




Primer of Liver Disease in SUD

Naoky Tsai, MD



Some functions of the liver include:

- Secreting bile into intestines to help with digestion
- Purifying blood to disarm harmful chemicals or toxins like drugs and alcohol to prevent them from causing damage
- Sending harmful chemicals to be secreted in the stool or through the kidneys and urine
- Producing proteins like albumin and prothrombin that assist in forming blood clots and healing
- Storing minerals and vitamins
- Removing bacteria from the bloodstream



Drug and substance use disease (SUD) remains a major medical problem including liver disease.

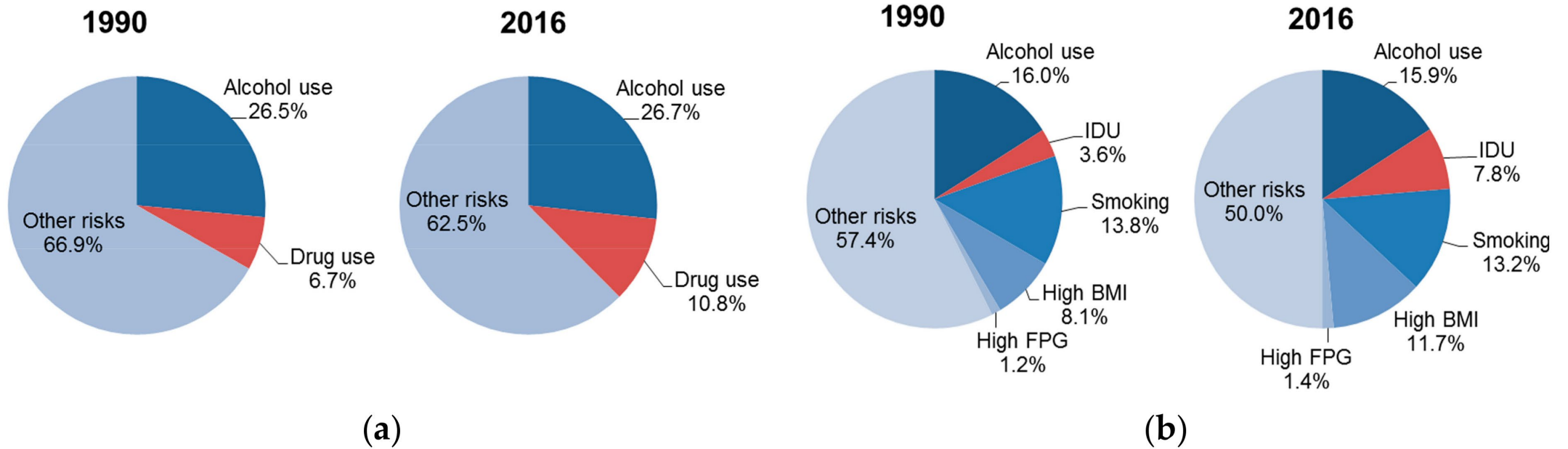
Objectives:

- Epidemiology
- Risk factors
- Clinical manifestations
- Pathogenesis of liver toxicity
- Management.

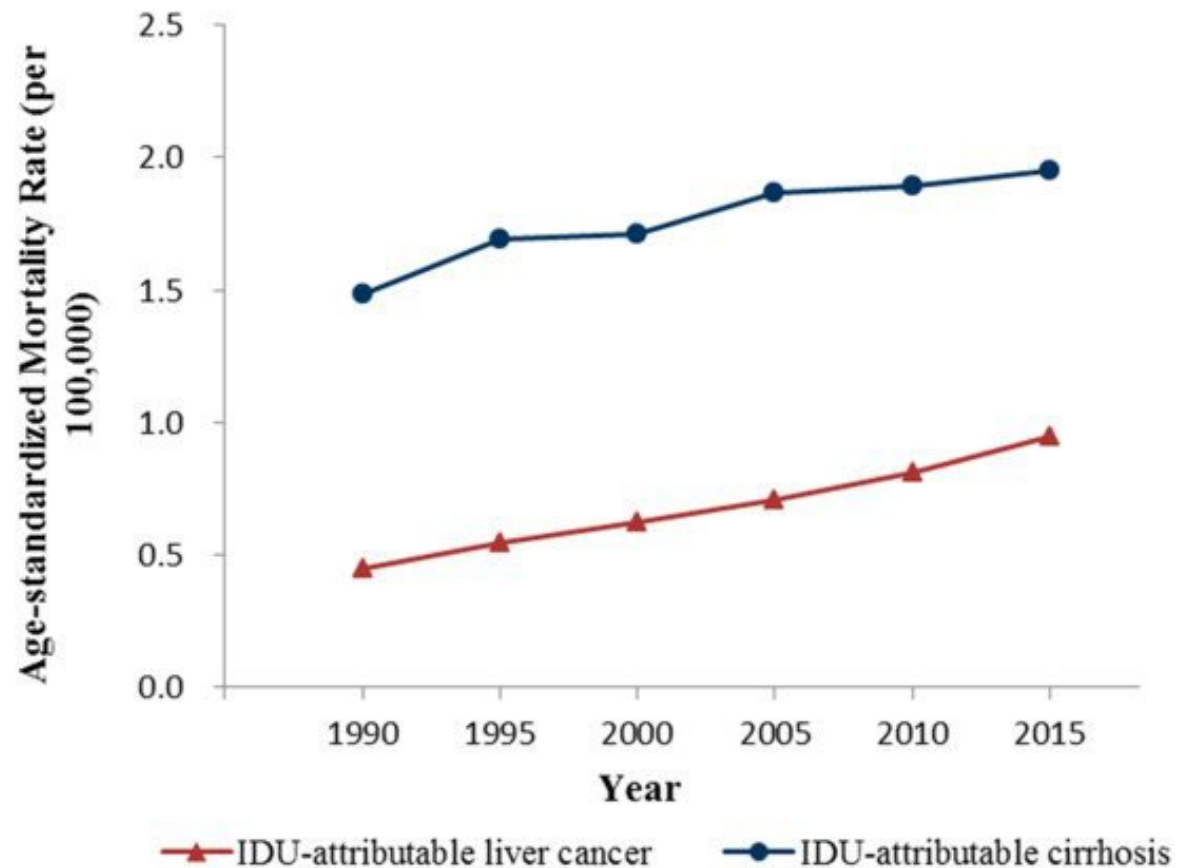
Int. J. Environ. Res. Public Health **2018**, *15*(1),
170; <https://doi.org/10.3390/ijerph15010170>

