

# Primary Care of the Solid Organ Transplant Patient

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The speaker has no conflicts of interest to disclose in relation to this content.

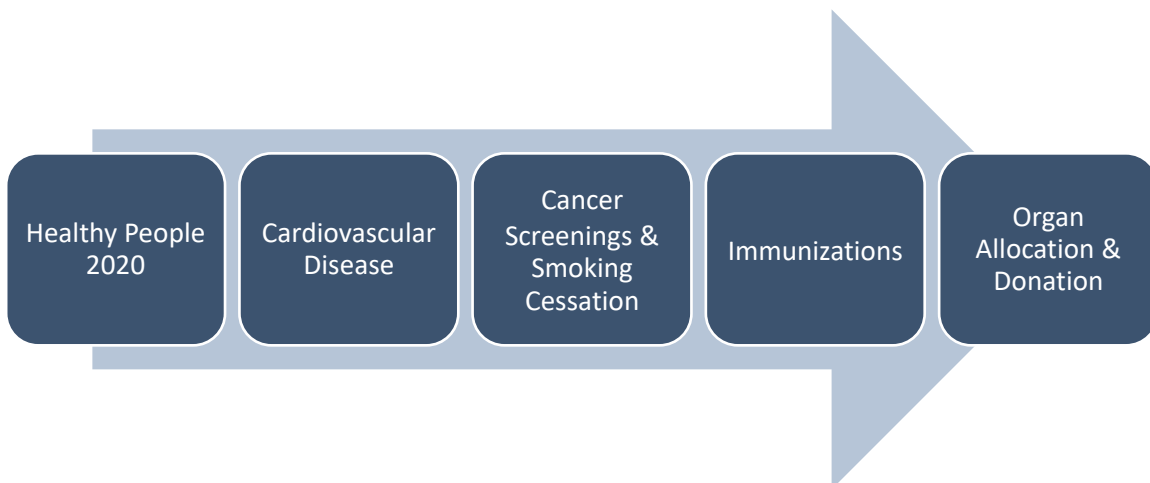
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## Learning Objectives

- Apply general principles and practices of disease prevention to solid organ transplant recipients.
- Outline unique patient populations that require additional disease screening.
- Create an immunization plan for a solid organ transplant recipient in both the pre and post-transplant setting.
- Identify reputable resources for public education and awareness on organ transplantation including organ donation.

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## Lecture Outline



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# Healthy People 2020



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## Healthy People 2020

- Department of Health and Human Services initiative for health promotion and disease prevention
- Mission:
  - Identify nationwide health improvement priorities
    - Cardiovascular disease, cancer screenings, smoking cessation, etc.
  - Increase public awareness and understanding of disease
  - Identify areas of research in the sector of public health

Healthy People 2020. Washington, DC: U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion [cited November 18<sup>th</sup>, 2019]. Available from: <https://www.healthypeople.gov/>

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# Prevention of Cardiovascular Disease



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## Cardiovascular Disease after Transplant

- Significant morbidity & mortality
  - Death from cardiovascular disease (CVD) is a leading cause of graft loss among kidney transplant recipients
  - Accounts for 50-60% of post-kidney transplant deaths
  - 10% of liver recipients will experience a CV event within the first year post-transplant
- Risk increases 3-5 fold in transplant recipients
  - Traditional risk factors: Diabetes Mellitus (DM), hypertension, hyperlipidemia, obesity
  - Transplant-specific risk factors related to immunosuppression

Fussner LA, et al. Liver Transpl. 2015;21(7):889-96.

Morales, JM, et al. J Hypertens. 2005 Sep;23(9):1609-16.

Padiyar A, et al. Prim Care. 2008 Sep;35(3):433-50.

Shirali AC, et al. Clin J Am Soc Nephrol. 2008 Mar;3(2):491-504.

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## Aspirin for Primary Prevention

- 2016 US Preventive Service Task Force: Consider daily low-dose aspirin for CVD and colorectal cancer primary prevention if:
  - Not at increased risk for bleeding
    - History of GI bleeding or peptic ulcer disease, steroids, thrombocytopenia, etc.
  - Adults aged 50 to 69 years with a  $\geq 10\%$  10-year CVD risk
  - Life expectancy of at least 10 years

Published Recommendations. U.S. Preventive Services Task Force. 2016  
<https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/aspirin-to-prevent-cardiovascular-disease-and-cancer>

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## Aspirin for Primary Prevention?

Trial	Population	Intervention	All-Cause Mortality	Major Bleeding
ASCEND, 2018	15,480 patients T2DM	ASA 100mg vs. placebo	9.7% vs. 10.2% (RR 0.94, 95% CI 0.85-1.04)	4.1% vs. 3.2% (rate ratio, 1.29; P=0.003)
ARRIVE, 2018	12,546 patients ASCVD risk $\sim 14\%$	ASA 100mg vs. placebo	At 5 years: 2.55% vs. 2.57% (HR 0.99; 95% CI 0.8-1.24)	GI: 0.87% vs. 0.46% (HR 2.11; P=0.0007)
ASPREE, 2018	19,114 patients > 70 years old	ASA 100mg vs. placebo	At 5 years: 12.7% (ASA) vs. 11.1% (HR 1.14; 95% CI 1.01-1.29)	N/A

\*The decision to initiate an aspirin regimen requires a patient-provider discussion, weighing the risks and benefits\*

T2DM = Type 2 Diabetes  
 ASA = Aspirin

Bowman, L et al. N Engl J Med. 2018;379(16):1529-1539.  
 Gaziano, JM, et al. Lancet. 2018;392(10152):1036-1046.  
 Mcneil JJ, et al. N Engl J Med. 2018;379(16):1519-1528.

