Kidney Transplantation

Part of the Continuum of care of Kidney Disease

A story of Failure and Success

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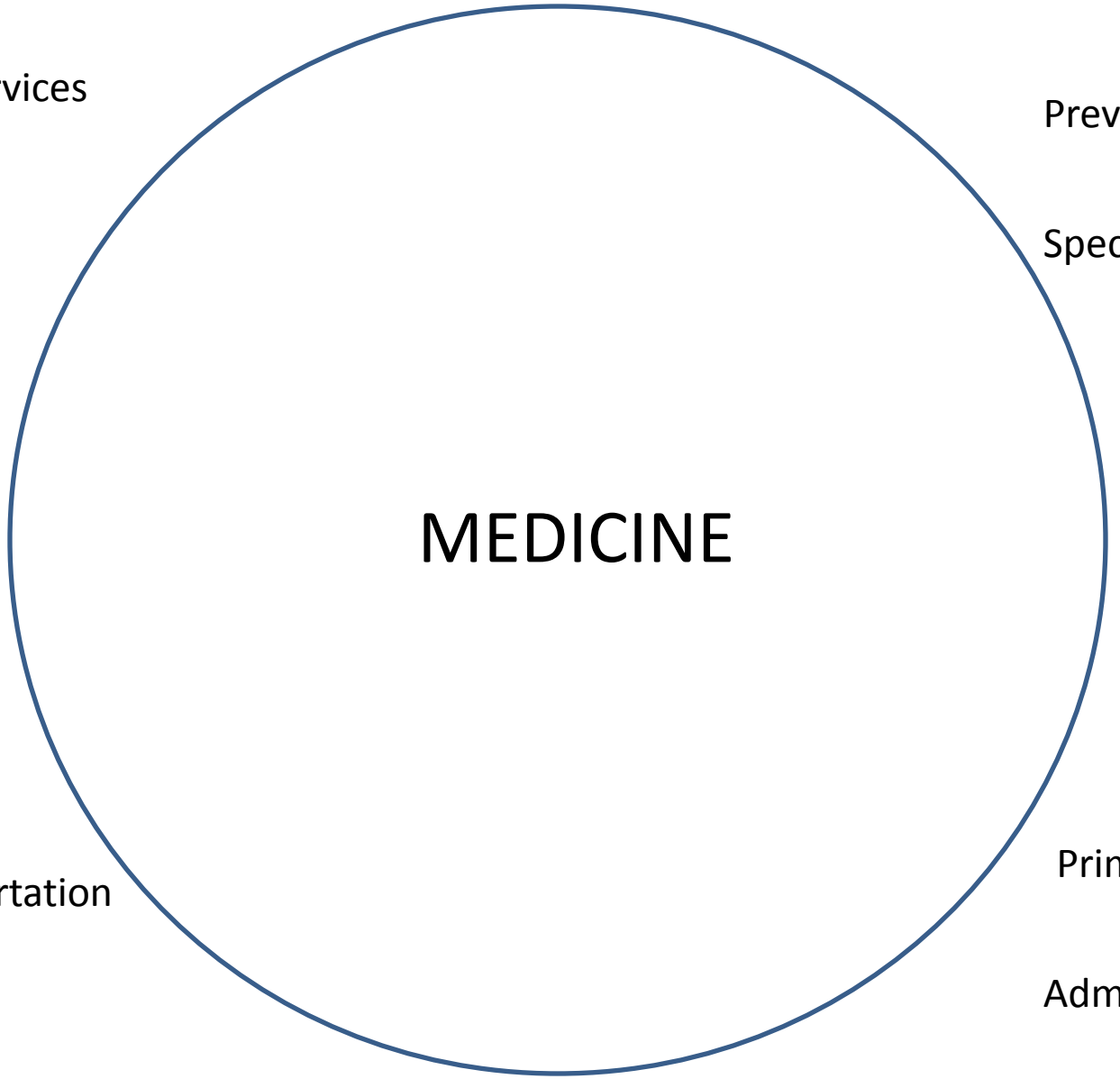
Conflict of Interest

- *I am employed by Alexion Pharmceuticals as a clinical researcher*
- *My talk does not address the use ofAlexion products or the off label use of other pharmaceutical products*
- *I have no conflicts of interest*

Agenda

- Introduction
  - Some terminology – Healthcare and Success
- Beginning with the punch line –
  - Renal Replacement Therapy - Transplantation as the preferred option
- Chronic Kidney Disease
  - A continuum of care through the lens of transplantation
- Questions

The World of Healthcare
20th C Services



Tertiary care facilities

Support services

Home health

Research

Hospice

Transportation

Information Technology

Preventative care

Specialty hospitals

Home health

Testing

Primary hospitals

Administration

What is Success when dealing with a Disease ?

Prevention -

Successful prevention: disease never occurs… Healthcare

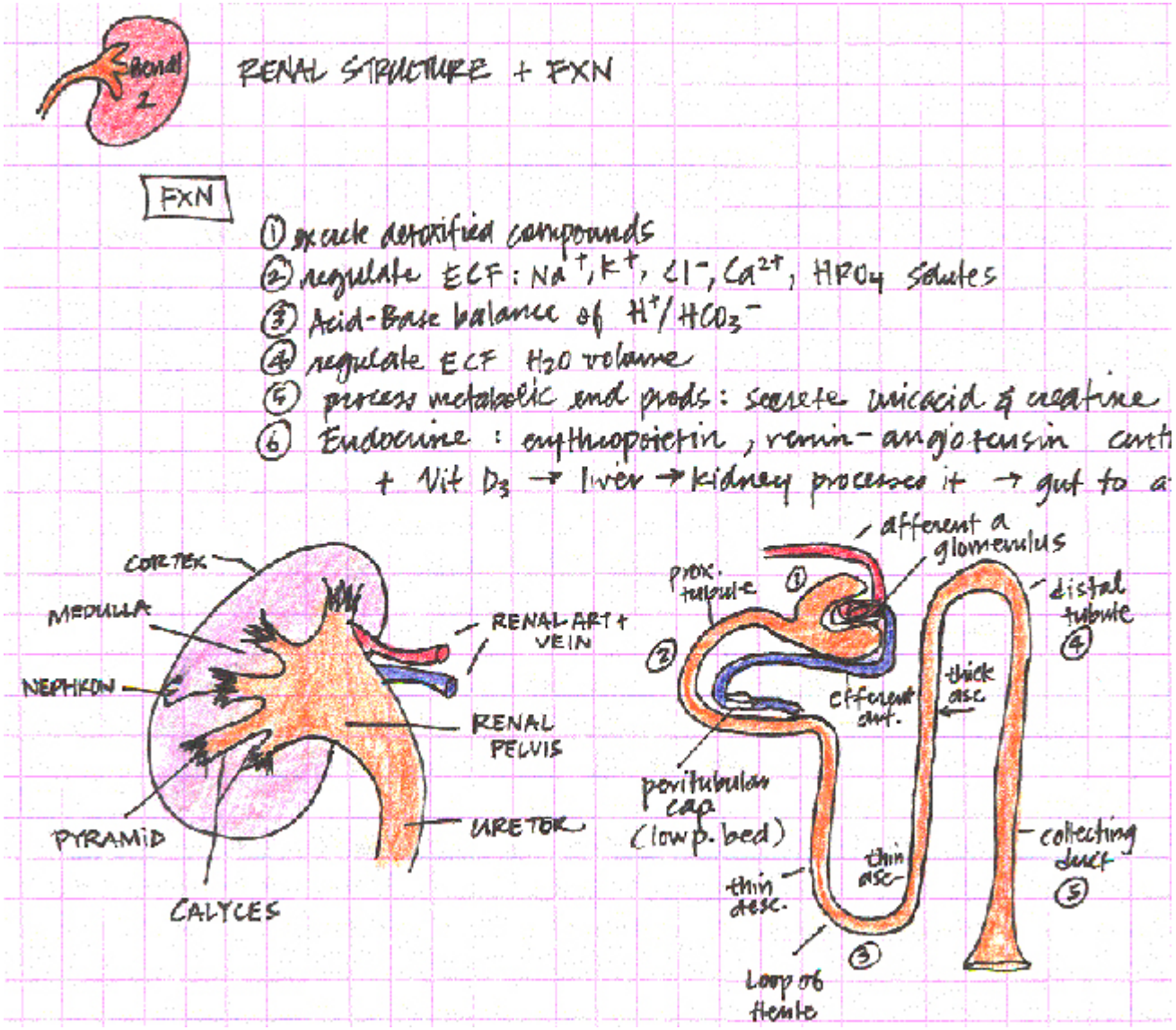
Treatment - dealing with failure… Medicine/Healthcare

