Substance Use Considerations with Organ Transplantation

Vanderbilt Transplant Advanced Practice Provider Symposium

VANDERBILT
School of Nursing

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Disclosures

I have no financial relationships or commercial interests pertaining to the material being presented today. I am not going to discuss any unapproved/investigational use of a commercial product. This presentation will provide a balanced view of therapeutic options and be free of promotional bias.

Presentation Agenda

- Introduction
- Case Scenarios
- Substances and Risks
  - Alcohol
  - Tobacco
  - Cannabis
  - Opioids
- Evaluation and Recommendations
- Conclusion

Case Scenario 1

Brenda is a middle-aged divorced female with alcoholic cirrhosis evaluated for a liver transplant. Past psychiatric history of anxiety, insomnia, remote eating disorder symptoms, and alcohol use disorder. At the time of listing, she had been sober from alcohol for 11 months, completed IOP, and attending AA regularly. She demonstrated good insight into her alcohol use and had recently started medications for her anxiety and insomnia. Additionally, she started seeing a local therapist and greatly benefited from that relationship. Her social supports included her aging parents and adult children who attended college out of state.

Case Scenario 2

Mary is a middle-aged female with a history of alcoholic cirrhosis. She is on the waiting list for liver transplant and has attended IOP for alcohol use disorder. She has reluctantly participated in AA. She also has a history of PTSD and is on chronic opioids. She has good family support and lives with her mother who does not drink or use substances. She helps care for her grandchildren and is otherwise unemployed. She is prescribed sertraline for PTSD.

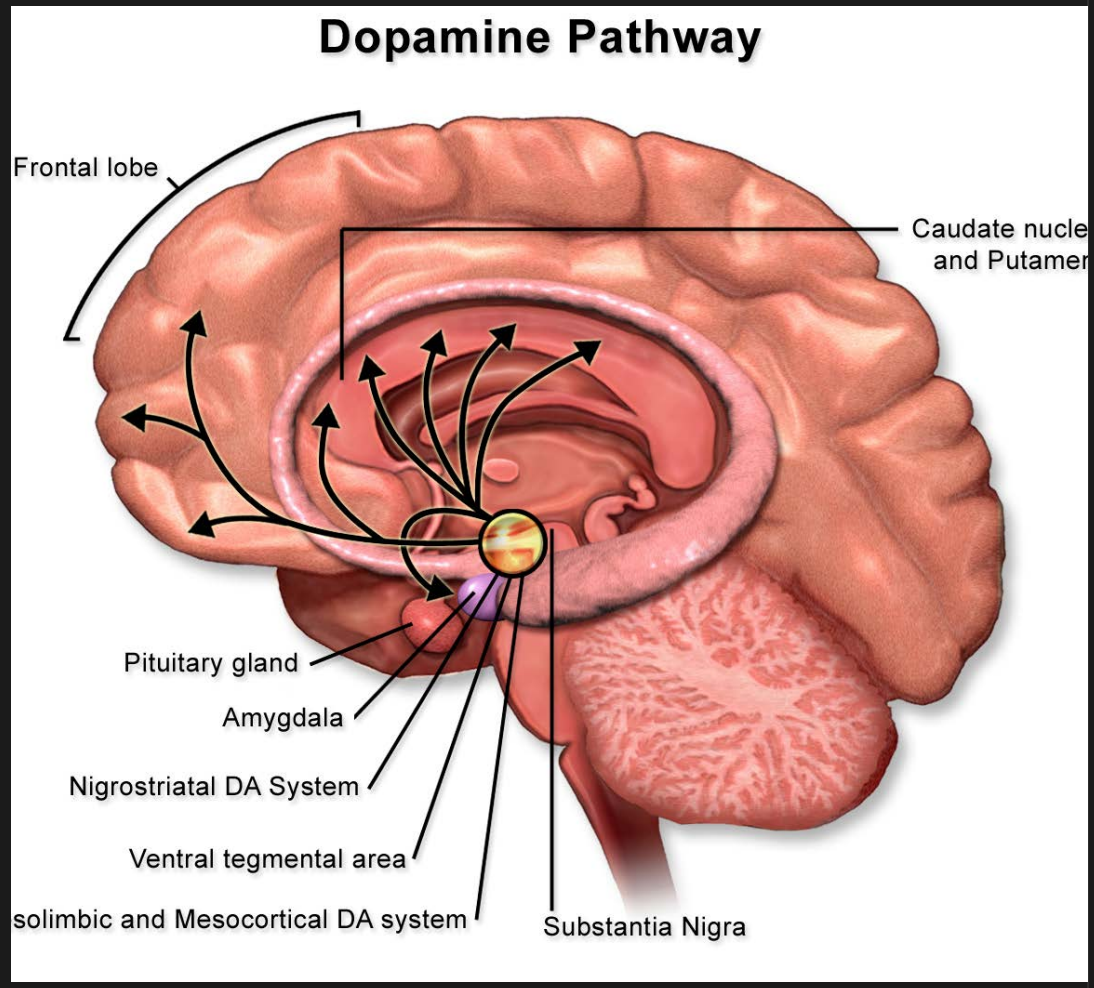
Risks

- What do you think are the risks for relapse?

