



Improving Awareness & Patient Outcomes

Mental Health in Kidney Transplant Recipients

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Presenters



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Objectives

- Review epidemiology and qualifications requirements of kidney-transplantation
- Understand post-transplant care and lifestyle
- Evaluate outcomes of mental health in kidney-transplant recipients
- Mental health services and resources for kidney-transplant recipients

Overview of Kidney Transplantation

- Patients with end-stage kidney disease have better long-term survival if they are placed on the waiting list and eventually undergo kidney transplantation than those who stay on dialysis¹
- Those who undergo transplantation often experience a better quality of life and a projected survival benefit of 10 years over those who remain on dialysis¹
- In 2022, more than 25,000 kidney transplants were performed in a single year¹
 - Deceased donor kidney transplants increased by 5 percent (19,636 in 2022)
 - 5,863 came from living donors
 - 1,086 of those living donors participated in a Kidney-Paired Donation program
 - 703 patients were under 18 when they received a kidney

1. <https://unos.org/news/in-focus/new-milestone-kidney-donation-and-transplant/>

Kidney Transplant Qualifications

Indications ¹	Contraindications ¹
<p>Most common etiologies of kidney failure:</p> <ul style="list-style-type: none">• Diabetes• Hypertension	<p>Absolute:</p> <ul style="list-style-type: none">• Inability to tolerate surgery due to severe cardiac or pulmonary disease, active malignancy, active infection, active drug abuse, and uncontrolled psychiatric disease
<p>Other causes of CKD/ESKD:</p> <ul style="list-style-type: none">• Prerenal (chronic or acute ischemia)• Intrinsic renal (glomerulonephritis, focal-segmental glomerulosclerosis)• Postrenal categories (reflux nephropathy, obstruction).	<p>Relative: (May vary across centers and regions)</p> <ul style="list-style-type: none">• Morbid obesity with a recommended body mass index (BMI) less than 40 kg/m• History of noncompliance with dialysis schedule or medication regimen• Frailty• psychiatric problems• limited life expectancy (defined as less than the anticipated waiting time for a kidney)

Patients who reach chronic kidney disease (CKD) stage 4, which correlates to an eGFR < 30 mL/min/1.73 m, should be seeing a nephrologist and educated about kidney failure and treatment options, including transplantation¹

1. Abramyan et al. StatPearls Publishing; 2023 Jan

Post Kidney Transplant Immunosuppression

- Maintenance immunosuppressive medication is a long-term treatment to prevent acute rejection and deterioration of graft function¹
- Treatment is started before or at the time of transplantation, and the initial medication may or may not be used with induction therapy¹
- Agents are used in combination to achieve sufficient immunosuppression, while minimizing the toxicity associated with individual agents¹

