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Disclosures

- Institutional research support: NIH, CDC, HRSA, NKF, Pharma: Johnson and Johnson, Merck, Takeda, Affymax, NxStage, Genzyme, Amgen, Abbott, Medtronic, BMS,
- Advisory Boards: WHO NCD research panel, WHO field protocol for NCD Dx and Rx, KDIGO, Kidney Health Australia, CARI, IKEA-J, Kidney and Urologic Institute Karachi
- Epidemiology consulting: Takeda, NxStage,
 Amgen, Merck, Affymax, Physician Nexus, GSK



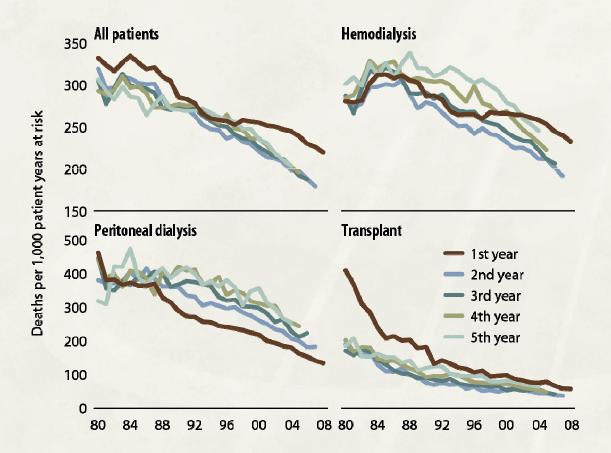
Current Status of dialysis outcomes in the United States

- Trends in both incident and prevalent based mortality
- The impact of three times per week hemodialysis on morbidity and mortality: impact of a long interdialytic interval
- Hospitalization and re-hospitalization
- Alternatives to three times per week HD in practice
 - Peritoneal dialysis
 - Frequent hemodailysis: 5+ days per week

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Adjusted all-cause mortality rates (from day 90), by modality & year of treatment

Figure 5.1 (Volume 2)

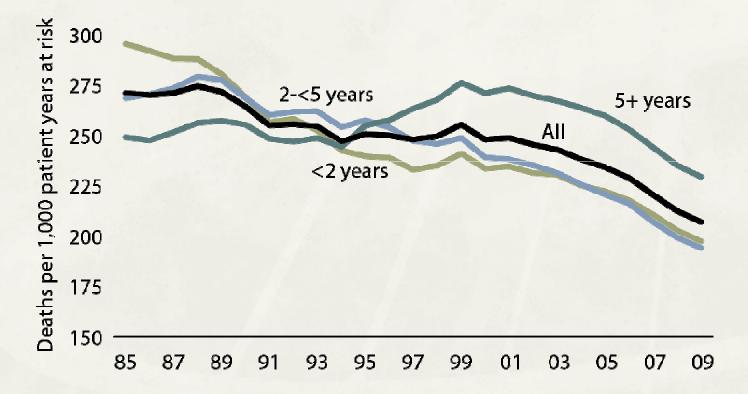


Incident ESRD patients. Adj: age/gender/race /primary diagnosis; ref: incident ESRD patients, 2005.

USRDS

Adjusted all-cause mortality rates in prevalent hemodialysis patients, by vintage

Figure 5.4 (Volume 2)

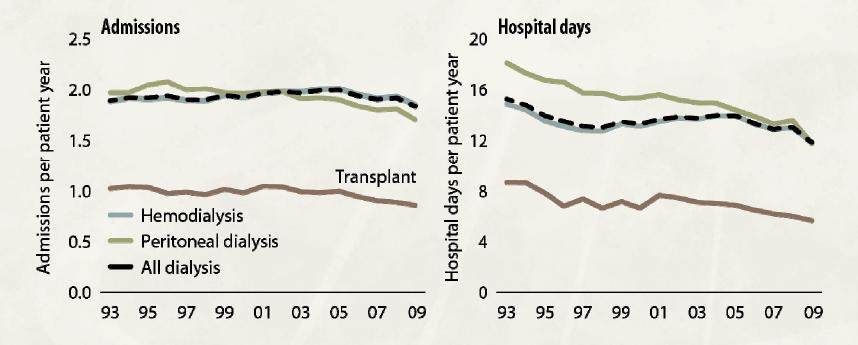


Incident hemodialysis patients. Adj: age/gender/race/primary diagnosis; ref: incident hemodialysis patients, 2005.