Successful treatment: benefits a target population and consistently yields best possible outcome

Successful treatments share specific characteristics

1. Testable -------- scientifically vetted
2. Equitable ------ apply equally to affected group
3. Cost effective -- pharmacoeconomic argument
4. Available -------- generally available

Kidney Function(s)



S. Wong, MD (internet notes)

The Early NHANES III Study

Analysis of Prevalence of CKD by Stage

Stage	Description	eGFR Range (ml/min/ 1.73 m^2)	Population (1,000's)	Population (%)
1	Kidney damage with normal or increase GFR	≥ 90	5,900	3.3 %
2	Mildly decreased GFR	60-89	5,300	3.0 %
3	Moderately decreased GFR	30-59	7,600	4.3 %
4	Severely decreased GFR	15-29	400	0.2 %
5	Kidney Failure	< 15	300	0.1%

- Adapted from NHANES III (2000)

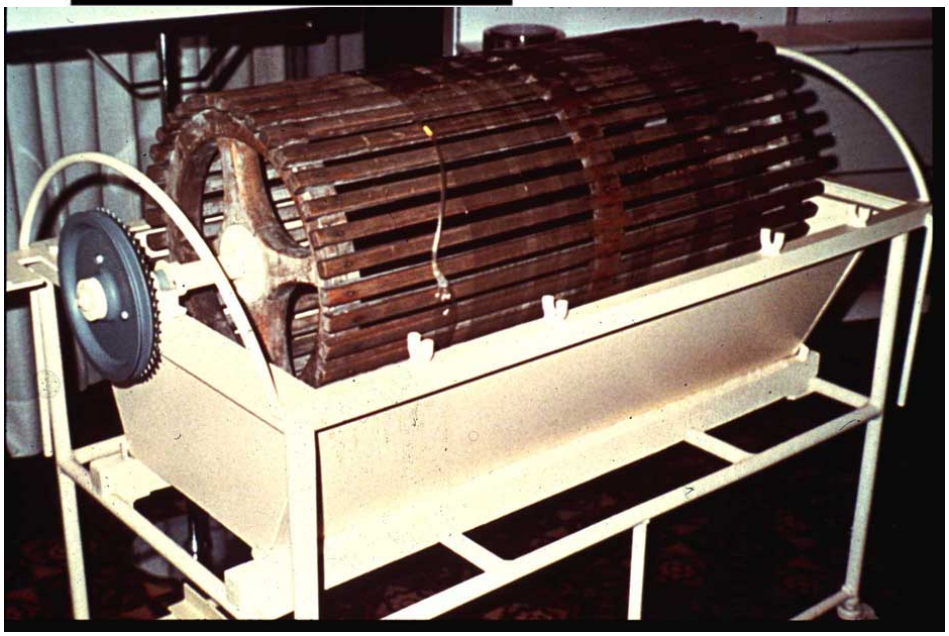
CKD Management – Thinking Ahead
Renal Replacement Therapy

