

Major Depressive Disorder in Chronic Kidney Disease

© 2019 Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD

September 2019 MRC2.CORP.D.00453



This program is paid for by Otsuka Pharmaceutical Development & Commercialization, Inc.

Speakers are paid consultants for Otsuka Pharmaceutical Development & Commercialization, Inc.

Objectives

- Overview of Major depressive disorder (MDD) and Chronic kidney disease (CKD)/End Stage Renal Disease (ESRD).
- Discuss the high prevalence of depression in patients with CKD.
- Discuss how overlap of symptomatology between MDD and CKD makes diagnosing depression in the setting of CKD challenging.
- Discuss the association of MDD with poor outcomes in CKD.
- Discuss potential risk factors and mechanism of MDD in CKD.
- Discuss the cycle between MDD and ESRD.
- Address challenges in MDD management considerations in CKD patients.



Major Depressive Disorder (MDD)

- Persistent feelings of sadness and hopelessness and lose of interest in activities they once enjoyed⁵.
- Depression is the most common diagnosis among patients seen by psychiatrists in the US¹.
- MDD is a serious, chronic, disabling illness affecting more than 350 million people worldwide².
- MDD results in a substantial burden of disease to both the individual and society
 - 4th leading cause of disability worldwide³.
 - By 2020 will be second leading cause³.
- Residual symptoms are common and cause significant psychosocial and occupational functional impairment⁴.

Affects approximately 8% of American adults in a given year¹

1..Duffy FF et al. *Psychiatr Serv*. 2008;59(10):1148-1154 2. World Health Organization. *Fact Sheet on Depression*. (2012) http://www.who.int/mediacentre/factsheets/fs369/en/index.html 3. Kessler RC. *Psychiatr Clin North Am*. 2012;35(1):1-14 4. Zimmerman M et al. *Compr Psychiatry*. 2007;48(2):113-117. 5. <u>https://www.psycom.net/depression-definition-dsm-5-diagnostic-criteria/</u>





Stages of CKD

- Chronic kidney disease (CKD) is defined as the presence of kidney damage that persists for more than 3 months¹.
- CKD is subdivided into five stages according to glomerular filtration rate (GFR) category^{1,2}.



Table and figure adapted from National Kidney Foundation Website²

1. Thomas R et al. Prim Care. 2008; 35(2): 329-vii. 2.. National Kidney Foundation. The Facts about Chronic Kidney Diseases. 2019 https://www.kidney.org/atoz/content/about-chronic-kidney-disease.



CKD Patient Journey



McCarley P. Patient Empowerment and Motivational Interviewing: Engaging Patients to Self-Manage Their Own Care. Nephr Nurs J. 2009;36:409-413.



Introduction: Facts about MDD in CKD



MDD, major depressive disorder; CKD, chronic kidney disease; ESRD; end stage renal disease;

1. Amira O. Niger J Cin Pract. 2011;14(4):460-3. 2. Palmer S et al. Kidney Int. 2013;84(1):179-91. 3. Teles F et al. Clinics (Sao Paulo). 2014;69(3):198-202. 4. Bautovich A et al. Aust N Z J Psychiaty. 2014;48(6):530-41.



Depression in CKD: Prevalence

- Depression is common in patients with chronic physical health problems¹.
- The prevalence of depression in CKD has been reported to be greater than the depression rates seen in the general population and in other chronic diseases, except for chronic obstructive airways disease (COAD)².



CKD, chronic kidney disease

1. Bautovich A et al. Aust N Z J Psychiaty. 2014 ;48(6):530-41. 2. Palmer S et al. Kidney Int. 2013 ;84(1):179-91.



Depression and CKD: Symptom Overlap



CKD, chronic kidney disease

1. Shirazian S et al., *Kidney Int Rep* 2017: 2, 94-107. 2. https://www.aafp.org/news/health-of-the-public/20180219nchsdepression.html 3. https://www.kidney.org/news/one-seven-american-adults-estimated-to-have-chronic-kidney-disease 4. https://unckidneycenter.org/files/2017/10/commonsymptoms_ckd.pdf 5. https://www.mayoclinic.org/diseases-conditions/depression/symptoms-causes/syc-20356007



Depression in CKD: Mechanisms

- Depression seen in CKD patients can be caused by reaction to the diagnosis and treatment, natural course of the disease as well as the losses experienced¹.
- Studies suggest that the mechanism of depression in CKD, similarly to other chronic diseases, can be divided into **behavioral** and **biological** mechanisms^{2,3}.
- Different mechanisms of depression affect CKD and ESRD patients^{2,3}.



CKD, chronic kidney disease; ESRD; end stage renal disease;

1. Thomas R et al. JDMS. 2014; Vol 13, Issue 9 : 19-22 2. Shirazian S. Kidney Int Rep. 2019; 4:189–190. 3.. Shirazian et al. Kidney Int Rep. 2017; 2(1): 94–107



Depression in CKD: Risk Factors

- In CKD, risk factors for depression include¹:
 - Younger age
 - Female
 - Non-white race/ethnicity
 - Lower household income
 - Presence of comorbid conditions (lower eGFR and proteinuria > 1 g/g)
- In End-Stage Renal Disease (ESRD), coping with the long-term nature of renal replacement therapy may lead to depression. Other factors that predispose patients to developing depression include²:
 - Loss of a primary role in their occupation or family
 - Decreased physical and/or sexual function
 - Decline in cognitive skills

CKD, chronic kidney disease; $\,$ eGFR, estimated glomerular filtration rate $\,$

1.. Shirazian S. Kidney Int Rep. 2019; 4:189–190 2. Cohen SD et al, Clin J Am Soc Nephrol. 2007; 2: 1332–1342.



