Comprehensive Assessment of Solid Organ Transplant Recipients and Living Donors

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Disclosure: Fremonta Meyer, MD

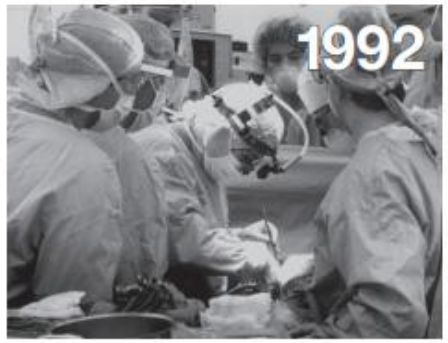
With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company in the past 24 months which could be considered a conflict of interest.

- Receive annual honorarium from Up To Date for writing chapter on topic unrelated to this presentation

Outline

- History and demographics/epidemiology of transplant
- Psychiatric assessment of prospective recipients
- When the transplant is the consequence of a substance use disorder: early liver transplant for alcoholic hepatitis
- Psychiatric contraindications to transplant: case example
- Post-transplant psychiatric considerations
- Demographics/epidemiology of living organ donation
- Psychiatric/psychosocial assessment of prospective living donors
- Potential psychological complications for donors: case example

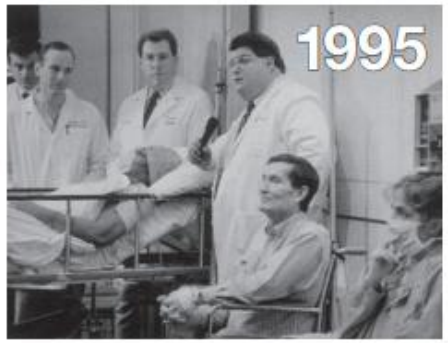
1954: kidney
1960's: liver, heart, pancreas
1980's: lung
1984: United Network of Organ Sharing (UNOS) founded in USA



Heart-Lung Transplant

First in New England

» Brigham and Women's Hospital (BWH) becomes the first hospital in Massachusetts to replace a patient's heart and lung in one operation.

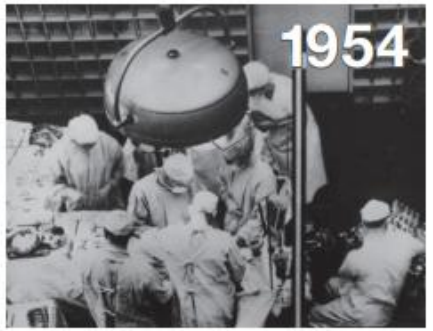


Triple Transplant

First in the U.S.

» BWH performs the nation's first triple organ transplant, removing three organs from a single donor – two lungs and a heart – and transplanting them into three recipients.