- Palliative care
- Peritoneal Dialysis
- Hemodialysis
- Transplantation

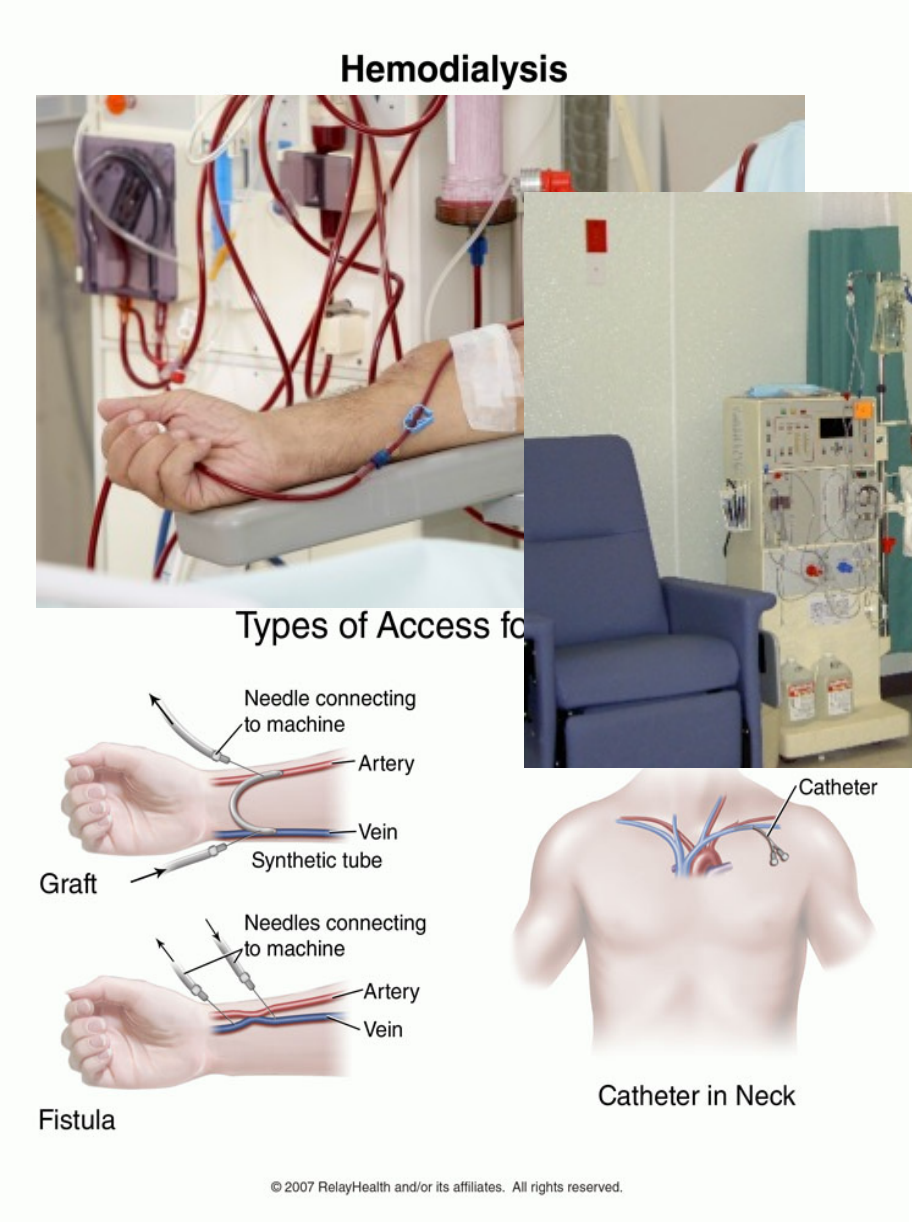
Hemodialysis

Then and Now

Artificial Kidney: 1947



Hemodialysis



Advantages

1. Target electrolytes
2. Tight control of fluid status
3. Professional contact
4. Community interaction

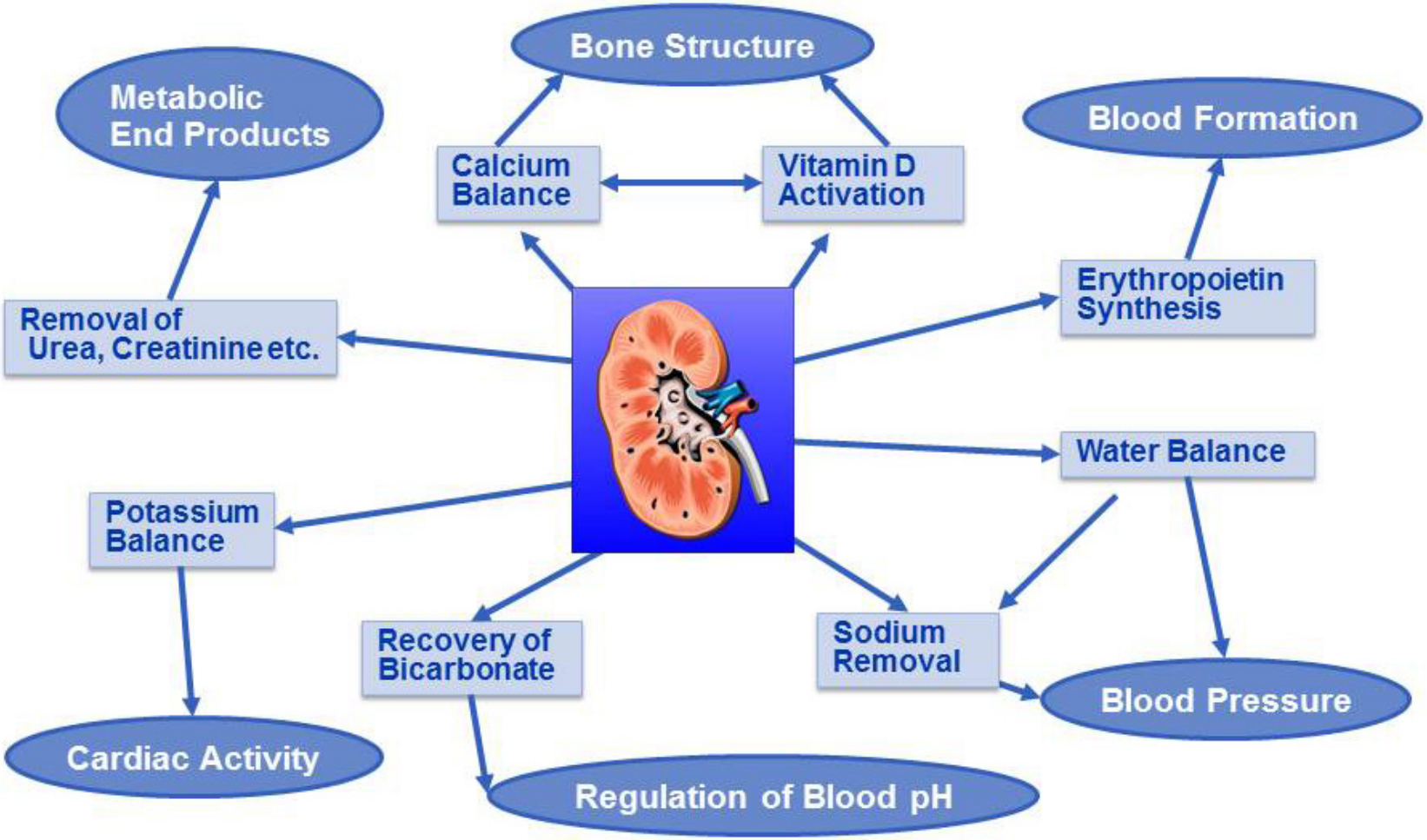
Disadvantages

1. Surgical / wound complications
2. Infection
3. Peak and valley results
4. Time / availability
5. Access to facilities/certified assist

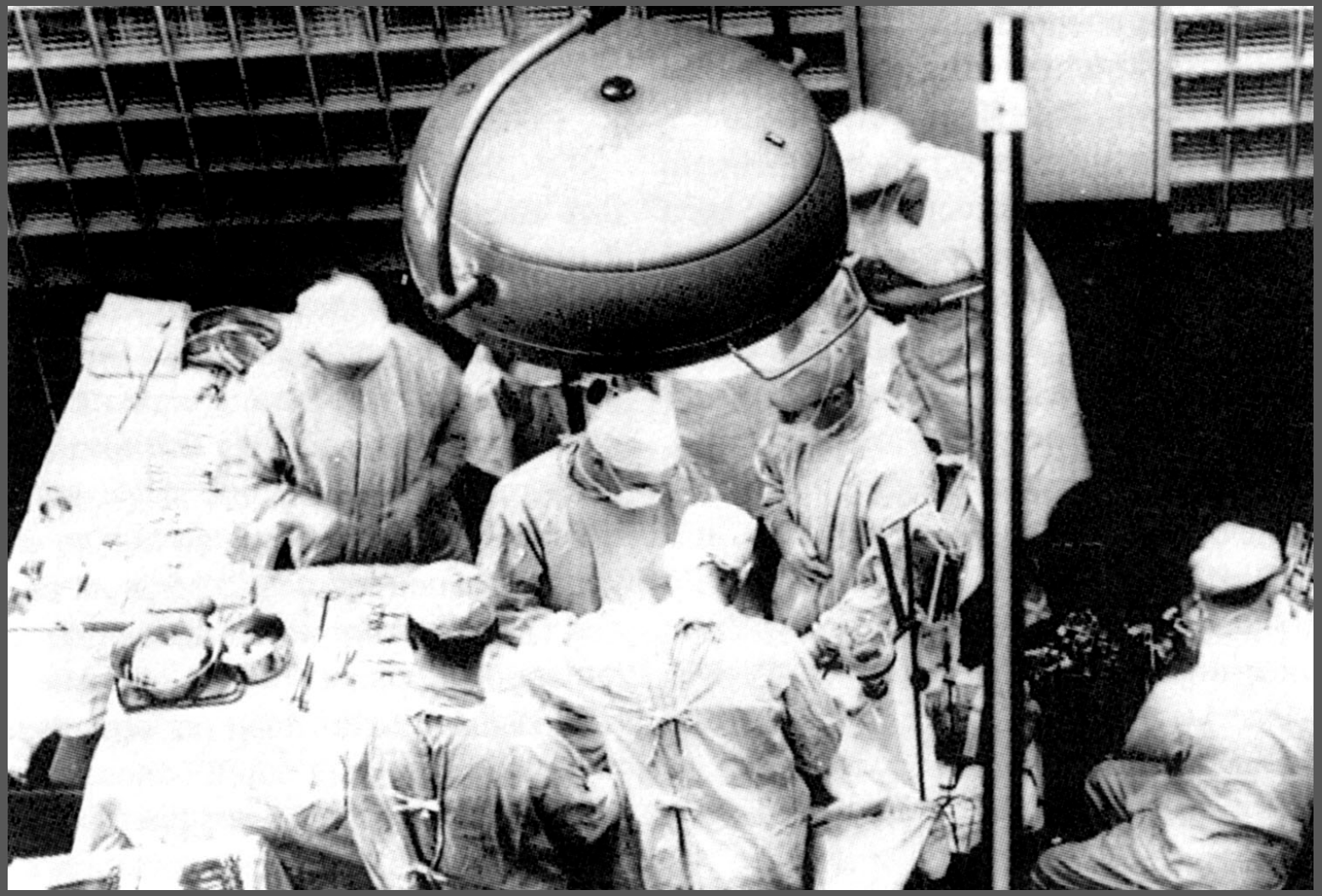
Peritoneal Dialysis

3. Weight gain
4. Diabetic control

Kidney Functions



Adapted from NephroCare 2013



Fears - Safety – Efficacy – Expectations
Transplant – safe alternative

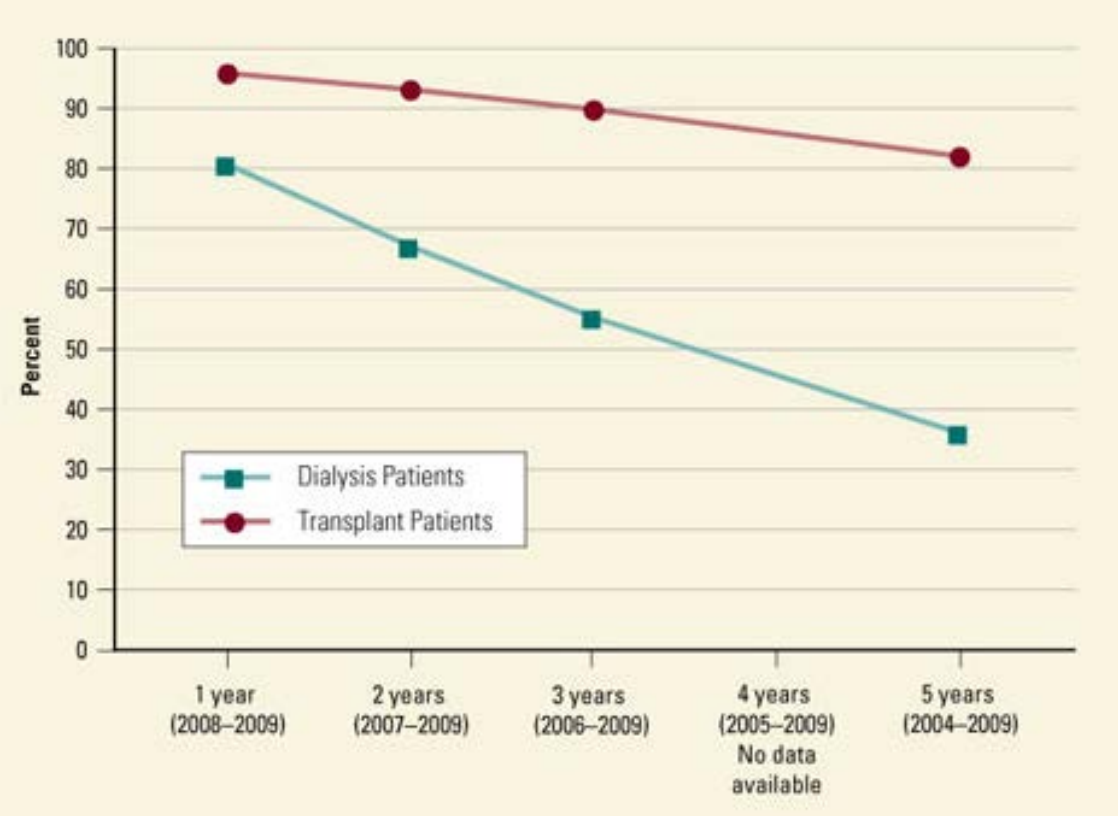
Table 11.1 Graft survival after first adult kidney only transplant from a DBD

