

# Comorbid Depression in Patients with ESRD Treated with Hemodialysis

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# Learning Objectives

- The goal of the lecture is to highlight recent scientific advances in the assessment, outcomes, and treatment of comorbid depression in patients with end stage renal disease.
- To provide practical suggestions for the implementation of depression screening programs in dialysis centers

# Question?

Which attitude best describes your center's approach to depression treatment.

- A. We regularly screen for depression and treat or refer as necessary, system works well.
- B. We screen for depression, but do not have the resources to adequately address all patients issues.
- C. System for addressing depression? What system?

# Question?

ASN 2013 -2014 – ~200 Dialysis Centers

Which attitude best describes your center's approach to depression treatment.

25%

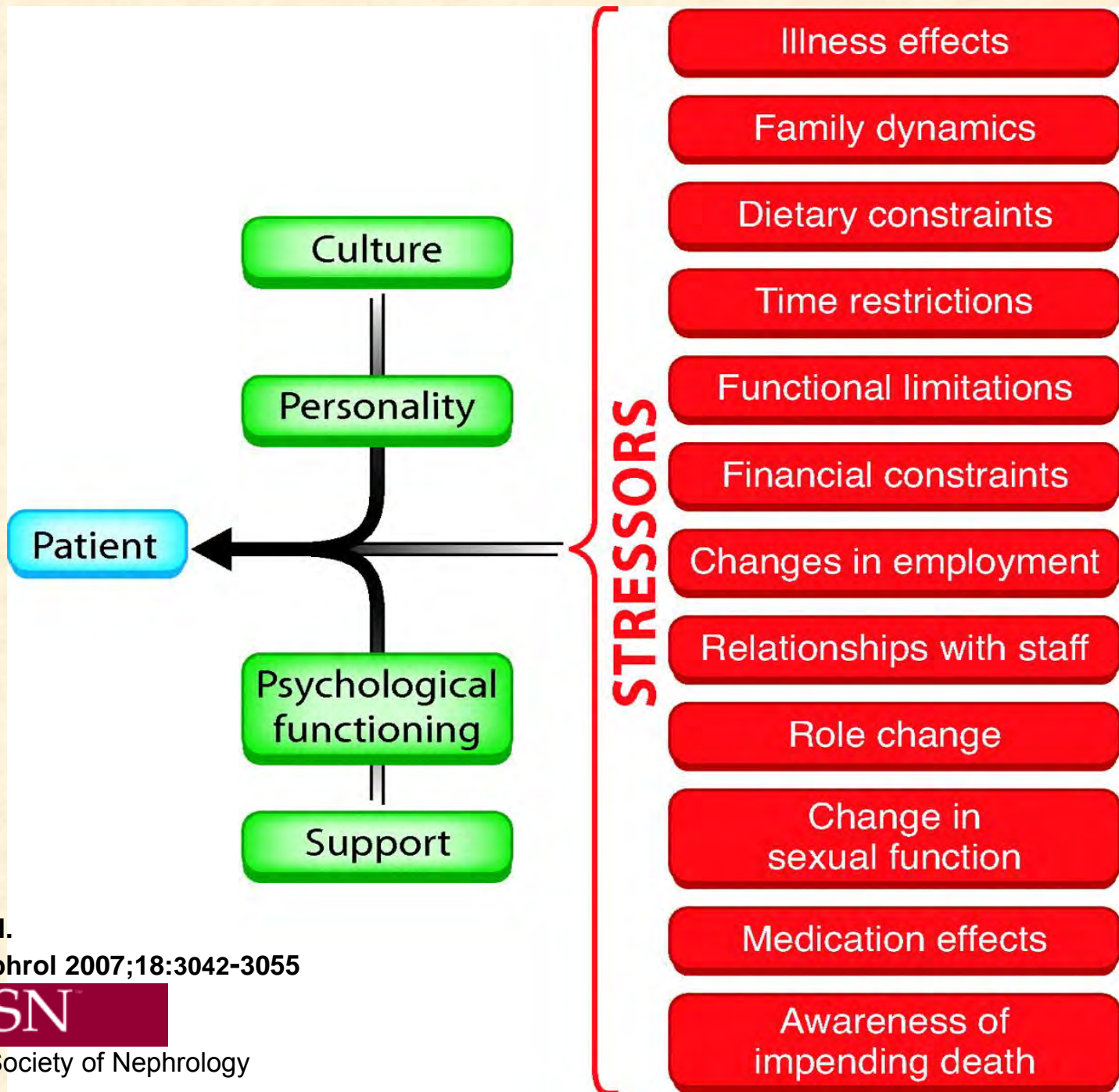
A. We regularly screen for depression and treat or refer as necessary, system works well.

