# Evaluation of Kidney Transplant Recipients

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# Disclosure

- Merck Co, Abbvie – Advisory Board

# Objectives

- **Access to transplantation and recipient selection**
- ”Evaluation visit”, what the patient should know
- General principles of recipient evaluation
- Cardiovascular morbidity and transplant
- Infectious disease and transplant
- Malignancy and transplant
- Respiratory and GI disease and transplant
- Obesity and transplant
- Adherence, psychiatry disorders and transplantation

## Recommendations

1. All patients with end-stage renal disease should be considered for kidney transplantation provided no absolute contraindications exist (Grade A).

Renal transplantation is the treatment of choice for many patients with ESRD. Despite an increased risk of death in the early post-transplant period, transplantation improves long-term survival and quality of life compared with dialysis.[7,14,15] A report from the United States Renal Data System (USRDS), in which a time-dependent non-proportional hazards model was adjusted for such covariates as age, race, gender and cause of ESRD in more than 250 000 patients initiating renal replacement therapy (RRT) between 1991 and 1996, revealed that the long-term mortality rate of patients who received a first deceased-donor renal transplant was 48–82% lower than that of patients who remained on the waiting list.[7]

# Canadian guideline

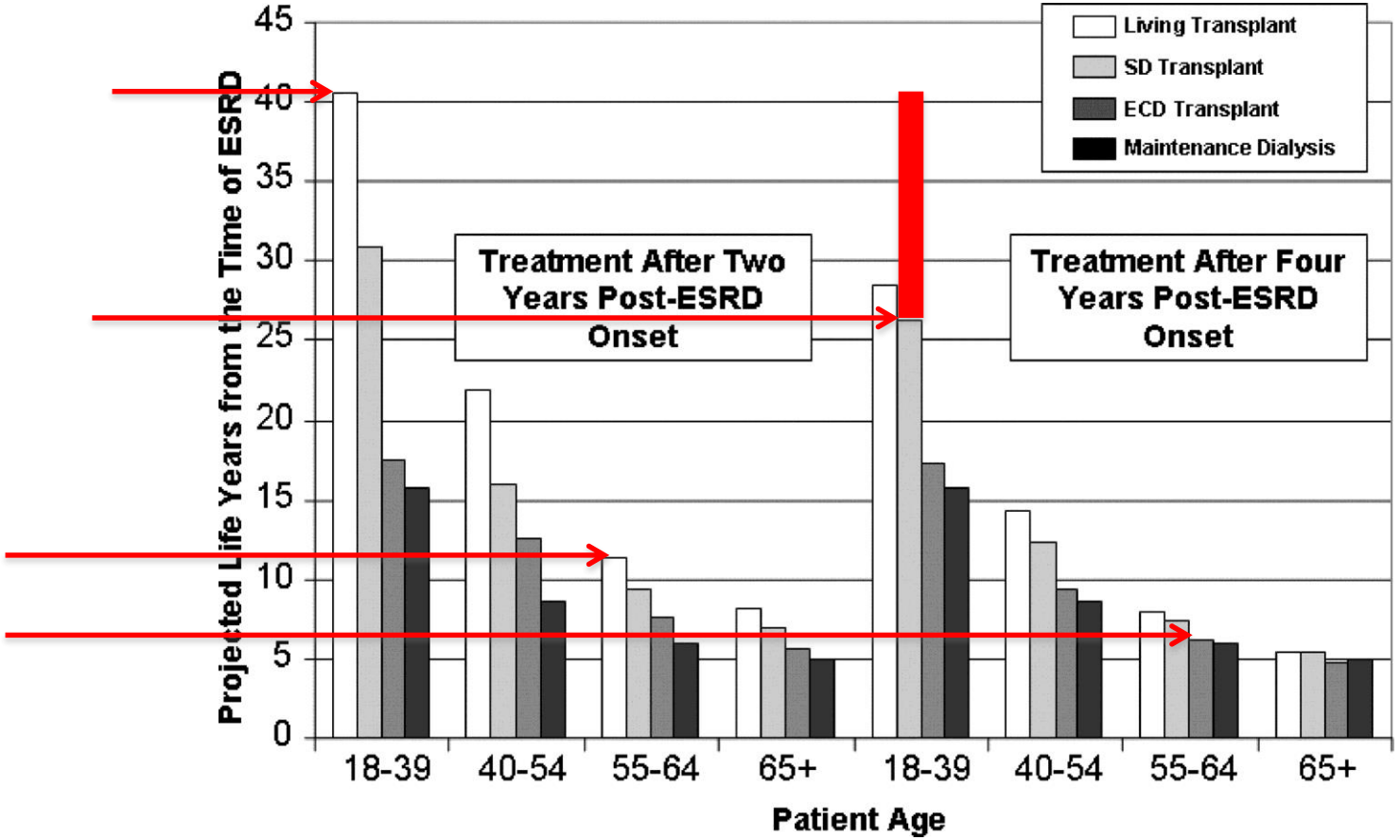
1. All patients with end-stage renal disease should be considered for kidney transplantation provided no absolute contraindications exist (Grade A).
2. Eligibility for kidney transplantation should be determined on medical and surgical grounds. Criteria for eligibility should be transparent and made available to patients and the public. Eligibility should not be based on social status, gender, race or personal or public appeal (Grade C).

Decisions should be made to serve the **best interests of the patient** and be based on medical and surgical grounds

# UK guideline

- Chronic Kidney Disease Stage 5 (CKD 5) includes pre-dialysis and transplant patients with eGFR < 15 ml/min/1.73m2 as well as patients on dialysis i.e. CKD 5, CKD 5T and CKD 5D.

# Projected life expectancy after ESRD onset by recipient age and treatment modality




Which Renal Transplant Candidates Should Accept Marginal Kidneys in Exchange for a Shorter Waiting Time on Dialysis?

Schold J D , and Meier-Kriesche H CJASN 2006;1:532-538

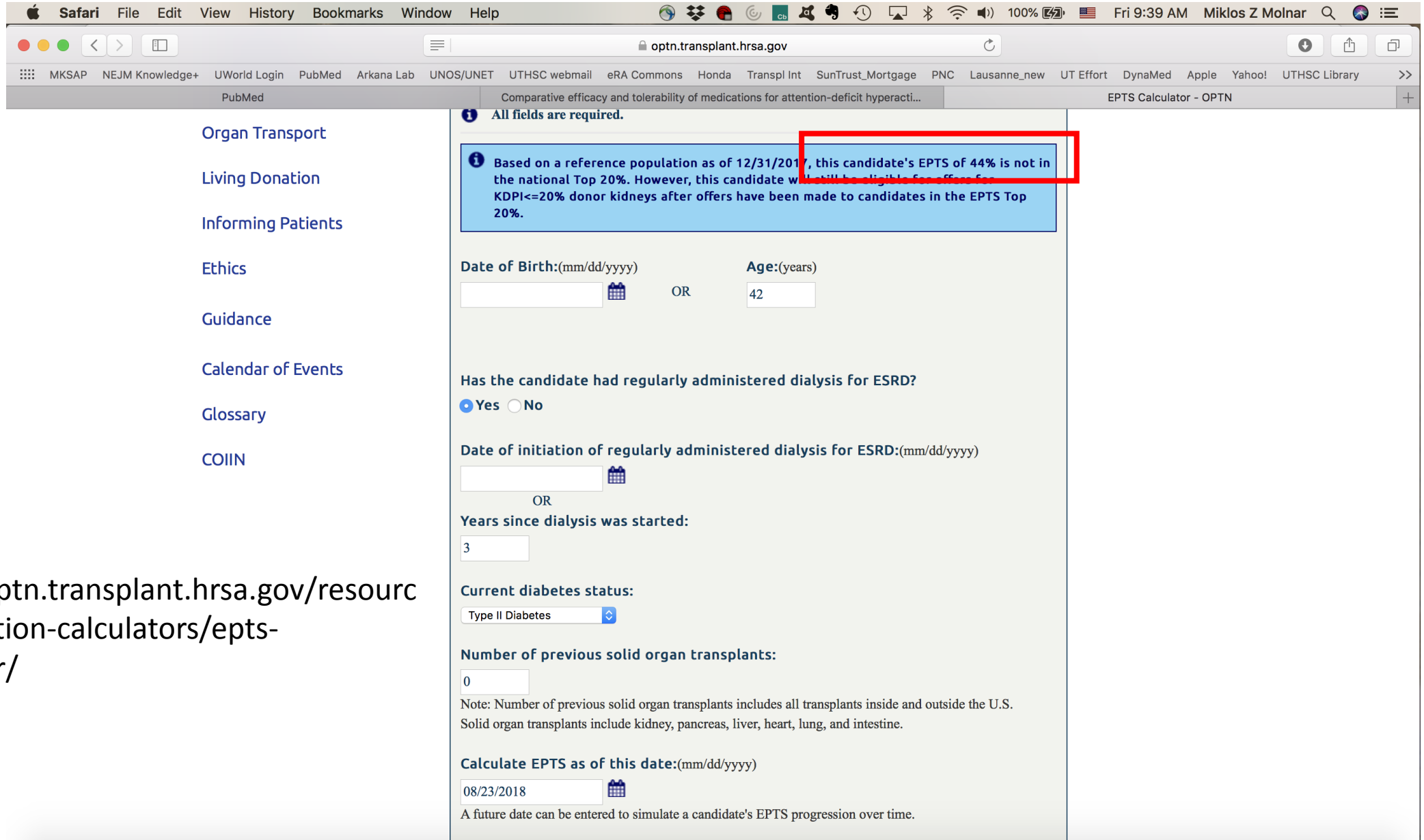
# Estimated Post Transplant Survival (EPTS) score

An Estimated Post Transplant Survival (EPTS) score is assigned to all adult candidates on the kidney waiting list and is based on four factors:

- Candidate time on dialysis
- Current diagnosis of diabetes
- Prior solid organ transplants
- Candidate age