BWH BRIGHAM AND WOMEN'S HOSPITAL



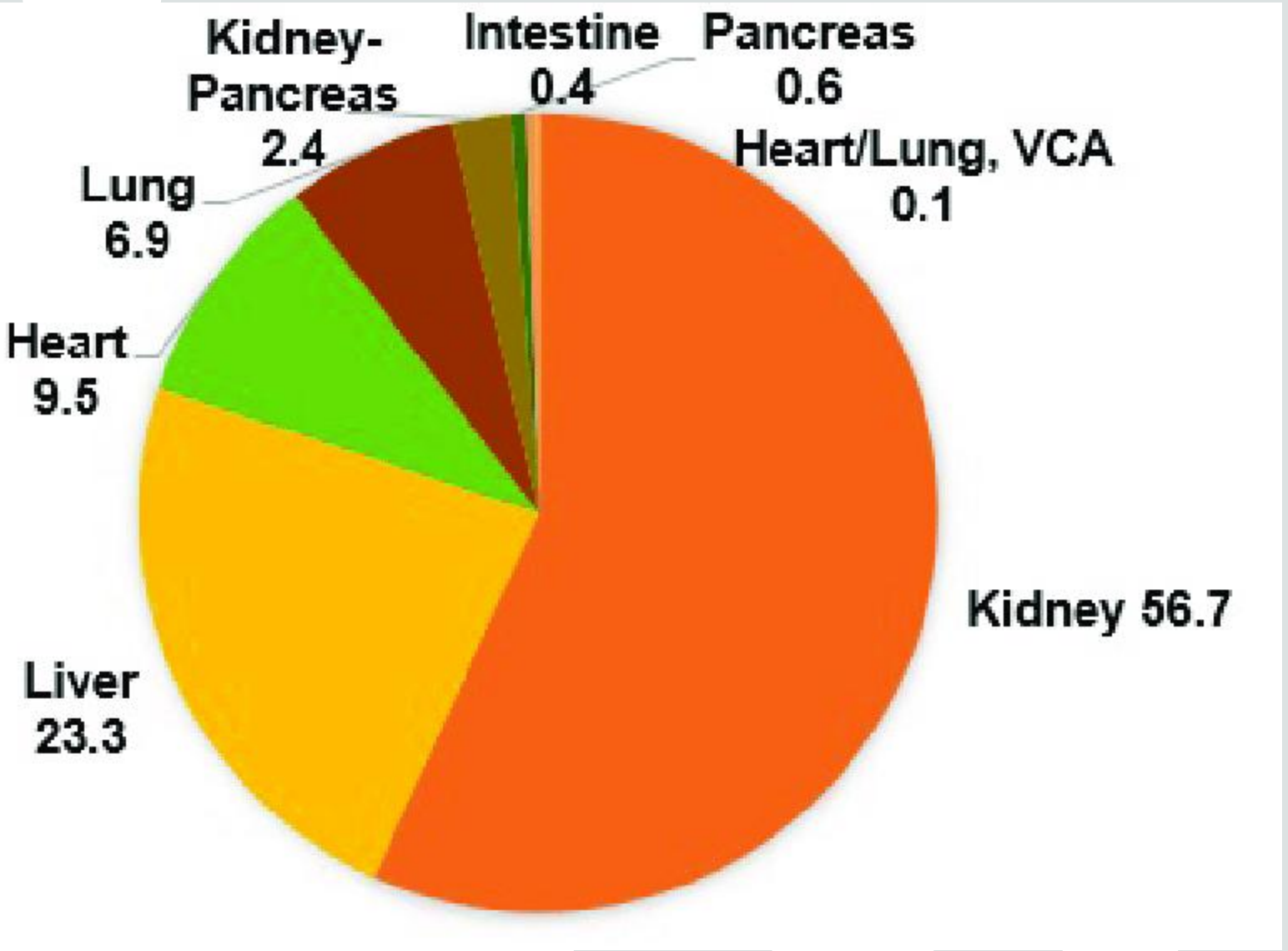
Human Organ Transplant

First in the World

» A surgical team led by Dr. Joseph Murray transplants a kidney from one identical twin to another. Dr. Murray receives the Nobel Prize in 1990 for this work and his subsequent development of immunosuppressive drugs to help prevent rejection of transplanted organs.

As of 2022, 1 million transplants have been performed in the US

2024: 48,000 in the US (highest # ever)



VCA=vascularized composite allografts (face and hand transplants)

Solid organ transplant survival rates

"Trading one disease for another"

Lung: 80% at 1 year, 65% at 3 years, 54% at 5 years, 32% at 10 years

Heart: 80-85% at 1 year, 50% at 10 years

Liver: 81% (living donor) and 76% (deceased donor) at 5 years *(living donors--only 5% of transplants in US)

Kidney: 81% (living donor) and 67% (deceased donor) at 10 years; better than dialysis

*Rana A, Gruessner A, Agopian VG. JAMA Surg 2015; 150: 252-259
*UNOS data

Surviving
Dialysis vs Cancer

Patients diagnosed with many forms of cancer
have better outcomes than dialysis patients.