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## New Onset Diabetes After Transplant

- NODAT risk highest in first 3 months post-transplant
  - At 1 year: 10-30% for those on CNI + corticosteroid (CS)
- Screening
  - Fasting BG, OGTT and/or HbA1c weekly x 4 weeks
  - Every 3 months for 1 year
  - Annually thereafter
  - Repeat screening after starting or increasing dose of CNI, mTORi, or CS
  - Follow WHO and ADA criteria for diagnosis

KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (Suppl 3): S71–S79.

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## Hypertension

- USPSTF: Screen adults aged 18 years or older
  - Obtain measurements outside of the clinical setting for diagnostic confirmation before starting treatment

KDIGO	AASLD	ISHLT (JNC)
<ul style="list-style-type: none"> <li>• 140/90</li> </ul>	<ul style="list-style-type: none"> <li>• 130/80</li> </ul>	<ul style="list-style-type: none"> <li>• ≥60: 150/90</li> <li>• &lt;60: 140/90</li> </ul>

KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (Suppl 3): S71–S79.

Lucey MR, Terrault N, Ojo L, et al *Liver Transpl.* 2013;19(1):3-26.

Costanzo MR, Costanzo MR, Dipchand A, et al. 2010;29(8):914-956.

Armstrong C; Am Fam Physician. 2014 Oct 1;90(7):503-4.

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## Hyperlipidemia

- Monitoring:
  - Kidney: 2-3 months post-transplant
  - After a change in immunosuppression + before mTORi usage
  - Annually thereafter
- Early initiation of therapy results in a greater reduction in CVD events

Padiyar A, et al. Prim Care. 2008 Sep;35(3):433-50.

KDIGO Clinical Practice Guideline for the Care of Kidney Transplant Recipients. American Journal of Transplantation 2009; 9 (Suppl 3): S71–S79.

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## Statin Benefit Groups

- LDL-C  $\geq 190$  mg/dL: High-intensity statin
- Age 40-75 years + DM
  - Moderate intensity statin
  - ASCVD  $\geq 7.5\%$ : High intensity statin
- Age 40-75 years and LDL-C  $\geq 70$  mg/dl and  $< 190$  mg/dl
  - ASCVD 5% to 20%: Moderate intensity
  - ASCVD  $\geq 20\%$ : High intensity statin
- Age  $> 75$  years clinical assessment and risk discussion

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019.

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## Statin Intensities

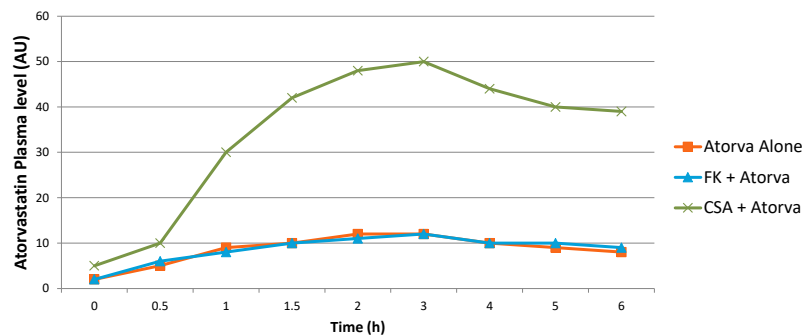
High Intensity	Moderate Intensity	Low Intensity
↓ LDL $\geq$ 50%	↓ LDL 30% to 50%	↓ LDL < 30%
Atorvastatin 40-80 mg Rosuvastatin 20-40mg	Atorvastatin 10-20mg Rosuvastatin 5-10mg Simvastatin 20-40mg Pravastatin 40-80mg Lovastatin 40mg Fluvastatin 40mg BID Pitavastatin 2-4mg	Pravastatin 10-20mg Lovastatin 20mg Simvastatin 10mg Fluvastatin 20-40mg Pitavastatin 1mg

Stone NJ. Et al. Circulation 2014;63:2889-2934

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## Statin Drug Interactions with Immunosuppressants

- Statin dose adjustments may be required due to CYP 3A4 and P-GP competitive inhibition with CNIs (CSA >> FK)
  - CSA inhibition of OATP1B1 → increased statin systemic exposure



Adapted from: Lemahieu WP, et al. Am J Transplant. 2005;5(9):2236-43.

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## Statin use in Special Populations

- Lung Transplant
  - Decreased risk of grade 2 or 3 primary graft dysfunction (PGD) and chronic rejection
- Heart Transplant
  - short/long-term rejection, cardiac allograft vasculopathy (CAV), and survival
  - Initiate 1-2 weeks after transplant regardless of cholesterol levels (Class I, level of evidence A)
    - Limited evidence supporting use of high intensity statin for CAV
    - Recommended statin doses:
      - Pravastatin 20-40mg
      - Atorvastatin 10-20mg
      - Rosuvastatin 5-20mg
      - Simvastatin 5-20mg

Raphael J, et al. J Heart Lung Transplant. 2017;36(9):948-956.

Sieg A, et al. Transplant Rev. 2016;30(3):178-86.