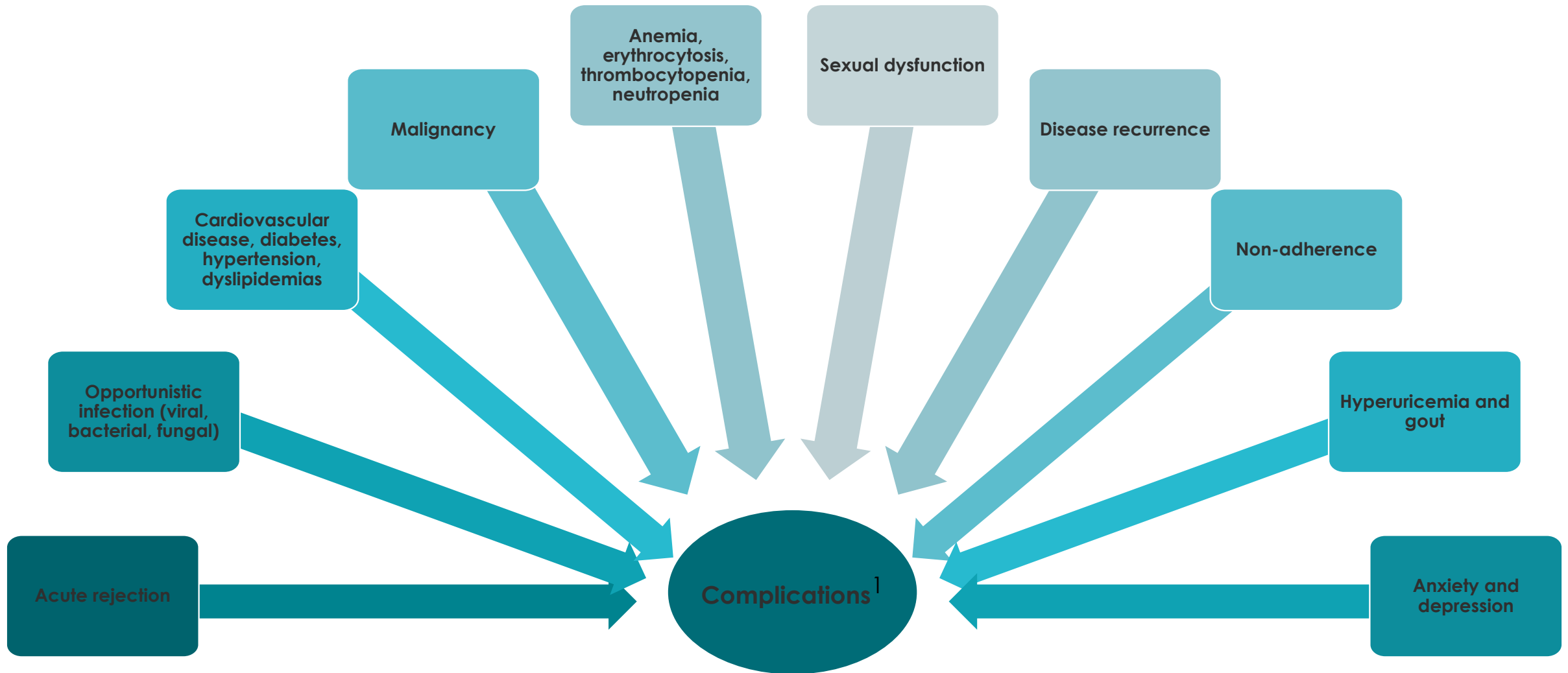
Examples of Adverse Events Associated with Immunosuppressive Medications²

New-onset diabetes mellitus	Delayed wound healing
Dyslipidemias	Diarrhea, nausea/vomiting
Hypertension	Proteinuria
Osteopenia	Decreased GFR
Anemia and leucopenia	

1. American Journal of Transplantation 2009; 9 (Suppl 3): S131–S155;

2. KDOQI US Commentary on the 2009 KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients.

Complications of a kidney transplant



1. KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. Am J Transplant. 2009

Mental health in solid-organ transplantation

Depression and anxiety common in transplant recipients¹

- According to BDI, 22% - 39% of kidney transplant recipients reported depressive symptoms with 10% - 20% expressing moderate – severe depression²

Depression in transplant patients may be associated with:³

- Medication non-adherence
- Sleep disorders
- Poor quality of life

Common Psychosocial Issues in Transplant Recipients and Caregivers⁴

- Emotional highs and lows from corticosteroids
- Stress of post-transplant regimens:
 - Medications
 - Frequent lab monitoring
 - Follow-up evaluations
 - Lifestyle restrictions
- Early complications - - acute graft rejection
- Acceptance of a deceased donor transplant
- Financial concerns of transplant surgery and post-transplant care

1. Dew MA, et al. Transplantation 2015.

2. Dobbels F, et al. AJKD 2008.

3. KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. Am J Transplant. 2009.

4. Terrie YC. US Pharm. 2017.

Depression and anxiety – epidemiology and diagnosis

DSM V Depression Diagnosis¹

- Mood + somatic symptoms for at least 2 weeks¹
- Symptoms must include either:
depressed mood or loss of interest/pleasure
- Symptoms not due to another medical condition

DSM V Anxiety Diagnosis²

- Chronic persistent worry for at least 6 months, with at least 3 of the following 6 symptoms¹:
 - Restlessness
 - Feeling “on-edge”
 - Fatigue
 - Difficulty concentrating
 - Irritability
 - Muscle tension and sleep disturbance
- Defined as anticipation of a future threat¹

Validated Screening Tools¹

- Beck Depression Inventory (BDI)
- Patient Health Questionnaire-9 (PHQ-9)
- Center for Epidemiologic Studies Depression Scale (CES-D)

Types of Anxiety Disorders²

- Generalized anxiety disorder (GAD)
- Specific phobia
- Social anxiety disorder (social phobia)
- Panic disorder
- Agoraphobia

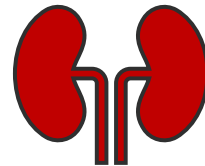
1. King-Wing Ma T, et al. Nephrology. 2016, 2. Cohen SD et al. CJASN. 2016.