83% **of lung cancer patients**
die 5 years after diagnosis

60% **of dialysis patients**
die 5 years after diagnosis

11% **of breast cancer patients**
die 5 years after diagnosis

9% **of skin cancer patients**
die 5 years after diagnosis

1% **of prostate cancer patients**
die 5 years after diagnosis

Ethnic and cultural considerations

- Black patients are referred for kidney and liver transplant less often and have longer wait list time
- Socioeconomic status: high-poverty neighborhood dialysis centers less likely to refer patients for renal transplant
- Black females, followed by Black males, have highest mortality after heart transplant

*Ladin K et al. Am J Transplantation 2009; 9: 669-674
*Higgins RSB, Fishman JA. Am J Transplantation 2006; 2556-62
*Patzer RE et al. JAMA 2015; 314: 582-94

Transplant Evaluation

- Organized by nurse coordinator
- Financial clearance
- Formal education by transplant physician and surgeon
- Social work evaluation, +/- psychiatry, psychology, neuropsychology
- Committee meeting
- Notification of decision within 10 days of meeting
- Wait list visits
- Possible dry runs

*Kuntz K, Weinland S, Butt Z. J Clin Psychol Med Settings 2015; 22: 122-135

Aims of Psychosocial Evaluation

- Ensure transplant will provide a survival and quality of life benefit for the candidate
- Optimize the candidate's psychosocial status prior to transplant
- Understand and manage expectations of candidate and family members
- Ensure optimal use of limited resource (given shortage of donor organs)
  - 10-15% of listed heart and lung transplant patients die before receiving a transplant

*Bailey P et al. Transplantation 2021; 105: 293-302
*Agren S et al. Clinical Transplantation 2017; 31:e12905

Supplemental elements of psychiatric assessment in solid organ transplant recipients

*Narrative of end organ medical diagnosis

*Oxygen dose/duration (lung), dialysis schedule/duration (kidney +/- liver)

*Family history of similar medical disease

*Pulmonary or cardiac rehab

*Adherence with meds, dialysis, fluid/salt restriction – self report and chart review/collateral

*What's their understanding of risks/benefits? Why do they want transplant – what are their goals?

Supplemental elements of psychiatric assessment in solid organ transplant recipients

*Do they know anyone who had a solid organ transplant?

*Have they read written material and/or watched educational videos provided by transplant team?

*Prior steroid-related neuropsychiatric symptoms

*History of delirium

*Spirituality; other coping strategies

*Baseline cognitive assessment–e.g. MOCA

Psychiatric assessment: Other

*Always request collateral from outside treaters

Important to make sure care can be coordinated if necessary in future

*Meet with family members if possible

*Be aware of possible symptom minimization

Early liver transplant (LT) for alcoholic hepatitis (AH)

- Defined as transplant performed without 6-month period of pre-LT alcohol abstinence
- *Rationale:* at least 25% of patients with severe AH die within 3 months without LT
- *Concern:* relapse to alcohol post-LT – steatosis, fibrosis, graft failure, lower survival
  - Relatively brief disease awareness compared to other liver diseases – could elevate risk
- 75% of alcohol relapses occur in first year
- Treatment post LT
  - Monitoring with biomarkers (combination of urinary ethyl glucuronide + carbohydrate deficient transferrin (CDT); phosphatidylethanol (PEth))
  - Medications e.g. naltrexone, acamprosate, gabapentin, topiramate – absence of supporting literature, but probably safe
  - Behavioral therapy

Sample criteria: early liver transplant for alcoholic hepatitis

- Severe alcoholic hepatitis nonresponsive to steroids and MELD>30
- First alcohol-related decompensating event with no prior knowledge or insight into the presence of alcohol use disorder
- SALT (Sustained Alcohol Use Post-Liver Transplant) score < 5
- Grade II or less hepatic encephalopathy (West Haven criteria)
- Strong/durable social supports
- No refractory psychiatric symptoms and no SUD other than alcohol, tobacco, cannabis

From: MGB Protocol for Severe Alcoholic Hepatitis and Liver Transplant Consideration

***SALT scoring:**

- >10 drinks/d at initial hospitalization (+4)
- Multiple prior rehab attempts (+4)
- Prior alcohol-related legal issues (+2)
- Prior non-cannabis illicit substance misuse (+1)