25%

B. We screen for depression, but do not have the resources to adequately address all patients issues.

50%

C. System for addressing depression? What system?



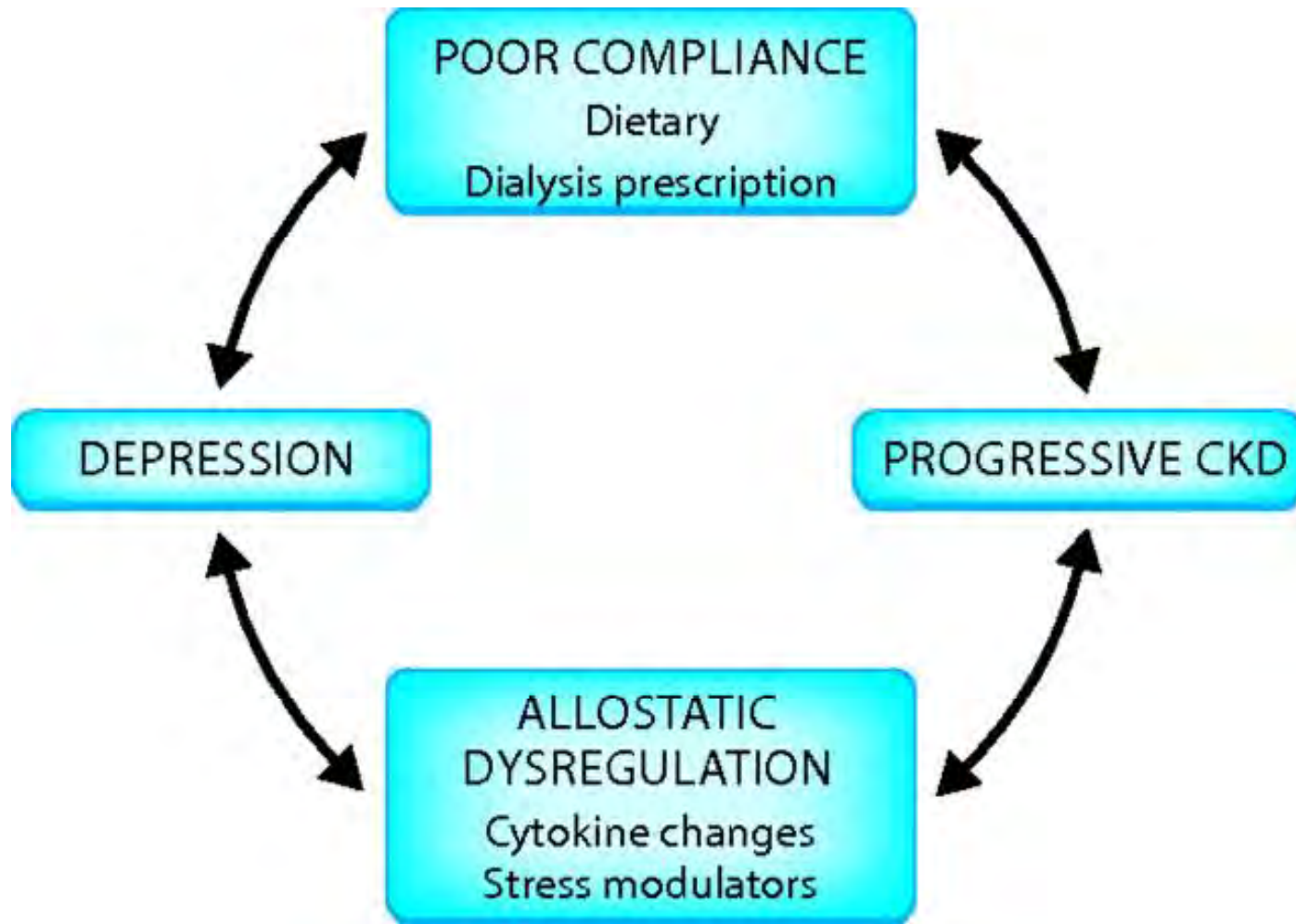
Cukor, D. et al.

J Am Soc Nephrol 2007;18:3042-3055

**JASN**

2007 American Society of Nephrology

Figure 3. Potential mechanism of vicious cycle between depression and ESRD



Cukor, D. et al. J Am Soc Nephrol 2007;18:3042-3055

# Impact of Depression in Dialysis

- Association of depressive symptoms and morbidity
  - Increased mortality
  - Higher peritonitis rates
  - Increased hospitalization
  - Lower QOL