Year of transplant	No. at risk on day 0	% Graft survival (95% confidence interval) One year		Two year		Five year		Ten year	
1998-2000	2890	90	(89-91)	88	(87-89)	82	(81-84)	71	(69-72)
2001-2003	2773	91	(90-92)	89	(88-90)	83	(81-84)		
2004-2006	2469	93	(92-94)	91	(90-92)	85	(84-87)		
2007-2010	2868	94	(93-94)						

Table 11.2 Patient survival after first adult kidney only transplant from a DBD

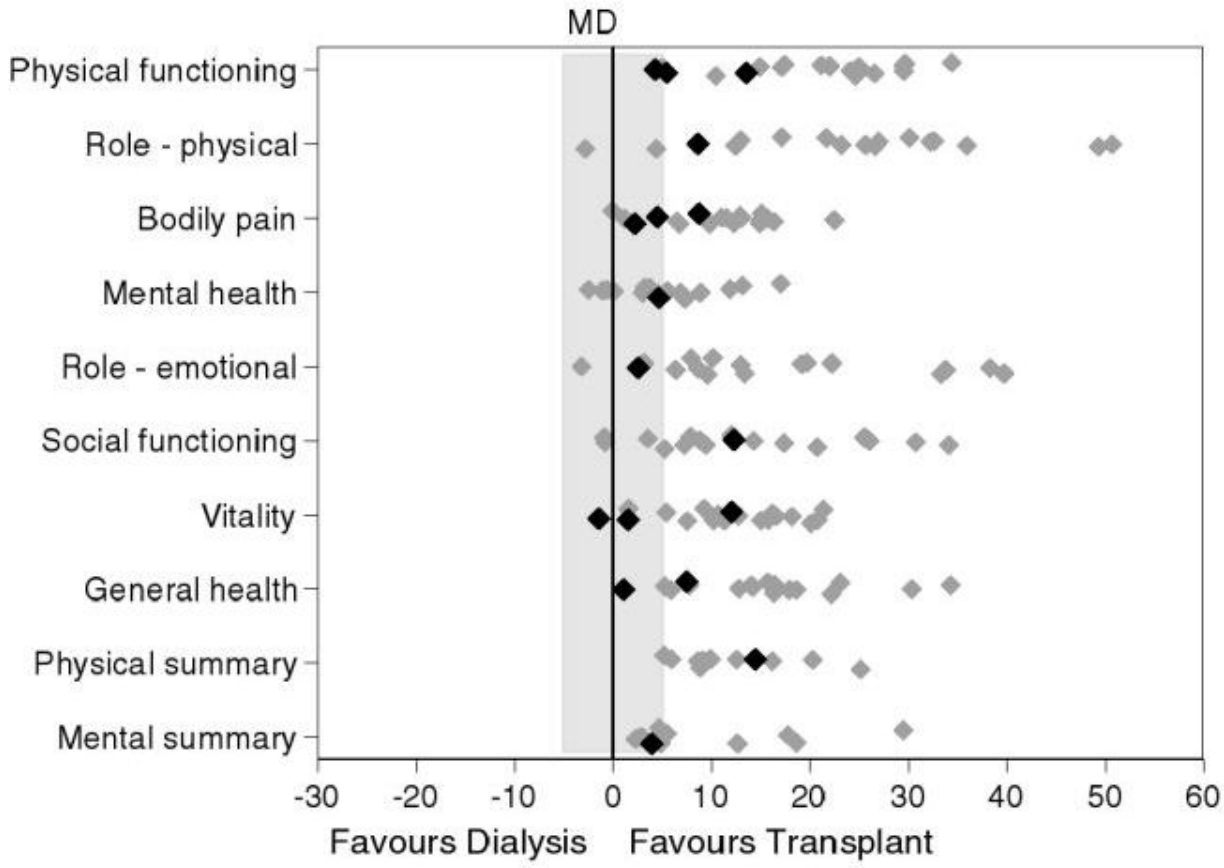
Year of transplant	No. at risk on day 0	% Patient survival (95% confidence interval) One year		Two year		Five year		Ten year	
1998-2000	2890	95	(94-96)	93	(92-94)	87	(86-88)	75	(73-77)
2001-2003	2773	95	(94-96)	93	(92-94)	88	(86-89)		
2004-2006	2469	97	(96-97)	95	(94-96)	90	(88-91)		
2007-2010	2868	96	(95-97)						

Survival Benefit
Transplant versus Dialysis



USRDS annual report 2011

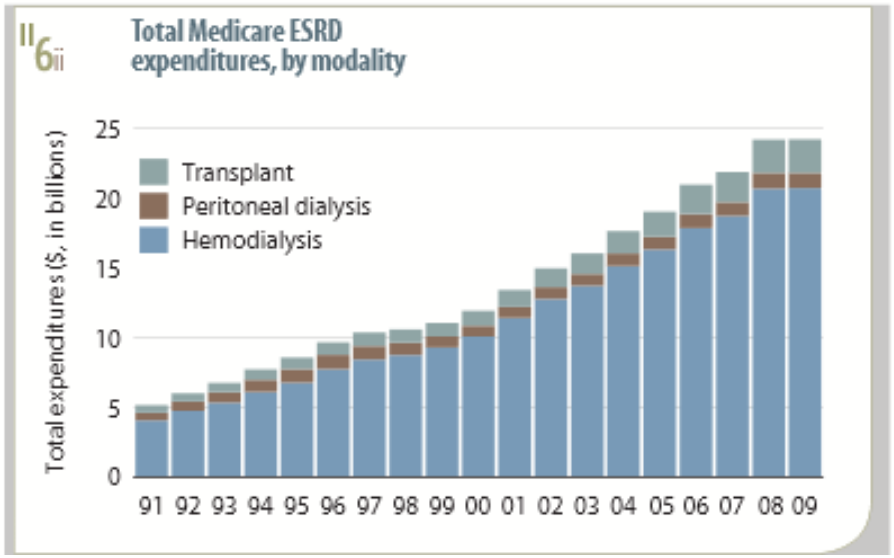
Improved Quality of Life Transplant versus Dialysis



Short form health survey - SF36

Tonelli M, et al., AJT 2011; 11(10)

Cost Effective
Transplant versus Dialysis



USRDS annual report 2011

What is the Success when dealing with ESRD?

Prevention: Ideal but limited

✔Successful treatment: benefits the target population and consistently yields <u>best possible outcome</u>

Characteristics of a successful treatment:

- ✔ 1. Testable -------- scientifically vetted
- ✔ 2. Equitable ------ apply equally to affected group
- ✔ 3. Cost effective -- pharmacoeconomic argument
- ✔ 4. Available -------- generally available

Transplantation is the preferred treatment for <u>ESRD</u>

What about the rest of 'Kidney Disease?'

Kidney Disease = Chronic Kidney Disease

- Many terms used interchangeably to describe a state of chronic reduced kidney function
  - Chronic Renal Insufficiency
  - Chronic Renal Failure
  - Renal Insufficiency
  - Renal dysfunction
  - Diabetic nephropathy*
  - Chronic rejection (if patient had prior transplant)
  - Chronic nephropathy
  - Hypertensive nephrosclerosis*
  - Etc. etc. etc.

