

Depression and Chronic Illness: Focus on CKD & ESRD

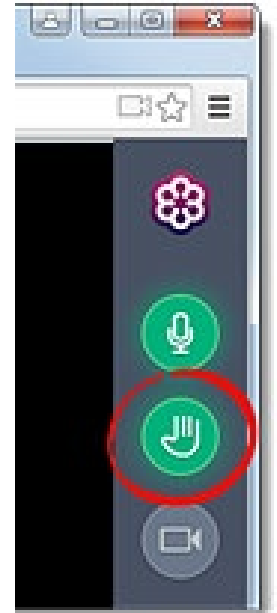
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Welcome

- Thank you all for being part of this call today.
- All phone lines are muted. Please use the raise hand or chat box features to ask questions.
- This session will be recorded





Depression and Chronic illness - Focus on CKD & ESRD



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Objectives

- To identify the association between depression and chronic medical illness
- To discuss the impact of depression in patients with chronic kidney disease (CKD) & end-stage renal disease (ESRD)
- To evaluate treatment interventions in patients with depression and CKD & ESRD

Major Depressive Disorder

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
- Note: Do not include symptoms that are clearly attributable to another medical condition
- PLUS four of the following symptoms:
 - Insomnia or hypersomnia nearly every day
 - Psychomotor retardation or agitation (observable by others)
 - Poor appetite and weight loss, or increased appetite and weight gain (a change of >5% of body weight in a month)
 - Fatigue or loss of energy nearly every day
 - Feelings of worthlessness or excessive or inappropriate guilt
 - Diminished ability to think or concentrate, or indecisiveness
 - Recurrent thoughts of death or suicide
- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the physiological effects of a substance or another medical condition.

Prevalence Of Major Depression

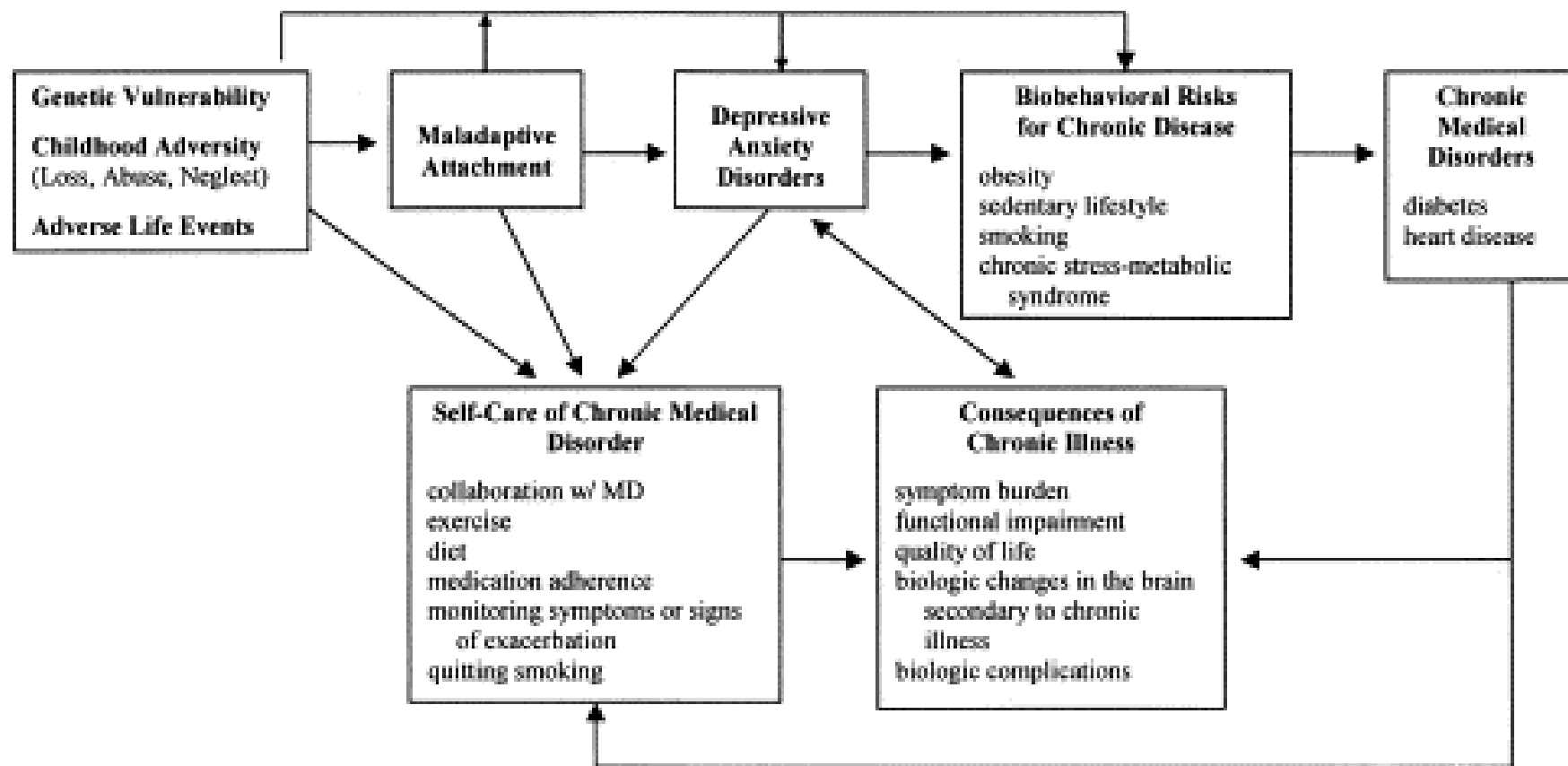
- General population: 8.1 % (lifetime – 17%)
- Heart disease 15% to 23%
- Diabetes: 11% to 15%
- HIV: 4% to 23%
- CKD: 21%; ESRD: 20% - 25%
- Stroke: 9% -31%
- Parkinson's disease: 20% -30%
- Multiple sclerosis: 16%-30%