Adjusted hospital admission rates & days, by modality

Figure 3.2 (Volume 2)

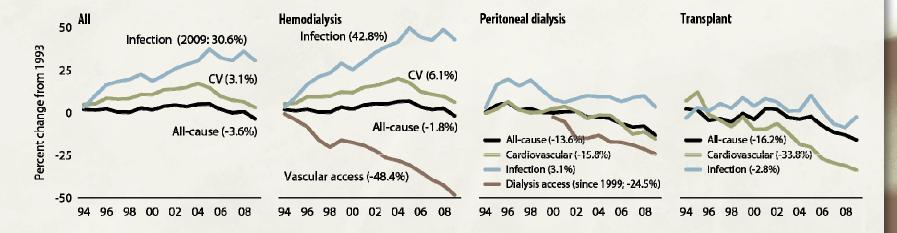


Period prevalent ESRD patients. Adj: age/gender/race/primary diagnosis; ref: ESRD patients, 2005.



Change in adjusted all-cause & causespecific hospitalization rates, by modality

Figure 3.1 (Volume 2)



Period prevalent ESRD patients. Adj: age/gender/race/primary diagnosis; ref: ESRD patients, 2005.



State of Dialysis in the United States

- Slow progress in overall Prevalent mortality(10% decline over 20+ years)
- Slightly better improvement in incident based death rates over the last 20 years (20-30% decline)
- Hospitalization rates are still very high for CVD, Infections and other causes
- Hemodialysis is the dominant dialysis therapy based on 3 times per week



Original Article

Long Interdialytic Interval and Mortality among **Patients Receiving Hemodialysis**

Robert N. Foley, M.B., David T. Gilbertson, Ph.D., Thomas Murray, M.S., and Allan J. Collins, M.D.

