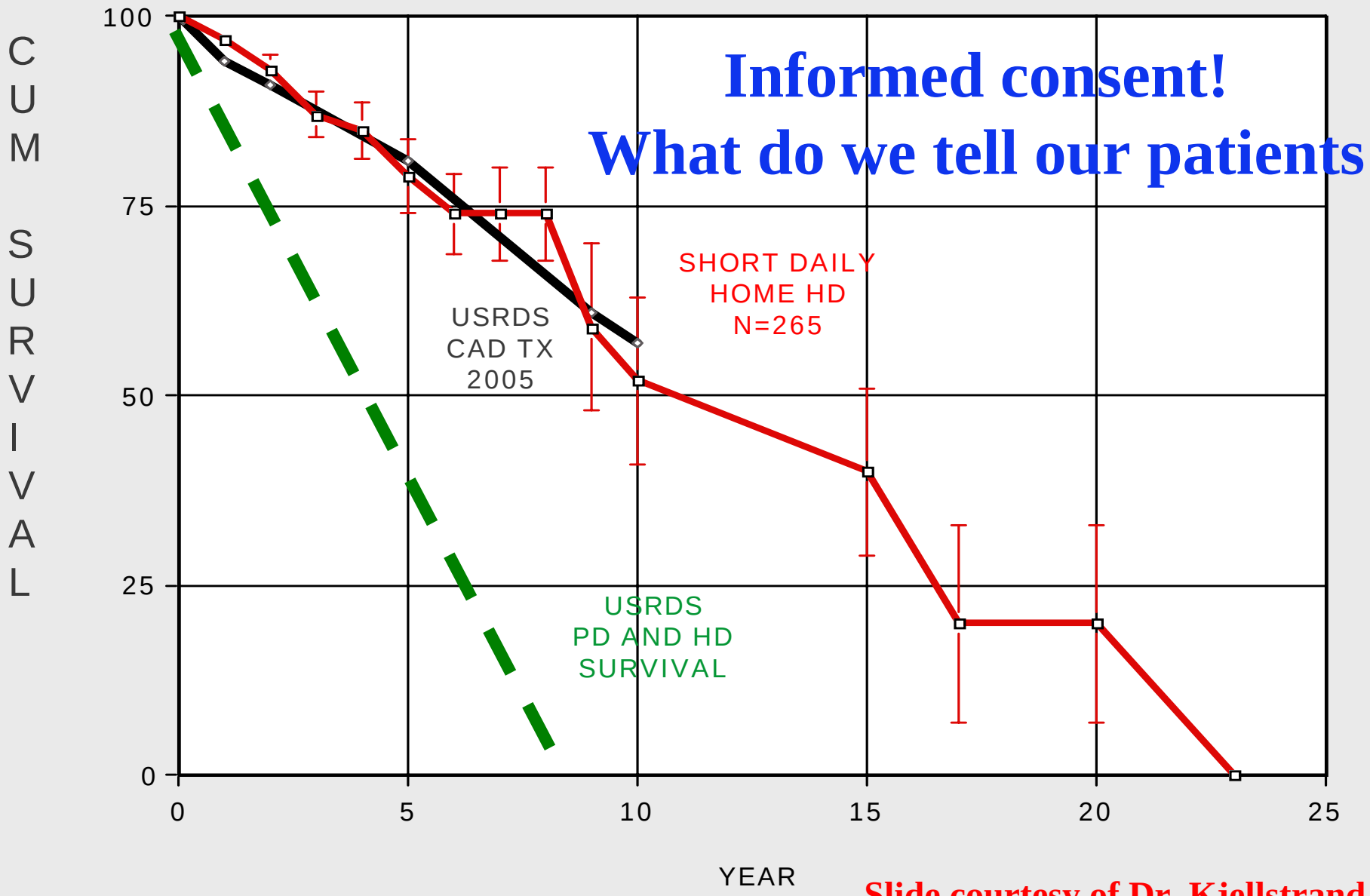
Kjellstrand et al. NDT May 2008



Slide courtesy of Dr. Kjellstrand



Slide courtesy of Dr. Kjellstrand


Informed consent!
What do we tell our patients
CUM SURVIVAL
100
75
50
25
0
0
5
10
15
20
25
YEAR
SHORT DAILY
HOME HD
N=265
USRDS
CAD TX
2005
USRDS
PD AND HD
SURVIVAL
Slide courtesy of Dr. Kjellstrand

Conclusion

- "All patients suitable for home dialysis should do PD first" **NO!**

- All patients need to be given

  "Options for Renal Replacement"

- Options should include

  "Informed Consent"

Thanks!