Possible Causes Of Increased Prevalence Of Major Depression In Chronic Illnesses

- Secondary psychological reaction to the development of the disease;
- Secondary to the complications or aversive symptoms of that disease;
- Secondary to the side effects from medication used to treat these illnesses;
- Direct pathophysiologic effect on the brain (i.e., stroke, or multiple sclerosis)
- Indirect physiologic effects (i.e., increasing cytokine levels or other inflammatory factors that affect the brain)

A Conceptual Model Of Interaction Between Major Depression And Medical Illness



Depression and Chronic Medical Illness

- Amplifies physical symptoms associated with medical illness
- Comorbidity increases impairment in functioning
- Decreases adherence to prescribed regimens
- Adverse health behaviors (diet, exercise, smoking)
- Increases mortality



Relationship Of Depression To Physical Symptom Perception

- Interferes with adaptation to chronic aversive disease symptoms and is associated with heightened awareness and focus on symptoms
- DM: Depressive symptoms significantly correlate with 9 - 11 symptoms traditionally associated with poor glucose control (e.g., polyuria, polydipsia)
- Hepatitis C: Higher depressive symptom severity correlates with impairment from the symptoms of fatigue
- CAD: More symptomatic reports of chest pain and fatigue

Depression And Functional Impairment

- Additive functional impairment
- More work lost days and cut-back days
- Additive disability
- Decrements in Quality-Adjusted Life Years
- Independently predicts increased rate of functional decline in patients ≥ 65 yrs of age
- Predictive of functional impairment over time then is severity of physical illness

Medical Utilization And Costs

- Increased medical costs in depressed elderly patients.
- Total ambulatory costs were 43% to 52% higher and total ambulatory and inpatient costs were 47% to 51% higher in depressed compared with non-depressed elderly patients after adjustment for chronic medical illness.
- More primary care appointments and medications
- Longer length of stay
- Increased cardiac rehospitalization rate

Increased Cardiac Risk & Mortality

- Increased risk of death from cardiovascular disease, especially in men

Possible mechanisms:

- Decreased heart rate variability
- Increased platelet aggregation
- Higher levels of inflammatory risk markers (C-reactive protein and interleukin-6)
- Decreased adherence to lifestyle changes, such as exercising, quitting smoking, and taking medications.

Impact Of Depression In Patients With CKD And ESRD

Chronic Kidney Disease To End-stage Renal Disease

- CKD – slight decrease in kidney function to severe decrements leading to uremia
- Uremia - lack of appetite, dysgeusia, nausea and vomiting, fatigue, lack of interest, somnolence, delirium, seizures
- ESRD/ESKD - worse medical outcomes- autonomic dysregulation and behavior non adherence

Chronic kidney disease classification based upon glomerular filtration rate and albuminuria

| GFR stages | GFR (mL/min/1.73 m ²) | Terms |
|--------------------|-----------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|
| G1 | ≥90 | Normal or high |
| G2 | 60 to 89 | Mildly decreased |
| G3a | 45 to 59 | Mildly to moderately decreased |
| G3b | 30 to 44 | Moderately to severely decreased |
| G4 | 15 to 29 | Severely decreased |
| G5 | <15 | Kidney failure (add D if treated by dialysis) |
| Albuminuria stages | AER (mg/day) | Terms |
| A1 | <30 | Normal to mildly increased (may be subdivided for risk prediction) |
| A2 | 30 to 300 | Moderately increased |
| A3 | >300 | Severely increased (may be subdivided into nephrotic and non-nephrotic for differential diagnosis, management, and risk prediction) |

The cause of CKD is also included in the KDIGO revised classification but is not included in this table.

GFR: glomerular filtration rate; AER: albumin excretion rate; CKD: chronic kidney disease; KDIGO: Kidney Disease Improving Global Outcomes.

Data from:

1. KDIGO. Summary of recommendation statements. *Kidney Int* 2013; 3 (Suppl):5.
2. National Kidney Foundation. *K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification*. *Am J Kidney Dis* 2002; 39 (Suppl 1):S1.

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Depression Scales Cut Off

- Patient health questionnaire (PHQ-9):10
- Beck depression inventory (BDI):14 to16
- Center for epidemiologic studies depression Scale (CESD):18
- Cutoff score is higher than in general population





Prevalence Of Depression In CKD And ESRD

- 3-4 times higher than the general population & 2-3 times higher than other chronic illnesses.
- Pt. who screen positive for depression should be referred to a qualified professional to confirm the diagnosis with the clinical interview
- ESRD receiving dialysis: Prevalence - 39% (screening questionnaires) & **23%** (clinical interview)
- CKD: Prevalence - 27% (screening questionnaires) & **21%** (clinical interview)
- Minorities – higher rates (black, Hispanic) - less likely to use antidepressants. Some studies had mixed results

Depression And Outcomes In CKD

- **Adverse medical outcomes** –
 - Hospitalizations
 - Acute kidney injury
 - Faster rate of decline in eGFR
 - ESRD
 - Mortality
- **Adverse psychosocial outcomes** -
 - Poor quality of life
 - Poor social support
 - Sexual dysfunction

Depression And Outcomes In ESRD

- Fatigue, poor sleep quality, pain, pruritus, sexual dysfunction
- Poor psychosocial outcomes, lower quality of life
- Increased ED visits, hospitalizations, and, accumulated hospital days
- Higher cardiovascular events, peritonitis and withdrawal from dialysis and suicide
- 1.5 times increased mortality in patients on dialysis (independent of confounding factors)

Risk Factors For Depression

| Patients with ESRD | |
|--------------------------------|---------------------------------------------------------|
| Younger age | Longer duration of dialysis |
| Female | Diabetes, CAD |
| White race | Cerebrovascular disease and peripheral vascular disease |
| | |
| Patients with CKD | |
| Younger age | Lower family income, unemployment |
| Female | Hypertension |
| Black race, Hispanic ethnicity | Smoking status |
| Lower education | Diabetes, CAD |