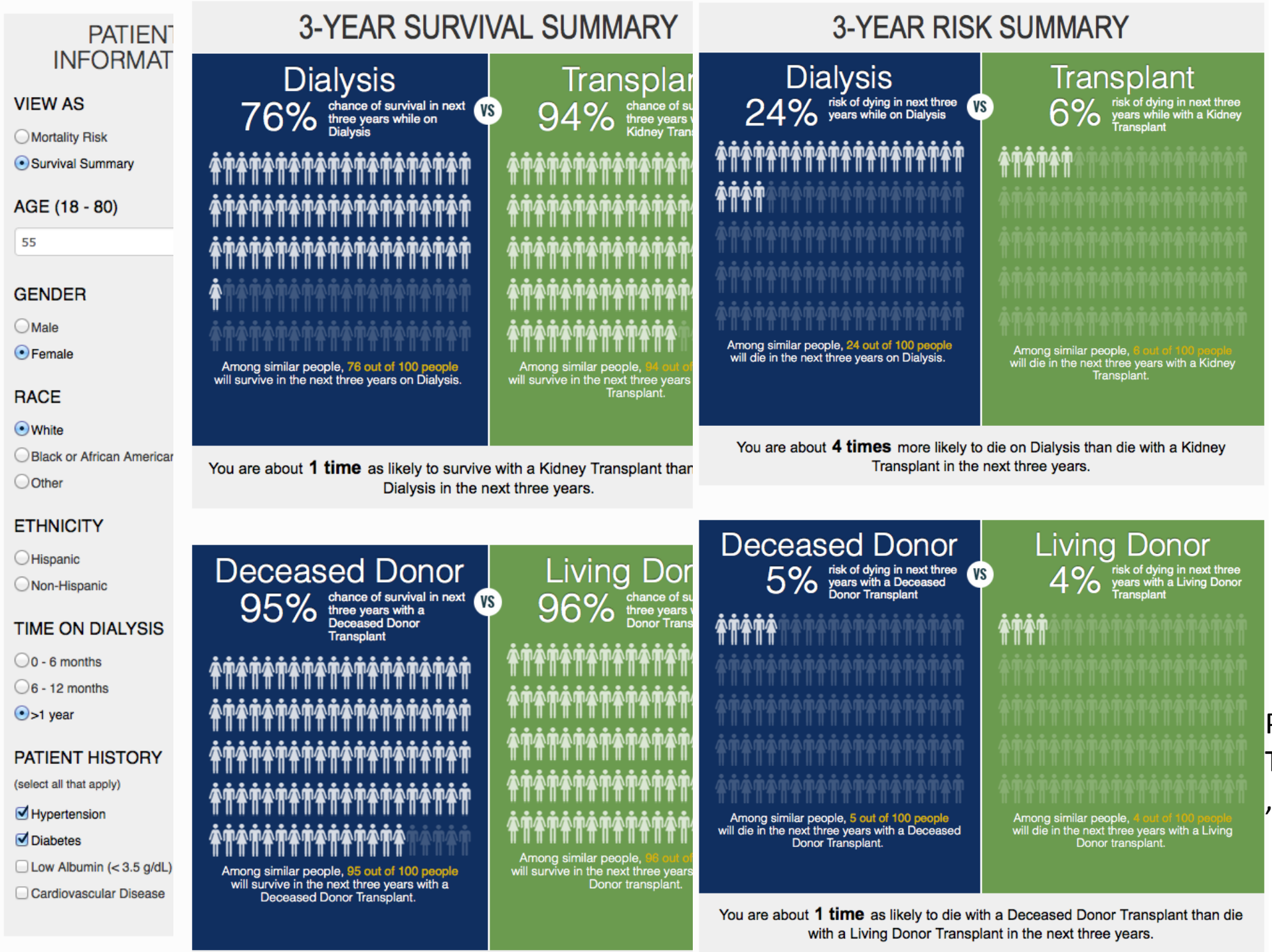
A candidate's EPTS score can range from 0% to 100%. The candidates with EPTS scores of 20% or less will receive offers for kidneys from donors with KDPI scores of 20% or less before other candidates at the local, regional, and national levels of distribution. **The EPTS score is not used in allocation of kidneys from donors with KDPI scores greater than 20%.**

# Estimated Post Transplant Survival (EPTS) score



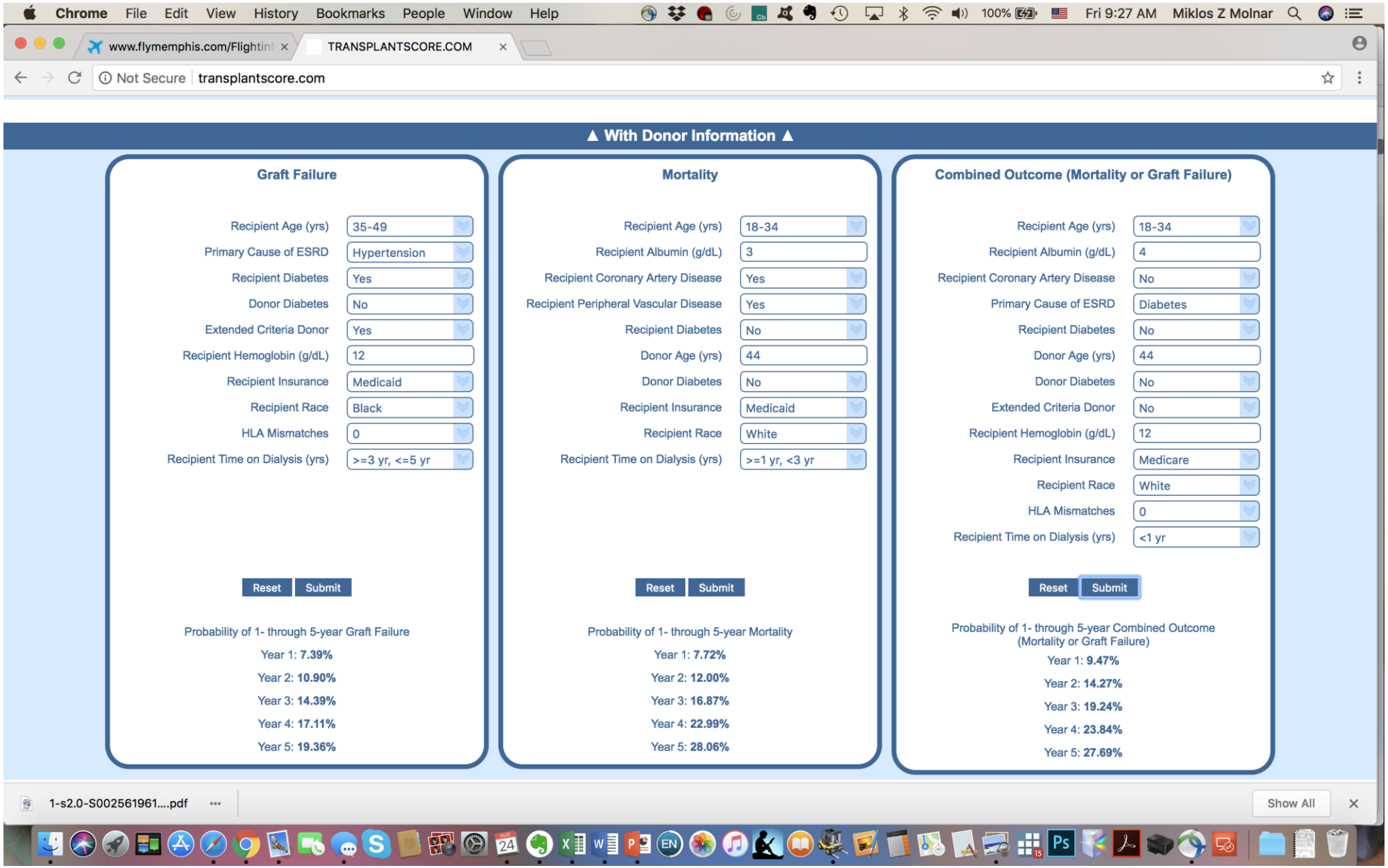

https://optn.transplant.hrsa.gov/resources/allocation-calculators/epts-calculator/

http://ichoosekidney.emory.edu




Patzer RE, Transplantation, 2016

# www.transplantscore.com




Molnar MZ, Transplantation, 2017

# More Accurate Prediction

**TABLE 7.**

**Predicted combined outcome using our new main model, EPTS score and model based on equation of Kasiske's article for 4 different patients**

| | Our new model with all variables | | | | |
|---|---|---|---|---|---|
| **Probability (%) of the event** | **First year** | **Second year** | **Third year** | **Fourth year** | **Fifth year** |
| Patient 1A ("good"): No comorbidities and with relatively low of albumin and hemoglobin | 8 | 12 | 17 | 21 | 24 |
| Patient 1B ("good"): No comorbidities and with relatively high of albumin and hemoglobin | 7 | 10 | 14 | 18 | 21 |
| Patient 2A ("bad"): With all comorbidities and with relatively low of albumin and hemoglobin | 33 | 47 | 58 | 67 | 73 |
| Patient 2B ("bad"): With all comorbidities and with relatively high of albumin and hemoglobin | 29 | 41 | 52 | 61 | 67 |
| **Probability (%) of the event** | **EPTS model** | | | | |
| | First year | Second year | Third year | Fourth year | Fifth year |
| Patient 1A ("good"): No comorbidities and with relatively low of albumin and hemoglobin | 6 | 10 | 13 | 17 | 20 |
| Patient 1B ("good"): No comorbidities and with relatively high of albumin and hemoglobin | 6 | 10 | 13 | 17 | 20 |
| Patient 2A ("bad"): With all comorbidities and with relatively low of albumin and hemoglobin | 9 | 13 | 18 | 23 | 27 |
| Patient 2B ("bad"): With all comorbidities and with relatively high of albumin and hemoglobin | 9 | 13 | 18 | 23 | 27 |
| **Probability (%) of the event** | **Kasiske et al model** | | | | |
| | *First year* | *Second year* | *Third year* | *Fourth year* | *Fifth year* |
| Patient 1A ("good"): No comorbidities and with relatively low of albumin and hemoglobin | 14 | 22 | 30 | 38 | 45 |
| Patient 1B ("good"): No comorbidities and with relatively high of albumin and hemoglobin | 14 | 22 | 30 | 38 | 45 |
| Patient 2A ("bad"): With all comorbidities and with relatively low of albumin and hemoglobin | 15 | 23 | 32 | 40 | 48 |
| Patient 2B ("bad"): With all comorbidities and with relatively high of albumin and hemoglobin | 15 | 23 | 32 | 40 | 48 |

Molnar MZ, Transplantation, 2017

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# What the recipient needs to know

- Risks of the surgical procedure
- Risks and side effects of immunosuppressive drugs
- Risk of rejection
- Risk of infection
- Risk of neoplasia after transplantion
- The duration of immunosuppressive therapy, as long as the allograft survives
- Importance of compliance
- Live versus cadaveric donation
- Mean survival of the allograft. Currently, the half-life of a renal allograft from a cadaver is 13-15 years and from a live donor is 20-30 years (half-life: period of time after which half of transplants no longer survive)
- The statistical success of the center where the transplant is to be performed
- What happens when the allograft fails: restarting dialysis and possible re-transplantaton, success of a second allograft.
- Pregnancy and birth control

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# European guidelines

## ERBP Guideline on kidney donor and recipient evaluation and perioperative care - 2017

**CLINICAL PRACTICE GUIDELINES**

**Assessment of the Potential Kidney Transplant Recipient**

**UK Renal Association**

**5th Edition, 2010**

**Final Version 12.01.11**

# North American guidelines

COMMENTARY

## Canadian Society of Transplantation consensus guidelines on eligibility for kidney transplantation

CMAJ • November 8, 2005 • 173(10) |

Greg Knoll, Sandra Cockfield, Tom Blydt-Hansen, Dana Baran, Bryce Kiberd, David Landsberg, David Rush, Edward Cole, for the Kidney Transplant Working Group of the Canadian Society of Transplantation

**Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation. 2009;9(Suppl 3):S1-S157.**

# Pre-transplant Recipient Evaluation

## Routine tests

- Full medical history and physical exam
- CBC and chemistry panel
- PT and PTT
- Blood type
- HBV and HCV serology
- HIV screen
- EBV
- VZV
- CMV test
- Pelvic exam and Pap smear??????
- Chest X-ray
- ECG
- HLA tissue typing and cytotoxic antibodies
- VDRL screen
- Lipid profile
- Abdominal U/S

Kasiske BL, et al. *Am J Transplant.* 2001;1 (suppl 2):1-95.