N Engl J Med Volume 365(12):1099-1107 **September 22, 2011**

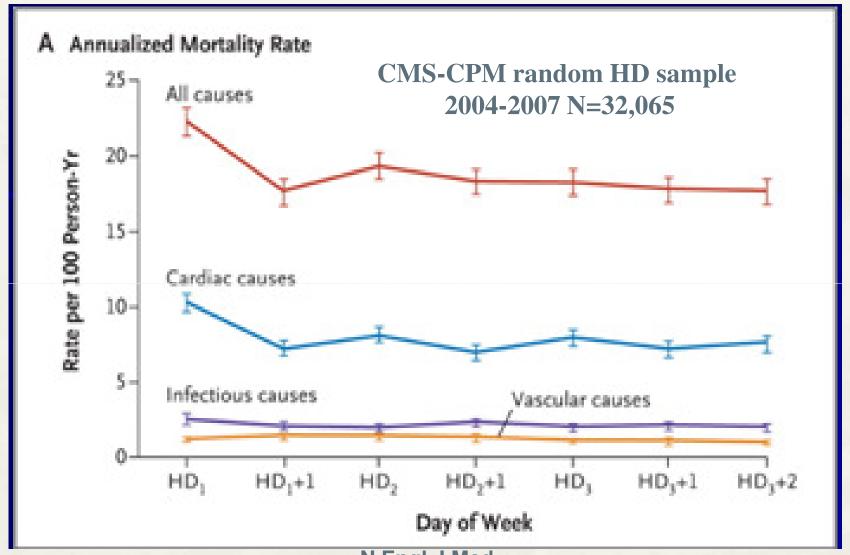








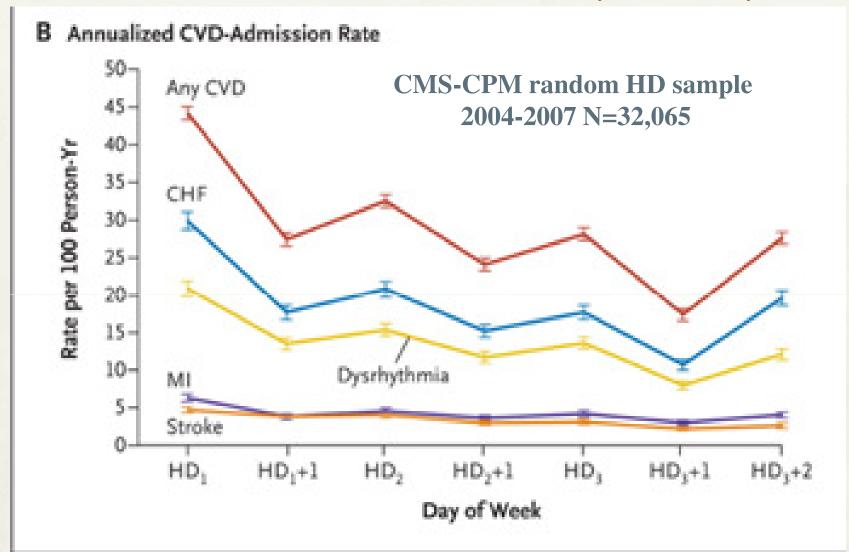
Annualized Mortality Rates on Different Days of the Dialysis Week.



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N Engl J Med Volume 365(12):1099-1107 September 22, 2011

Annualized CVD Admission Rates on Different Days of the Dialysis Week.



N Engl J Med Volume 365(12):1099-1107 September 22, 2011

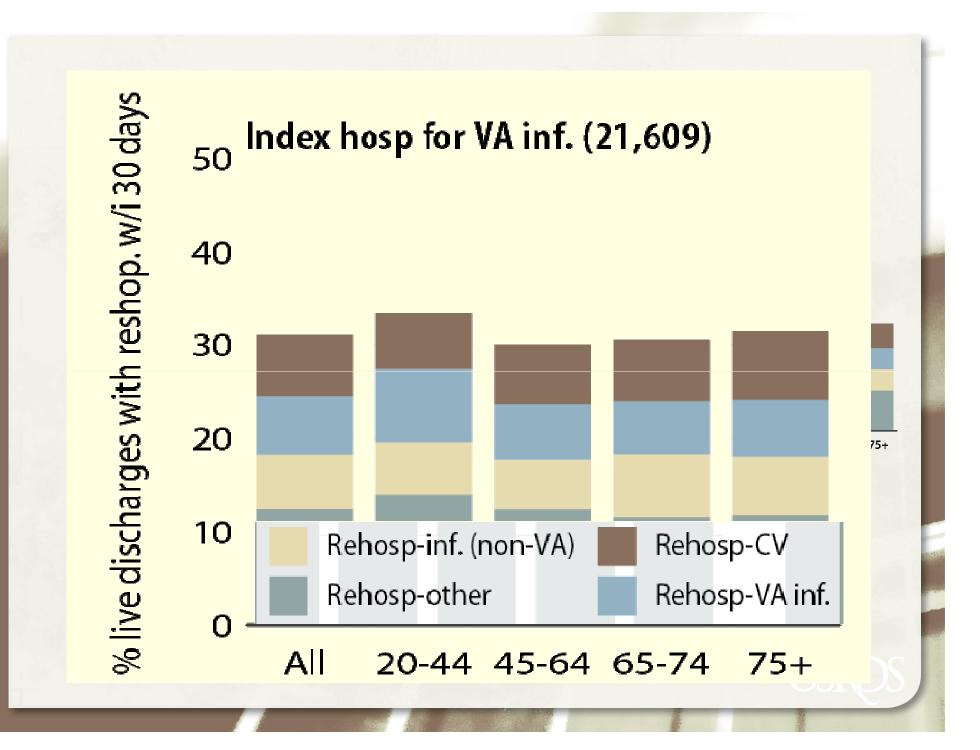
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Mortality and Morbidity on three times per week hemodialysis

- The long interdialytic interval (two days off) is associated with substantial morbidity and mortality.
- Congestive Heart failure, Arrhythmias and Acute Myocardial Infarctions are the lead causes of hospitalization after the long interdialytic interval.
- This is only the tip of the iceberg!
 - Re-hospitalization within 30 days are substantial.