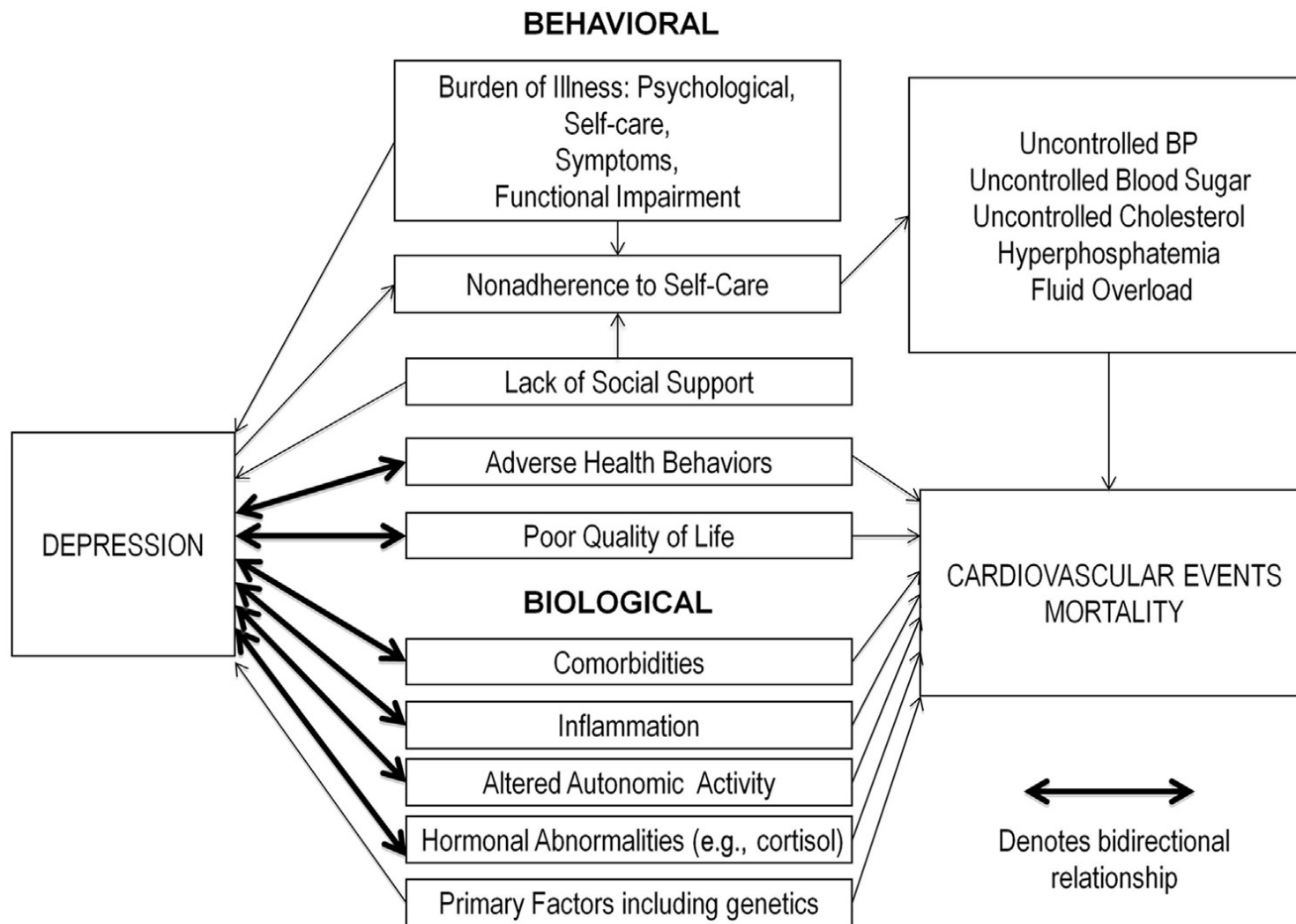


Depression And Coping In Adults Undergoing Dialysis For ESRD

- A cross-sectional study conducted at several dialysis centers in Malaysia
- The Beck Depression Inventory II (BDI-II) and the Brief COPE scale were used to measure depression and coping skill, respectively
- 274 ESRD patients - 183 hemodialysis and 91 continuous ambulatory peritoneal dialysis patients
- **Behavioral disengagement** and **self-blame** were identified as predictors for depression
- Better outcomes - Good interpersonal and treatment control, and greater understanding of their illness