Kimmel, KI, 2000

Troidle, AJKD 2003

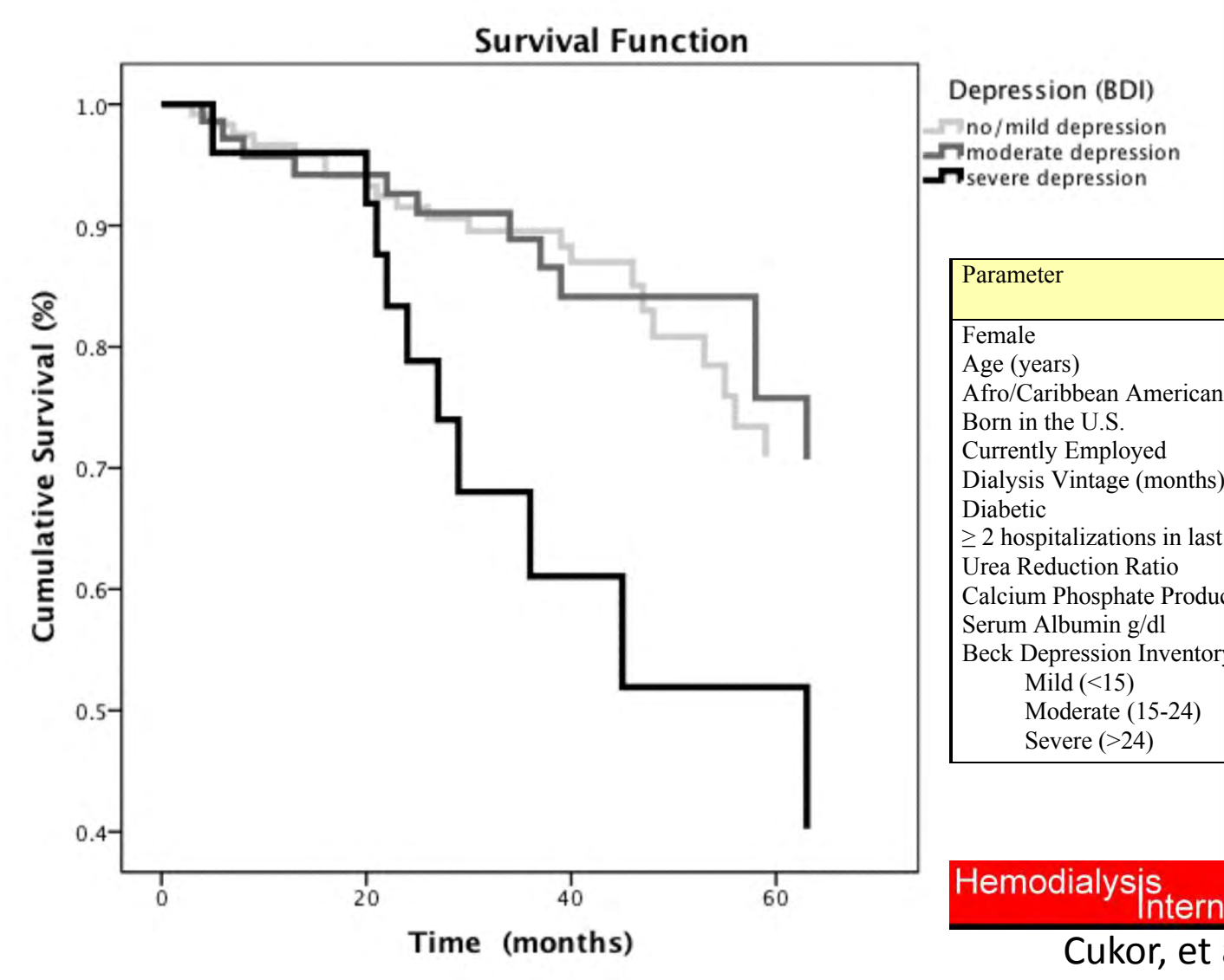
Lopes, KI, 2004

Hedayati, AJKD 2005

Farrokhi, AJKD 2014

“the presence of depressive symptoms significantly increased the risk of death by 51% (adjusted HR, 1.51; 95% CI, 1.35-1.69;  $I^2 = 40\%$ ;)”

# Cox Regression Survival Function Across Depression Severity



Parameter	Full Sample (n=130) Mean ± SD or %
Female	58%
Age (years)	57.6 ± 13.6
Afro/Caribbean American	84%
Born in the U.S.	48%
Currently Employed	17%
Dialysis Vintage (months)	54.8 ± 54.3
Diabetic	31%
≥ 2 hospitalizations in last year	39%
Urea Reduction Ratio	70.7 ± 10.5
Calcium Phosphate Product	49.5 ± 15.8
Serum Albumin g/dl	3.83 ± .86
Beck Depression Inventory	12.6 ± 10.2
Mild (<15)	55%
Moderate (15-24)	32%
Severe (>24)	13%



# Section Summary/Points to take home

- The psychological response to dialysis treatment is individual and varied.
- Depression is the most prominently studied psychological response.
- Comorbid depression is associated with lower QOL, behavioral adherence, increased hospitalization and morbidity.

# **SCREENING FOR DEPRESSION**

# What is “Depression”?

“Depression is characterized by feelings of helplessness, hopelessness, inadequacy, and sadness. However these are symptoms of several disorders and can also occur in normal individuals” -

Wolman, B. B. (1973). *Dictionary of behavioral science*

# DSM 5

- Major depressive episode vs major depressive disorder
- Dysthymia

# DSM 5 Criteria for Major Depressive Disorder (MDD)

- Depressed mood or a loss of interest or pleasure in daily activities for more than two weeks.
- Mood represents a change from the person's baseline.
- Impaired function: social, occupational, educational.
- Specific symptoms, at least 5 of these 9, present nearly every day:
  - 1. Depressed mood or irritable most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad) or observation made by others (e.g., appears tearful).
  - 2. Decreased interest or pleasure in most activities, most of each day
  - 3. Significant weight change (5%) or change in appetite
  - 4. Change in sleep: Insomnia or hypersomnia
  - 5. Change in activity: Psychomotor agitation or retardation
  - 6. Fatigue or loss of energy
  - 7. Guilt/worthlessness: Feelings of worthlessness or excessive or inappropriate guilt
  - 8. Concentration: diminished ability to think or concentrate, or more indecisiveness
  - 9. Suicidality: Thoughts of death or suicide, or has suicide plan

# Dysthymia

- Now called 'chronic depression'
- overwhelming yet chronic state of depression, exhibited by a depressed mood for most of the days, for more days than not, for at least 2 years.
- No more than 2 months without experiencing two or more of the following symptoms:
  - poor appetite or overeating
  - insomnia or hypersomnia
  - low energy or fatigue
  - low self-esteem
  - poor concentration or difficulty making decisions
  - feelings of hopelessness