- What do you think are the abstinence prognostic factors?

What do we know about substance use disorders?

- Addiction is a brain disease
- Chronic illness and relapse rates are high
- Increased risk of morbidity and mortality
- Decreased life expectancy
- Risk for overdose
- Can result in end stage organ disease



https://www.simplypsychology.org/brain-reward-system.html

Substance Use Concerns with Transplant

- Relapse
  - Direct or indirect damage to graft
  - Rejection
  - Med non-adherence

- Early identification and referral to treatment improves outcomes

ALCOHOL

https://healingproperties.org/alcohol-use-disorder/

What is “risky drinking ?”

HOW MUCH ALCOHOL IS TOO MUCH?

Binge Drinking

A pattern of drinking that brings a person’s blood alcohol level to 0.08. Typically this means having four or five drinks over a two-hour period.

Heavy Drinking

Binge drinking over five or more days in one month, or consuming a certain amount of drinks in a week: typically, for men it’s defined as having 15 or more drinks, and for women it’s 8 drinks or more.

Alcohol Use Disorder

A chronic disease characterized by uncontrolled drinking and preoccupation with alcohol.

JED

The Jed Foundation

https://www.jedfoundation.org/resource/understanding-the-mental-health-and-drinking-connection

How much is one “drink?”

WHAT IS A STANDARD U.S. DRINK?

Alcohol-by-volume will vary by drink, so it is always important to check labeling for exact amount. For example, a *light* beer may have 4.2% alcohol, while a *regular* beer may contain 5% alcohol.

SOURCE: NIAAA

12 oz. beer at
5% alcohol

5 oz. wine at
12% alcohol

1.5 oz. hard liquor at
40% alcohol

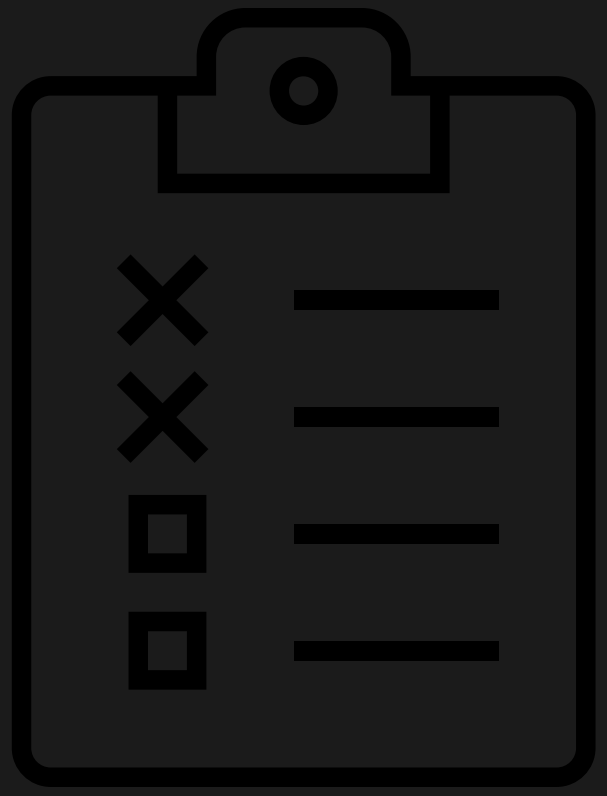
https://www.recoveryanswers.org/resource/guide-drinking-levels/

DSM 5 Criteria

Table 1. DSM V Diagnostic Criteria for Alcohol Use Disorder (22)
1. Alcohol is often taken in larger amounts or over a longer period than was intended
2. There is persistent desire or unsuccessful efforts to cut down or control alcohol use
3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol or recover from its effects
4. Craving or a strong desire or urge to use alcohol
5. Recurrent alcohol use resulting in a failure to fulfil major role obligations at work, school or home
6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol
7. Important social, occupational or recreational activities are given up or reduced because of alcohol use
8. Recurrent alcohol use in situations in which it is physically hazardous
9. Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol use
10. Tolerance defined as either a need for markedly increased amounts of alcohol to achieve desired effect or markedly diminished effect with continued use of the same amount of alcohol.
11. Withdrawal, as manifested by either the characteristic withdrawal syndrome for alcohol or alcohol is consumed to relieve or avoid withdrawal symptoms.
The presence of at least two criteria indicates alcohol use disorder. The grading of severity of alcohol use disorder is defined in terms of the number of criteria present e.g. two or three criteria indicate mild severity, 4 to 5 criteria indicate moderate severity and six or more criteria indicate high severity. (Additionally, the presence or absence of physiological dependence is specified.)