# Pretransplant Recipient Evaluation

## Elective tests

- Voiding cystourethrogram
- **Pharmacologic or exercise stress test**
- **Noninvasive vascular study**
- Barium enema and lower endoscopy
- **PSA test**
- **Mammogram**
- **Coronary angiogram**

**CT angio for diabetic patient**

**Siddqi N, et al. In: Danovitch GM, ed. *Handbook of Kidney Transplantation.* 2005:169-192.**

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# ERBP Guideline

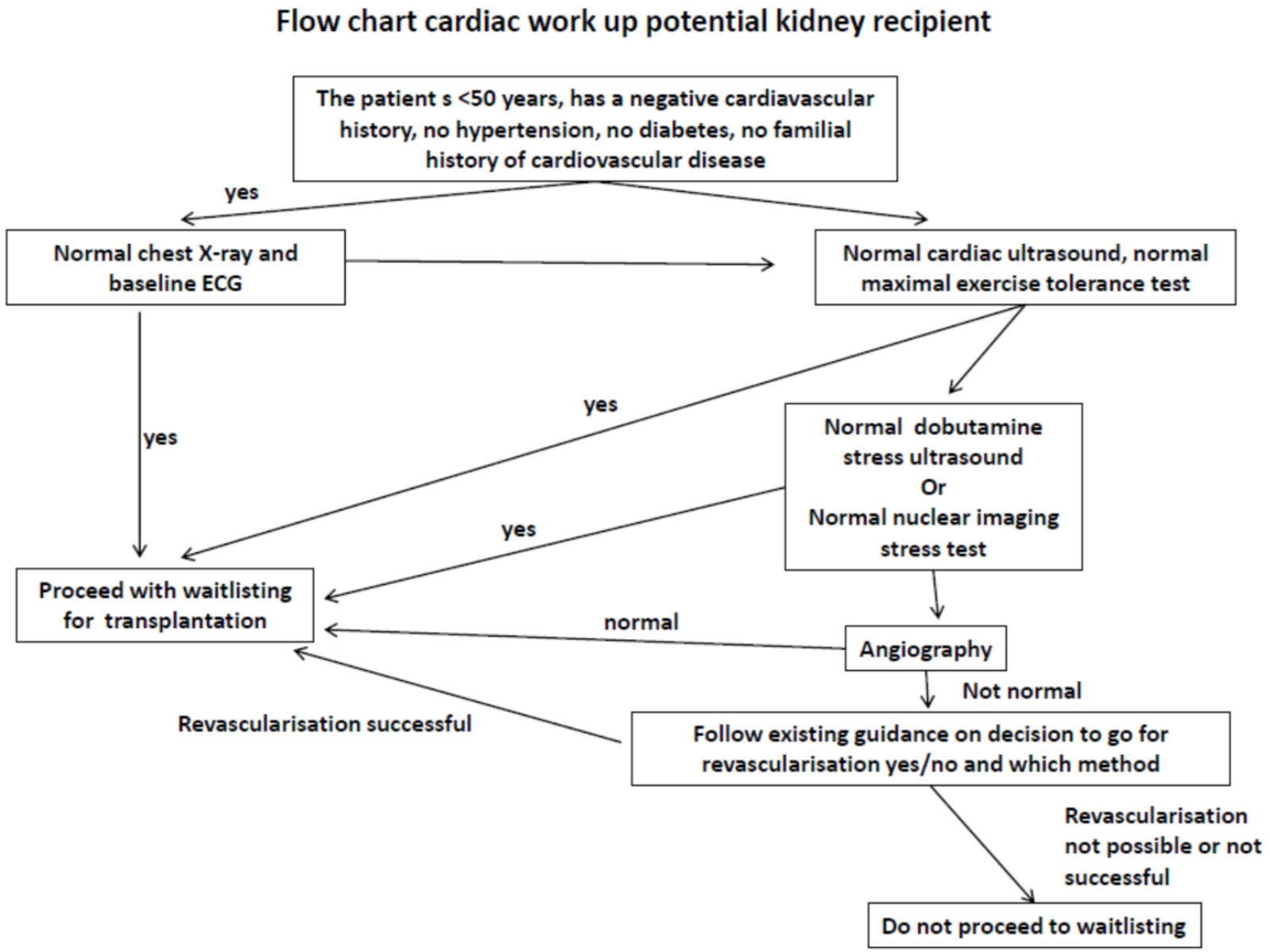
We recommend that basic clinical data, physical examination, resting ECG and chest-X ray are a sufficient standard work-up in asymptomatic low risk kidney transplant candidates. (**1C**)

We recommend performing a standard exercise tolerance test and cardiac ultrasound in asymptomatic high risk patients (older age, diabetes, history of cardiovascular disease). In patients with a true negative test, further cardiac screening is not indicated. (**1C**)

We recommend performing further cardiac investigation for occult coronary artery disease with non-invasive stress imaging (Myocardial perfusion or Dobutamine Stress Echocardiography) in kidney transplant candidates with high risk and a positive or inconclusive exercise tolerance test. (**1C**)

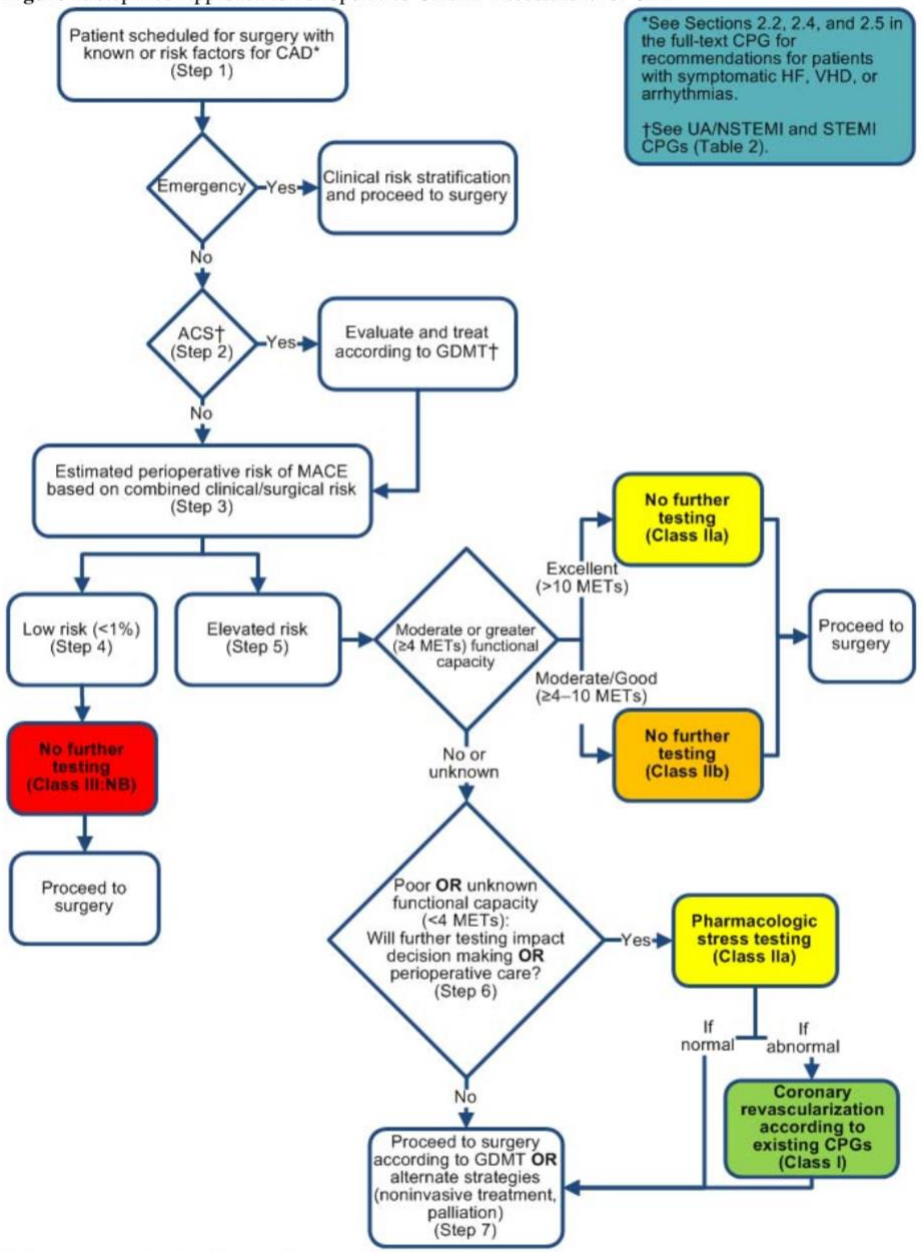
We recommend performing coronary angiography in renal transplant candidates with a positive test for cardiac ischemia. Further management should be according to the current cardiovascular guidelines. (**1D**)

# ERBP Guideline



# 2014 ACC/AHA guideline

**Figure 1.** Stepwise Approach to Perioperative Cardiac Assessment for CAD




Colors correspond to the Classes of Recommendations in Table 1.

The ACC/AHA does not recommend routinely screening asymptomatic patients facing intermediate to high risk surgery if their functional status allows them to **perform 4 or more metabolic equivalent tasks,** however, the relevance of these findings to patients with ESRD is not known. As a consequence, ACC/AHA guidelines are in conflict with current practice in many units for ESRD patients facing kidney transplant.