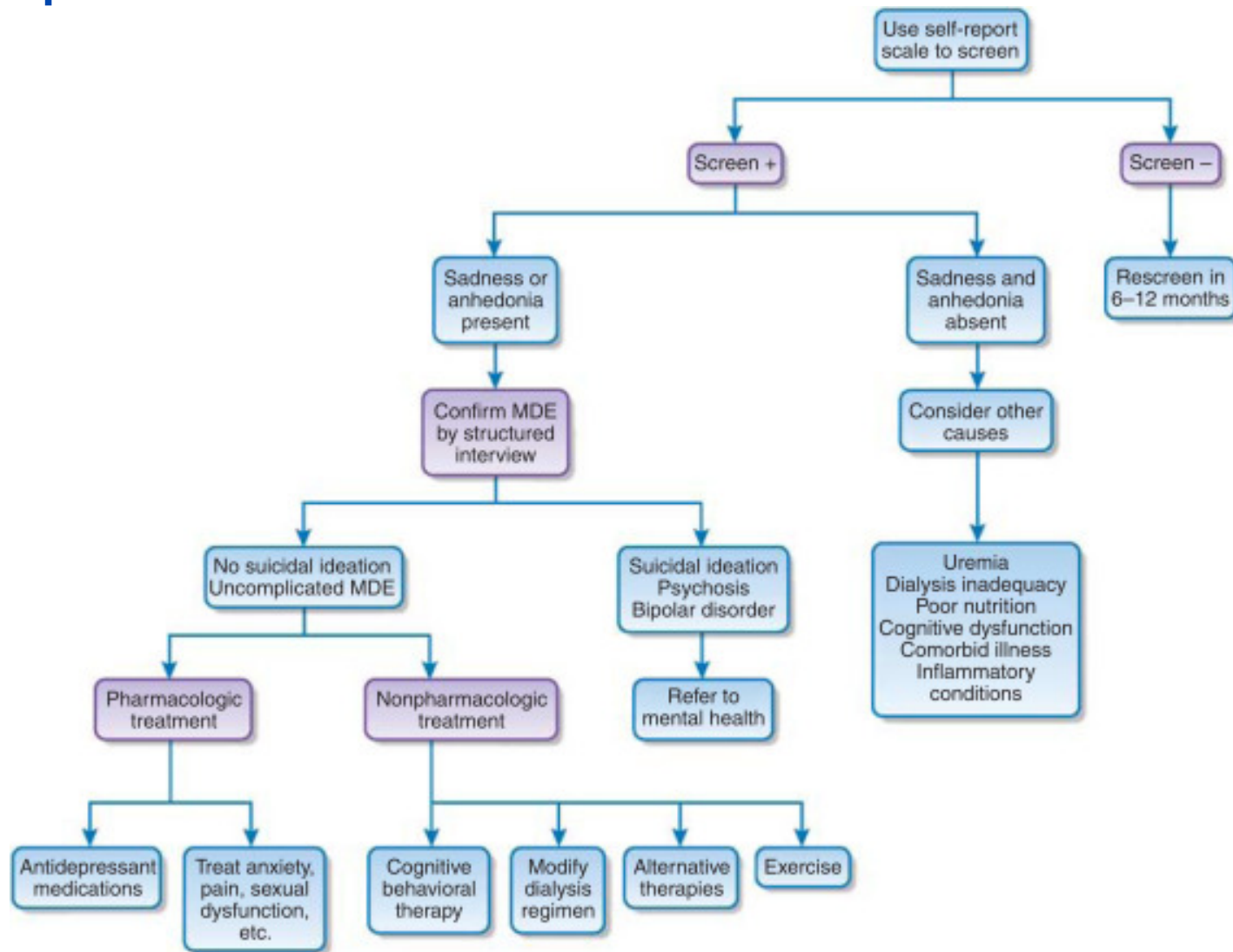
Ibrahim et al. Depression and coping in adults undergoing dialysis for ESRD. Asia Pac Psychiatry. 2013:35-40.

Mechanisms Of Depression And Adverse Medical Outcomes



Treatment Interventions In Patients With Depression And CKD/ESRD

Proposed Algorithm For Management Of Depression In Patients With CKD & ESRD





Treatment Of Depression

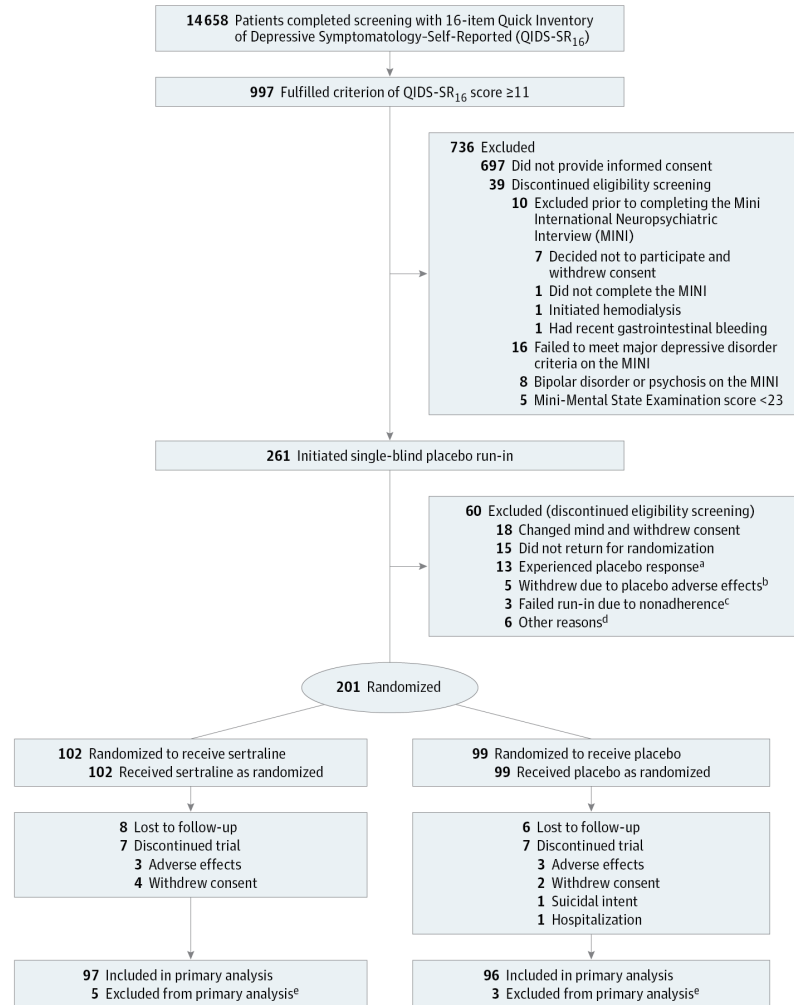
- Combination of antidepressant and psychotherapy has been shown to be more effective in chronic illnesses
- Collaborative care models have shown consisted improvement in medical outcome
- Limited studies in patients with CKD/ESRD
- Undertreated in both patients with CKD & ESRD
- 31% -35% received antidepressant medications