https://www.semanticscholar.org/paper/Alcohol-Use-Disorders%3A-Implications-for-the McDonough/02e77885a2efaebe73954294a59bc6002c340b05

Screening Tools



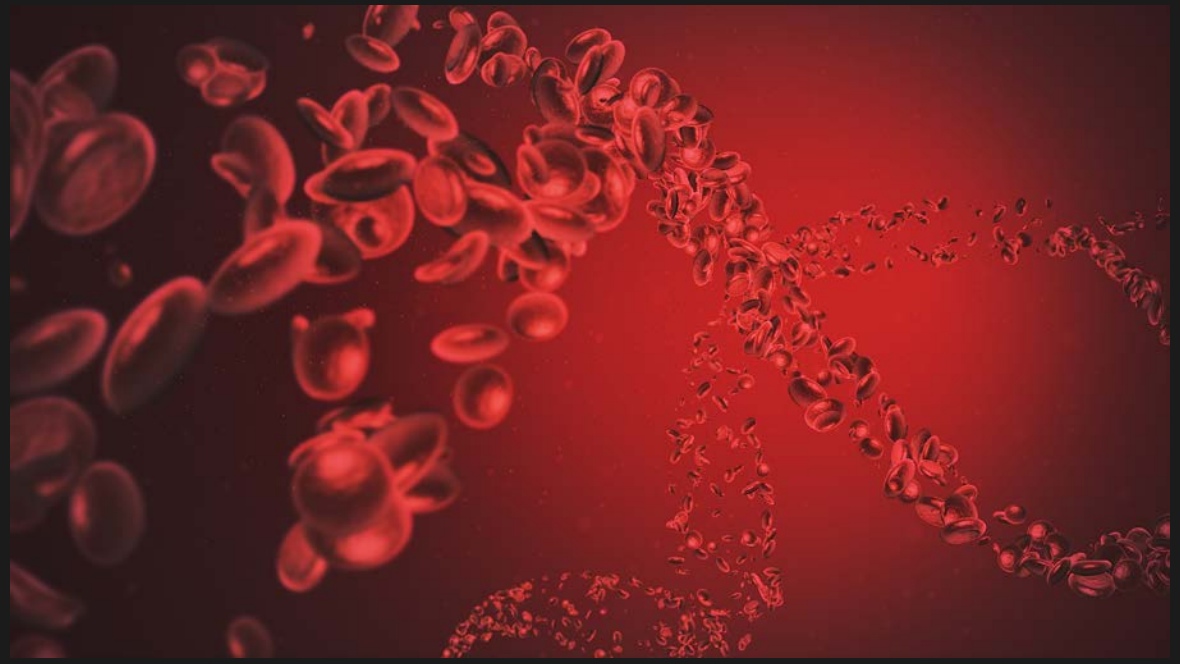
https://www.sciencedirect.com/topics/medicine-and-dentistry/alcohol-use-disorders-identification-test

Alcohol Users Disorders Identification Test (AUDIT)

Questions	Scoring System 0	1	2	3	4	Your Score
How often do you have a drink that contains alcohol?	Never	Monthly or less	2 - 4 times per month	2 - 3 times per week	4+ times per week	
How many standard alcoholic drinks do you have on a typical day when you are drinking?	1 - 2	3 - 4	5 - 6	7 - 8	10+	
How often do you have 6 or more standard drinks on one occasion?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often in the last year have you found you were not able to stop drinking once you had started?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often in the last year have you failed to do what was expected of you because of drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often in the last year have you needed an alcoholic drink in the morning to get you going?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often in the last year have you had a feeling of guilt or regret after drinking?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
How often in the last year have you not been able to remember what happened when drinking the night before?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily	
Have you or someone else been injured as a result of your drinking?	No		Yes, but not in the last year		Yes, during the last year	
Has a relative/friend/doctor/health worker been concerned about your drinking or advised you to cut down?	No		Yes, but not in the last year		Yes, during the last year	