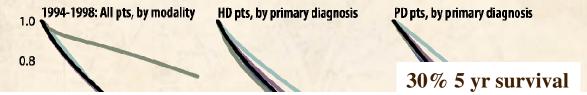
Re-hospitalizations are a major problem

- Almost double the rate of the non-dialysis population in Medicare
- Cardiovascular disease and infections are the major source of re-hospitalization
- The rates have not changed over the last decade (data in 2011 ADR)
- How do the different therapies stackup on morbidity and mortality?

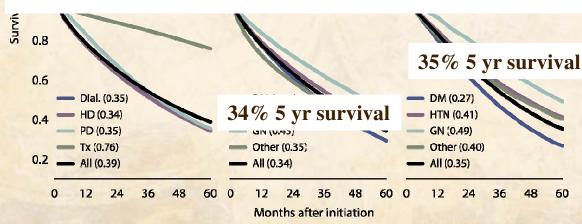


Adjusted five-year survival, by modality & primary diagnosis

Figure 6.7 (Volume 2)



Classic Cox outcome modeling does not address substantial selection bias between HD and PD



patients, 2005, used as reference cohort. Modality letermined on first ESRD ervice date; excludes patients transplanted or dying during the first 90 days. Five-year survival probabilities noted in parentheses. Dialysis patients followed from day 90 after initiation; transplant patients followed from the transplant date.

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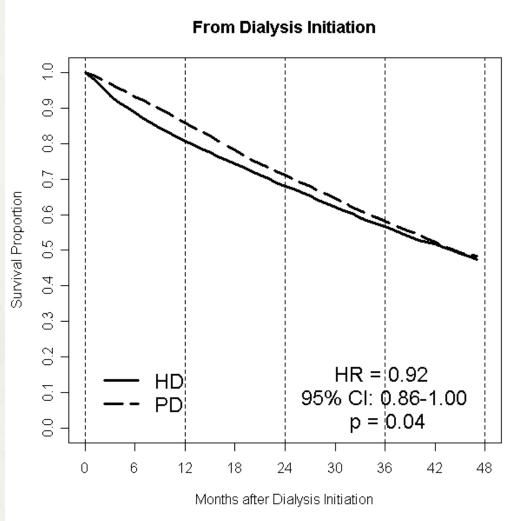


Eric D. Weinhandl, Robert N. Foley, David T. Gilbertson, Thomas J. Arneson, Jon J. Snyder, and Allan J. Collins