Costanzo MR, et al. J Heart Lung Transplant. 2010;29(8):914-56.

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## Cancer Screenings and Smoking Cessation

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## Cancer Screenings\*

### Men

- Prostate:
  - Consider PSA testing in those 55 to 69 years
  - Not recommended in men  $\geq 70$  years
- Colon cancer:
  - Screening starting at 45 to 75 years
  - Colonoscopy every 10 years
  - Flexible sigmoidoscopy: every 5 years
  - Stool-based tests: annually

### Women

- Cervical: Every 3 years (ages 21-65)
- Breast: Biennial screening with mammography (ages 50-74 years)
- Colon cancer:
  - Screening starting at 45 to 75 years
  - Colonoscopy every 10 years
  - Flexible sigmoidoscopy: every 5 years
  - Stool-based tests: annually

\*For recipients at average risk for development of cancer

*Published Recommendations. U.S. Preventive Services Task Force. <https://www.uspreventiveservicestaskforce.org/BrowseRec/Search?s=cancer>*

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## Skin Cancer Screening

Patient Characteristic	Screening Recommendation
<b>High risk:</b> Caucasian + $\geq 1$ of the following: <ul style="list-style-type: none"> <li>• Thoracic organ</li> <li>• Age &gt; 50 years</li> <li>• Male</li> </ul>	Within 2 years of transplantation
<b>High risk:</b> African American + $\geq 1$ of the following: <ul style="list-style-type: none"> <li>• Thoracic organ</li> <li>• Age &gt; 50 years</li> <li>• Male</li> </ul>	Within 5 years of transplantation
<b>Low Risk:</b> <ul style="list-style-type: none"> <li>• Caucasian with no additional risk factor</li> <li>• Hispanic and Asian SOT Recipients</li> </ul>	Within 5 years of transplantation
Low Risk African American	No consensus reached

Crow LD, et al. Transpl Int. 2019;32(12):1268-1276.

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## Special Populations

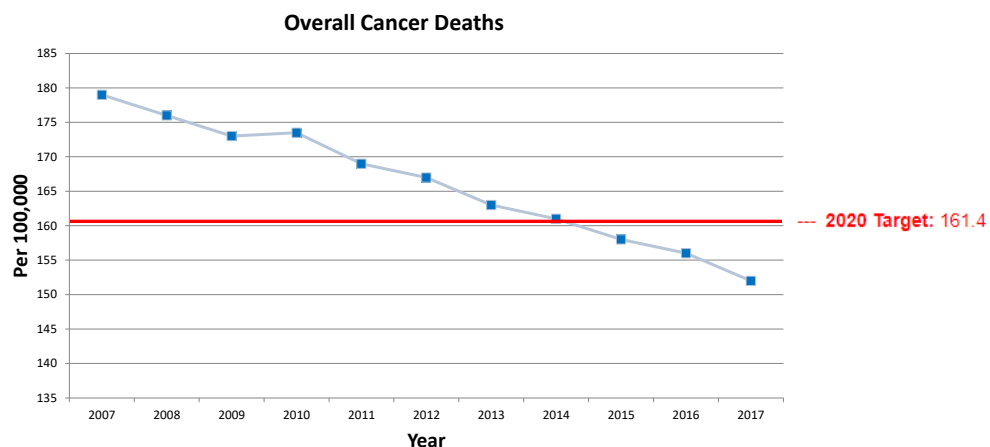
- Hepatocellular Carcinoma:
  - Consider chest/abdomen CT every 6 to 12 months for the first 3 years
  - Consider serial measurement of alpha-fetoprotein (AFP) in those with elevated AFP pre-transplant
- Primary Sclerosing Cholangitis and IBD:
  - Annual colonoscopy with biopsies
- High risk for renal cell carcinoma (acquired cystic, family hx, smokers)
  - Native kidney ultrasound (annually or biennially)

Lucey MR, et al. Liver Transpl. 2013;19(1):3-26.

Al-Adra D, Al-Qaoud T, Fowler K, Wong G. CJASN. 2021;CJN.14570920.

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## Cancer: Healthy People 2020



Adapted From: Bridged-race Population Estimates; Centers for Disease Control and Prevention, National Center for Health Statistics and U.S. Census Bureau (CDC/NCHS and Census)

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## Smoking Cessation

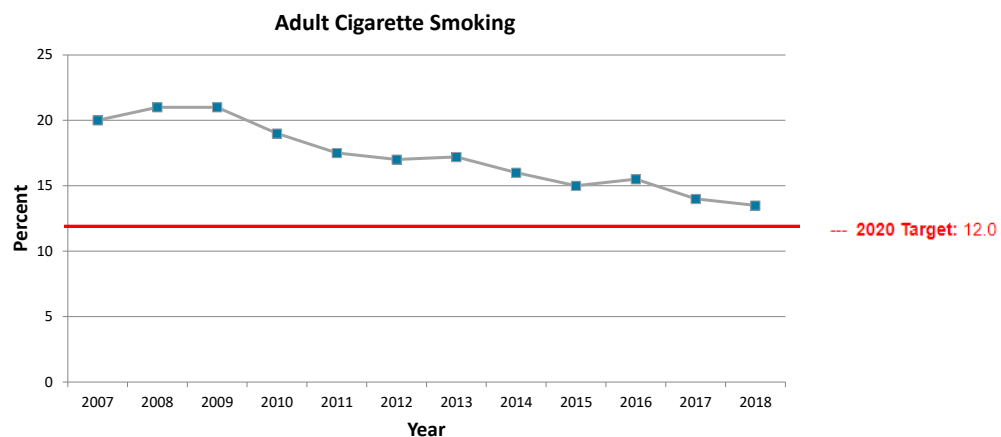
- Leading preventable cause of death in the United States
- Smoking is associated with:
  - Alteration in mucociliary clearance, disruption of respiratory epithelium, and inhibition of phagocytic alveolar macrophages
  - Increased risk for bacterial pneumonia, oral candidiasis, and cryptococcal meningitis
- Use should be assessed at every visit
  - Provide behavioral interventions and pharmacotherapy for cessation

Pourbaix A, et al. Clin Infect Dis. 2020.