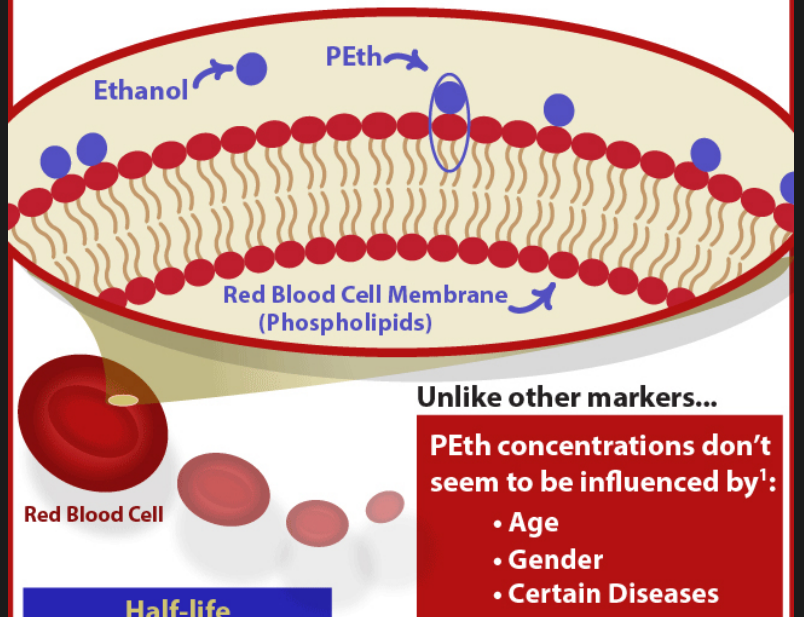
Scoring: 0-7 = sensible drinking, 8-15 = hazardous drinking, 16-19 = harmful drinking and 20+ = possible dependence

PEth Test



Direct Alcohol Biomarker Testing
Phosphatidylethanol (PEth)

During a series of processes, Phosphatidylethanol (PEth) accumulates in human red blood cells when the body is exposed to ethanol. Since it is formed only when the body is exposed to ethanol it is called a direct alcohol biomarker. The accumulation in red blood cells make it easy to test by collecting blood specimens.



Unlike other markers...

PEth concentrations don't seem to be influenced by[1]:
- Age
- Gender
- Certain Diseases
- Other Substances

Half-life
3-5 Days[1]

Detectability
2-4 Weeks

According to a combination of research, analysis demonstrates good efficiency of PEth for detecting chronic heavy drinking[1]

Sensitivity

Window of Detection

Benefits:
Highly sensitive, collection can be done anywhere*, no notice needed for collection*, mid-term window of detection

1. Guido Viel, (et al.) (2012) *International Journal of Molecular Sciences*, 13,14788-14812, doi: 10.3390/ijms131114788
* When collected via USDTL BloodSpot® collection

USDTL® Advancing The Gold Standard

https://www.usdtl.com/media/infographics/direct-alcohol-biomarker-testing-phosphatidylethanol-peth

Alcohol Treatment

1. Inpatient detox/rehab
2. Intensive Outpatient Program
3. Alcoholics Anonymous
4. Licensed Alcohol and Drug Abuse Counselor

FDA Approved Medications

	Action	Precautions	Adverse Reactions and Common Side Effects	Adult Dosage
Oral naltrexone	Blocks opioid receptors; reduces reward in response to alcohol use	Must be opioid-free 7 to 10 days. If opioid analgesia needed, larger doses required and respiratory depression deeper and prolonged. Monitor liver function.	Precipitates severe withdrawal if concurrently taking opioids; hepatotoxicity at supratherapeutic doses. Nausea, vomiting, and somnolence.	50 mg PO daily.
Naltrexone depot injection	Same as oral naltrexone but effects last 30 days.	Same as oral naltrexone.	Same as oral naltrexone, plus site reaction and greater somnolence.	380 mg gluteal IM injection monthly.
Acamprosate	Mechanism unknown but believed to reduce glutamatergic hyperexcitability.	Evaluate renal function. Moderate Kidney Disease (adjust dose for CrCl 30-50 mL/min).	Mild diarrhea.	666 mg PO TID. If creatinine clearance 30-50 mL/min: 333 mg PO TID.
Disulfiram	Inhibits intermediate metabolism of alcohol which can cause flushing, nausea, dizziness, and tachycardia if patient uses alcohol.	Monitor liver function. Warn patient to avoid alcohol in diet, OTC medications, toiletries. Psychosis or severe myocardial disease relatively contraindications	Disulfiram-alcohol reaction, hepatotoxicity.	250 mg PO daily (range 125 mg to 500 mg)

https://www.researchgate.net/figure/FDA-Approved-Medications-for-Alcohol-Use-Disorders_tbl1_266380512

Alcohol Use Disorder and Organ Transplant

Pre-transplant evaluation

- Evaluation of addiction (PEth, AUDIT)
- Relapse risk (SALT, AI?)
- Physical assessment and medical work-up

Selection criteria

- Longer period of abstinence may result in lower relapse rate
- No consensus on minimum abstinence period
- 6 month “rule”
- Early liver transplant

Sustained Alcoholuse post-Liver Transplantation (SALT)

Variable	Points
More than 10 drinks per day at initial hospitalization	+4
Multiple prior rehabilitation attempts	+4
Prior alcohol-related legal issues	+2
Prior illicit substance use	+1