Chronic Kidney Disease (CKD)
Kidney Disease Outcome Quality Initiative (KDOQI)

- Anatomical or Structural Defect
  - Abnormal imaging study
    - (i.e. Polycystic Kidney Disease, nephrosclerosis)
  - Abnormal Renal Biopsy
    - (i.e., MPGN, TMA)
  - Proteinuria (spot UProt/creat >30 mg/g)

- Functional Component
  - Abnormal eGFR (Low or High)
    - A biomarker (calculated measure) of kidney function

- Time Component (chronic)
  - Finding present ≥ 3months

KDOQI CKD Definition

- eGFR < 60 ml/min/1.73 m^2 ≥3 months

OR

- Spot urine albumin/creatinine ratio of >30 mg/g in at least 2 urine samples

Chronic Kidney Disease

Quality of life

Length of life

Social impact

Financial impact

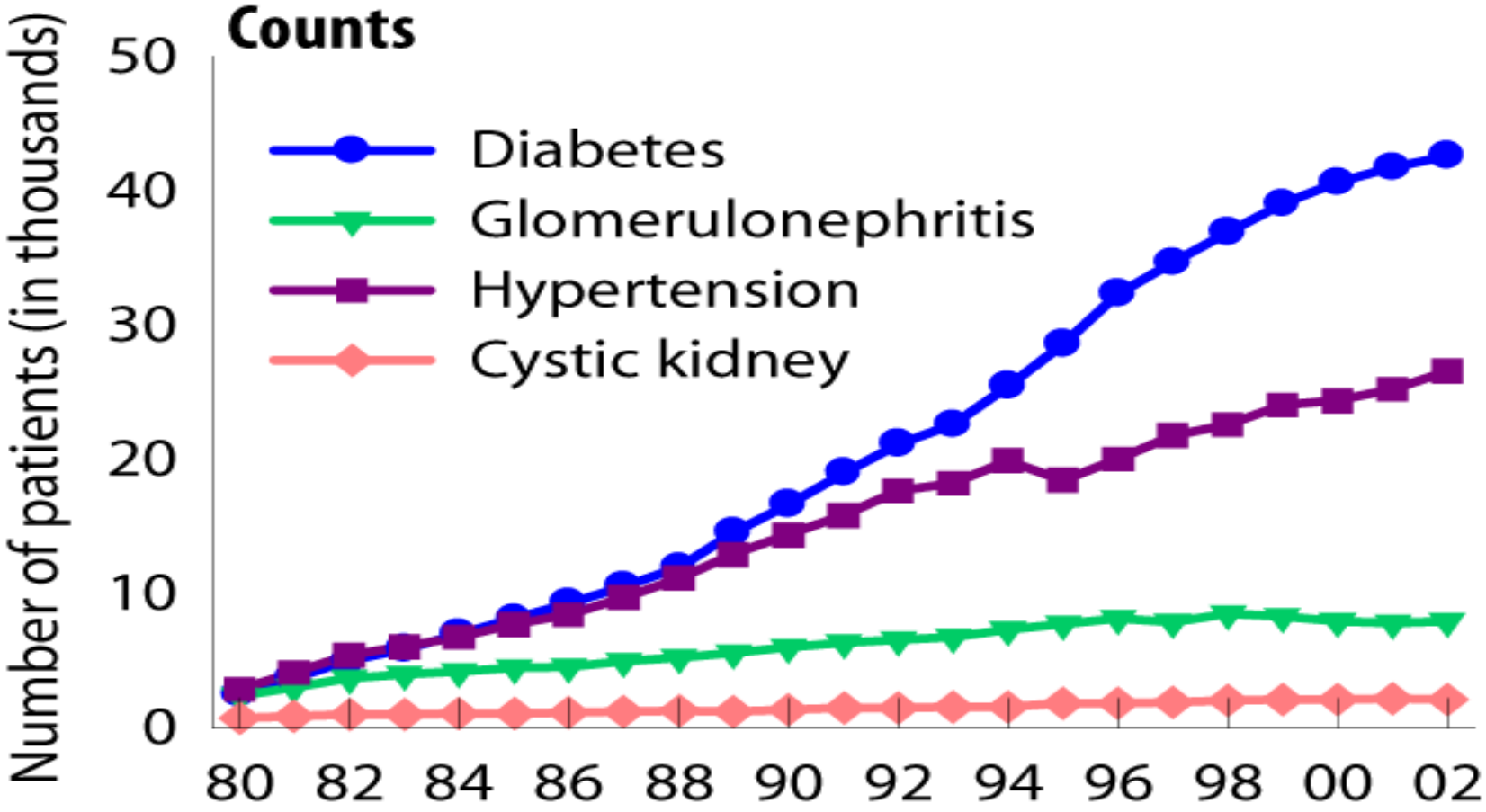
Family

Community

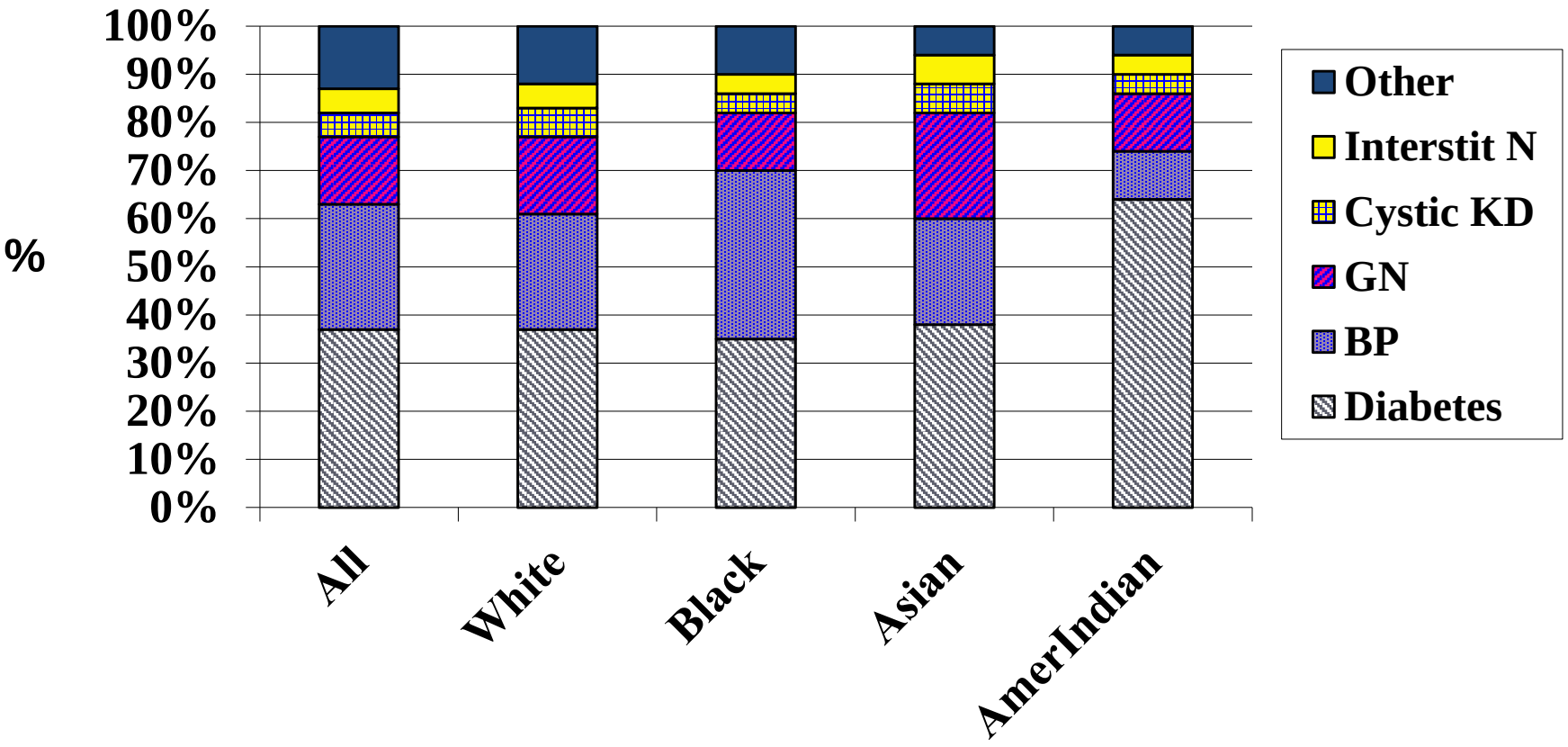
CKD – Risk Factors

- Diabetes Mellitus
- Hypertension
- Cardiovascular Disease
- Obesity
- Metabolic Syndrome
- Age and Race
- Acute Kidney Injury
- Malignancy
- Family history of CKD
- Infections like Hep C and HIV
- Kidney Stones
- Autoimmune diseases
- Nephrotoxic drugs
  - like NSAIDS
  - Calcineurin inhibitors (CNI)
- Prior transplant
  - Chronic rejection
- History of antibody mediated rejection (AMR)
- History of delayed graft function (DGF)

CKD – Most Common Etiologies



Etiologies CKD by Race



USRDS Annual Data Report

High Blood Pressure
Endemic Native American Healthcare Risk for CKD

Hypertension

NHANES data is not available.