J Am Soc Nephrol 21:499-506, 2010

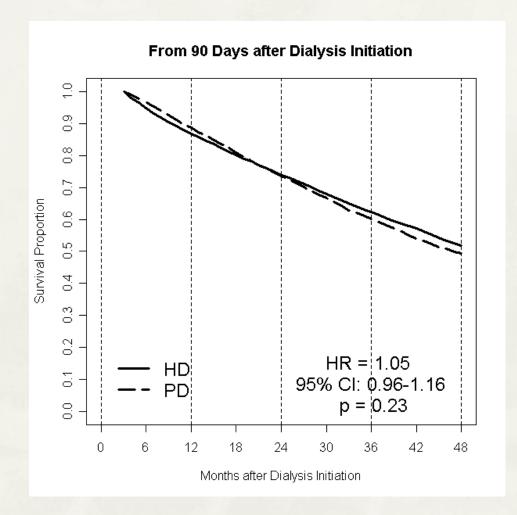


Survival from Day 0 Intention-to-treat analysis

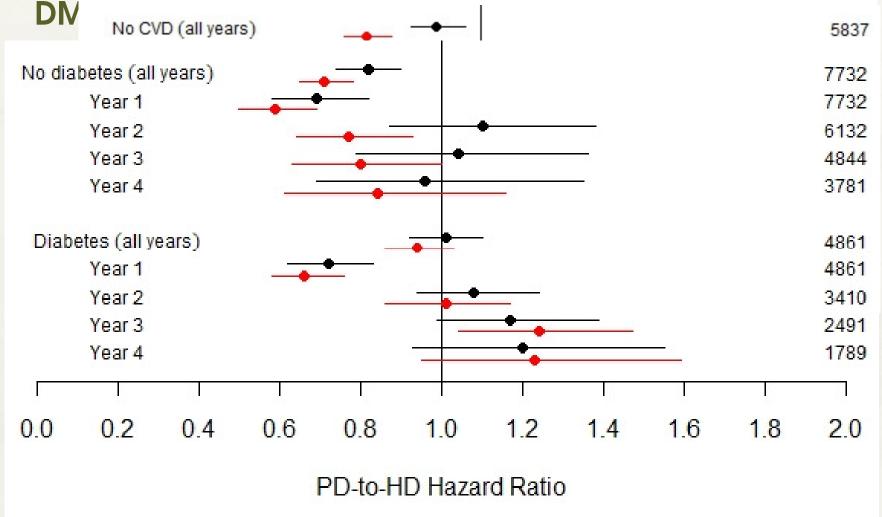


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Survival from Day 90 Intention-to-treat analysis



Mortality Hazard Ratios (PD vs HD) Follow-up from Day 0; subgroups by Age, CVD, and



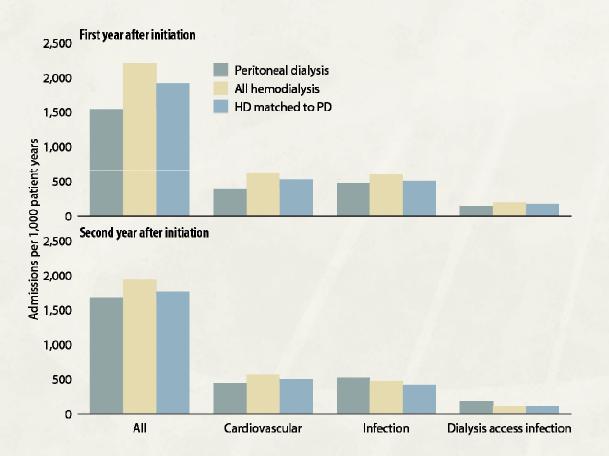
PD-to-HD Hazard Ratio

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Unadjusted rates of hospitalization in 2006–2007 matched incident hemodialysis & peritoneal dialysis patients: all patients

Figure 3.8 (Volume 2)



Incident hemodialysis & peritoneal dialysis patients age 20 & older, 2006–2007; unadjusted. First-year rates show admissions from day 90 to one year after initiation; second-year rates include patients alive & uncensored at the end of the first year.

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Comparative Mortality in NxStage System One Users and Matched Controls from the Thrice-Weekly In-center Hemodialysis Population

- Once again home hemodialysis populations are highly selected for the therapy
 - Lack of balance between controls and treatment groups such as in an RCT
 - Matching of populations or statistical matching with probability weighting
- Direct matching results
- Presented NKF Spring Clinical Meeting 2011.

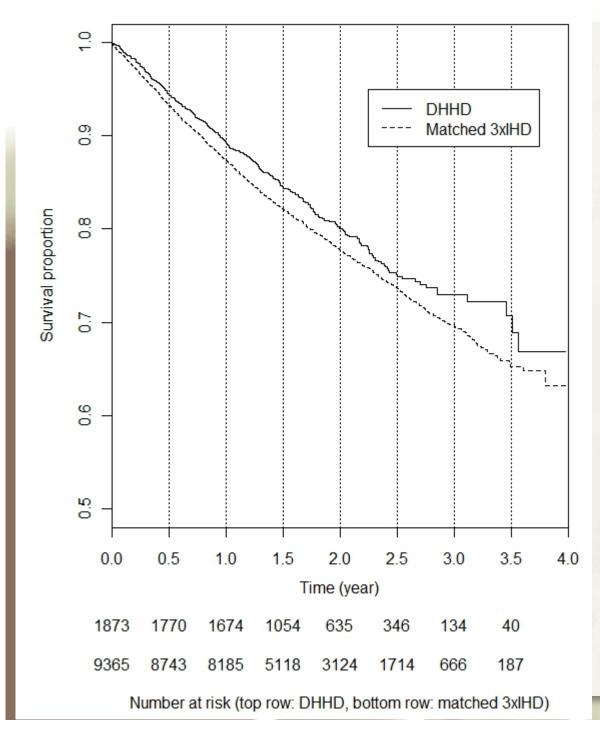


All-cause Mortality

- Rates per 100 patient-years
 - Frame of reference: 205 deaths per 1000 pt-yr in '08 period-prevalent dialysis patients (USRDS)

| | DHHD | IHD | Difference |
|-----|------|-----|------------|
| ITT | 110 | 127 | -17 |
| AT | 112 | 137 | -25 |