Lee et al. (2019)

Relapse and Complications

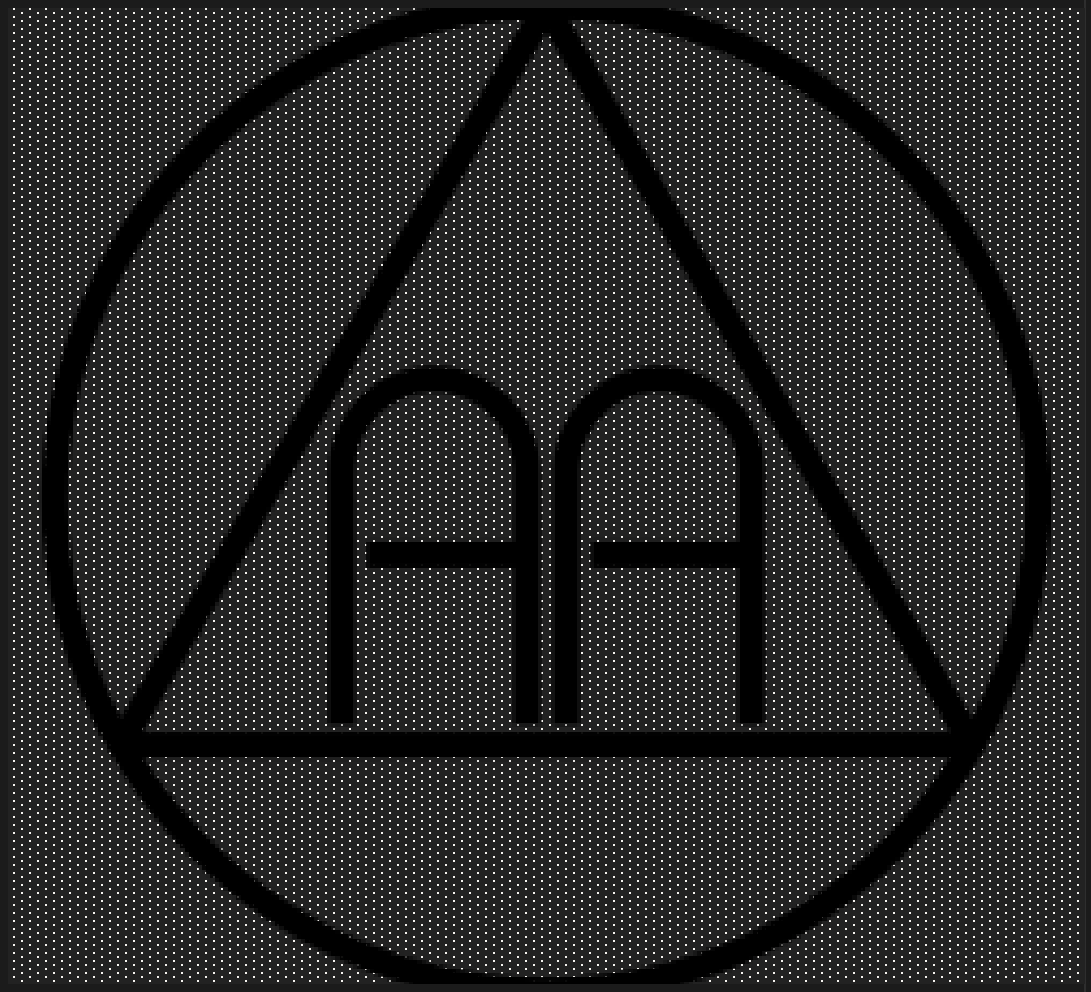
- 10-50% of patients do relapse and 10-20% at harmful levels
- Complications of heavy alcohol use:
  - Non-adherence
  - Rejection
  - Increased rates of steatohepatitis
  - Cirrhosis risk: 15% at 3 years, 32% at 5 years, and 54% at 10 years

Predictors of Relapse Post-transplant

- Diagnosis of an AUD and severity
- Comorbid psychiatric diagnosis
- Polysubstance abuse
- Poor social support
- Family history of AUD
- Ongoing tobacco use

Predictors of Long-Term Sobriety

- Substitute activities
- Relationships supporting ongoing sobriety
- Negative re-enforcement for drinking behaviors
- Sources that provide hope and improved self-esteem