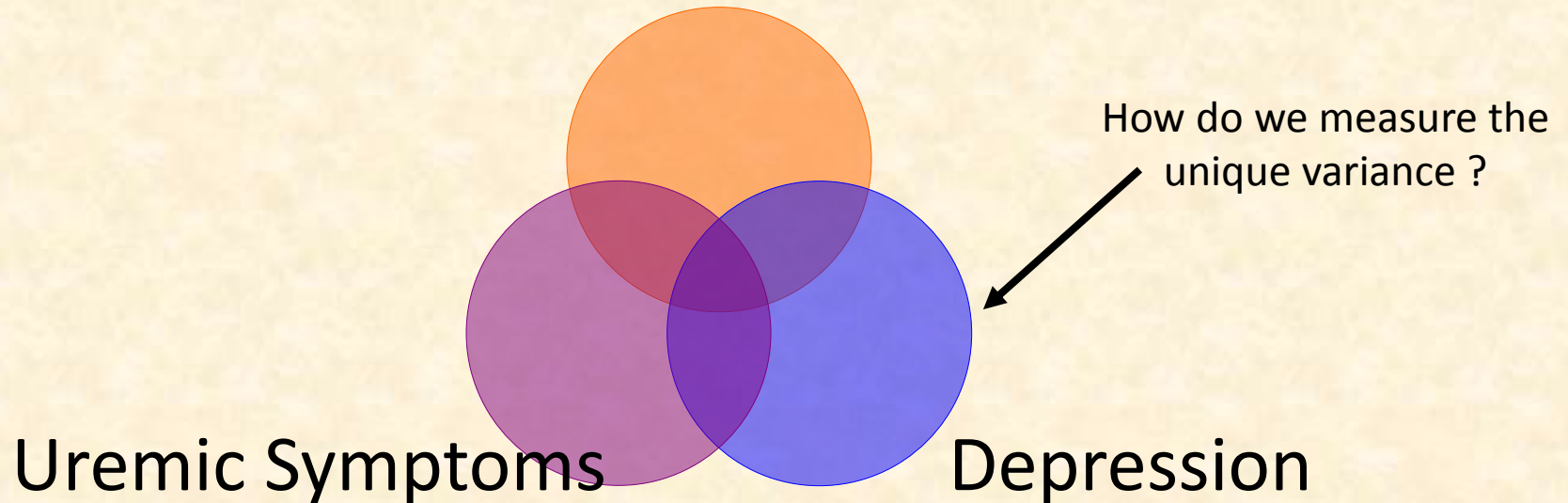
# Diagnosing Depression

- Most nephrologists not qualified to perform DSM-5 gold standard assessment
- You CAN assess patients yourselves
- – Screening tools identify high risk, not diagnostic

Criterion contamination: overlap of depressive symptoms & physical illness makes diagnosis difficult

# Overlapping Symptoms

## Medication Side Effects





# Screening Instruments

## **Quick Inventory of Depressive Symptomatology-Self Report(QIDS-SR) Scale**

New scale can be self report or clinician administered, used in Star\*D

## **Beck Depression Inventory-II (BDI-II)**

21-item self-report instrument. High scores reflect the presence and severity of depressed mood.

## **Hamilton Rating Scale for Depression (HAM-D)**

The total HAM-D provides an indication of depression and, over time, provides a valuable guide to progress.

## **Center for Epidemiologic Studies Depression Scale (CES-D)**

includes 20 items that survey mood, somatic complaints, interactions with others, and motor functioning.

## **SF-36 Health Survey**

A 36-item short-form was constructed to survey health status in the Medical Outcomes Study.

## **Kidney Disease Quality of Life Questionnaire (KDQOL-SF)**

assesses the quality of life of patients with kidney disease.

# Section Summary/Points to take home

- Depression can be difficult to define
- Screening instruments can identify high levels of depressive affect
- Outstanding questions
  - how often should we screen? (at initiation and every 6 months)
  - At what level of depression should we intervene?
    - Complex algorithm including: Depression severity, Depression length, suicidality, patient willingness, available resources

# Question

Have you ever encountered a dialysis patient who had a comorbid depression?

- A. Yes, and I attempted to treat the depression
- B. Yes, and I made a referral.
- C. Yes, but wasn't sure what to do.
- D. No, I haven't encountered a depressed patient

# Question

ASN ~ 200 Dialysis Centers

Have you ever encountered a dialysis patient who had a comorbid depression?

- 21% A. Yes, and I attempted to treat the depression
- 23% B. Yes, and I made a referral.
- 53% C. Yes, but wasn't sure what to do.
- 3% D. No, I haven't encountered a depressed patient

# Depression Treatment in General

- Psychopharmacological Interventions
- Psychotherapy Interventions
- Other interventions

# Pharmacological Interventions

- Identified 28 studies evaluating pharmacokinetic parameters in CKD for 24 antidepressants.
- Drug clearance in CKD 3-5 was markedly reduced for selegiline, amitriptyline, venlafaxine, desvenlafaxine, milnacipran, bupropion, reboxetine and tianeptine.
- There were nine non-randomized trials, all suggesting benefit for the antidepressant under investigation. Side-effects were common, but mild in most patients.
- Conclusions: The evidence on effectiveness of antidepressants versus placebo in patients with CKD is insufficient, and in view of the high prevalence, a well-designed RCT is greatly needed.