Age-adjusted percentage of persons 18 years of age and over who have high blood pressure, 2004-2008.

	American Indian/Alaska Native	Non-Hispanic White	American Indian/Alaska Native/Non-Hispanic White Ratio
Men and Women	34.5	25.7	1.3
Men	38.7	26.7	1.4
Women	30.2	24.7	1.2

Source: CDC 2010. Health Characteristics of the American Indian and Alaska Native Adult Population: United States, 2004-2008. Table 4.
http://www.cdc.gov/nchs/data/nhsr/nhsr020.pdf [PDF | 304KB]

Percent of adults age 18 and over with hypertension whose blood pressure is under control
Not available at this time.

Age-adjusted percentage of persons 18 years of age and over who have high blood pressure, 2010. National Health Interview Survey (NHIS)

American Indian/ Alaska Native	Non-Hispanic White	American Indian/Alaska Native/Non-Hispanic White Ratio
30.0	23.9	1.3

Source: CDC 2011. Summary Health Statistics for U.S. Adults: 2010. Table 2.
http://www.cdc.gov/nchs/data/series/sr_10/sr10_252.pdf [PDF | 1.6MB]

Native Americans CKD
Etiology

Diabetes (DM) = #1 cause of kidney failure

Native Americans have a high incidence of diabetes

13-15% of Native Americans >18y have diabetes

High Blood Pressure (HTN) = #2 cause of kidney failure

~30% of adult Native Americans have HTN

Together: DM and HTN = ~ 75% of kidney failure

Kidney Disease - Therapeutic Windows

- Prevention

  prevent and/or treat CKD risk factors

- Management of CKD

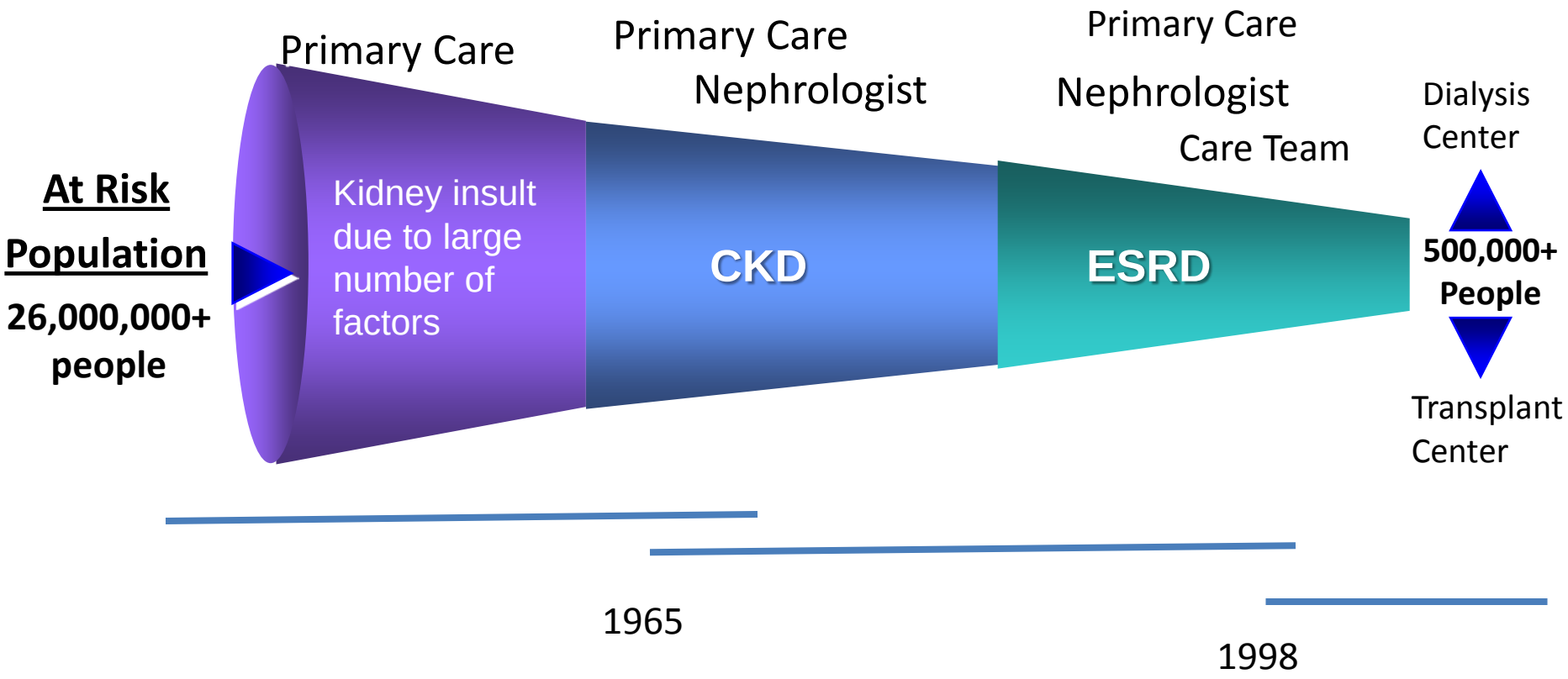
  stages 1 & 2 (eGFR >60): management guidelines DM and HTN and patient education

  stages 3 & 4 (eGFR 15-60) therapeutic guidelines for related complications (anemia, ESRD preparation)

- Renal replacement therapy (RRT)

  Patient education, evaluation and collaboration with dialysis and/or transplant center