Published Recommendations. U.S. Preventive Services Task Force. 2015.

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## Smoking Cessation: Healthy People 2020



Adapted from: National Health Interview Survey (NHIS); Centers for Disease Control and Prevention, National Center for Health Statistics (CDC/NCHS)

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# Immunization of the Solid Organ Transplant Recipient



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## Vaccinations

- Transplant recipients are at an increased risk for vaccine-preventable illnesses
- Review vaccination status pre-transplant and vaccinate candidates
  - Document seroconversion when available
  - Re-evaluate at the time of listing
- Advisory Committee on Immunization Practices (ACIP)

Danziger-Isakov, L, et al. Clin Transplant. 2019;;e13563.

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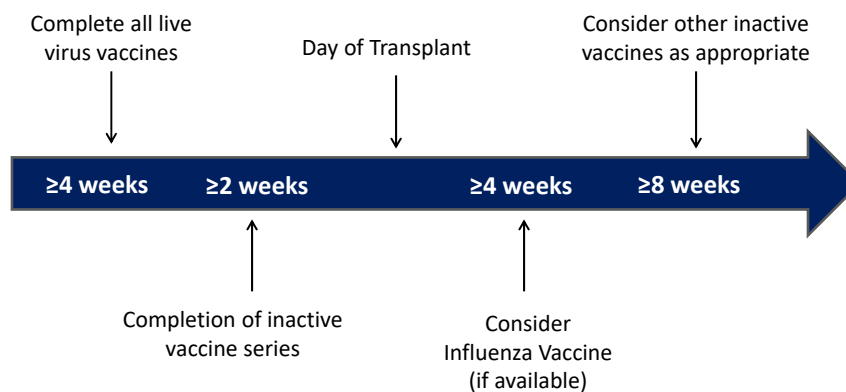
## Live Virus Vaccinations

- Generally considered contraindicated post-transplant
  - Varicella zoster, BCG, Smallpox, intranasal influenza, MMR, etc.
  - Avoid if  $\geq 20$  mg/day of prednisone for  $\geq 14$  consecutive days
  - Withhold for 2 months following discontinuation of anti-rejection medications
  - Living donors should avoid live vaccines within 4 weeks of donation

Rubin LG, et al. Clin Infect Dis 2014;58:e44–100.

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## Timeline of Vaccinations



Rubin LG, et al. Clin Infect Dis 2014;58:e44–100.

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## Influenza Vaccination

- Prevented an estimated 1.6-6.7 million illnesses from 2010 through 2016
- Risk of influenza-associated complications higher in SOT:
  - Secondary viral, bacterial, and fungal pneumonia
  - Allograft dysfunction and acute rejection
  - Death
- Influenza vaccination recommended annually for recipients:
  - Decrease in pneumonia, ICU admission, use of invasive ventilation, and death
  - Lower risk of graft loss and death in kidney transplant recipients

Manuel O, et al. Clin Transplant. 2019;33(9):e13511.

Kumar D, et al. Clin Infect Dis. 2018;67(9):1322-1329.

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## Influenza Vaccine Concerns

- Patients with contraindications
  - Consider oseltamivir prophylaxis for up to 12 weeks at the start of influenza season
- Suboptimal immunologic response
  - Influenza antibody titers are frequently undetectable at one year
  - Response varies from 15-70% based on immunosuppression, time post-transplant, organ type
- Theoretical immune stimulation and organ rejection

Grohskopf LA, et al. MMWR Recomm Rep 2019;68(No. RR-3):1–21.

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## Definitions

### Seroconversion

- Negative pre-vaccination titer that reached post-vaccination titers  $>1:40$   
OR
- 4-fold increase in antibody titer

### Seroprotection Rate

- Antibody titers  $\geq 1:40$  post-vaccination  
AND
- Proportion of vaccines achieving this titer

### Geometric Mean Concentration (GMC)

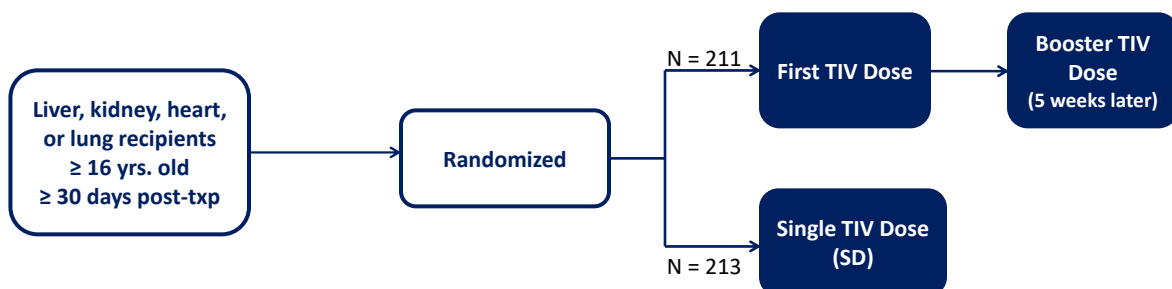
- Average antibody concentration

European Agency for the Evaluation of Medicinal Products (EMA) . Committee for Proprietary Medicinal Products (CPMP). 12 March 1997.  
 WHO Expert Committee on Biological Standardization: fifty-second report. Geneva: World Health Organization; 2016.