MDD in CKD: Association with Poor Outcomes

- Depression is associated with an increased risk for adverse clinical outcomes and poor health in patients with CKD^{1,2}.
- Depressive symptoms such as low motivation, impaired concentration, and apathy can significantly affect treatment adherence of patients in ESRD³.
- Decrease in treatment compliance is one of the potential pathways through which depression may affect mortality and morbidity in patients with late stage CKD³.
- Depression, more so than clinical and sociodemographic variables taken together, has been shown to negatively impact health related quality of life in CKD patients⁴.



MDD, major depressive disorder; CKD, chronic kidney disease; ESRD; end stage renal disease;

1. Finkelstein F O et al. *Kidney Int.* 2008; 74: 843–845 2. Palmer S et al. *Kidney Int* .2013 ;84(1):179-91 3. Asher D R et al. 2012. *Hemodial Int.* 2012; 16(3): 387–393 4. Bautovich A et al. *Aust N Z J Psychiaty*. 2014 ;48(6):530-41.



Cycle Between Depression and ESRD

- The interactions between depression and CKD are dynamic and multifactorial¹.
- Depression possibly affects medical outcomes in ESRD patients through².
 - Modification of immunologic and stress responses .
 - Impact on nutritional status.
 - Reduction of compliance access to, prescribed dialysis and medical regimens.



Figure adapted from Cukor D et al ²

CKD, chronic kidney disease; ESRD; end stage renal disease;

;

1. Bautovich A et al. Aust N Z J Psychiaty. 2014 ;48(6):530-41 2. Cukor D. et. al., J Am Soc Nephrol, 2007: 18, 3042-3055.



Depression in CKD: Challenges in Diagnosis

Several factors make the diagnosis of depression in CKD challenging. The barriers to diagnosis include: patient factors, physician factors, and issues related to syndromal diagnosis ¹.

Patient Factors ¹	Physician Factors ¹	Issues Related to Syndromal Diagnosis ¹
 Denial of their illness Unwillingness to consider antidepressant medication Stigma associated with a mental illness 	 Frequently do not inquire about the symptoms of depression Perceived lack of time for busy nephrologists to perform formal psychiatric evaluations 	 Depressive symptoms can overlap with complications of uremia, as well as with other medical and psychiatric disorders

CKD, chronic kidney disease

1. Cohen SD et al, Clin J Am Soc Nephrol. 2007; 2: 1332-1342.



MDD in CKD: Screening and Management

Conservative Approach¹

 Screen only patients with signs of depression

Aggressive Approach¹

• Screen all new CKD or ESRD patients periodically (every 6 months to 1 year)

- There are pharmacological and non-pharmacological approaches available for the management of depression in CKD².
- A combination of pharmacological and nonpharmacological treatments has been shown to be more effective than either alone¹.
- Pharmacokinetics, drug-to-drug interactions and adverse event profile will impact the decision on which antidepressant to use².
- Examples of non-pharmacological treatments include electroconvulsive therapy, cognitive behavioral therapy (CBT), exercise therapy and changes to the dialysis regimen².
- There is limited evidence to suggest that treatment of MDD is efficacious or that treatment changes clinical outcomes in patients with CKD³.

MDD, major depressive disorder; CKD, chronic kidney disease; ESRD; end stage renal disease;

1. Shirazian S et. al., Kidney Int Rep, 2017: 2, 94-107. 2. Bautovich A et al. Aust N Z J Psychiaty.. 2014;48(6):530-41. 3. Hedayati,, SS and Finkelstein, FO. Am J Kidney Dis. 2009; 54(4): 741–752.



MDD in CKD: Barriers to Treatment

There are several barriers to treatment in patients with depression and CKD or ESRD¹.



MDD, major depressive disorder; CKD, chronic kidney disease; ESRD; end stage renal disease;

1. Shirazian S et. al., Kidney Int Rep, 2017: 2, 94-107 2. Bautovich A et al. Aust N Z J Psychiaty. 2014;48(6):530-41.



Summary



MDD, major depressive disorder; CKD, chronic kidney disease; ESRD; end stage renal disease;

17

1. Shirazian et al. *Kidney Int Rep.* 2017; 2(1): 94–107 2. Palmer S et al. *Kidney Int*. 2013; 34(1):179-91 3. Shirazian S et al., *Kidney Int Rep*. 2017; 2, 94-107 4. Shirazian S. *Kidney Int Rep*. 2019; 4:189–190 5. Bautovich A et al. *Aust N Z J Psychiaty.*. 2014; 48(6):530-41. 6. Finkelstein FO et al. *Kidney Int*. 2008; 74: 843–845



Conclusion

Given that depression has been associated with poor outcomes in CKD, the identification and appropriate management of depression in those with CKD is extremely important and needs to be given greater priority ¹.





Major Depressive Disorder in Chronic Kidney Disease

© 2019 Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD

September 2019 MRC2.CORP.D.00453