Kidney Disease - Continuum of Care



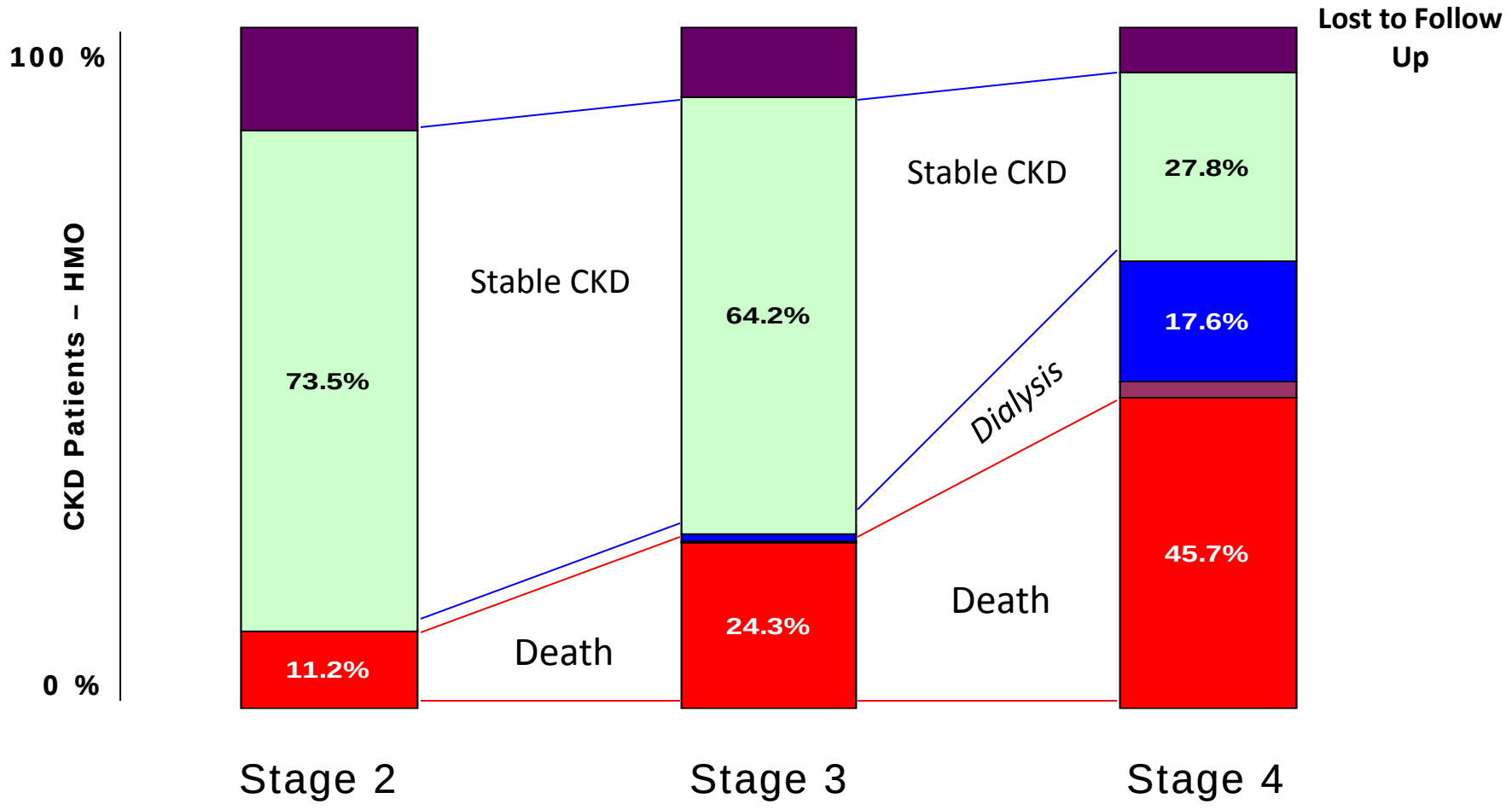
Modified –
Fresenius corporation 2012

CKD Patients Need Special Attention

CKD "*Death Before Dialysis*" is Prominent

- Early recognition and intervention for CKD can prevent early death before dialysis
- In one study of a large HMO, CKD patients were more likely to die than reach RRT