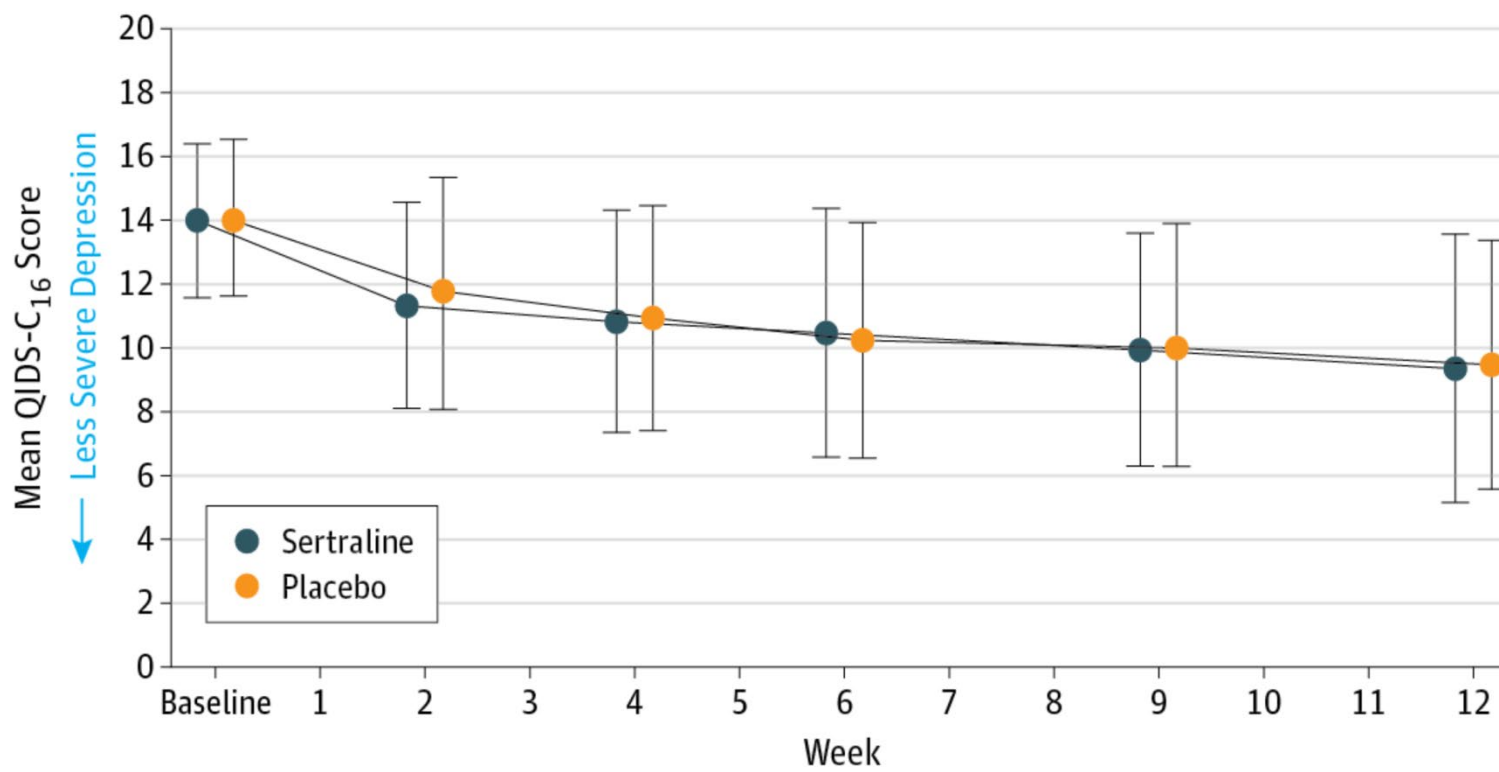
Antidepressants

- In ESRD – data is sparse & inconclusive
- Monitor closely for side effects and drug interactions.
- Fluoxetine, Citalopram, Paroxetine, sertraline
- Venlafaxine, duloxetine, mirtazapine, bupropion
- dose reduction is recommended
- Meta-analysis showed SSRI significantly improved depressive symptoms – 1st line.
- Ongoing RCTs

Patient Enrollment In The Chronic Kidney Disease Antidepressant Sertraline Trial (CAST)



Effect Of Sertraline On Depressive Symptoms In Patients With CKD Without Dialysis Dependence: The CAST Randomized Clinical Trial