Systematic review and meta-analysis of mental health in solid-organ transplant recipients

Determine strength of association of depression and anxiety on transplant mortality and common transplant-related comorbidities¹

Inclusion¹

- Studies published between 1981-2014 in solid-organ transplant recipients
- Evaluated depression or anxiety in relation to any of 8-transplant related outcomes:
 - All-cause mortality
 - Graft loss
 - Death-censored graft loss
 - Acute or chronic graft rejection, cancer
 - Infection
 - Rehospitalization after index hospitalization for transplant



Studies¹

- Majority of studies in heart transplant patients
- 47,800 kidney transplant recipients
- 59% of studies examined depression and 44% both depression and anxiety
- 74% studies utilized standardized diagnostic assessments
 - Structured clinical interview for DSM-III or IV and/or psychometrically validated clinical scales
- Depression and anxiety studied in 24 and 10 studies, respectively

65% greater mortality risk in patients with depression¹

1. Dew MA, et al. Transplantation 2015.

Depressive symptoms and kidney transplant outcomes

Single-center Brazilian study¹

- Evaluated relationship between depression and patient and graft outcomes
- 64 recipients of first successful kidney transplants surveyed over 4 months
- Patients took Beck Depression Inventory
 - ❖ Group 1: BDI \geq 10 (Depressed patients, n = 25)
 - ❖ Group 2: BDI < 10 (Not-depressed patients, n = 39)

Frequency of negative outcomes significantly greater in patients with depression¹

Outcome	Group 1	Group 2
Chronic allograft nephropathy	36% (n=9)	28% (n=11)
Return to dialysis	16% (n = 4)	0
Death with a functioning graft	8% (n=2)	2.5% (n=2)

Suggested association between moderate-severe depression and negative outcomes in kidney transplant recipients¹

1. Rocha G, et al. Transplantation Proceedings 2001.

Depressive disorder in renal transplantation: analysis of Medicare claims

Incidence, risk factors and associated outcomes for depression evaluated in large cohort of kidney transplant recipients¹

Inclusion¹

- 1st kidney transplant recipients between 1995-2003 with Medicare as primary insurance (n=47,899)
- Claims histories searched for evidence of depression during first 3 years post-transplant including transplantation hospitalization until:
 - Graft failure, death or loss of Medicare coverage
- ICD 9 code 311 “depression not elsewhere classified”
- Patients with at least 6 and 12 months of Medicare coverage before transplantation used to identify patients with pre-transplantation depression

Outcomes¹

- Association of post-transplantation depression with demographic and clinical characteristics of recipients and donors
- Relationship between depression and occurrence during first 3 years post-transplant:
 - Graft failure
 - Return to dialysis – censoring at death with functioning graft
 - Death with a functioning graft – censoring at return to dialysis therapy

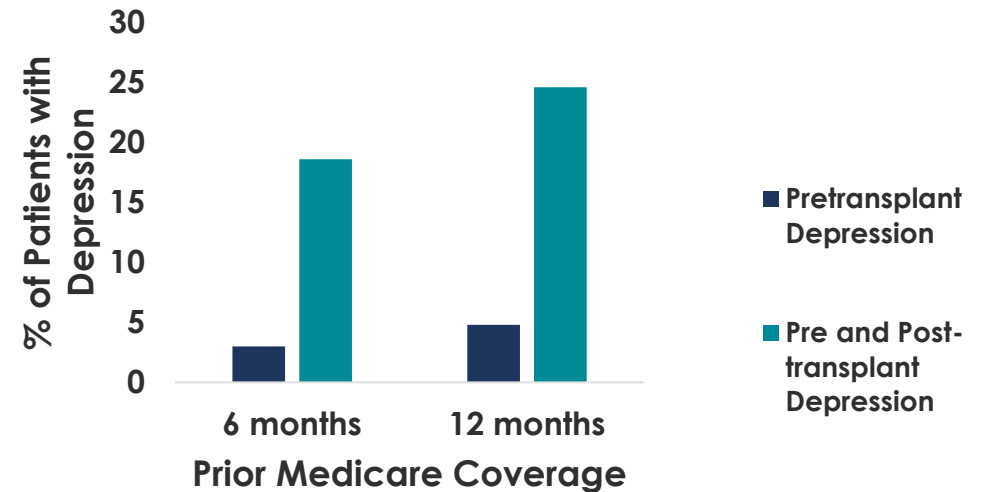
1. Dobbels F, et al. AJKD 2008.