Absolute Contraindications to Transplant Listing

- Active suicidal or homicidal ideation
- Active psychosis
- Dementia
- Personality disorders impeding collaborative work with transplant team
- Persistent lack of social support

Case

- 67yo married mother with interstitial lung disease on mycophenolate diagnosed 6 years ago, worsening after spontaneous pneumothorax year prior, on 3-4L continuous home oxygen
- Support team comprised of son, daughter, family friend; siblings not supportive of transplant
- Husband -> known Alzheimer's dementia. Wandering. No home care yet
- Cognitive concerns – childhood "slow learner"
- MOCA 18/30 – delayed recall 0/5, 1/5 cues, 4/5 multiple choice; borderline semantic fluency
- Neuropsych testing substantiated concerns
- Patient declined for listing

Delirium after solid organ transplant

- Lung: 37-44%; Liver: 17-47%; Heart 9%; Kidney: 4.7%; (underestimates?)
- Predictors:
  - Liver – alcohol use/abuse, hepatic encephalopathy, antidepressant use, older age, intubation duration, higher MELD score
  - Kidney – frailty, older age
  - Lung – worse preop cognition, obesity
- Outcomes
  - Mortality, longer LOS, increased ICU and ventilation time, higher cost of care
  - Increased risk of primary graft dysfunction and graft loss (lung, kidney)

- May herald apathy and cognitive decline

*Chu NM, Segey DL, McAdams-DeMarco N. Curr Transplant Rep 2021; 8: 118–126

Effect of transplant on mental health

20% kidney, 30% liver, up to 60% of heart develop mood/anxiety disorders in 1st year

Heart: Elevated risk with pretransplant psychiatric disorder, female gender, longer hospitalization, more impaired functional status, lower social support*

***Psychiatric distress in early aftermath of transplant bears stronger relationship to morbidity/mortality than distress occurring pre-transplant

*Dew MA et al. Psychosomatics 2001; 42:300
*Rosenberger EM et al. Curr Opin Organ Transplant 2012; 17: 188-92

Post-transplant psychological issues

Physical discomfort, medication side effects, altered body image

Frequent hospitalizations

Worry about transplant failure – rejection; other organ failures

Inability to work – feel like burden

Social isolation – due in part to infection risk

Emotional management – e.g. irritability with caregivers

Counterbalances: Spirituality/prayer, responsibility of living with a blessing (*donor letter), professional/family/peer support, regular exercise and dietary adjustments

*Yang FC et al. Transplantation Proceedings 2020; 52: 3226-3230
*Fatma C et al. QOL Research 2021; 30:1619-27

Post-transplant psychological issues

- Naivete – after initial positive post-op course and normalization of end-organ function, pts can feel immune to complications – may result in reduced self-care and vigilance over time

- Nonadherence to medication increases over time – up to 36% in long run, highest in kidney pts

*Dabbs AD, Hoffman LA, Swigart V et al. Soc Sci Med 2004; 59: 1473-1484
*Rynar LZ, Merchant MS, Dilling DF. Clinical Transplantation 2018; 32:e13263
*Dew MA et al. Transplantation 2007; 83: 858-73

Calcineurin inhibitors (tacrolimus, cyclosporine)

Impair transcription of IL-2 and several other cytokines in T lymphocytes

Tacrolimus – IR BID; XR QD

Trough level – 12 or 24 hr post-dose; weekly until 3 months posttransplant; then monthly

Metabolized by CYP3A4 and P-glycoprotein

Impact on levels:

 : Paxlovid, azole antifungals, HIV protease inhibitors, macrolide antibiotics, grapefruit juice, fluvoxamine, nefazodone

 : enzyme inducing AED's (carbamazepine, phenytoin, primidone, phenobarbital), rifampin, St. John's Wort, modafinil

Side effects of calcineurin inhibitors

- Nephrotoxicity
- Hypertension
- Glucose intolerance and diabetes mellitus
- Neurotoxicity
  - Tremor – 35-55%
  - Posterior reversible leukoencephalopathy (PRES) – headache, visual changes, seizures
- Pain syndrome – lower limbs (symmetrical)
- Hyperuricemia/gout
- Hyperkalemia
- Hypomagnesemia