Antidepressants for depression in stage 3-5 chronic kidney disease: a systematic review of pharmacokinetics, efficacy and safety with recommendations by European Renal Best Practice (ERBP). Nagler, et al. Nephrol Dial Transplant. 2012

# Pharmacological Intervention

- 1 RCT in dialysis patients – 14 patients Fluoxetine vs Placebo ( effect at 4 weeks, no effect at 8 weeks) (Blumenfield (1997))
- Observational studies show moderate reductions in depression scores, but plagued by high rates of drop out, expectancy effects, and non-blinded assessment - Textbook of Somatic Medicine (2017) Cukor, Rosenthal, Kimmel & Levenson
- Getting patients to sufficiently take an SSRI is very challenging (Finkelstein (2000), Weisbord 2016, Weisbord (2017))

# Recommendations

- Citalopram or Sertraline – SSRI's with fewest identified complications for ESRD. R/O Mania
- Common side-effects include: Sexual dysfunction, weight gain, GI & CNS symptoms, Risk of bleeding
- Typical treatment – initiation at  $\frac{1}{2}$  recommended dose – will not work until reach adequate dose



# Other Interventions

- Exercise – Very modest effect in general, smaller for patients with increased comorbid illness/disability
  - Cochrane Review of Exercise Interventions for Depression
  - Exercise Training in Patients Receiving Maintenance Hemodialysis: A Systematic Review of Clinical Trials
- Frequent hemodialysis – no significant impact on BDI score
  - Chertow G, NEJM 2010

# Psychotherapy

- Group CBT in Brazil 85 subjects with high BDI
- RCT
- Stronger effect for CBT than standard care at 12 weeks.
- Strong attendance
  - Duarte P, et al Cognitive-behavioral group therapy is an effective treatment for major depression in hemodialysis patients, *Kidney Int* 2009 76:4, 414-420.

# Study Objective

To demonstrate the feasibility and effectiveness of a modified  
Cognitive Behavioral Intervention in End Stage Renal Disease  
Patients being treated with Hemodialysis.

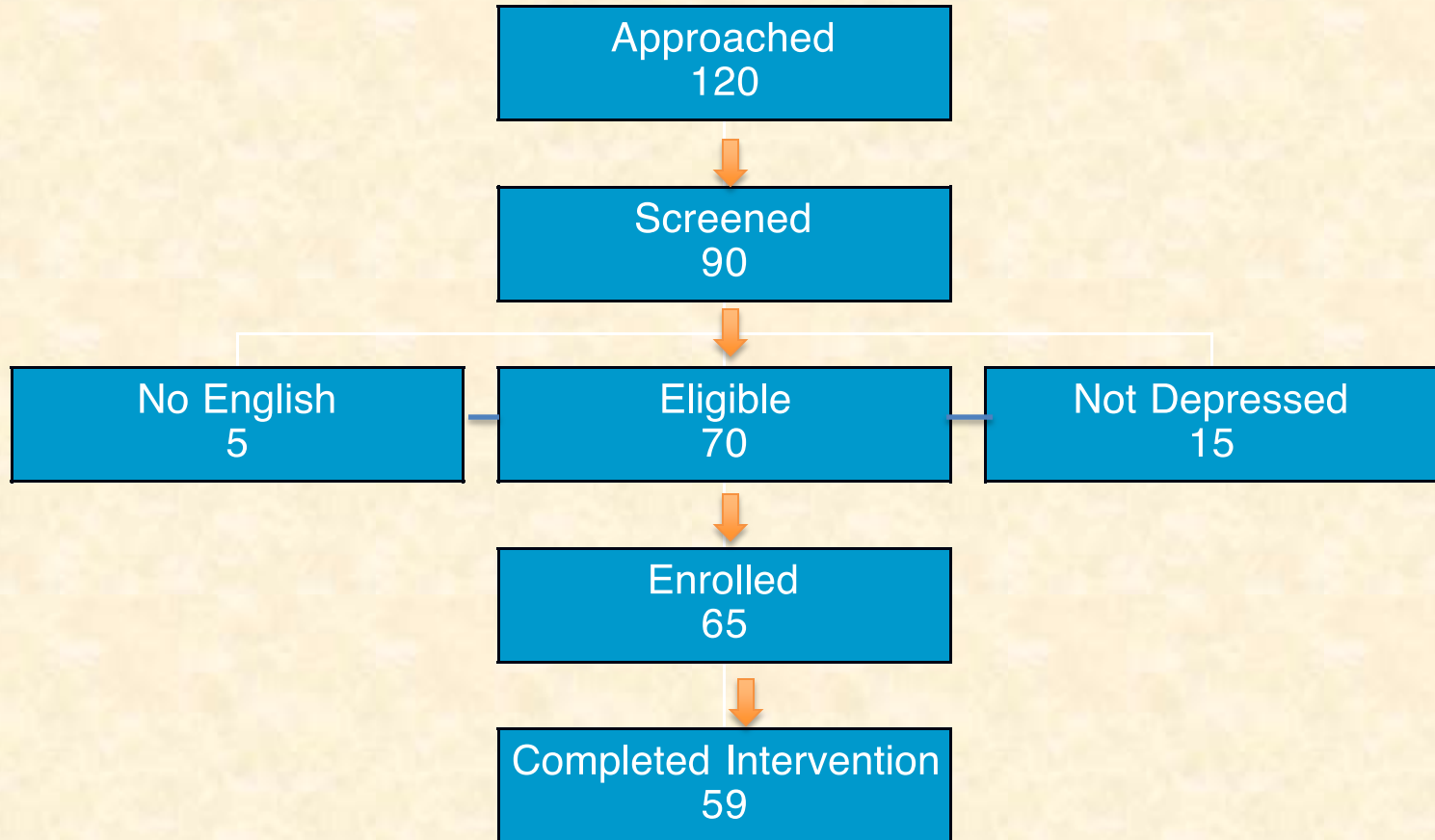
K-23 NIDDK “Cognitive Behavioral Treatment of  
Depression in ESRD Patients on Dialysis” 2007-2012.