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## Booster Doses: TRANSGRIPE 1-2

Purpose: Assess the safety/efficacy of a booster dose of the trivalent influenza vaccine (TIV) in transplant recipients



Primary Outcome: Seroconversion at 10 weeks post-vaccination

Secondary Outcomes: Seroprotection rate, vaccine mean titers, microbiologically confirmed influenza cases

Cordero E, et al. Clin Infect Dis. 2017;64(7):829–838.

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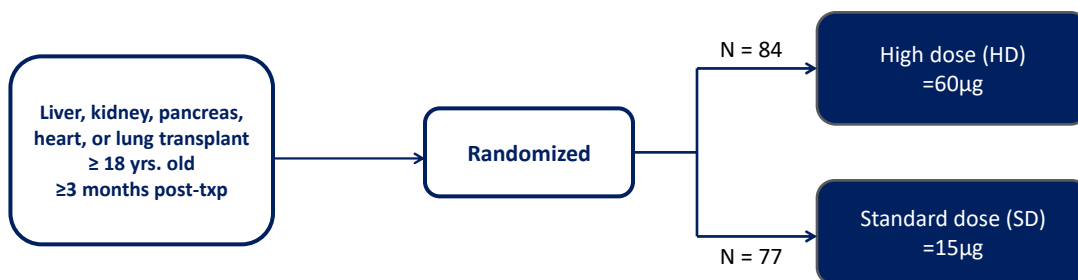
## Booster Doses: TRANSGRIPE 1-2

- Baseline Characteristics:
  - Kidney (44%) and liver (37%) recipients on tacrolimus (80%) and MMF (67%)
  - Average age 55 years, majority >12 months post-transplant (60%)
- Results:
  - Seroconversion:
    - Booster: achieved effective seroconversion for all influenza strains
    - Control: achieved effective seroconversion only for influenza B
  - Seroprotection:
    - Higher in the booster arm for the 3 types of influenza virus studied
    - A (H1N1) [54% vs. 43.2%], A (H3, N2) [56.9% vs. 45%], and influenza B [83.4% vs. 71.8%]
  - No difference in influenza rates or long term immunity (> 1 year)

Cordero E, et al. Clin Infect Dis. 2017;64(7):829–838.

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## High Dose vs. Standard Dose



Primary Outcome: Seroconversion to at least 1 of the 3 vaccine antigens at 4 weeks post-vaccination  
 Secondary Outcomes: Influenza infection, hospitalization, biopsy proven acute rejection

Natori Y, et al. Clin Infect Dis. 2018;66(11):1698–1704.

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## High Dose vs. Standard Dose

- Baseline Characteristics:
  - Kidney (39%), liver (22%) and lung (14.5%) recipients
  - Tacrolimus (73%), MMF (67%) and prednisone (76%)
  - Average age 57 years (18-86 years)
  - Median time from transplant: 38 months (IQR 12-89.5 months)
- Results:
  - Seroconversion: higher in HD group (78.6% vs. 55.8%; P= 0.002)
  - Seroconversion rates were not different between groups
  - MMF doses of >2g/day associated with lower rates of seroconversion
  - No difference in secondary outcomes

Natori Y, et al. Clin Infect Dis. 2018;66(11):1698–1704.

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## Acute Rejection and Influenza Vaccination

Citation	Population	Vaccine	De novo DSA	Rejection	Other
Katerinis, et al.	Kidney (N=151)	Adjuvanted influenza A (H1N1) vaccine	2 independent treatment cohorts: 17.8% in cohort 1 11.9% in cohort 2	2 patients	High rate of de novo DSA, low MFI  Disappeared 6 months after vaccination
Brakemeier, et al.	Kidney (N=60)	Adjuvanted influenza A (H1N1) vaccine	3/60 (5%)	2/3 with biopsy proven AMR 1 graft loss	MFI of 1265, 350, and 443
Candon, et al.	Kidney (N=66)	Trivalent 2005-2006 influenza vaccine	3/66 (4.8%)	No clinical signs of rejection at 3 months	All DSAs found at baseline were also detected on day 30 following vaccination. No change in MFI
Kimball, et al.	Heart (N=29)	Trivalent 1998 influenza vaccine	2/29 (6.9%)	No difference compared to rates of BPAR pre-vaccination	Minimal antibody production and only to minor HLA antigens

Katerinis I, et al. Am J Transplant. 2011;11(8):1727-33.  
 Brakemeier S, et al. Nephrol Dial Transplant. 2012;27(1):423-8.

Candon S, et al. Am J Transplant. 2009;9(10):2346-54.  
 Kimball P, et al. Transplantation. 2000;69(11):2449-51.