Side effects of calcineurin inhibitors

- Gastrointestinal – anorexia, n/v/d, pain
- Alopecia
- Gingival hyperplasia (cyclosporine)
- Infections – bacterial, viral (CMV), fungal
- Malignancy
  - Squamous cell carcinoma of skin
  - Lymphoproliferative disorders

Psychotropics most dependent on renal excretion

- Lithium
- Gabapentin
- Pregabalin
- Topiramate
- Paliperidone

*Renal disease decreases protein binding of medications (due to uremia, hypoalbuminemia, drug interactions).

Therefore, free drug concentration more reliable than total drug concentration (e.g. valproate)

Psychotropics requiring dose adjustment in renal impairment

- Anticonvulsants: gabapentin, oxcarbazepine, pregabalin (*dose after dialysis), topiramate, lithium
- Antidepressants: bupropion, citalopram, paroxetine, venlafaxine (*dose after dialysis), desvenlafaxine; avoid duloxetine in dialysis pts
- SGAs: brexpiprazole (not aripiprazole--excreted in feces), clozapine, risperidone; paliperidone (avoid in ESRD)
- Procognitive agents: amantadine, galantamine, memantine, rivastigmine
- Sedative/hypnotics for sleep: no clear need to adjust
- Stimulants: no clear need to adjust

*Goldberg JF and Stahl SM. Practical Psychopharmacology. Cambridge: Cambridge UP, 2021.

Kidney Transplantation
Saves Lives

There are **not enough kidneys** available.

On average,
20
people die every day
while waiting
for a transplant

In the U.S.
100,000+
patients
need a kidney transplant
& **5,000+** will die yearly.

In Georgia,
Only 1/3
of kidney transplants
are made possible
by living donors
every year.

6-8 years
kidney transplant median wait time

Every 14 minutes
someone is added
to the **kidney transplant list**

3,000
new patients
added to the wait list each month

3 Types of Living Donation

Matching Donors to Recipients

There are three categories of living donations:

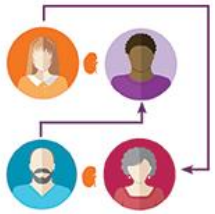
#1 Directed Donation:

This is when the donor specifically chooses who will receive the transplant.

#2 Non-Directed Donation:

This is when the donor is neither related to nor known by the person in need. He or she makes the donation purely out of selfless reasons. The recipient is determined primarily by medical compatibility.

#3 Paired Donations (Kidney Only):



This involves at least two pairs of living-kidney donors and transplant candidates who do not have matching blood types. The transplant candiates "trade" donors so that each recipient receives a kidney from the donor with a compatible blood type.

Living donation is not as rare as you might think.

47%

of all transplanted organs in the U.S. are from living donors.

The need for living-liver donors is a big one. 30 million Americans have some form of liver disease.

1 person = 1 million

UPMC LIFE CHANGING MEDICINE | DONATE LIFE

Surgeons transplant a genetically edited pig kidney into patient Tim Andrews on Jan. 25. Image: Kate Flock/Mass General

Mass General Brigham

Surgeons Transplant Engineered Pig Kidney Into Fourth Patient

A 66-year-old man from New Hampshire became the fourth person to receive a pig's kidney.

Living liver donors

- Most commonly: adults donating left lateral segment to children with biliary atresia – less volume (20%) is removed

- Right lobe living liver donor hepatectomy (adult to adult) – only a few centers
  - 40% morbidity (much higher than kidney donation)
  - 3% psychological complications

- Age < 60 to proceed

Living kidney donation: medical basics

- Loss of 25-35% of renal function
- 4-5 hr surgery, laparoscopic; largest incision 3-4in; 1-2 nights in hospital
- No lifting, pushing, pulling anything over 15 lbs for 3 months
- No NSAIDs and no protein supplements for life
- Donor medical expenses covered by separate fund
- Donation status may affect candidacy & premiums for health, disability, life insurance in future
- Need to provide health info to transplant center at 1 week post-op, 6 months, 1 year and 2 years post-donation