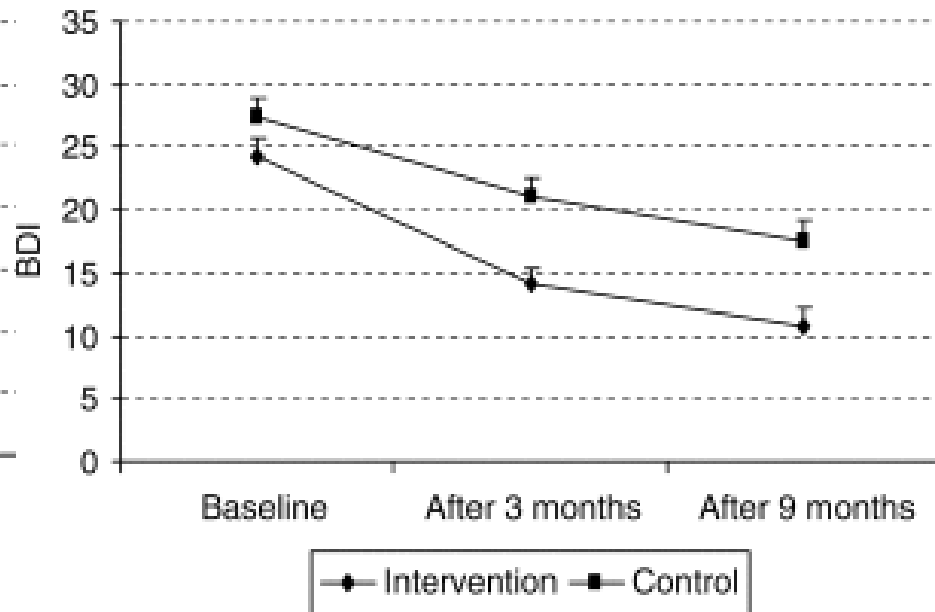
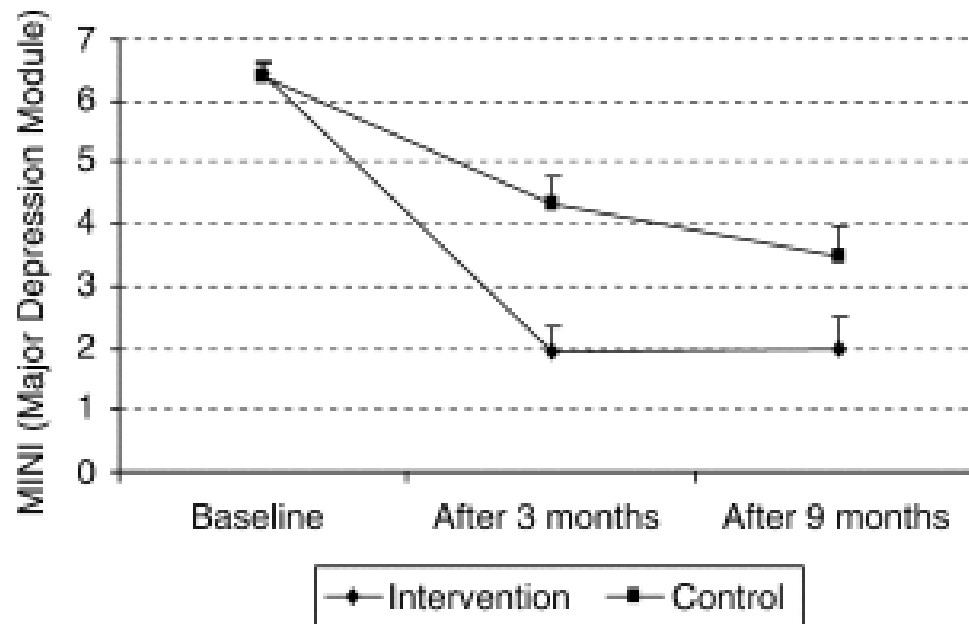
No. of participants

| | | | | | | |
|------------|----|----|----|----|----|----|
| Sertraline | 97 | 95 | 87 | 83 | 81 | 81 |
| Placebo | 96 | 94 | 91 | 88 | 81 | 81 |

Nonpharmacological Interventions

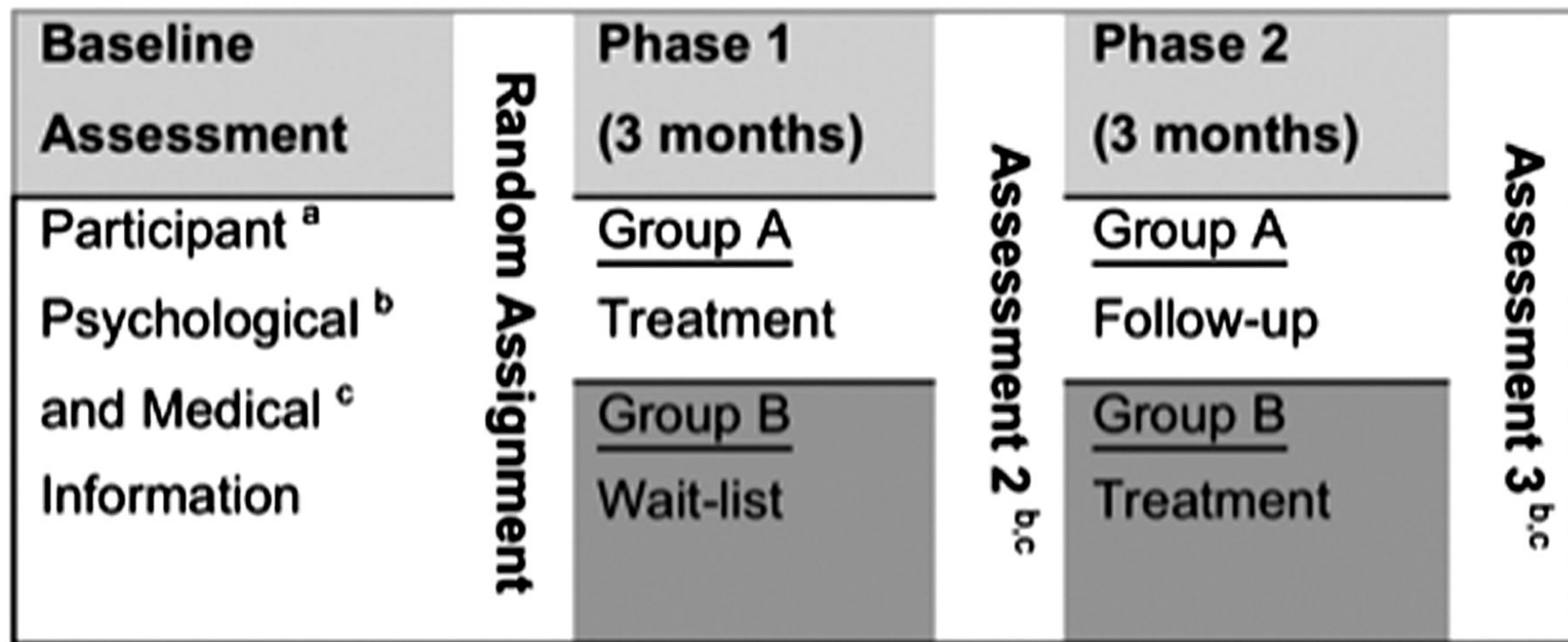
- **Cognitive behavior therapy -**
 - Designed to treat dysfunctional cognition, negative emotions, and maladaptive behaviors
- Several studies have shown an improvement of depressive symptoms with its use
- Significantly improved depressive symptoms and quality of life
- Improved sleep quality, inflammation adherence to fluid restrictions in patient with ESRD