# Study Design

Random Assignment

Baseline	3 Months	Assessment 2	3 Months	Assessment 3
Demographics <sup>1</sup>	<u>Group A</u> Intervention (10 sessions Of CBT)	Psychological Measures <sup>2</sup>	<u>Group A</u> No intervention	Psychological Measures <sup>2</sup>
Psychological Measures <sup>2</sup>	<u>Group B</u> Wait-list	Medical Ratings <sup>3</sup>	<u>Group B</u> Intervention (10 sessions Of CBT)	Medical Ratings <sup>3</sup>
Medical Ratings <sup>3</sup>				

# Patient Flow



# Baseline Demographic Information (N=65)

Gender	65% women
Self-Identified Race	94% Afro/Caribbean American
U.S. Born	28%
Transplant History	14%
Dialysis Vintage	50 ± 31 months
Serious Comorbidity	94%

# Baseline Medical Information (N=65)

Referent

Diabetes	30%	8.3% in US
Hypertension	68%	24% in US
URR	$71 \pm 11$	Goal > 70
Serum Albumin	$4.0 \pm .36$	Goal > 4
Calcium phosphate	$54.8 \pm 17.5$	Goal <55
Mini-mental	$27.6 \pm 2.3$	Intact >25

# Baseline Psychiatric Information (N=65)

Any SCID Axis I	68%	
SCID MDD	55%	
Any SCID Axis II	50%	
Beck - Depression	23.3 ± 9.6	Moderate
Hamilton - Depression	15.2 ± 6.4	Low Moderate
Beck - Anxiety	14.4 ± 11.2	Mild
Quality of Life	101.6 ± 26.0	Poor (average for hemo samples)