1

Abstinence

2

Sobriety

3

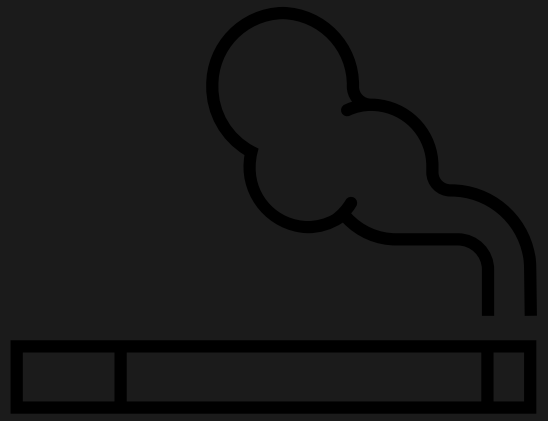
Recovery

https://recovered.org/treatment/the-treatment-process/recoveryabstinence

TOBACCO

https://thriveworks.com/blog/tobacco-use-disorder/

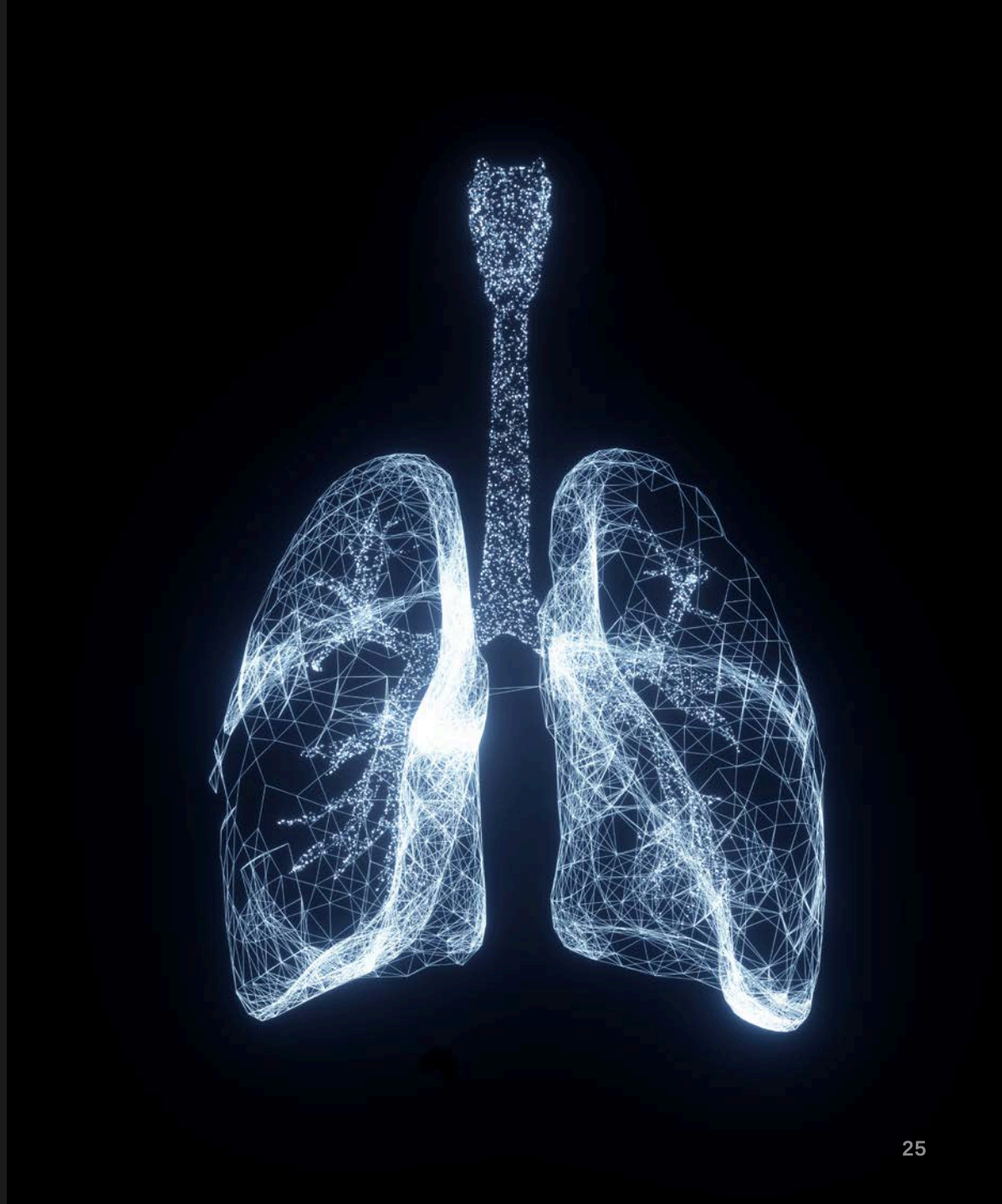
General Population Risks



- Cardiovascular disease
- Respiratory illness
- Stroke
- Malignancy
- Impairs wound healing
- Increases risk for infection
- Accelerates the development of renal disease
- Increases postsurgical complications