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## Varicella Vaccination

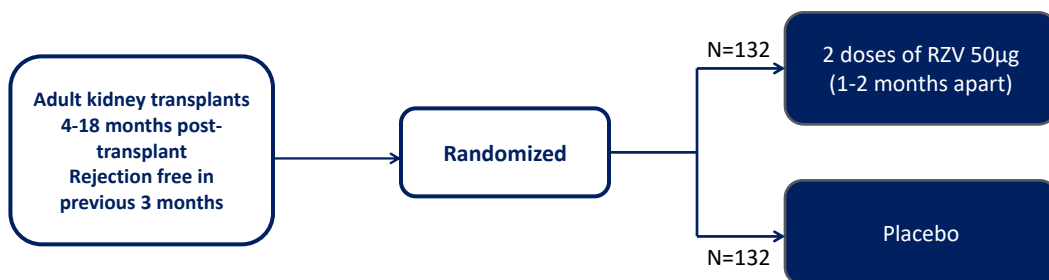
- Primary varicella can lead to severe complications post-transplant
- Vaccination pre-transplant is indicated in VZV-negative patients
  - Can be administered as early as 9 months of age
  - Confirmatory serologic testing, revaccinate if seroconversion does not occur
  - Varicella virus vaccine, live (Varivax®): Administer  $\geq 4$  weeks before transplant
- Herpes Zoster Vaccine
  - Recombinant zoster vaccine (RZV) should be given to patients age  $\geq 50$  years
  - RZV can be administered one year after resolution of a shingles episode

Danziger-Isakov L, et al. Clin Transplant. 2019;33(9):e13563.

Rubin L, et al. Clinical Infectious Diseases, Volume 58, Issue 3, 1 February 2014, Pages e44–e100

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## Immunogenicity and Safety of RZV In Kidney Transplant Recipients



Primary Outcome: Vaccine response rate (VRR) 2 months after the second vaccine dose

\*VRR met if the LL of the 95% CI for anti-gE Ab concentration was  $\geq 60\%$

Vink P, et al. Clin Infect Dis. 2020;70(2):181-190.

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## Immunogenicity and Safety of RZV In Kidney Transplant Recipients

- Baseline Characteristics:
  - Average age 52 years, ~70% Caucasian, 88% with PRA < 19%
- Results:
  - VRR in the RZV group was 80.2% (95% CI, 71.9%–86.9%)
  - Anti-gE antibody GMC ratio of 14.0 (95% CI, 10.90– 17.99; P< .0001)
- Humoral and cellular immune responses persisted through 1 year
- No BPAR occurred within 30 days after the last vaccine dose

Vink P, et al. Clin Infect Dis. 2020;70(2):181-190.

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## Pneumococcal Vaccine

- Recommended for ages 6-64 years who have not received PCV13
  - Single dose of PCV13 followed 8 weeks later by PPSV23
  - PPSV23 should be repeated 5 years after the first dose
  - Administer 2 to 6 months after SOT if not administered before
  - Titers decline post-transplant, but the optimal monitoring strategy and intervention for a declining titer is uncertain

Rubin L, et al. Clinical Infectious Diseases, Volume 58, Issue 3, 1 February 2014, Pages e44–e100.  
<https://www.cdc.gov/vaccines/vpd/pneumo/hcp/who-when-to-vaccinate.html>

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## Complement Component Deficiency

- C5 inhibitors (eculizumab and ravulizumab)
  - MenACWY + MenB at least 2 weeks prior to starting therapy
  - Consider antibiotic prophylaxis for the duration of therapy
- Functional or Anatomic Asplenia
  - MenACWY + MenB
  - PCV13 followed by PPSV23 ≥ 8 weeks later
  - *H. influenzae* type b vaccine (Hib)
- MenACWY-D (Menactra®) and PCV13 should not be co-administered
  - Reduced IgG Ab for 3 serotypes of pneumococcus when PCV7 was administered with MenACWY-D
  - Not seen with MenACWY-CRM (Menveo®)
  - PCV13 should be administered first and MenACWY-D (Menactra®) 4 weeks later

Rubin L, et al. Clinical Infectious Diseases, Volume 58, Issue 3, 1 February 2014, Pages e44–e100.  
 MMWR Morb Mortal Wkly Rep. 2011;60(40):1391-1392

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## Meningococcal Vaccines

Brand Name	Meningococcal Serotypes	Vaccine Type	Number of Doses	Interval	Other
Menactra®	A,C,W,Y	Conjugate	2	≥ 8 weeks	Must be separated from PCV13 by 4 weeks
Menveo®	A,C,W,Y	Conjugate	2	≥ 8 weeks	Can co-administer with PCV13
Menomune®	A,C,W,Y	Polysaccharide	1	--	Not recommended for patients on C5 inhibitors
Bexsero®	B	Recombinant	2	≥ 4 weeks	
Trumenba®	B	Recombinant	2	6 months	Can also be given as a 3 dose schedule (0, 1-2, 6 months)

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## SARS-CoV-2 Vaccination in SOT

- 34 SOT (10 kidney, 24 heart) recipients vs. 116 matched controls
- Median time from transplant: 11.1 (IQR: 7.3-15.8) years
- Anti-SARS-CoV-2 antibody response rate after 2<sup>nd</sup> dose:
  - 58.8% of SOT recipients vs. 100% of control group
- Antimetabolite-containing regimens negatively influenced immune response:
  - 33% receiving MPA vs. 79% that did not