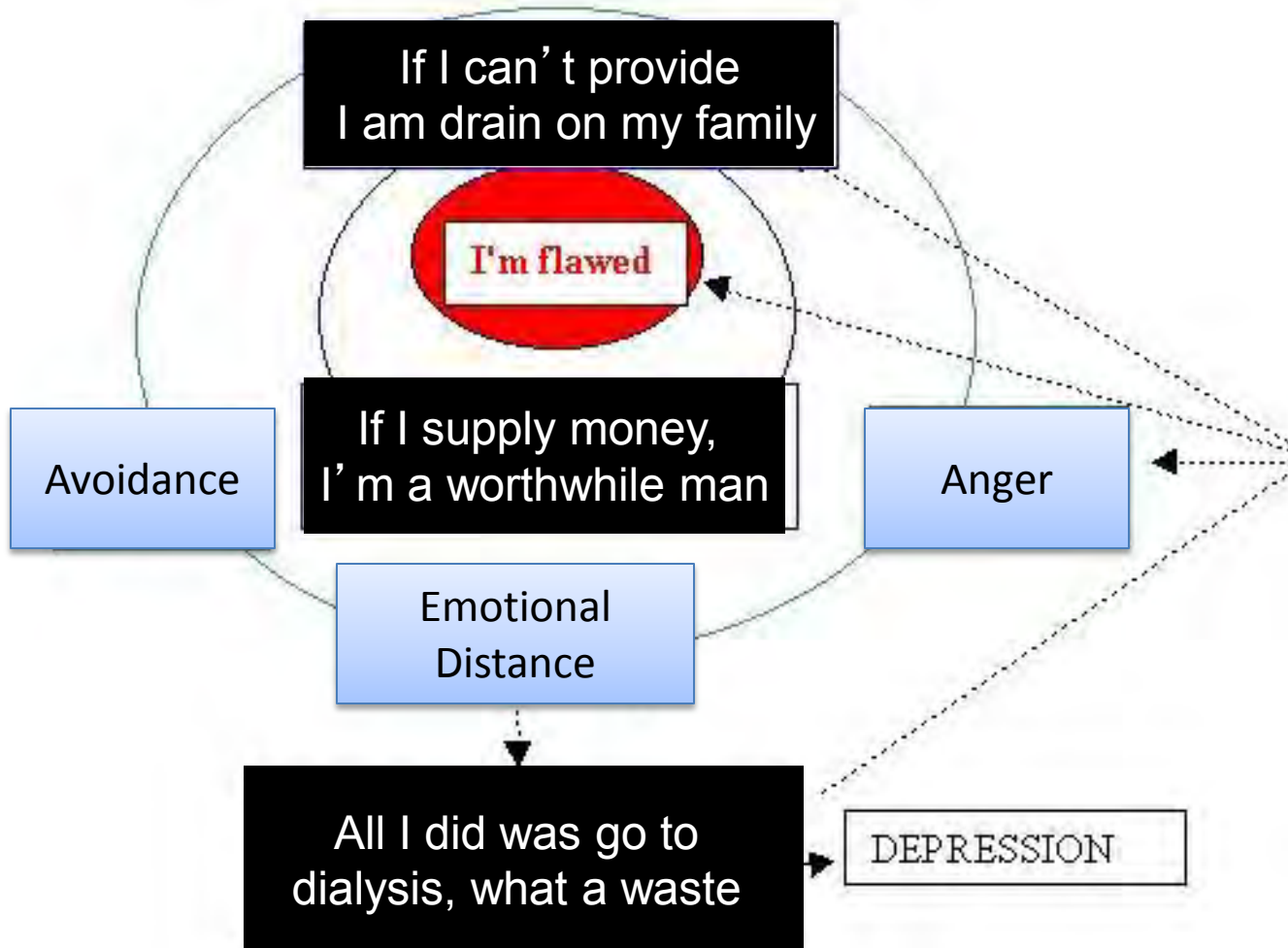


# CBT Intervention

- Individual
- 10 sessions
- Chair-side
- Homework
- Focused on
  - Psycho-education (Depression vs. Illness)
  - Behavioral Activation (modified for HD)
  - Cognitive Restructuring (modified for HD)

# CBT of Depression in ESRD Patients

Challenging the Depressed Dialysis Patient  
Form 4.3



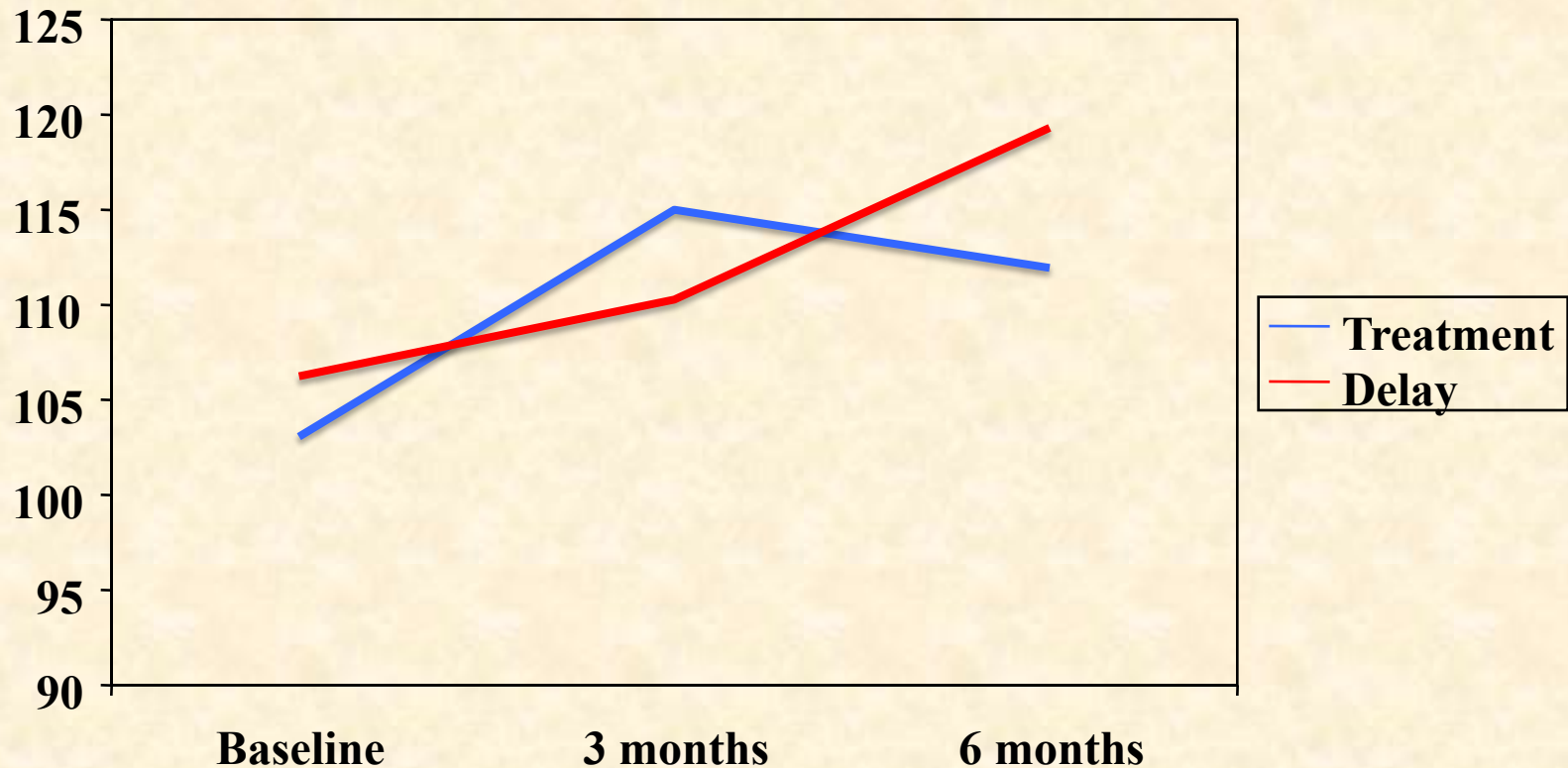
# Hamilton-D ratings pre and post treatment for the treatment (n=31) and control (n=29) groups