Tobacco in Organ Transplant

- Post transplant complications
  - Vascular disease, graft loss, mortality
- Lung transplant specific
  - Decreased survival, CKD, cancer
- Post-transplant relapse rates – 20% or higher



Assessment and Treatment

Clinical interview

Urine Nicotine Screen

Nicotine Replacement Therapy

FDA Approved pill medications: Chantix and Zyban (bupropion SR)

CANNABIS

https://www.healthywomen.org/your-health/smoking-marijuana-affect-academic-performance

Cannabis in Organ Transplant

- Legalization
- No consensus amongst transplant centers
- Define “use”
  - recreational, medical, cannabis use disorder, self medicating psychiatric disorder
- Medical and cognitive concerns
- Infectious complications
- Potential drug interactions

Assessment and Treatment

- Clinical interview
- Urine Drug Screen
- Behavioral/Cognitive Behavioral Therapies and Contingency Management
- Medications?

OPIOIDS

https://www.nlc.org/resource/opioid-use-disorder-city-actions-and-opportunities-to-address-the-epidemic/

Opioids in Organ Transplant

- Lack of research
- Highest use of prescription opiate pre-transplant -> increased post-transplant death and graft loss
- Define “use”
  - Appropriate prescription use or misuse/abuse?
- Refer to treatment and consider Medication Assistance Treatment (MAT)

Medication Assisted Treatment

Figure 1

How OUD Medications Work in the Brain

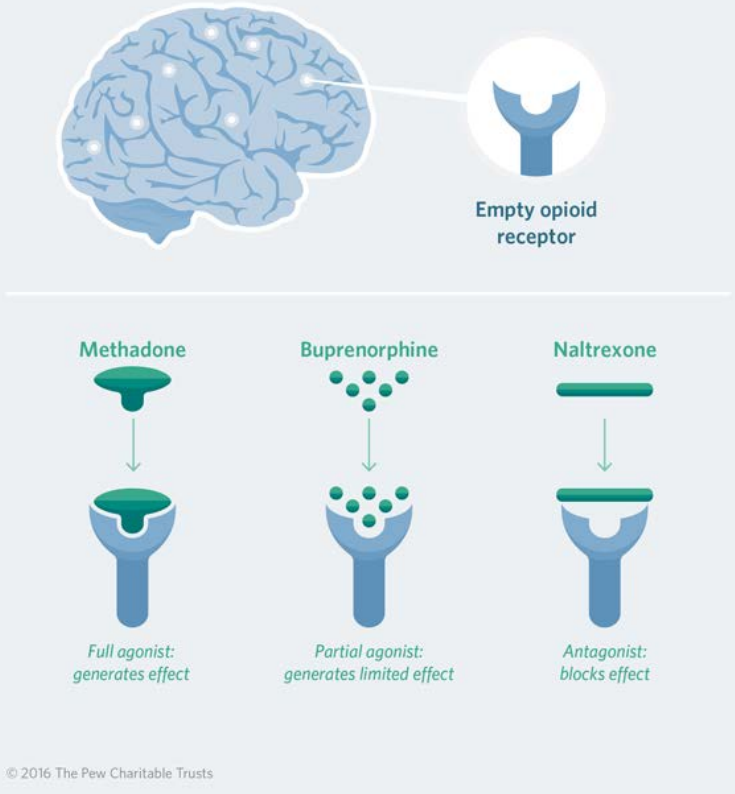


Table 1

FDA-Approved Drugs Used in MAT[21]

Medication	Mechanism of action	Route of administration	Dosing frequency	Available through
Methadone	Full agonist	Available in pill, liquid, and wafer forms	Daily	Opioid treatment program
Buprenorphine	Partial agonist	Pill or film (placed inside the cheek or under the tongue)	Daily	Any prescriber with the appropriate waiver
		Implant (inserted beneath the skin)	Every six months	
Naltrexone	Antagonist	Oral formulations	Daily	Any health care provider with prescribing authority
		Extended-release injectable formulation	Monthly	

https://www.pewtrusts.org/en/research-and-analysis/fact-sheets/2016/11/medication-assisted-treatment-improves-outcomes-for-patients-with-opioid-use-disorder