Effectiveness Of CBT In Chronic Hemodialysis Patients Diagnosed With Major Depression



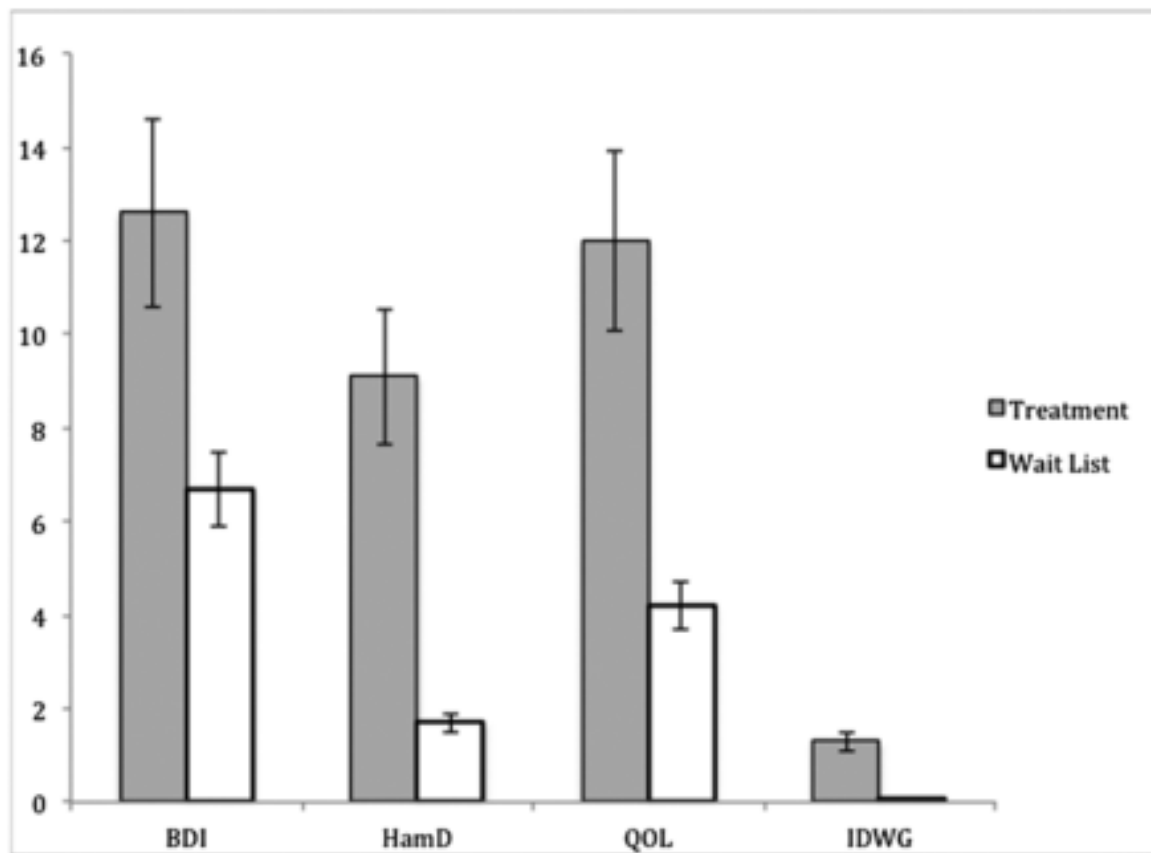
Duarte et al. Cognitive-behavioral group therapy is an effective treatment for major depression in hemodialysis patients. *Kidney Int.* 2009;76(4):414-21

Crossover Study Design To Study Depression In HD Patients With Elevated Depressive Affect



Cukor et al. Psychosocial intervention improves depression, quality of life, and fluid adherence in hemodialysis. J Am Soc Nephrol. 2014 ;25(1):196-206.