**Table 2. Published Recommendations for Testing for CAD in Asymptomatic Kidney Transplantation Candidates**

| Reference | Recommendations |
|---|---|
| 2012 AHA Scientific Statement | Noninvasive stress testing may be considered in kidney transplantation candidates with no active cardiac conditions on the basis of the presence of multiple CAD risk factors regardless of functional status (Class IIb, Level of Evidence C) |
| | Relevant risk factors among transplantation candidates include diabetes mellitus, prior cardiovascular disease, >1 y on dialysis, LV hypertrophy, age >60 y, smoking, hypertension, and dyslipidemia; the specific number of risk factors that should be used to prompt testing remains to be determined, but the committee considers ≥3 to be reasonable |
| 2007 ACC/AHA Perioperative Guidelines for Noncardiac Surgery[7] | No testing recommended if functional status ≥4 METS<br>If functional status <4 METS or unknown, then consideration of noninvasive stress testing is recommended based on the following clinical risk factors<br>Ischemic heart disease<br>Compensated or prior heart failure<br>Diabetes mellitus<br>Renal insufficiency<br>Cerebrovascular disease<br>Recommendations for testing are stronger if ≥3 clinical risk factors are present but may be considered in those with 1–2 risk factors |
| 2007 Lisbon Conference[13] | Acknowledges that there are no data establishing that screening of asymptomatic patients in itself prevents cardiac events; noninvasive and/or invasive testing should be considered in highest-risk patients with the following conditions<br>Diabetes mellitus<br>Prior cardiovascular disease<br>Multiple cardiac risk factors such as >1 y on dialysis, LV hypertrophy, age >60 y, smoking, hypertension, and dyslipidemia<br>Does not specify the number of risk factors to justify testing |
| 2005 NKF/KDOQI Guidelines[12] | Noninvasive stress testing recommended for<br>All patients with diabetes; repeat every 12 mo<br>All patients with prior CAD<br>If not revascularized, repeat every 12 mo<br>If prior PCI, repeat every 12 mo<br>If prior CABG, repeat after first 3 y and then every 12 mo<br>Repeat every 24 mo in "high-risk" nondiabetic patients defined as<br>≥2 traditional risk factors<br>Known history of CAD<br>LVEF ≤40%<br>Peripheral vascular disease |
| 2001 AST Guidelines[16] | Noninvasive stress testing recommended for patients at "high risk," defined as renal disease from diabetes, prior history of ischemic heart disease, or ≥2 risk factors<br>Coronary angiography for possible revascularization before transplantation recommended for patients with a positive stress test<br>Revascularization before transplantation recommended for patients with critical coronary lesions |

Noninvasive stress testing may be considered in kidney transplantation candidates with no active cardiac conditions based on the presence of multiple CAD risk factors regardless of functional status.

Relevant risk factors among transplantation candidates include diabetes mellitus, prior cardiovascular disease, more than 1 year on dialysis, left ventricular hypertrophy, age greater than 60 years, smoking, hypertension, and dyslipidemia.

The specific number of risk factors that should be used to prompt testing remains to be determined, but the committee considers 3 or more as reasonable (*Class IIb; Level of Evidence C*).

Lentine KL, Circulation, 2012

# Lentine KL, Circulation, 2012

- It is reasonable to evaluate kidney transplantation candidates with echocardiographic evidence of significant pulmonary hypertension for underlying causes (eg, obstructive sleep apnea, left heart disease) (*Class IIa; Level of Evidence C*).

- It may be reasonable to confirm echocardiographic evidence of elevated pulmonary arterial pressures in kidney transplantation candidates by right heart catheterization (*Class IIb; Level of Evidence C*). Echocardiographic evidence of significant pulmonary hypertension in this population is defined by right ventricular systolic pressure more than 45 mm Hg or ancillary evidence of right ventricular pressure overload.

- If right heart catheterization confirms the presence of significant pulmonary arterial hypertension (as defined by mean pulmonary artery pressure >25 mm Hg, pulmonary capillary wedge <15 mm Hg, and pulmonary vascular resistance of >3 Wood units) in the absence of an identified secondary cause (eg, obstructive sleep apnea, left heart disease), referral to a consultant with expertise in pulmonary arterial hypertension management and advanced vasodilator therapies is reasonable (*Class IIa; Level of Evidence C*).

# Lentine KL, Circulation, 2012

- Beta-blockers before renal transplantation, continuing the medication perioperatively and postoperatively is recommended to prevent rebound hypertension and tachycardia (*Class I; Level of Evidence A*).
- Among patients being considered for renal transplantation with clinical markers of cardiac risk (diabetes mellitus, prior known coronary heart disease, prior heart failure, extracardiac atherosclerosis) and those with unequivocal myocardial ischemia on preoperative stress testing, it is reasonable to initiate beta-blockers preoperatively and to continue them postoperatively provided that dose titration is done carefully to avoid bradycardia and hypotension (*Class IIa; Level of Evidence C*).
- Perioperative initiation of beta-blockers in beta-blocker–naıve patients may be considered in kidney transplantation candidates with established coronary heart disease or 2 or more cardiovascular risk markers to protect against perioperative cardiovascular events if dosing is titrated and monitored (*Class IIb; Level of Evidence C*).
- Initiating beta-blocker therapy in beta-blocker– naıve patients the night before and/or the morning of noncardiac surgery is not recommended (*Class III; Level of Evidence A*).

# Lentine KL, Circulation, 2012

- It is reasonable to continue aspirin indefinitely after renal transplantation in patients with known CAD, following the ACC/AHA guidelines for secondary prevention for patients with coronary artery disease (*Class IIa; Level of Evidence B*).

- For patients undergoing renal transplantation who are taking statin therapy, it is recommended that statin treatment be continued perioperatively and postoperatively (*Class I; Level of Evidence B*).

- For patients undergoing renal transplantation in whom preoperative evaluation established unequivocal evidence of atherosclerosis, it is reasonable to initiate low- to moderate-dose statin therapy preoperatively and to continue treatment postoperatively (*Class IIa; Level of Evidence B*).

# Cardiac disease – Canadian guideline about stress-test

- history, physical examination, electrocardiogram (ECG) and a chest radiograph (Grade A)
- I. Symptomatic patients or patients with a prior history of CAD including
  - Previous history of myocardial infarction (Grade A)
  - Symptoms of angina (Grade A)
  - Signs or symptoms of congestive heart failure (Grade A)
- II. Asymptomatic patients with
  - Diabetes (type 1 or type 2) (Grade B)
  - Multiple risk factors for CAD (3 or more) (Grade B)
    - age > 50 years
    - prolonged duration of chronic kidney disease
    - family history of CAD (first-degree relative)
    - significant smoking history
    - dyslipidemia (high-density lipoprotein level < 0.9mmol/L or total cholesterol > 5.2 mmol/L),
    - BMI≥ 30 kg/m2
    - history of hypertension
- Very high-risk patients should be considered for angiography even with a negative non-invasive test (Grade C).

# Cardiac disease – Canadian guideline

- Patients with IHD should be re-evaluated on a regular basis.
- Re-evaluation should occur annually in all patients who are at high risk (see previous recommendation for high-risk groups) (Grade C)
- All high-risk patients on the waiting list should be treated aggressively with risk-factor reduction strategies (Grade A) (**????)**

# Eligibility - HPT

## Hyperparathyroidism

- Hyperparathyroidism is not an absolute contraindication to kidney transplantation, but should be fully investigated.

- Parathyroidectomy should be considered prior to kidney transplantation for those who have failed medical management or have severe, persistent complications of hyperparathyroidism

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# ERBP Guideline - HIV

We recommend that HIV per se in not a contra-indication for kidney transplantation. (**1C**)

We recommend wait-listing HIV patients only if

1) they are compliant with treatment, particularly HAART therapy

2) their CD4+ T cell counts are > 200/μL and have been stable during the previous 3 months

3) HIV RNA was undetectable during the previous 3 months

4) no opportunistic infections occurred during the previous 6 months

5) they show no signs compatible with progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis, or lymphoma. (**1C**)

We suggest that the most appropriate anti-retroviral therapy should be discussed before transplantation with the infectious diseases team in order to anticipate potential drug interactions after transplantation. (**Ungraded Statement**)

# HCV positive donor to HCV negative recipient

- Waiting times for kidney transplants exceed 3 to 5 years in many parts of the United States.
- Yet more than 500 high-quality kidneys from deceased donors with hepatitis C virus (HCV) infection are discarded annually.
- Direct-acting antiviral agents, which are associated with high HCV cure rates and manageable side effects, have created the potential to substantially increase the number of kidney transplants by making HCV-infected kidneys available to HCV-negative candidates on the waiting list.

# THINKER trial – UPenn (NEJM, Goldberg Ds, 2017)

- Zepatier was used
- Only genotype 1
- Intravenous glucocorticoids and rabbit antithymocyte globulin were administered to all recipients, followed by oral tacrolimus, mycophenolate mofetil, and prednisone.
- The HCV viral load was measured in recipients on postoperative day 3; Zepatier (elbasvir–grazoprevir) was initiated when the results became positive, and therapy was maintained for 12 weeks.

# THINKER trial – UPenn (NEJM, Goldberg Ds, 2017)

- 10 patients
- On day 3 after transplantation, all recipients had detectable HCV RNA; viral loads ranged from less than 15 IU per milliliter (detectable but unquantifiable) to 193,000 IU per milliliter
- Nine recipients had HCV genotype 1a infection; none had identifiable NS5A resistance.
- All recipients were cured of HCV; a cure was defined as a sustained virologic response 12 weeks after the end of treatment.

# THINKER trial – UPenn (NEJM, Goldberg Ds, 2017)

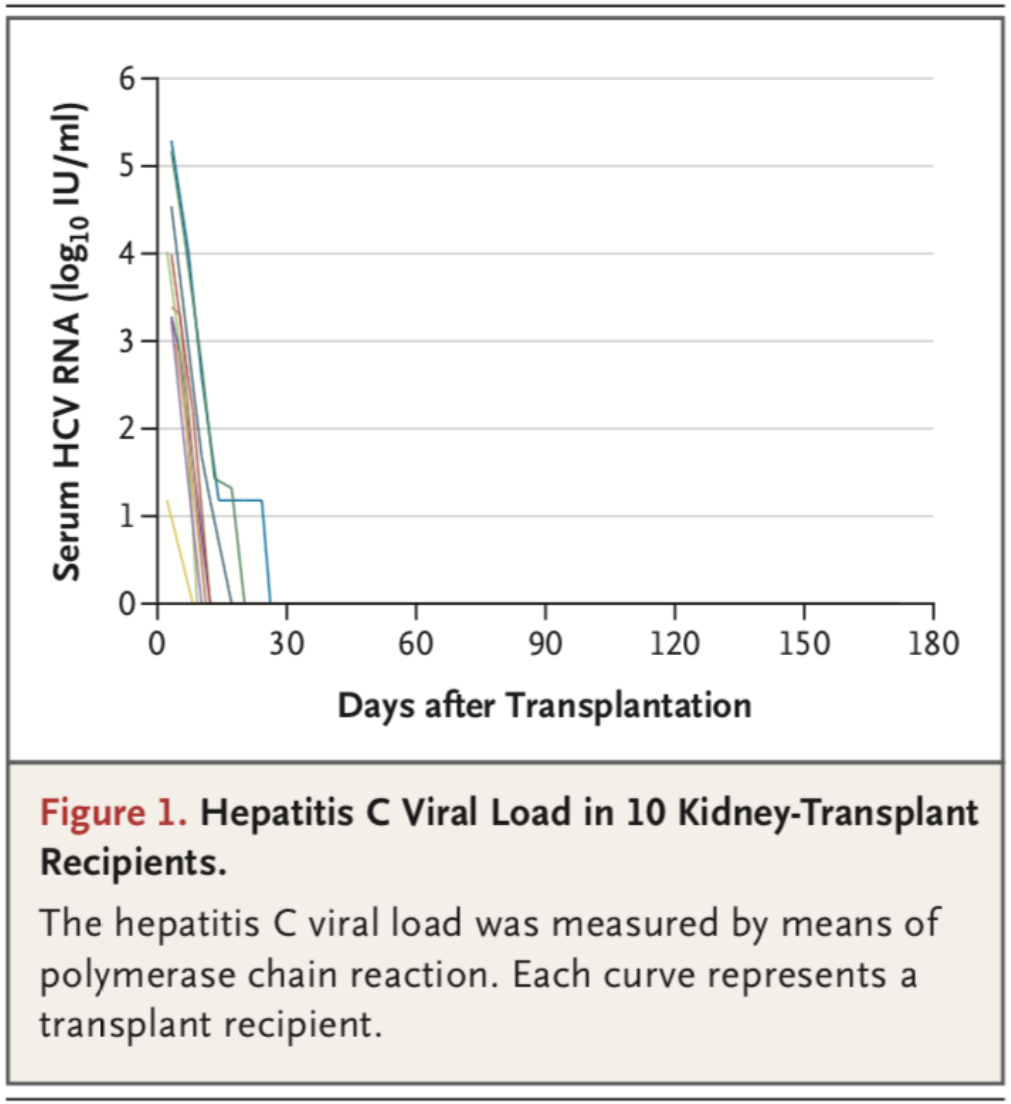


**Figure 1. Hepatitis C Viral Load in 10 Kidney-Transplant Recipients.**

The hepatitis C viral load was measured by means of polymerase chain reaction. Each curve represents a transplant recipient.