- **Global Mortality Burden of Cirrhosis and Liver Cancer Attributable to Injection Drug Use, 1990–2016: An Age–Period–Cohort and Spatial Autocorrelation Analysis**
- [Jin Yang](#)¹, [Yunquan Zhang](#)², [Lisha Luo](#)³, [Runtang Meng](#)⁴, [Chuanhua Yu](#)^{5,6}

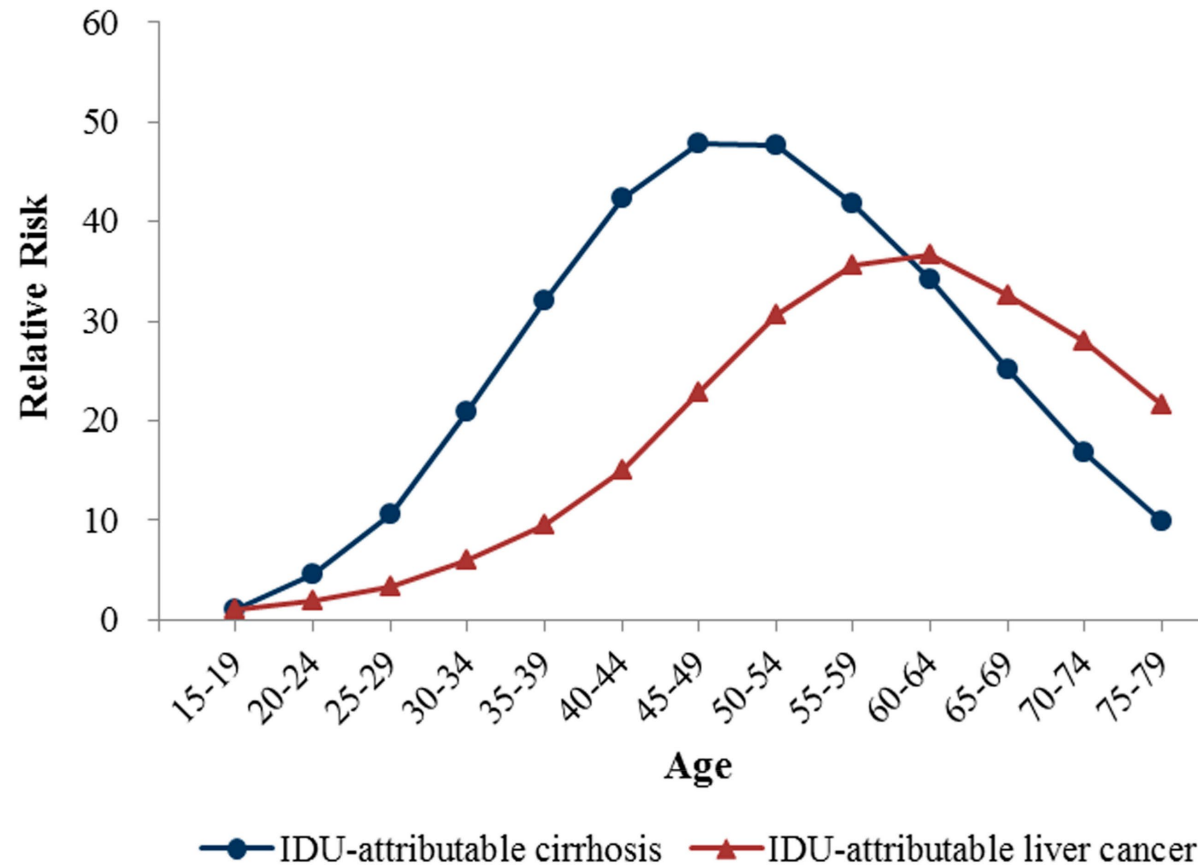
Risk-specific disease mortality on the global level in 1990 and 2016 for (a) cirrhosis; (b) liver cancer. IDU: injection drug use; BMI: body-mass index; FPG: fasting plasma glucose.