Dobbels et al - results

Effect of Pre-transplantation Depression on Estimates of Cumulative Incidence of Depression 3 Years Post-transplantation¹

Cumulative incidence of depression post-transplantation ¹			
Cohort	1 year	2 years	3 years
1 inpatient claim or 2 outpatient claims in one year	5.05%	7.29 %	9.1%
1 Medicare claim*	6.74%	10%	12.86%

*30%-40% increase in cumulative incidence

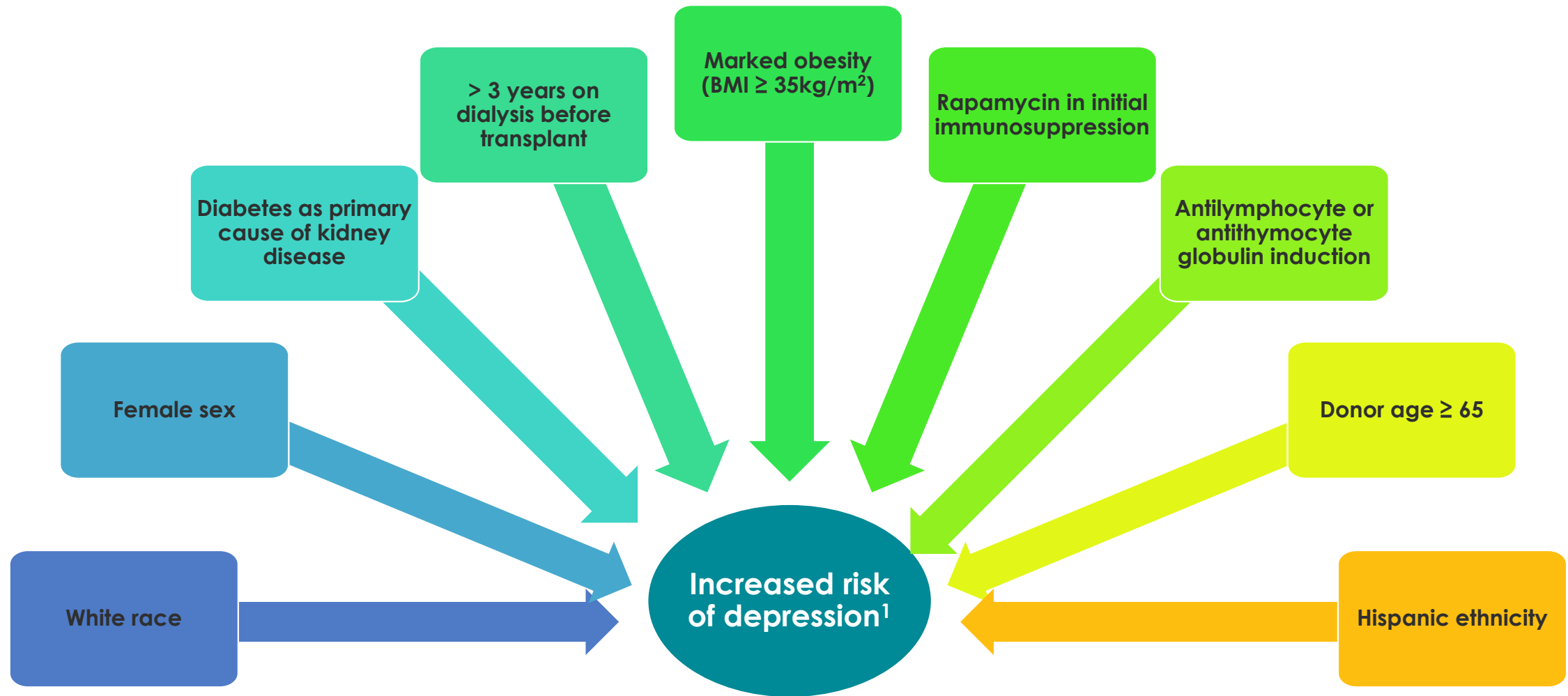


Association between depressive disorder and outcomes¹

Outcome	HR (CI)	P-value
Graft Failure	2.1 (1.94 – 2.27)	< 0.001
Return to dialysis	1.97 (1.76-2.19)	< 0.001
Death with functioning graft	2.24 (2 – 2.5)	< 0.001