Evaluation and Recommendations

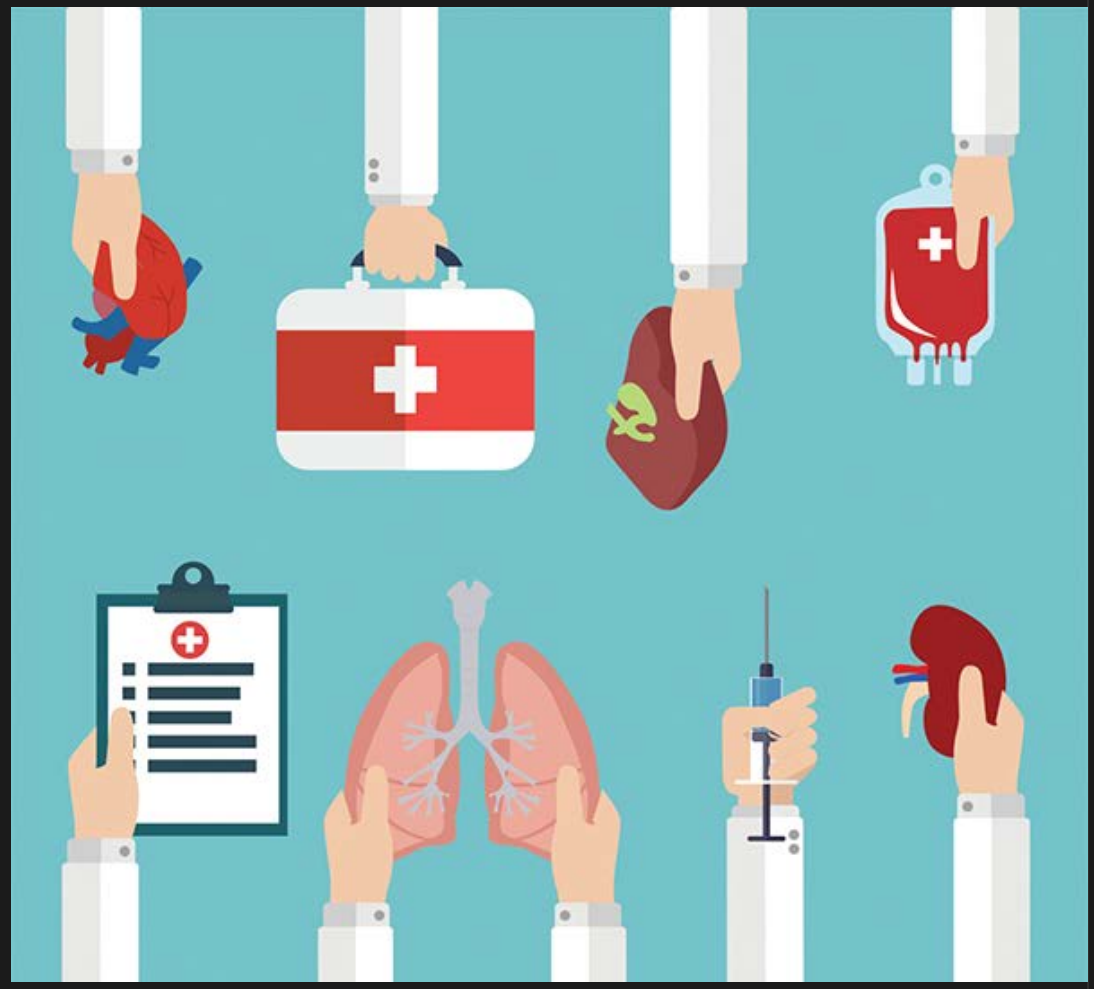
https://aviaryrecoverycenter.com/disease-addiction/

Role of the Provider

- Thorough pre-transplant assessment
  - Medical history
  - Psychiatric history
  - Drug and alcohol history
  - Psychosocial
- Support people
- Review all records
- Random screening (Peth, UDS, and nicotine)

Conclusion

- Lack of national guidelines
- Utility, justice, and respect
- Equal consideration
- Contraindications
- Considerations



https://journalofethics.ama-assn.org/issue/organ-transplantation

Cystic Fibrosis Video

- https://www.youtube.com/watch?v=2RO3zsh3xDw

What happened to Brenda

Brenda received a liver donation from one of her adult children. Her ex-husband re-entered their lives as the post-transplant caregiver for her donor. Her post-transplant course was complicated by need for prolonged biliary drain placement and pain. Additionally, her adult children returned to college, and she was living alone. She developed worsening anxiety and depression symptoms and unfortunately relapsed on alcohol 3 months post-transplant.

Brenda continued

Brenda was referred back to Transplant Psychiatry shortly after her relapse. Her SSRI was increased to target her depression and anxiety symptoms, and she was started on naltrexone which showed some initial benefit with managing cravings. She re-engaged in AA and is willing to attend an IOP. She is currently looking for a new therapist that takes Medicare since her insurance changed with transplant.

What happened to Mary

Mary underwent liver transplant in 2019. Since transplant she has remained sober from alcohol and has no desire to return to drinking. She does not participate in AA but attends her psychiatric appointments on a regular basis. Her sertraline was later changed to Cymbalta to help with both anxiety and chronic pain. She switched from oral opioids to fentanyl patches and later became involved with the MAT program at Vanderbilt. She is now off pain medications and uses Suboxone as a maintenance medication. She still lives with her mother who has played an important role in her recovery.

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Questions?

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