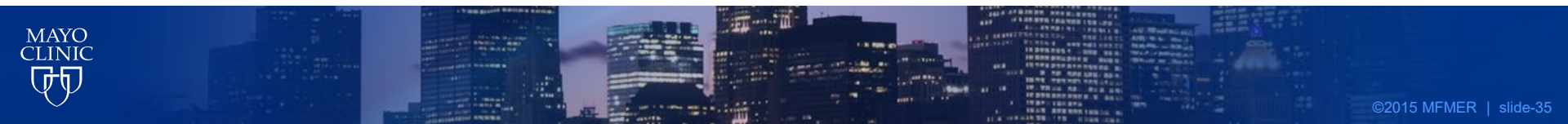
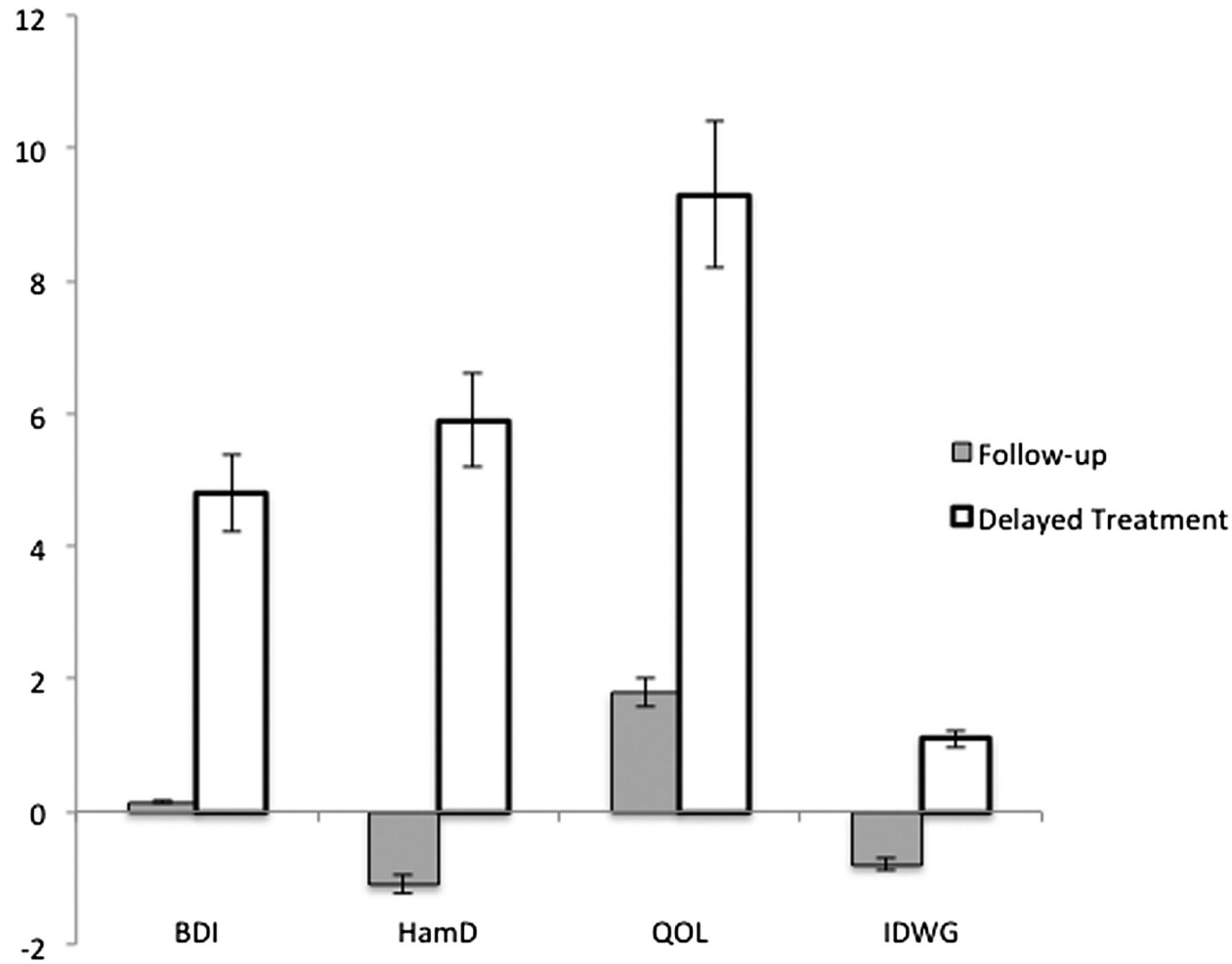
Model-adjusted Mean Change For The Treatment And Wait-list Groups In Phase 1



Cukor et al. Psychosocial intervention improves depression, quality of life, and fluid adherence in hemodialysis. J Am Soc Nephrol. 2014 ;25(1):196-206.



Model-adjusted Mean Change For The Treatment And Wait-list Groups In Phase 2



Results

- 89% in the treatment-first group were not depressed at the end of treatment compared with 38% in the wait-list group (P=0.01).
- The treatment-first group experienced greater improvements in **quality of life**, and interdialytic weight gain than the wait-list group.

Exercise Therapy

- Recent review showed exercise improve depressive symptoms
- ***Aerobic exercise*** – MC training in HD patients

Intradialytic - indoor stationary bicycle

Interdialytic - walking, mild jogging to cycling

- 35 % improvement in depression after 6 months of aerobic exercise on non dialysis days
- Home-based exercise training improved outcomes



Resistance Exercise Training

- Improved various health-related measures such as muscle and body composition and quality of life.
- Limited evidence regarding aspects related to mental health and depression
- One small study (8 HD patients) showed improvement in mental component of SF36 questionnaire



Recommendations For Exercise Training

- Minimum program length of 6 months with at least 35 min per exercise session to attain significant improvement in psychological –related parameters
- Interruptions for long periods of time will likely cause benefits to be lost.
- Intradialytic exercise is optimal, has low drop-out rates

Mitrou et al. Exercise training and depression in ESRD: a review. *Semin Dial.* 2013;26 (5):604-13

Barriers To Treatment

- Already high medication burden
- Unwillingness to follow certain recommendations such as home exercise
- Nephrologists often do not start therapy for depression – 82% believe its PCP's responsibility
- Non availability of resources - especially for combined behavioral and medical intervention

Future ?

- Need for cognitive behavior strategies integrated with CKD education
- Collaborative care model
- Patient-centered outcomes in clinical kidney research
- RCTs studying various treatment modalities

References

- Hedayati et al. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. *Kidney Int.* 2012;81:247-55.
- Hedayati et al. Prevalence of major depressive episode in CKD. *Am J Kidney Dis.* 2009;54(3):424-32
- Katon WJ. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biol Psychiatry.* 2003;54(3):216-26.
- Yu et al. Associations between depressive symptoms and incident ESRD in a diabetic cohort. *Clin J Am Soc Nephrol.* 2014;9(5):920-8
- Palmer et al. Antidepressants for treating depression in adults with end-stage kidney disease treated with dialysis. *Cochrane Database Syst Rev.* 2016 May
- Barcellos et al. Effects of exercise in the whole spectrum of chronic kidney disease: a systematic review. *Clin Kidney J.* 2015;8:753–765.
- Mitrou et al. Exercise training and depression in ESRD: a review. *Semin Dial.* 2013;26 (5):604-13
- Shirazian et al. Depression in Chronic Kidney Disease and End-Stage Renal Disease: Similarities and Differences in Diagnosis, Epidemiology, and Management. *Kidney Int Rep (2017) 2*, 94–107
- Duarte et al. Cognitive-behavioral group therapy is an effective treatment for major depression in hemodialysis patients. *Kidney Int.* 2009;76(4):414-21
- Cukor et al. Psychosocial intervention improves depression, quality of life, and fluid adherence in hemodialysis. *J Am Soc Nephrol.* 2014 ;25(1):196-206.
- Ibrahim et al. Depression and coping in adults undergoing dialysis for end-stage renal disease. *Asia Pac Psychiatry.* 2013:35-40.



Questions?