Marinaki S, Adamopoulos S, Degiannis D, et al. *American Journal of Transplantation*. 2021

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## Consensus Recommendations

- Pre-transplant vaccination of all SOT candidates is a priority
- SARS-CoV-2 vaccination of SOT recipients and their household members/caregivers
- Continuation of a stable immunosuppression regimen at the time of vaccination to avoid the risk of organ rejection
- Continued adherence of all SOT recipients to protective measures (i.e. masking, social distancing) regardless of vaccination status

<https://www.myast.org/statement-covid-19-vaccination-solid-organ-transplant-recipients>

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## Vaccine References

- IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromised Host
- Best Practices Guidance of the Advisory Committee on Immunization Practices (ACIP)
- CDC Website
- American Society of Transplantation Infectious Diseases Community of Practice (AST-IDCOP)

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## Organ Donation and Allocation

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## Kidney Allocation System (KAS)

- Worsening supply-demand mismatch
- Goals
  - Minimize allograft longevity mismatch
  - Improve access to transplantation for candidates from racial/ethnic minority groups, pediatric patients, and highly sensitized candidates
  - Increase utilization of high Kidney Donor Profile Index (KDPI) kidneys

Friedewald J, et al. Surg Clin North Am. 2013;93(6):1395-406.

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## Scoring Tools

- Estimated Post-Transplant Survival (EPTS)
  - Tool to estimate the survival of a kidney transplant recipient
  - Utilizes age, diabetic status, time on dialysis, and prior transplants
  - Lower EPTS score suggests longer post-transplant survival
- KDPI
  - Developed to improve risk stratification for survival of DCD kidneys
  - Variables include: donor age, height, weight, ethnicity, history of HTN, DM, COD, serum creatinine, HCV status, and DCD status

HTN= hypertension COD= cause of death

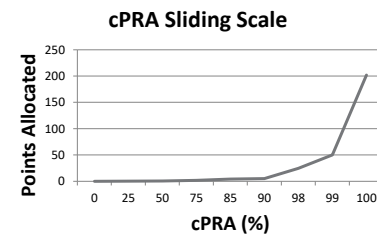
HCV = hepatitis C virus DCD= donation after cardiac death

Friedewald J, et al. Surg Clin North Am. 2013;93(6):1395-406.

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## Broadening Access

- Highly sensitized patients
  - “Sliding scale” for assigning points based on cPRA
  - Regional +/- national priority if cPRA 99-100%
- Historically Disadvantaged Candidates
  - Time spent on chronic dialysis
  - Candidates that may have had a delay in transplant referral
- Blood Type B Candidates
  - Historically low transplant rates
  - Allocation of blood subtype A<sub>2</sub> or A<sub>2</sub>B kidneys



Adapted from: Stewart DE, et al. Am J Transplant 2016;16:1834-47.

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## Allocation Occurs in Four Sequences

- A: Top 20% KDPI kidneys to top 20% EPTS candidates
- B: KDPI from 20% to 35%
  - Pediatric candidates will receive priority for all kidneys with KDPI < 35%
- C: KDPI 20% to 85%
  - EPTS not a factor, based on points for waiting time, HLA-DR matching, and cPRA
- D: KDPI >85% (formerly ECD kidneys)
  - Opt-in system aimed to benefit older candidates
  - Allocated solely on wait time to local/regional candidates

Friedewald J, et al. Surg Clin North Am. 2013;93(6):1395-406.

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## Liver Allocation & Distribution

- Previous Distribution Process
  - Based on geographic boundaries of donor service areas (DSAs) and transplant regions
  - BUT average MELD score at transplant varies as much as 10 points between DSAs
- New system emphasizes medical urgency and distance from donor hospital:
  - Highest priority to status 1A and 1B within 500 nautical miles
  - Next offered to candidates within distances of 150, 250 and 500 nautical miles
  - MELD/PELD Score

Elwir S, et al. Gastroenterol Hepatol (N Y). 2016;12(3):166-70.  
 United Network for Organ Sharing 2020 website. <https://unos.org/policy/liver-distribution/>. Accessed January 28<sup>th</sup>, 2020.

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## MELD Exception Points

- When severity of illness or risk are not captured by MELD:
  - Cholangiocarcinoma & hepatocellular carcinoma
  - Cystic fibrosis
  - Hepatic artery thrombosis
  - Hepatopulmonary syndrome
  - Portopulmonary hypertension
- Exception requests now reviewed by National Liver Review Board
  - Promotes equity by creating greater consistency in the review and application of exception scores for candidates nationwide

United Network for Organ Sharing 2020 website. <https://unos.org/policy/liver-distribution/>. Accessed January 28<sup>th</sup>, 2020.

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## Lung Allocation

- Updated in 2005 from a waiting time system to a Lung Allocation Score (LAS) for patients ages 12 and older
  - LAS estimates wait list urgency and post-transplant survival
- Consists of 18 objective items, prioritizing a higher LAS score
  - Age, diagnosis, O<sub>2</sub> requirements, predicted FVC, cardiac index, etc.
  - Other factors: ABO type, proximity to donor hospital, size
- Stark change in the underlying disease state prioritized for transplant upon implementation

Gries CJ, et al. Chest 2007;132:1954-61.

Egan TM, et al. Am J Transplant. 2006;6(5 Pt 2):1212-27.