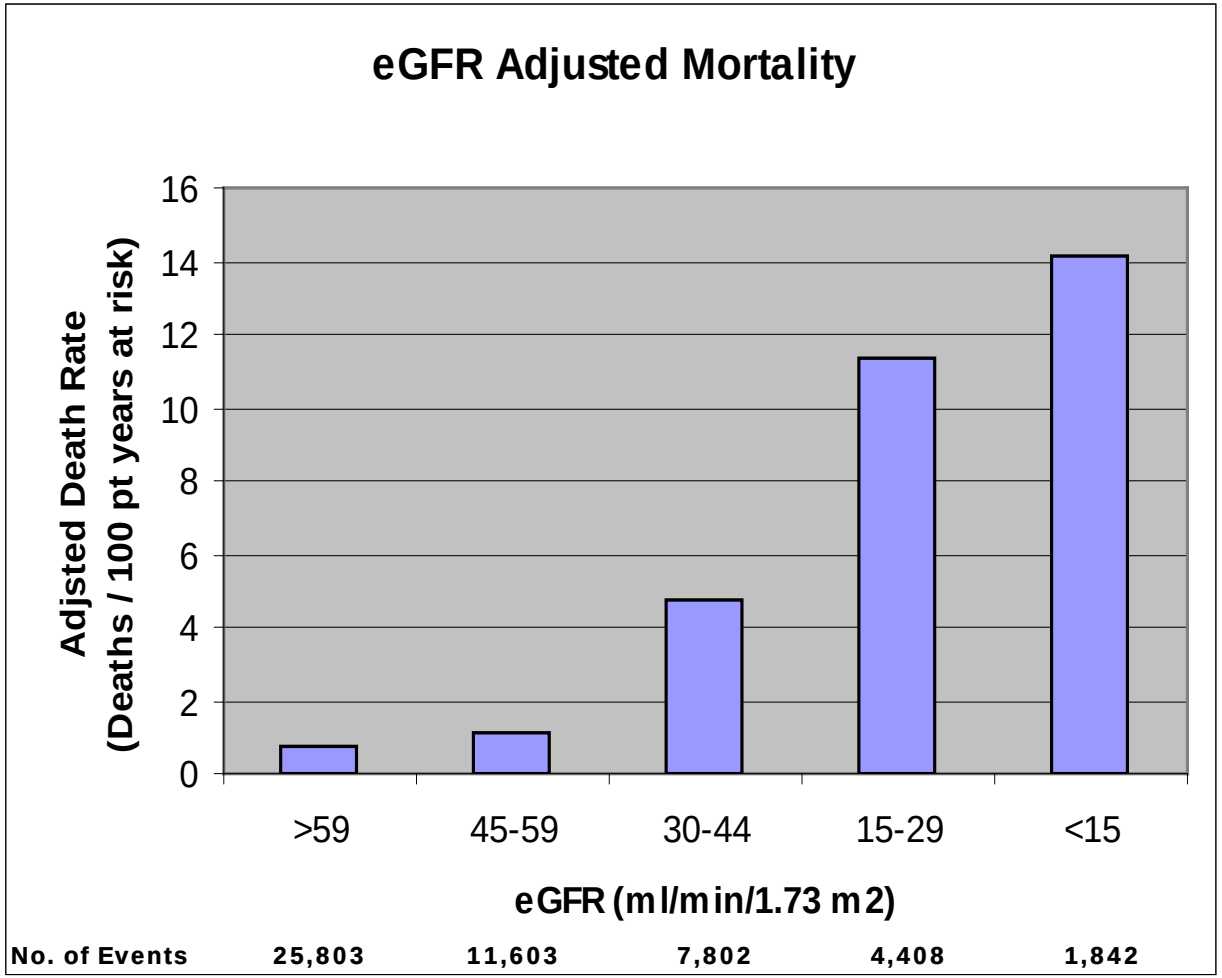
Modified/Fresenius corporation



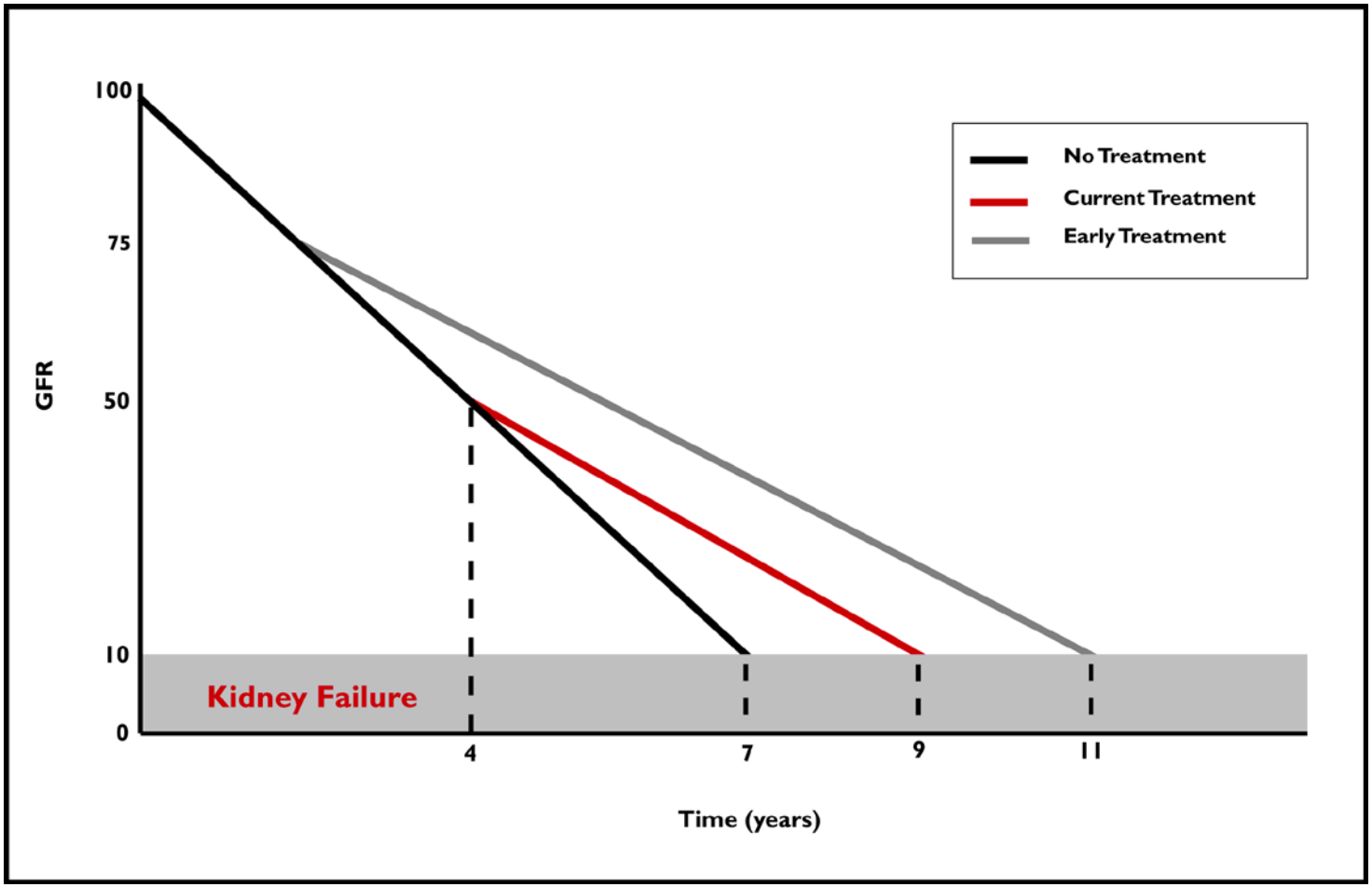
CKD Patients Need Special Attention

eGFR & Mortality

eGFR < 60 ml/min/m2 ➔ Increase Risk of Death



CKD - Management



Chronic Kidney Disease

through the lens of transplantation

Assumptions

- The patient will progress to ESRD
- The initial treatment will be dialysis (often for years)

Goals for Treatment of CKD

- Prolong the dialysis free course
  - Protect the kidneys (remember that the same factors that affect native kidneys affect transplants)
- Maintain health while on dialysis
  - (6% year over year mortality)
- Prepare patient and family for transplantation
  - Protect the patient from treatments that may adversely affect his/her ability to obtain a transplant

ESRD - treatment of choice is Transplantation

CKD Management

Key areas of focus (Eye to the Future)

1. Hypertension
2. Anemia
3. Diabetic control
4. Preparation for RRT

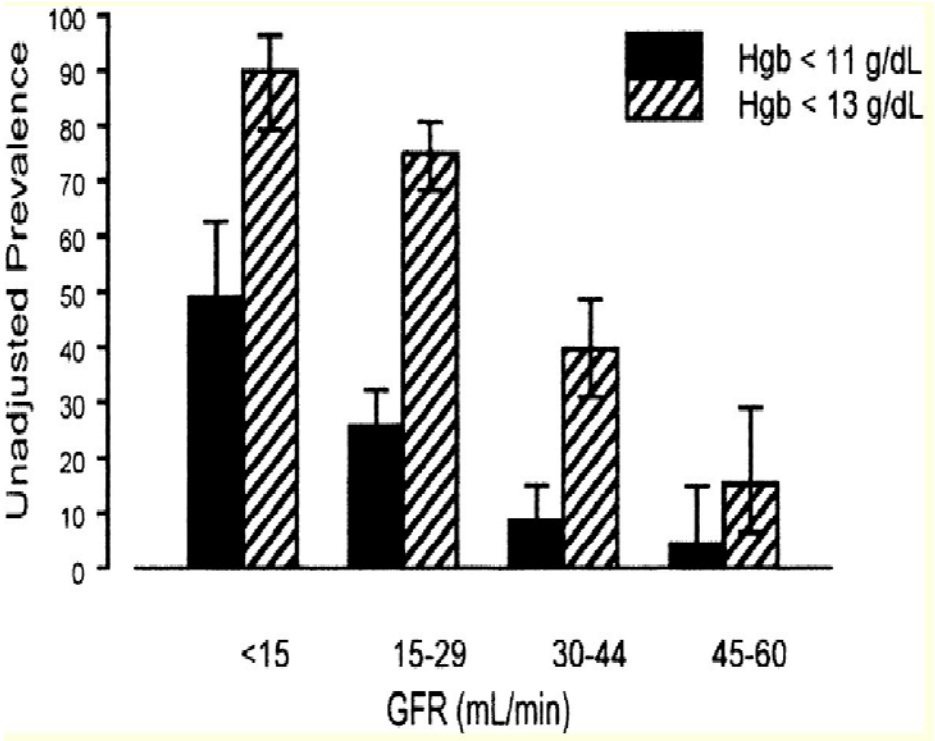
CKD – Hypertension

Thinking ahead – Hypertension injures ALL kidneys

- Single most important measure is BP control
  - Target BP <130/80 with minimal proteinuria
  - Lower (125/70) if significant proteinuria (1g)
- ACEIs and ARBs slow the progress of CKD (both diabetic and non-diabetic)
- Decrease the sodium intake - 2.5g/day
- Most patients require 2+ agents

CKD – Anemia

- Associated with a decrease in quality of life
  - Subjective Diagnosis
  - Most apparent in later stage disease
- Due to decrease in EPO production in the kidney.



CKD Management – Anemia - think ahead

Correct Anemia with an Eye to the Future

- Erythropoietin
  Epoetin alfa: Procrit ® , Epogen®
  Darbepoietin Alpha: ARANESP ®
- Recommended target Hb 11-12g (<13)
  ≥13g Hb associated with increased mortality due to CHF
- Correct iron stores
- AVOID transfusions
  - Sensitize patients –
    - Decrease opportunity for future transplant
    - Decrease success of future transplant
  - If transfusion necessary - insist on LEUKOREDUCED blood only (Leukofiltration)
    - Defend your patient's opportunity for future transplant

*CHOIR study
(correction hemoglobin and outcomes in renal insufficiency)

CKD Management – Think Ahead

Diabetic Control in a Changing Renal Environment

- Kidneys metabolize LMW proteins
- When kidney loses function
  - Ability to metabolize small proteins decreases and insulin is a small protein
  - Endogenous or exogneous insulin lasts longer
  - Oral therapies may have prolonged affect
  - CKD patients may suffer severe hypoglycemic episodes
  - Patient education and/or insulin dose adjustment
  - Close attention to oral therapy dosing
- Prepare patient to expect the opposite with successful transplant
  - A transplant does not make diabetes worse
  - may require greater attention to maintain tight control

CKD Management – Thinking Ahead
Renal Replacement Therapy

- Palliative care
- Peritoneal Dialysis
- Hemodialysis
- Transplantation

CKD Management – Thinking Ahead
Renal Replacement Therapy - RRT

- Preparation

1. Peritoneal Dialysis
    - Abdominal operations – communicate with the surgical team
    - Diet/weight loss
    - Early training
    - Early placement

2. Hemodialysis
    - Avoid needless Veni-puncture & insertion of catheters – patient and staff education
    - Early placement of vascular access

– HD/PD
    - Opportunity to CHANGE MIND

CKD Management – Thinking Ahead
Renal Replacement Therapy - RRT

Options – what's best for your patient's situation?

1. Peritoneal Dialysis
    - Prior abdominal operations
    - Home environment
    - Bathing – Swimming
2. Hemodialysis
    - Access
    - Transportation
    - Assistance
    - Cardiovascular status
3. Transplantation
    - Malignancy – Spectrum from in situ to Melanoma
    - Infection – active / bacterial / viral
    - Recurrent disease risk (ie., MGPN II, C3 nephropathy, FSGS)
    - Environment – Access
    - Personal responsibility - Compliance

CKD Management – Thinking Ahead
Renal Replacement Therapy - RRT

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Transplantation Renal Replacement Therapy Option of choice? The Issues…

1. High success rate post-transplant
   a. High incidence of renal disease
   b. Highest referral rate to transplant centers
   c. Once listed – transplanted at same rate as rest of list
   d. Once transplanted – 1, 3, 5 y graft survival high compared to other races
2. Low percapita rate of transplantation
   a. Cost: Medicare but no non-direct transplant costs and 80% reimbursement
   b. PsychoSocial issues
   c. Location – location – location