Hamilton x time  $F(2) = 15.6, p < .001$

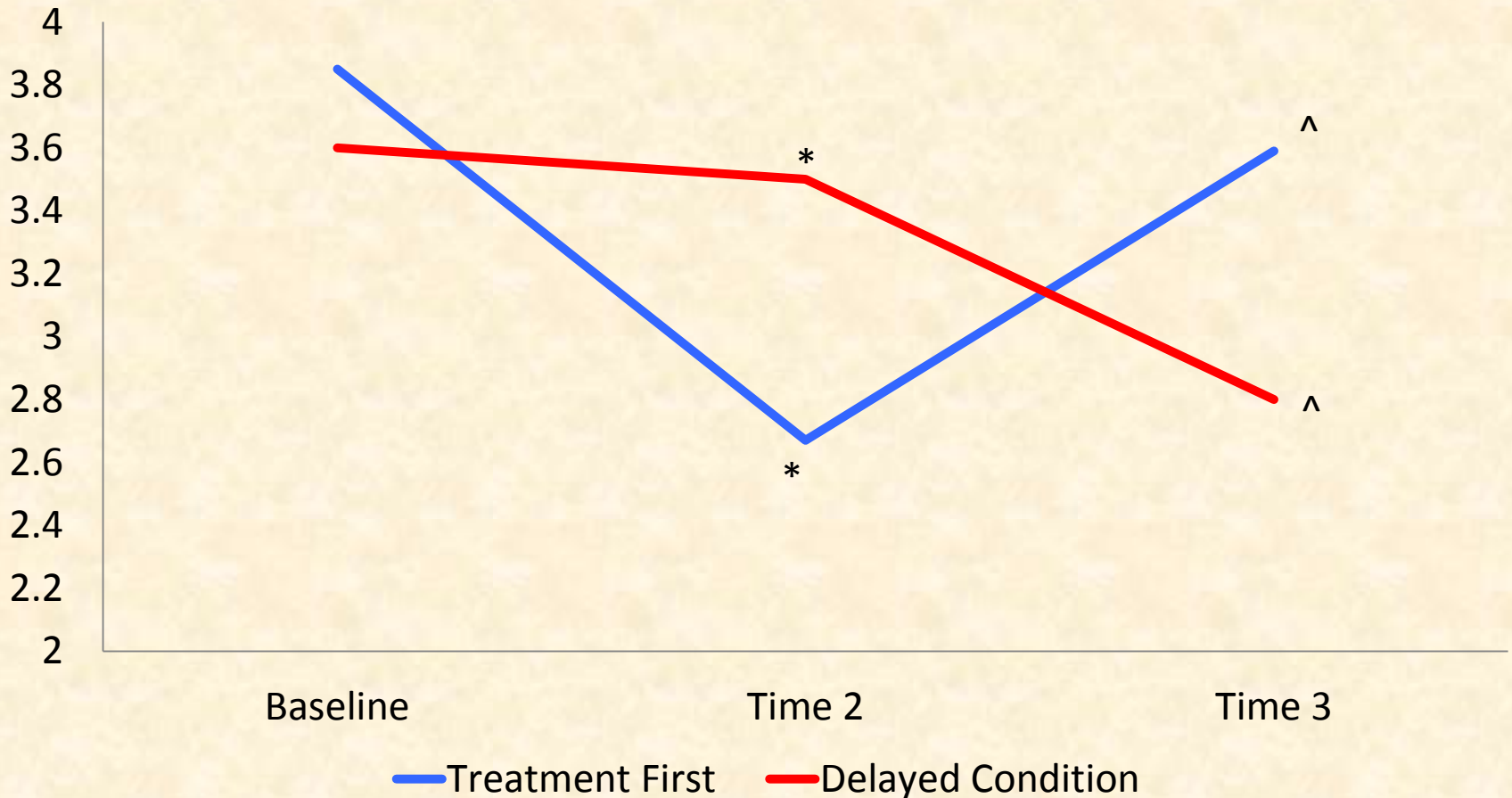
\*  $t(52) = -2.07, p < .05$

# Quality of Life ratings pre and post treatment for the treatment (n=31) and control (n=29) groups



QOL x time  $F(2) = 3.5, p < .05$

# Average Inter-Dialytic Weight Gain (IDWG) for the treatment (n=31) and delayed-control (n=29) groups



IDWG x time  $F(2) = 11.8, p < .01$

\*  $t(52) = -3.07, p < .05$

# Section Summary/Points to take home

- Pharmacotherapy is understudied, but probably effective – cautious approach warranted
- CBT holds promise for depression intervention
- Well-designed clinical trials are needed!
  - Can depression treatment be effectively integrated into dialysis care on a larger scale?
  - Does effective treatment mediate increased morbidity/mortality risk?

**ASCEND:  
A Trial of Sertraline vs. CBT for End-stage  
Renal Disease Patients with Depression**

Treatment Options for Depression in  
Patients Undergoing Hemodialysis

# Study Sites

- Seattle, WA:
- Dallas, TX:
- Albuquerque, NM:



# Conclusions

- Depression is a common comorbidity in ESRD
- Hemodialysis patients should be screened regularly
- Interventions should be made available that reduce barriers to care
- Treating depression is not only good mental health care, but good medical care

**THANK YOU!**