1. Adapted from Dobbels F, et al. AJKD 2008.

Patient and transplant characteristics associated with depression



1. Dobbels F, et al. AJKD 2008.

Depressive symptoms and mortality in patients after kidney transplantation: a prospective prevalent cohort study

Prospective cohort study¹

- Determine if severity of depressive symptoms and presence of clinically potential significant depression is associated with increased mortality and death-censored graft loss after renal transplant

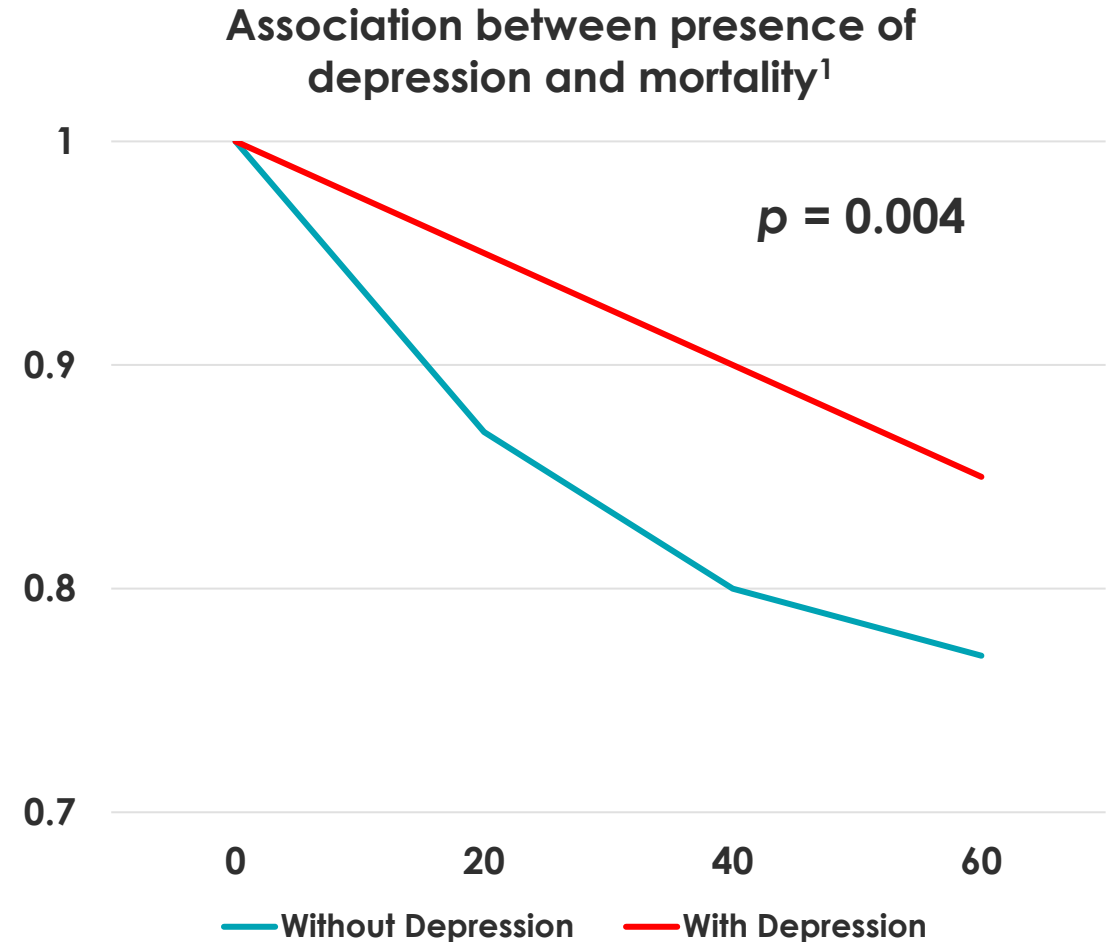
Inclusion¹

- Patients completed Hungarian version of CES-D questionnaire used to measure severity of depressive symptoms
- Cutoff score ≥ 18 used to determine an estimate of the frequency of clinically significant depression
- Patients completed Hungarian version of CES-D questionnaire used to measure severity of depressive symptoms