# EXPANDER Trial (Durand CM, Annals, 2018)

- 10 patients
- Prophylactic Zepatier (elbasvir–grazoprevir) BEFORE surgery
- Recipients of kidneys from donors with genotype 1 infection continued receiving GZR–EBR for 12 weeks after trans-plantation; those receiving organs from donors with genotype 2 or 3 infection had sofosbuvir, 400 mg, added to GZR–EBR for 12 weeks of triple therapy.

# EXPANDER Trial (Durand CM, Annals, 2018)

- Among 10 HCV D+/R- transplant recipients, no treatment-related adverse events occurred, and HCV RNA was not detected in any recipient 12 weeks after treatment.

*Table 2.* Donor HCV Characteristics and Recipient HCV Status After Transplant

| Donor-Recipient Pair | Genotype | Donor | | Recipient | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | HCV RNA Level, *IU/mL* | HCV Antibody Status | HCV RNA Level, *IU/mL* | | | | HCV Antibody Status at FW12 | Positive PPs, *n* | |
| | | | | POD1 | TW1 | TW12 | FW12 | | Baseline | FW8 |
| 1 | ND* | 467 | Positive | <15 | <15 | <15 | <15 | Negative | 0 | 0 |
| 2 | ND* | 104 | Positive | <15 | <15 | <15 | <15 | Positive | 0 | 0 |
| 3† | ND* | <15‡ | Positive | <15 | <15 | <15 | <15 | Negative | 2 | 1 |
| 4 | 1a/3 | 46 733 | Positive | <15‡ | <15 | <15 | <15 | Negative | 0 | 0 |
| 5† | 1a | 62 400 | Positive | <15 | <15 | <15 | <15 | Positive | 4 | 8 |
| 6 | 1a | 4 645 289 | Positive | 94 | <15 | <15 | <15 | Negative | 1 | 0 |
| 7 | 3 | 2 090 042 | Positive | <15‡ | <15 | <15 | <15 | Positive | 0 | 0 |
| 8 | 2 | 1 760 000 | Positive | 136 | 55 | <15 | <15 | Positive | 5 | 2 |
| 9 | ND | 131 | Positive | <15 | <15 | <15 | <15 | Negative | 3 | 6 |
| 10 | 1a | 1 140 000 | Positive | 32 | <15 | <15 | <15 | Positive | 1 | 2 |

FW = follow-up week; HCV = hepatitis C virus; ND = not determined; POD = postoperative day; PP = peptide pool; TW = treatment week.
* Because of insufficient viral RNA.
† The donor received substantial blood products, and the specimen being tested may have been hemodiluted.
‡ The target was detected but not quantifiable.

# EXPANDER Trial (Durand CM, Annals, 2018)

- In conclusion, this open-label nonrandomized study showed that DAA prophylaxis for non–HCV- infected recipients of kidneys from HCV-infected donors was safe and well-tolerated.

- No treatment-related adverse events or cases of chronic HCV occurred.

- This strategy should be studied further in carefully monitored clinical trials.
- If confirmed in larger studies, this approach should markedly expand organ options and reduce mortality for kidney transplant candidates without HCV infection.

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# Suggested malignancy wait time

- Prostate – 2 years
- Liver – Transplant not recommended with liver transplant
- Multiple myeloma – Transplant not recommended
- Lymphoma – 2 to 5 years
- Leukemia – 2 years
- Malignant melanoma – 5 years
- In situ or superficial melanoma – 2 years
- Squamous cell carcinoma – Surveillance
- Basal cell carcinoma – None
- Cervical/uterine – 2 to 5 years

# Suggested malignancy wait time

- Testicular – 2 years
- Kaposi’s sarcoma – 2 years; second transplant contra-indicated
- Breast cancer – 2 to 5 years
- Lung cancer – 2 years
- Bladder cancer – 2 years, In situ – None
- Renal cell carcinoma small low-grade tumor – 2 years
- Renal cell carcinoma large high-grade tumor – 5 years
- Colon cancer stage 1 – 2 years
- Colon cancer stage 2 or higher – 5 years

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# Respiratory diseases

- Patients with the following respiratory conditions and severity are not candidates for kidney transplantation:
- Requirement for home oxygen therapy (Grade C)
- Uncontrolled asthma (Grade C)
- Severe cor pulmonale
- Severe chronic obstructive pulmonary disease (COPD)–pulmonary fibrosis or restrictive disease with any of the following parameters (Grade C):
- - best forced expiratory volume in 1 s (FEV1 ) < 25% predicted value
- - PO2 room air < 60 mmHg with exercise desaturation, SaO2 < 90%
- - > 4 lower respiratory infections in the last 12 months
- - moderate disease with evidence of progression

# Gastrointestinal diseases

- Acute pancreatitis
- Inflammatory bowel disease
- Diverticulitis should be evaluated and considered for partial colectomy
- HBV, HCV?????

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# ERBP Guideline - Obesity

We recommend that patients with a BMI > 30 kg/m² reduce weight before transplantation.

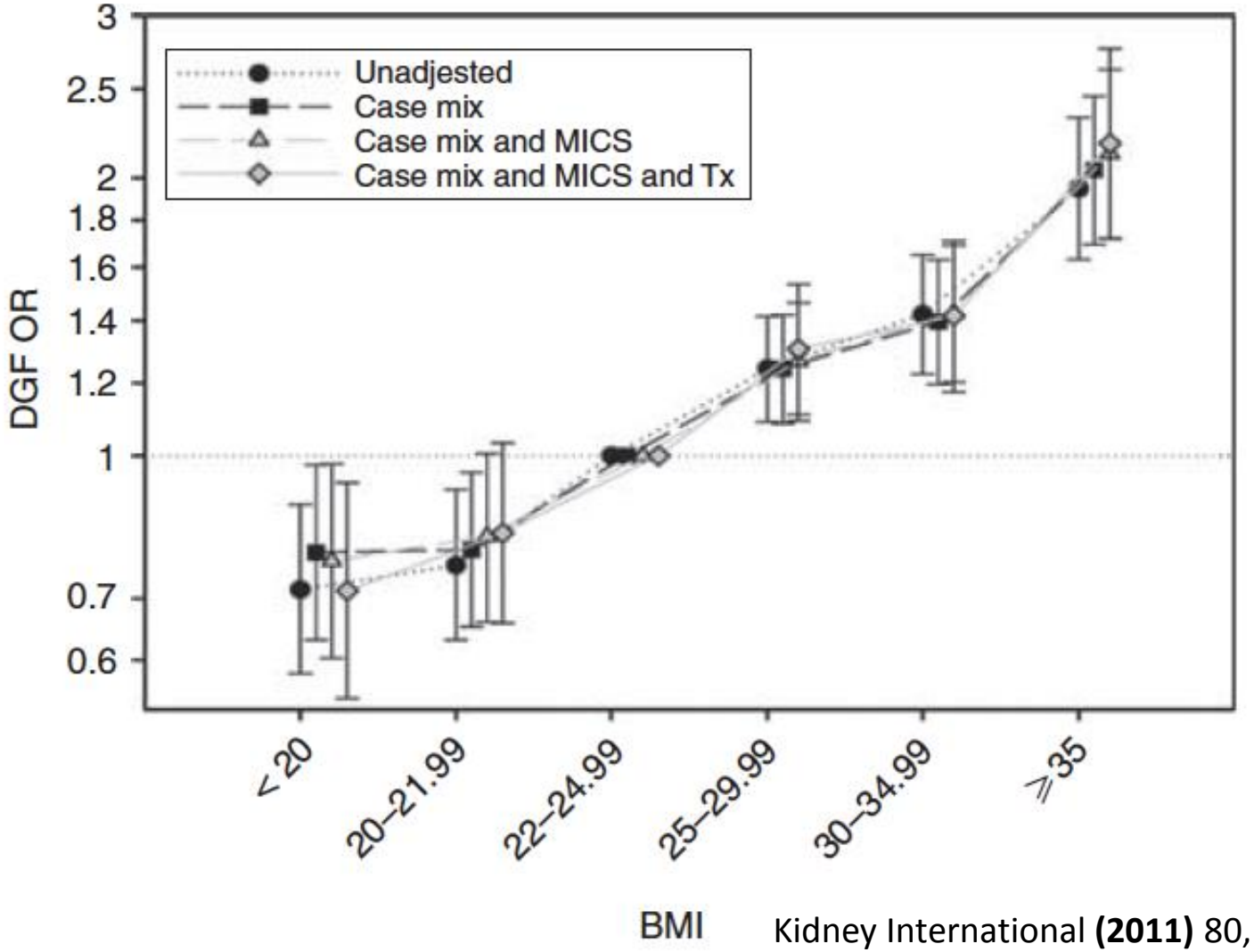
(**Ungraded Statement**)

# Obesity – UK guidelines

- We suggest that obese patients (BMI >30 kg/m2) present technical difficulties and are at increased risk of peri-operative complications. They should be screened rigorously for cardiovascular disease and each case considered individually.
- Although obesity is not an absolute contra-indication to transplantation, individuals with a BMI >40 kg/m2 are less likely to benefit. (2B)