Living kidney donors: medical and psychological effects

- RELIVE study: 80% reported average or above average health for age at follow-up
- 1% reported negative impacts of donation on health
  - Higher risk if obesity at time of donation
- Predictors of depression post-donation:
  - Non-Caucasian race
  - Younger age
  - Longer recovery post-donation
  - Greater financial burden
  - Feelings of moral obligation

*Gross CR et al, Am J Transplantation 2013; 13: 2924-34
*Jowsey SG et al, Am J Transplantation 2014; 14: 2535-44

Donor psychosocial evaluation

- Identify any risks for poor psychosocial outcomes
- Ensure understanding of risks, benefits and outcome of donation for her/himself and the recipient
- Assess ability to cope with major surgery and related stress
- Assess donor motives – free of guilt, undue pressure, enticements, impulsive response
- Review employment and family relationships that might be affected by donation
- Ensure adequate social support – family support; availability of post-operative care/transportation

Can be done by LICSW (master's level), psychologist or psychiatrist

Donor psychosocial evaluation (cont)

- Donation consistency with past beliefs/behaviors
  - Donor on driver's license
  - History of altruistic behaviors, volunteering
  - Values, lifestyle, faith
- Relationship with transplant candidate
  - Duration
  - Type/closeness
    - Internet/social media only: may require further eval
  - Expectations for change in relationship
  - Feelings of obligation/desire for forgiveness
  - Coercion
    - Ex: assistance with living expenses/college; employee/employer; family pressure; faith community pressure

Follow-up psychosocial care of donors

- Follow up after decline of candidacy at least once routinely
  - Reasons include medical diagnoses (e.g. cancer), misattributed paternity

- Follow up after donation surgery at least once routinely
  - More often if new psychiatric symptoms; known complications for donor or complications/death of recipient

Independent living donor advocate evaluation

Represent, advocate, protect, promote best interest of living donor

- Can be LICSW, physician, psychologist, RN, clergy or ethicist
- Assess willingness, competence
  - Emphasis on voluntariness and ability to withdraw up until the moment of getting anesthesia
- Assess motivations
- Assess pressure/coercion
  - Donor should be seen alone
- Rule out valuable consideration which is illegal (financial compensation beyond travel/housing/lost wages)
- Understand donor's experience with loss/grief (in case of recipient death)

*Lapointe Rudow D et al. J Clin Psychol Med Settings 2015; 22: 136-49

Case: donor psychological complications

- 41-year-old female nurse with h/o borderline personality disorder in remission after DBT; one prior suicide attempt by overdose in late teens
- Psychosocially cleared for kidney donation to father
- Donated in swap to unrelated recipient; father had medical complications and has not yet received another organ
- Surgery complicated by persistent abdominal pain with late onset ipsilateral adrenal hemorrhage seen on CT, later found to have large growth in fibroids, s/p hysterectomy; fibroids found to be necrosed
- Psychiatry consult 9 months postop for mood swings, paranoia toward transplant team and nurse coordinator
- “Do not understand why the recipient wouldn’t want to write to me or meet me if they are doing well”
- Father considering transition to palliative care

Summary

- Transplant recipient and donor psychosocial evaluations should be as comprehensive as possible in order to forecast future difficulties
- Few “absolute” psychosocial contraindications to candidacy but many “relative” concerns
- Evaluations should include active efforts to improve/remediate any areas of concern
- Clinicians involved in pre-transplant evaluations should maximize their familiarity with post-transplant issues (ideally by consulting on and/or following patients)
  - Improves forecasting

With gratitude…

*Transplant Psychiatry and Social Work colleagues – Maureen Cassady, MD; Angela Lombardo LICSW, Kaitlyn Randor LICSW

*Brigham Lung Transplant team (Adil Sheikh MD, Hilary Goldberg MD)

*Dept of Psychiatry at MGB–Nomi Levy-Carrick MD, Maurizio Fava MD, David Silbersweig MD

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