1. Novak M, et al. Psychosom Med. 2010.

Novak et al – results


- ❖ Prevalence of depression was 22% (CES-D \geq 18) with only 2% of patients taking an antidepressant¹
- ❖ Presence of depression (CES-D > 18) associated with significantly higher mortality (21% vs 13%, $p = 0.004$)¹
- ❖ Multivariate Cox proportional hazard model¹
 - Baseline CES-D score and depression significantly associated with mortality
 - CES-D: HR_(for each 1-point increase) = 1.02; 95% CI 1-1.04
 - Depression: HR_(presence) = 1.66; 95% CI 1.12-2.47
 - Baseline CES-D score significantly predicted death censored graft loss
 - HR_(for each 1-point increase) = 1.03; 95% CI 1.01-1.05



1. Adapted from Novak M, et al. Psychosom Med. 2010.

Management of depression in transplant recipients

Antidepressant Medications ¹	Advantages ¹	Monitoring ¹
Selective serotonin reuptake inhibitors (SSRIs)	Most commonly prescribed	Monitor for drug interactions with immunosuppressant medications
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	Minimal adverse effects and high therapeutic index	<ul style="list-style-type: none"> CYP3A4 inhibition ↑ plasma concentration of calcineurin inhibitors and mammalian target of rapamycin inhibitors

- In  transplant patients with depression, 92% of patients were taking an antidepressant¹
- 8% also receiving weekly psychotherapy¹

- Tricyclic antidepressants and monoamine oxidase inhibitors rarely used due to adverse effects and drug interactions¹

Pharmacists integral for monitoring complex and comprehensive transplant drug therapy¹

1. Terrie YC. US Pharm. 2017.

Mental Health Services for Kidney Transplant Recipients

- **American Kidney Fund:**
 - <https://www.kidneyfund.org/kidney-donation-and-transplant/life-after-transplant-rejection-prevention-and-healthy-tips/mental-health-and-support-after-transplant>
- **National Health Service (United Kingdom)**
 - <https://www.nhsbt.nhs.uk/organ-transplantation/kidney/living-with-a-kidney-transplant/support-and-emotional-wellbeing/>
- **Be the match:**
 - <https://bethematch.org/patients-and-families/life-after-transplant/coping-with-life-after-transplant/emotional-recovery/>
- **Otsuka Patient Education Network (OPEN)**
 - <https://www.otsukapatiented.com/>

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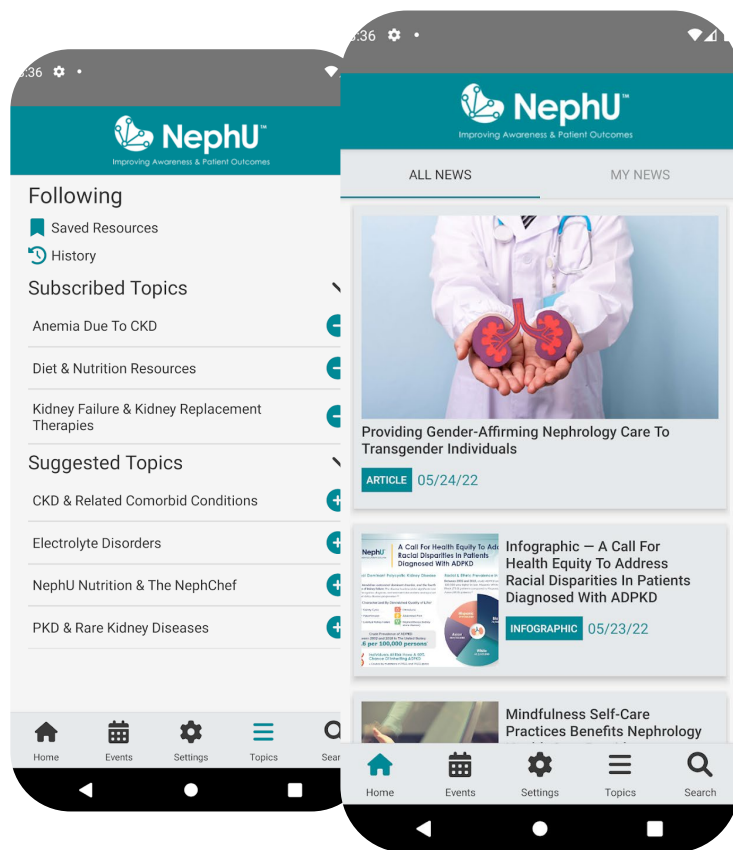
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