# Higher recipient body mass index is associated with post-transplant delayed kidney graft function

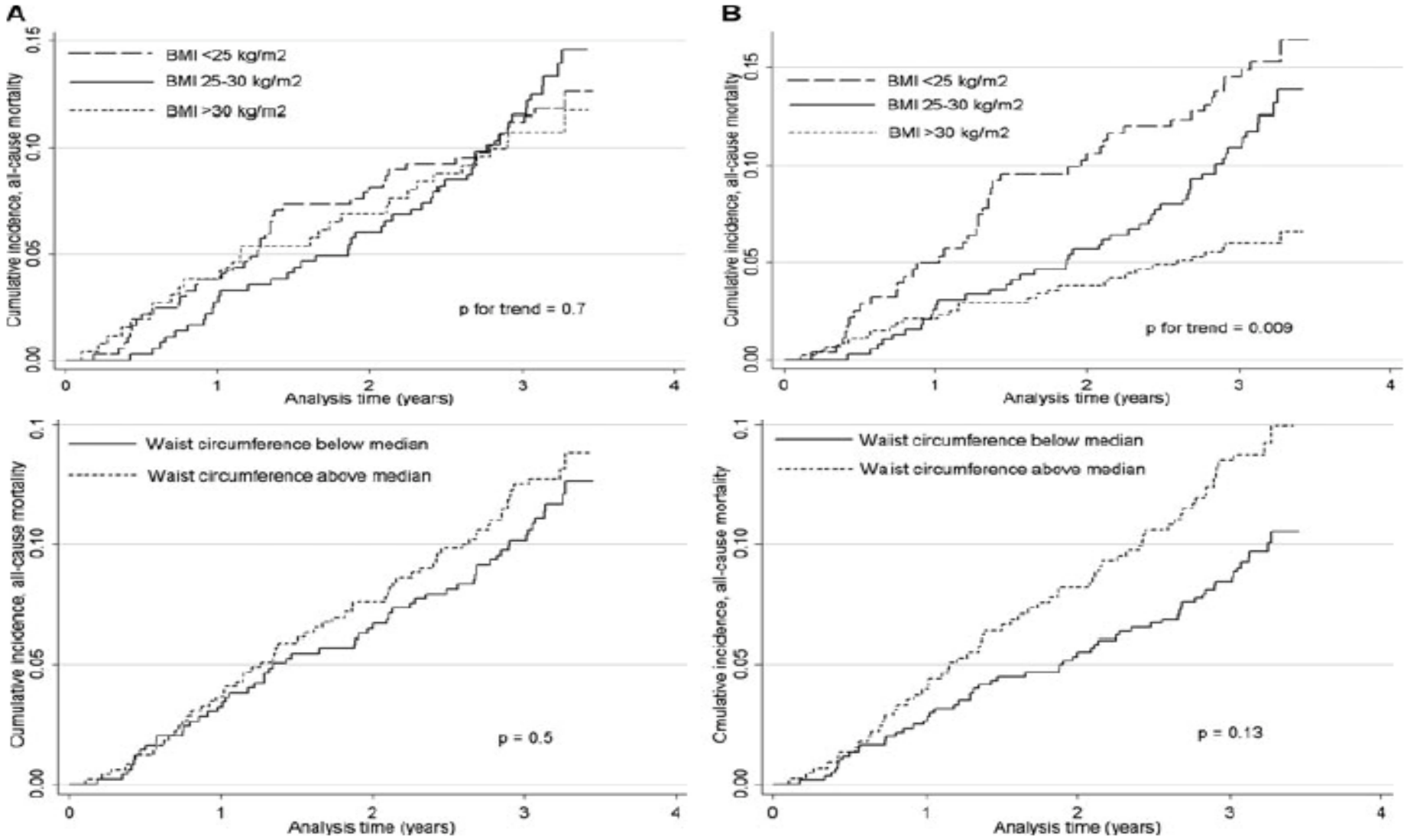
Miklos Z. Molnar[1,2], Csaba P. Kovesdy[3,4], Istvan Mucsi[2,5,6], Suphamai Bunnapradist[7], Elani Streja[1], Mahesh Krishnan[8] and Kamyar Kalantar-Zadeh[1,7,9]




Kidney International **(2011)** 80, **218–224;**

# Body Mass Index, Waist Circumference and Mortality in Kidney Transplant Recipients

C. P. Kovesdy[a,b,*], M. E. Czira[c], A. Rudas[c], A. Ujszaszi[c], L. Rosivall[d], M. Novak[c,e], K. Kalantar-Zadeh[f], M. Z. Molnar[c,d,f] and I. Mucsi[c,d,g]

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# Associations of Body Mass Index and Weight Loss with Mortality in Transplant-Waitlisted Maintenance Hemodialysis Patients

M. Z. Molnar[a,b], E. Streja[a,c], C. P. Kovesdy[d,e], S. Bunnapradist[f], M. S. Sampaio[f], J. Jing[a], M. Krishnan[g], A. R. Nissenson[g], G. M. Danovitch[g,h] and K. Kalantar-Zadeh[a,b,f,*]

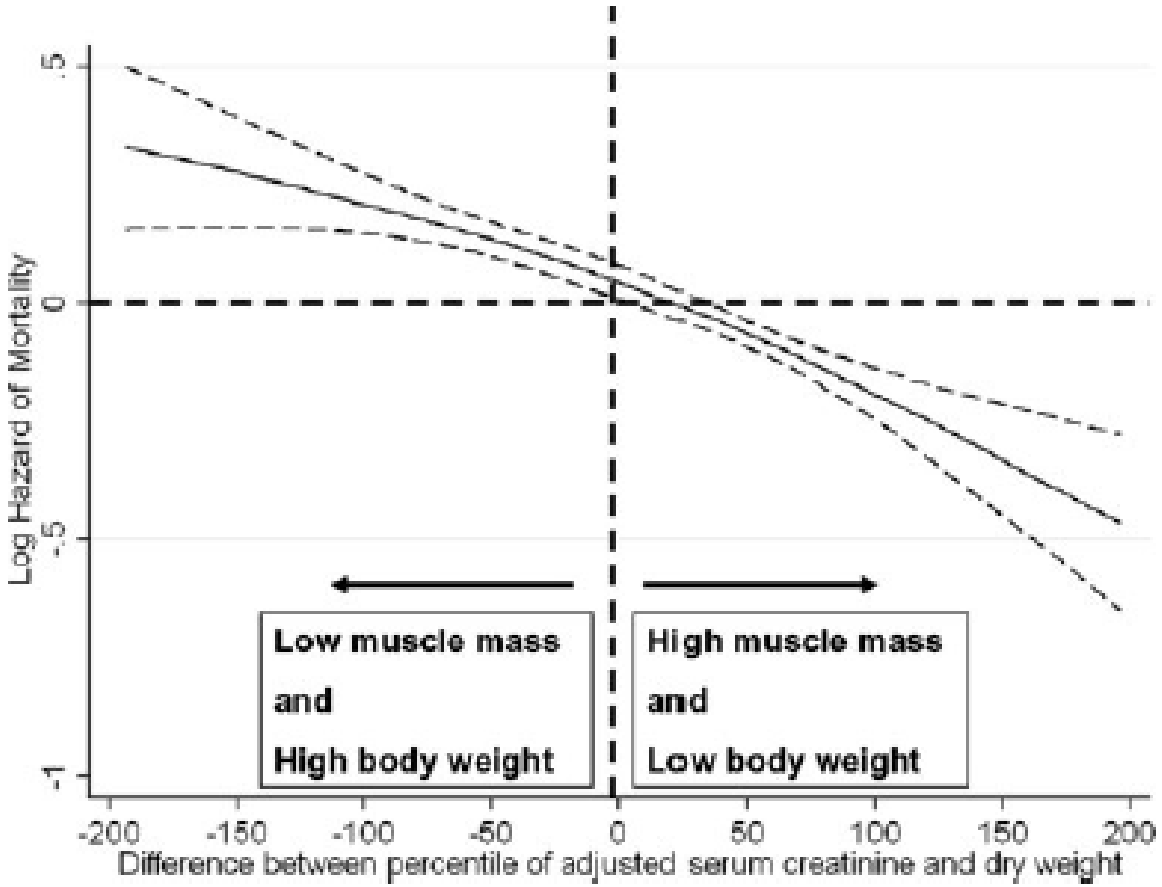


**Figure 7: Cubic splines models of Cox proportional regression to examine the mortality predictability of the combinations of the dry weight and in adjusted serum creatinine levels over a 6-year observation period (7/2001–6/2007).** The Y-axis shows the logarithm of the risk ratio of all-cause mortality over 6 years based on a multivariable Cox regression spline model, adjusted for case-mix. Dashed lines are 95% point wise confidence levels. Each patient received a percentile score between −100 and +100 according to the percentile rank of the change in dry weight or adjusted serum creatinine. The *difference* between adjusted serum creatinine concentration and dry weight in each patient also resulted in a number between −200 and +200.

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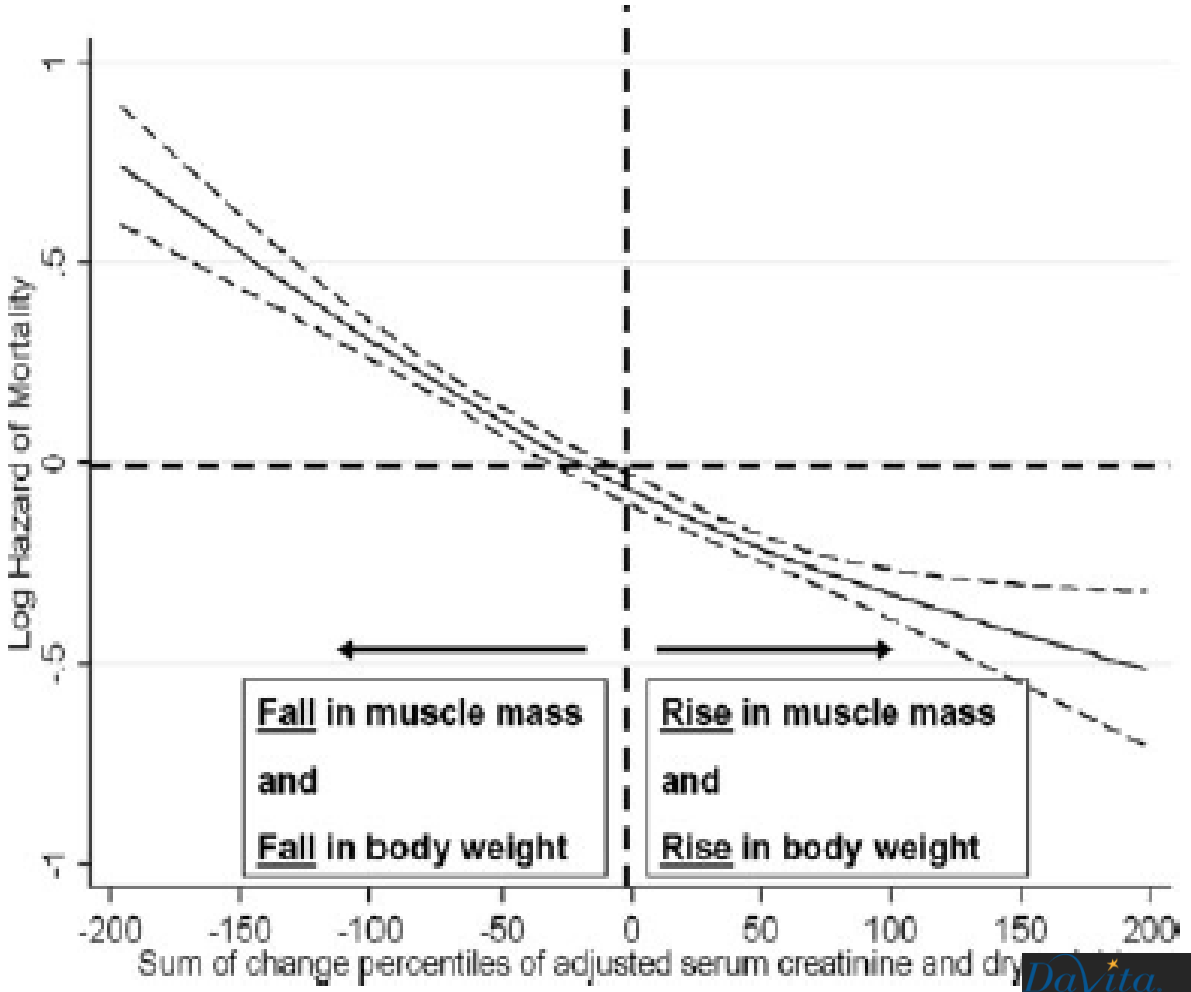