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ITT analysis

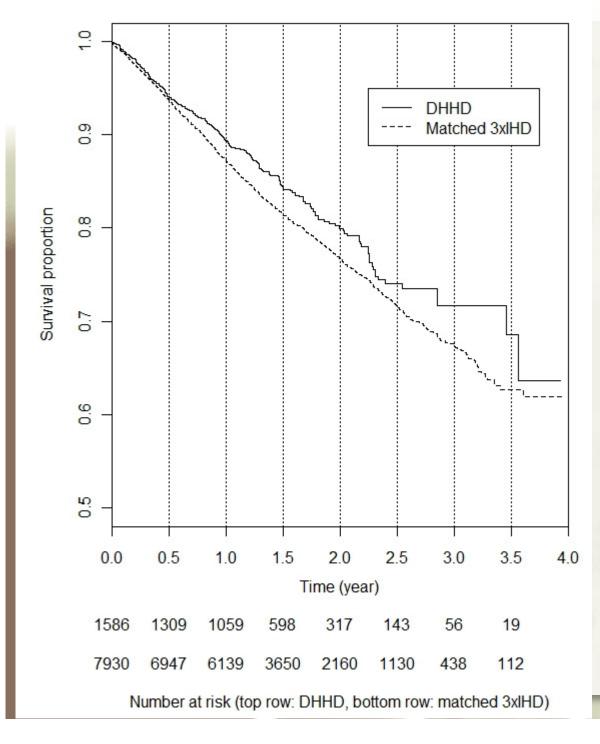
HR 0.87 95% CI (0.78, 0.97)

Survival at 1 year DHHD 89.4% IHD 87.4%

Survival at 2 years
DHHD 80.1%
IHD 77.8%

Survival at 3 years
DHHD 72.9%
IHD 69.8%

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AT analysis

HR 0.82 95% CI (0.72, 0.94)

Survival at 1 year DHHD 89.4% IHD 87.3%

Survival at 2 years
DHHD 80.0%
IHD 76.7%

Survival at 3 years
DHHD 71.7%
IHD 67.6%

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Summary

- It appears it is time for the traditional three times per week hemodialysis to be modified based on the high morbidity and mortality based on the intermittent nature of the therapy
- PD therapy, in appropriate groups, is comparable as with HD
- Frequent hemodialysis 5-6 days per week has been shown in clinical trials to have some advantages, yet good criteria are needed to advance this therapy in practice
- One last thing to consider:



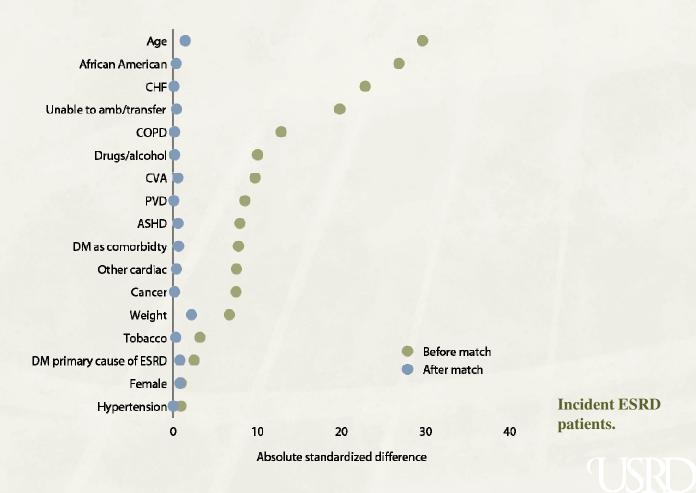
"Insanity: doing the same thing over and over again and expecting different results".

Albert Einstein



Absolute standardized differences before & after hemodialysis patients are matched to peritoneal dialysis patients

Figure 1.2 (Volume 2)



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