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## Heart Allocation

- Previous system
  - Three medical urgency statuses (1A, 1B, & 2)
  - Allocation rules for MCS patients were not aligned with prognosis
  - Geographic disparities
- Updated October 2018
  - Increased to six medical urgency statuses (1-6)
  - Better stratification of medically urgent cases
  - Clear definitions of MCS complications
  - Status 1 & 2 patients will draw organs from a 500-mile radius

MCS =mechanical circulatory support

Meyer DM, et al. Am J Transplant 2015;15:44-54.

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## Heart Allocation

Status	Criteria
1	ECMO (up to 14 days of support) Non-dischargeable BiVAD or RVAD Mechanical circulatory support with life-threatening ventricular arrhythmia
2	Intra-aortic balloon pump (up to 14 days of support) Ventricular tachycardia/ventricular fibrillation, mechanical support not required Mechanical circulatory support with device malfunction/mechanical failure
3	LVAD for up to 30 days Multiple inotropes or single high-dose inotropes with continuous hemodynamic monitoring Mechanical circulatory support with device infection or thromboembolism
4	Stable LVAD candidates after 30 days Inotropes without hemodynamic monitoring Re-transplant
5	Combined organ transplants
6	All other active candidates

Meyer DM, et al. Am J Transplant 2015;15:44-54.

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## Resources for Public Awareness on Organ Donation

- United Network for Organ Sharing (UNOS)
  - UNOS Ambassador Program
  - United for UNOS Movement
  - Allocation Calculators (MELD/PELD, EPTS, LAS, etc.)
- Organ Procurement and Transplantation Network (OPTN)
- Health Resources and Services Administration (HRSA) & [organdonor.gov](http://organdonor.gov)
- Scientific Registry of Transplant Recipients (SRTR)

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## Summary



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## Key Takeaways

- Transplant recipients are at an increase risk of immunosuppression-related complications and require close monitoring.
- Transplant pharmacists are in a unique position to ensure recipients are compliant with the appropriate preventative tests and vaccinations.
- Optimizing allocation processes and increasing public awareness to donation is critical.



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## Active Learning Questions



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Question 1: Which of the following is correct regarding cancer screenings among transplant recipients?

- A. African American lung transplant recipients over 60 years old should receive skin cancer screening within 5 years of transplant.
- B. Flexible sigmoidoscopies for routine colon cancer screening should be obtained every 10 years for transplant recipients ages 50-75.
- C. Male kidney transplant recipients over the age of 40 should receive skin cancer screening within 2 years of transplant
- D. Male transplant recipients should get annual prostate screening if over the age of 50 years.

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Question 2: Which of the following does not describe a transplant-specific benefit of statin therapy?

- A. Decreased incidence of grade 4 PGD post-lung transplant
- B. Decreased bronchiolitis obliterans syndrome post-lung transplant
- C. Decreased incidence of CAV
- D. Increased survival post-heart transplant

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Question 2: Which of the following does not describe a transplant-specific benefit of statin therapy?

- A. Decreased incidence of grade 4 PGD post-lung transplant
- B. Decreased bronchiolitis obliterans syndrome post-lung transplant
- C. Decreased incidence of CAV
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Question 3: Which of the follow is false regarding influenza vaccination post-transplant?

- A. Booster doses result in higher seroprotection and seroconversion rates
- B. High dose did not decrease the incidence of influenza
- C. Influenza vaccines can be administered as soon as 4 weeks post-transplant
- D. The annual influenza vaccine can increase DSA production and risk for antibody-mediated rejection

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Question 4: RK is a 62 year old female 2 weeks post-kidney transplant. Her course was complicated by TMA requiring eculizumab treatment. Which of the following is false?

- A. RK should receive either Menactra® or Menveo® along with Bexsero® or Trumenba®
- B. RK should receive antibiotic prophylaxis with penicillin during her course of eculizumab treatment
- C. Serologic testing is recommended to confirm meningococcal vaccine response
- D. Provider must be enrolled in REMS program

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- C. **Serologic testing is recommended to confirm meningococcal vaccine response**
- D. Provider must be enrolled in REMS program

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Question 5: Which of the follow is true regarding the kidney allocation process?

- A. Patients with a lower EPTS score will preferentially receive higher KDPI kidney allografts.
- B. Patients with low cPRA are awarded additional points to increase the likelihood of receiving an organ offer.
- C. Pediatric candidates receive priority for kidneys with KDPI < 35%.
- D. Waiting time no longer plays a role in waitlist priority.

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Question 5: Which of the follow is true regarding the kidney allocation process?

- A. Patients with a lower EPTS score will preferentially receive higher KDPI kidney allografts.
- B. Patients with low cPRA are awarded additional points to increase the likelihood of receiving an organ offer.
- C. **Pediatric candidates receive priority for kidneys with KDPI < 35%.**
- D. Waiting time no longer plays a role in waitlist priority.

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Question 6: Which of the following is true regarding organ allocation?

- A. The LAS predicts only post-transplant survival
- B. Heart allocation is now based on concurrent therapies used for care
- C. DSAs have replaced geographic distance from donor hospitals in determining liver allograft priority
- D. Kidney transplant has the smallest geographic donor pool

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Question 6: Which of the following is true regarding organ allocation?

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- C. DSAs have replaced geographic distance from donor hospitals in determining liver allograft priority
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## Primary Care of the Solid Organ Transplant Patient

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