**Figure 8: Cubic splines models of Cox proportional regression to examine the mortality predictability of the combinations of the changes in dry weight and in adjusted serum creatinine levels over a 6-year observation period (7/2001–6/2007).** The Y-axis shows the logarithm of the risk ratio of all-cause mortality over 6 years based on a multivariable Cox regression spline model, adjusted for case-mix. Dashed lines are 95% point wise confidence levels. Each patient received a percentile score between −100 and +100 according to the percentile rank of the change in dry weight or adjusted serum creatinine. The *sum* of the two percentile scores for each patient resulted in a number between −200 and +200.

# The Survival Benefit of Kidney Transplantation in Obese Patients

J. S. Gill[1,2,3], J. Lan[1], J. Dong[1], C. Rose[1], E. Hendren[1], O. Johnston[1] and J. Gill[1,2,*]

American Journal of Transplantation 2013; 13: 2083–2090

- Comparing 208,498 waitlisted dialysis patients with 118,662 kidney transplant recipients from the same period (1995-2007)
- Source of data: USRDS
- Stratified by BMI and race

**Table 3:** Risk of death in transplant recipients compared to wait-listed patients with the same body mass index 1 year after transplantation

| | SCD recipients | ECD recipients | LD recipient |
|---|---|---|---|
| BMI < 18.5 | 0.33 (0.26, 0.41) | 0.30 (0.21, 0.42) | 0.35 (0.24, 0.52) |
| BMI 18.5–24.9 | 0.34 (0.30, 0.39) | 0.37 (0.32, 0.42) | 0.20 (0.15, 0.26) |
| BMI 25.0–29.9 | 0.32 (0.28, 0.37) | 0.43 (0.38, 0.50) | 0.30 (0.22, 0.47) |
| BMI 30.0–34.9 | 0.32 (0.26, 0.39) | 0.42 (0.35, 0.51) | 0.23 (0.17, 0.32) |
| BMI 35.0–39.0 | 0.34 (0.26, 0.46) | 0.39 (0.24, 0.52) | 0.28 (0.14, 0.50) |
| BMI ≥ 40.0 | 0.52 (0.37, 0.72) | 0.54 (0.33, 0.78) | 0.34 (0.19, 0.59) |

Separate multivariate nonproportional hazards analyses with transplantation treated as a time-dependent covariate to account for the fact that patients switched treatment from dialysis to transplantation at different times. Models adjusted for differences in patients characteristics including age, gender, cause of ESRD, history of comorbid conditions (ischemic heart disease, cerebrovascular disease, congestive heart failure, peripheral vascular disease, cancer), year of wait-listing and propensity score for transplantation.

# The Survival Benefit of Kidney Transplantation in Obese Patients

**J. S. Gill[1,2,3], J. Lan[1], J. Dong[1], C. Rose[1],** *American Journal of Transplantation 2013; 13: 2083–2090*

**Table 4:** Risk of death in Black and White transplant recipients compared to wait-listed patients with the same body mass index 1 year after transplantation

| | SCD recipients | ECD recipients | LD recipient |
|---|---|---|---|
| BMI < 18.5 | | | |
| Black | 0.40 (0.30, 0.60) | 0.23 (0.11, 0.46) | 0.43 (0.18, 1.00) |
| White | 0.29 (0.21, 0.39) | 0.29 (0.21, 0.42) | 0.26 (0.21, 0.54) |
| BMI 18.5–24.9 | | | |
| Black | 0.35 (0.27, 0.59) | 0.42 (0.31, 0.57) | 0.26 (0.15, 0.35) |
| White | 0.29 (0.25, 0.35) | 0.35 (0.29, 0.41) | 0.22 (0.17, 0.25) |
| BMI 25.0–29.9 | | | |
| Black | 0.30 (0.22, 0.41) | 0.47 (0.35, 0.62) | 0.28 (0.23, 0.76) |
| White | 0.33 (0.28, 0.39) | 0.35 (0.26, 0.40) | 0.30 (0.20, 0.42) |
| BMI 30.0–34.9 | | | |
| Black | 0.34 (0.24, 0.49) | 0.53 (0.37, 0.75) | 0.30 (0.16, 0.32) |
| White | 0.33 (0.24, 0.41) | 0.36 (0.28, 0.41) | 0.23 (0.16, 0.33) |
| BMI 35.0–39.9 | | | |
| Black[1] | 0.41 (0.24, 0.78) | 0.77 (0.50, 1.22) | 0.40 (0.27, 0.66) |
| White | 0.35 (0.24, 0.49) | 0.42 (0.29, 0.62) | 0.32 (0.20, 0.52) |
| BMI ≥ 40.0 | | | |
| Black[2] | 0.56 (0.33, 1.08) | 0.76 (0.08, 1.12) | 0.75 (0.31, 1.80) |
| White | 0.54 (0.33, 0.82) | 0.44 (0.25, 0.76) | 0.22 (0.07, 0.67) |

Separate multivariate nonproportional hazards analyses with transplantation treated as a time-dependent covariate to account for the fact that patients switched treatment from dialysis to transplantation at different times. Models adjusted for differences in patients characteristics including age, gender, cause of ESRD, history of comorbid conditions (ischemic heart disease, cerebrovascular disease, congestive heart failure, peripheral vascular disease, cancer), year of wait-listing.

[1]There were n = 5785 Black patients with BMI 35.0–39.9 including n = 671 who received and ECD transplant during follow-up.

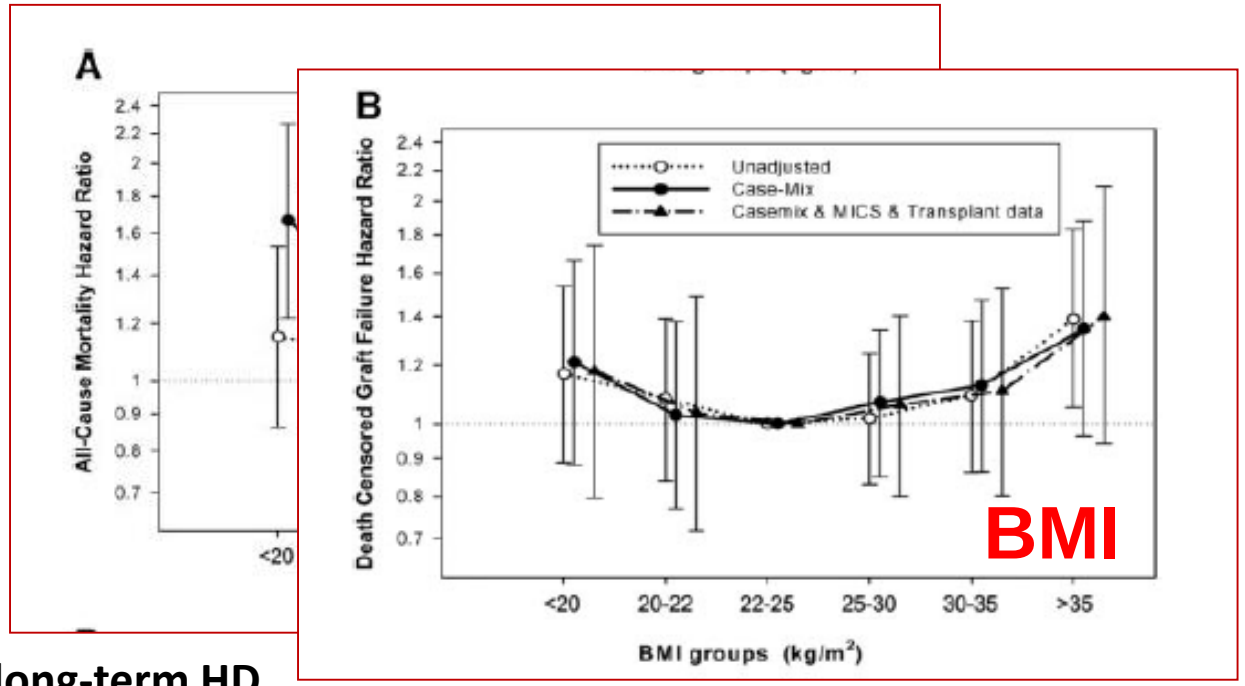
[2]There were n = 3832 Black patients with BMI ≥ 40 including n = 763, n = 335 and n = 350 who received and SCD, ECD and LD transplant during follow-up.

*CJASN ePress*. Published on May 26, 2011

# Associations of Pretransplant Weight and Muscle Mass with Mortality in Renal Transplant Recipients

**CJASN 2011**

*Elani Streja,*[*†] *Miklos Z. Molnar,*[*‡] *Csaba P. Kovesdy*[§‖] *Suphamai Bunnapradist*[¶] *Jennie Jing,*[*] *Allen R. Nissenson,*[¶**] *Istvan Mucsi,*[††] *Gabriel M. Danovitch,*[¶] *and Kamyar Kalantar-Zadeh*[*†¶]




**N= 10,090 long-term HD patients who underwent renal transplantation and were observed over a 6-year observation period (July 2001 to June 2007).**

Streja, Molnar … Kalantar-Zadeh, ***CJASN.*** 2011

DaVita Clinical Research

# Objectives

- Access to transplantation and recipient selection
- ”Evaluation visit”, what the patient should know
- General principles of recipient evaluation
- Cardiovascular morbidity and transplant
- Infectious disease and transplant
- Malignancy and transplant
- Respiratory and GI disease and transplant
- Obesity and transplant
- **Adherence, psychiatry disorders and transplantation**

# PS matched – 444 US Veteran

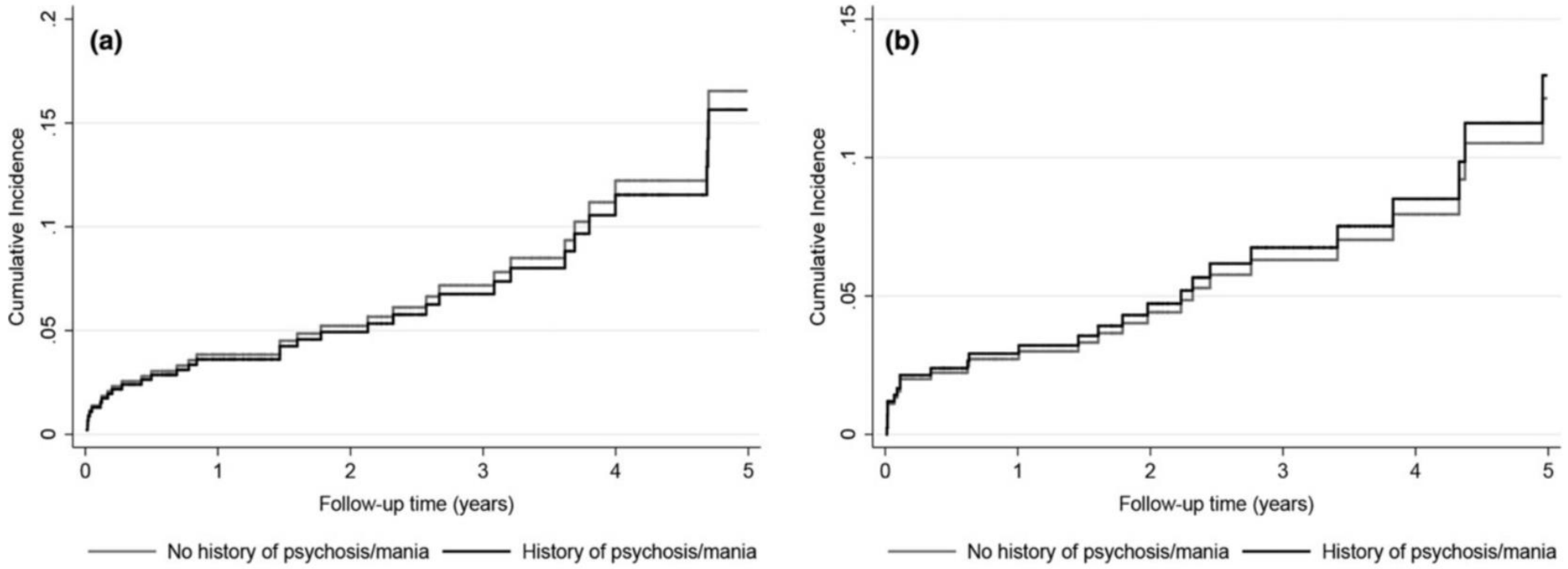



**Figure 2** Cumulative incidence of death with functioning graft (panel a) and graft loss (panel b) using competing risks regression models in the propensity-matched cohort.

Molnar MZ, TI, 2018

# PS matched – 444 US Veteran

**Table 2.** Association between history of psychosis and/or mania and post-transplantation outcomes using Cox proportional regression, competing risks regression, and logistic regression models in the propensity-matched cohort ($n$ = 442).

| History of psychosis and/or mania versus no. of history of psychosis and/or mania (ref.) | Hazard ratios (HRs) | 95% confidence interval of HRs | *P*-value |
|---|---|---|---|
| All-cause death | 1.04 | 0.51–2.14 | 0.913 |
| **History of psychosis and/or mania versus no. of history of psychosis and/or mania (ref.)** | **Subhazard ratios (SHRs)** | **95% confidence interval of SHRs** | ***P*-value** |
| Death with functioning graft | 0.94 | 0.42–2.09 | 0.881 |
| Graft loss | 1.07 | 0.45–2.57 | 0.874 |
| **History of psychosis and/or mania versus no. of history of psychosis and/or mania (ref.)** | **Odds ratios (ORs)** | **95% confidence interval of ORs** | ***P*-value** |
| Rejection | 1.23 | 0.60–2.53 | 0.567 |
| | **History of psychosis and/or mania** | **No of history of psychosis and/or mania** | ***P*-value*** |
| Immunosuppressive adherence: proportion of days covered for | | | |
| Tacrolimus (%) (mean ± SD) | 76 ± 21 | 78 ± 19 | 0.529 |
| Mycophenolic acid (%) (mean ± SD) | 78 ± 17 | 79 ± 18 | 0.666 |
| Immunosuppressive persistence: 30 days gap | | | |
| Tacrolimus | 54% | 54% | 0.998 |
| Mycophenolic acid | 49% | 48% | 0.949 |

HR, hazard ratio; OR, odds ratio; SHR, subhazard ratio.

**P* values for adherence are result of *t*-test and chi-squared test.

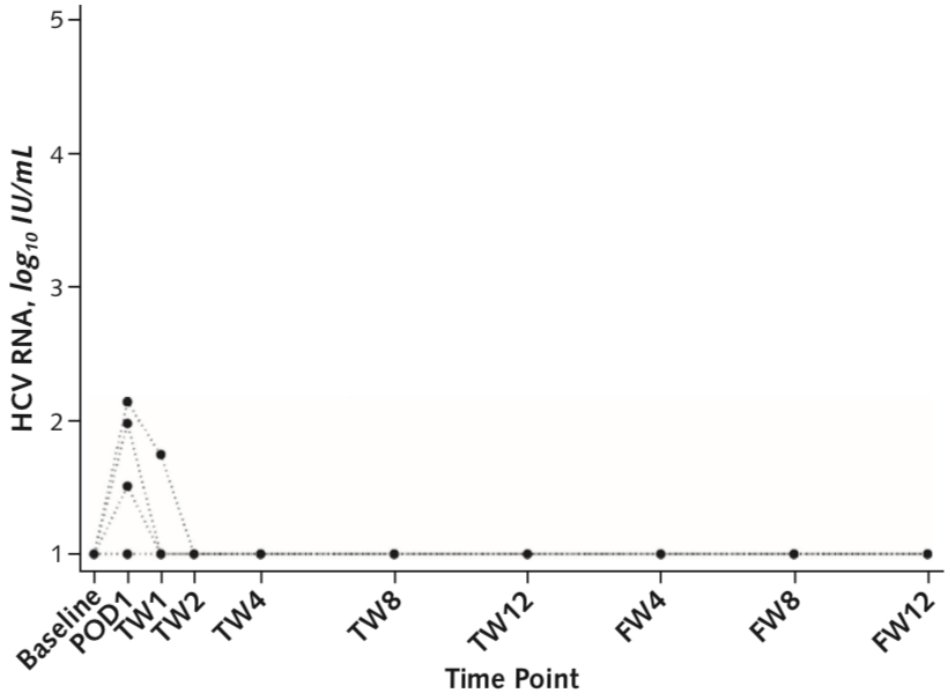
Molnar MZ, TI, 2018

**Thank you very much for your attention!**

**Questions?**

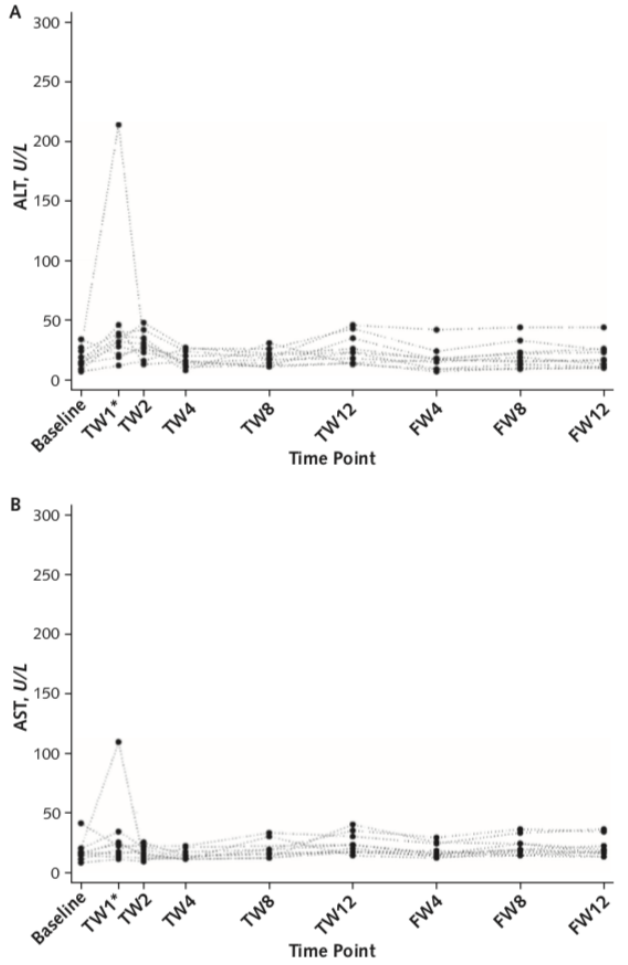
# EXPANDER Trial (Durand CM, Annals, 2018)

***Figure 1.*** Pre- and posttransplantation HCV RNA levels in non–HCV-infected recipients of kidneys from HCV-infected donors.




Shown are plasma HCV RNA levels before transplantation (baseline); during DAA treatment on POD1; at TW1, TW2, TW4, TW8, and TW12 after transplantation; and at FW4, FW8, and FW12 after DAA treatment. Lower limit of quantification is 15 IU/mL. DAA = direct-acting antiviral; FW = follow-up week; HCV = hepatitis C virus; POD = postoperative day; TW = treatment week.

***Figure 2.*** Posttransplantation liver function tests in non–HCV-infected recipients of kidneys from HCV-infected donors.




Shown are (**A**) ALT and (**B**) AST values measured at baseline and during posttransplantation follow-up. ALT = alanine aminotransferase; AST = aspartate aminotransferase; FW = follow-up week; HCV = hepatitis C virus; TW = treatment week.
* Missing for 1 patient.

# THINKER trial – UPenn (NEJM, Goldberg Ds, 2017)

- The median 6-month serum creatinine level was 1.1 mg per deciliter; inter-quartile range, 0.8 to 1.3 mg per deciliter), and the estimated glomerular filtration rate was 62.8 ml per minute per 1.73 m2 (interquartile range, 51.8 to 83.1).
- One recipient had delayed graft function
- transiently elevated aminotransferase levels developed in two recipients
- transient new class I donor- specific antibody level (1800 mean fluorescence intensity units) developed in one patient.
- Proteinuria (at an estimated level of 2 g per day of urinary protein excretion) developed in one patient who had IgA nephropathy before transplantation; in this patient, focal segmental glomerulosclerosis was detected on biopsy after a sustained virologic response was reached 12 weeks after the end of treatment.