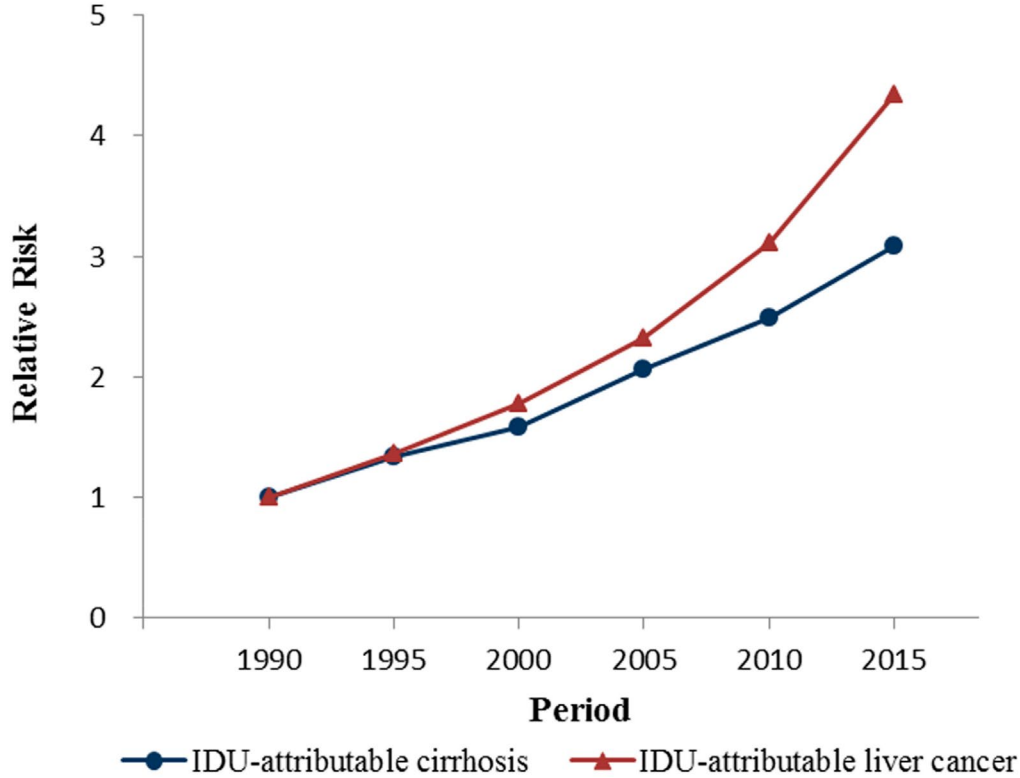
Mortality rates (age-standardized, per 100,000) of IDU-attributable cirrhosis and IDU-attributable liver cancer, 1990–2015, globally.



Age effects on mortality rates of IDU-attributable cirrhosis and IDU-attributable liver cancer.



Period effects on mortality rates of IDU-attributable cirrhosis and IDU-attributable liver cancer.



Key points in Liver Disease of SUD

- Always consider the possibility of multiple causes.
- Always think harm reduction

Etiologies of Liver disease in SUD

- Substances:
 - **Alcohol**
 - **Cigarette**
 - **Cocaine**
 - **Stimulants: Amphetamine, Meth, MDMA.**
 - **Cannabis? (Cannabidiol vs Delta Tetrahydrocannabinol THC).**
 - Sedatives: Benzo diazepam, Barbiturate.
 - Medications :
 - Acetaminophen
 - NSAIDS, Antibiotics, Antifungal, Antimycobactriums, ART.
 - Supplements
- Opportunistic infections:
 - Bacterial infection
 - Mycobacterial infection
 - Parasitic infection
 - Fungal infection
 - Viral Infections: HCV,HBV/HDV,HIV,HEV.
- Circulatory: Shock, Passive congestion.
- Nutritional deficiency: Vitamins, protein, sarcopenia.

Alcohol

- WHO: 2.8 million annual deaths, 4% of total global death burden annually.
- Pathogenesis: Poorly understood, oxidative stress from acetaldehyde, mitochondria damage.
- Clinical manifestation: Steatosis, steatohepatitis, cirrhosis, HCC.
- Treatment: Steroids in acute case, nutritional support, MAT, abstinence in long term.

UCSF Fresno Study M. Roytman et al

- Community Medical Centers

- Community Regional Medical Center
- Clovis Community Medical Center
- Fresno Heart and Surgical Hospital

- January 1, 2019 through December 15, 2020

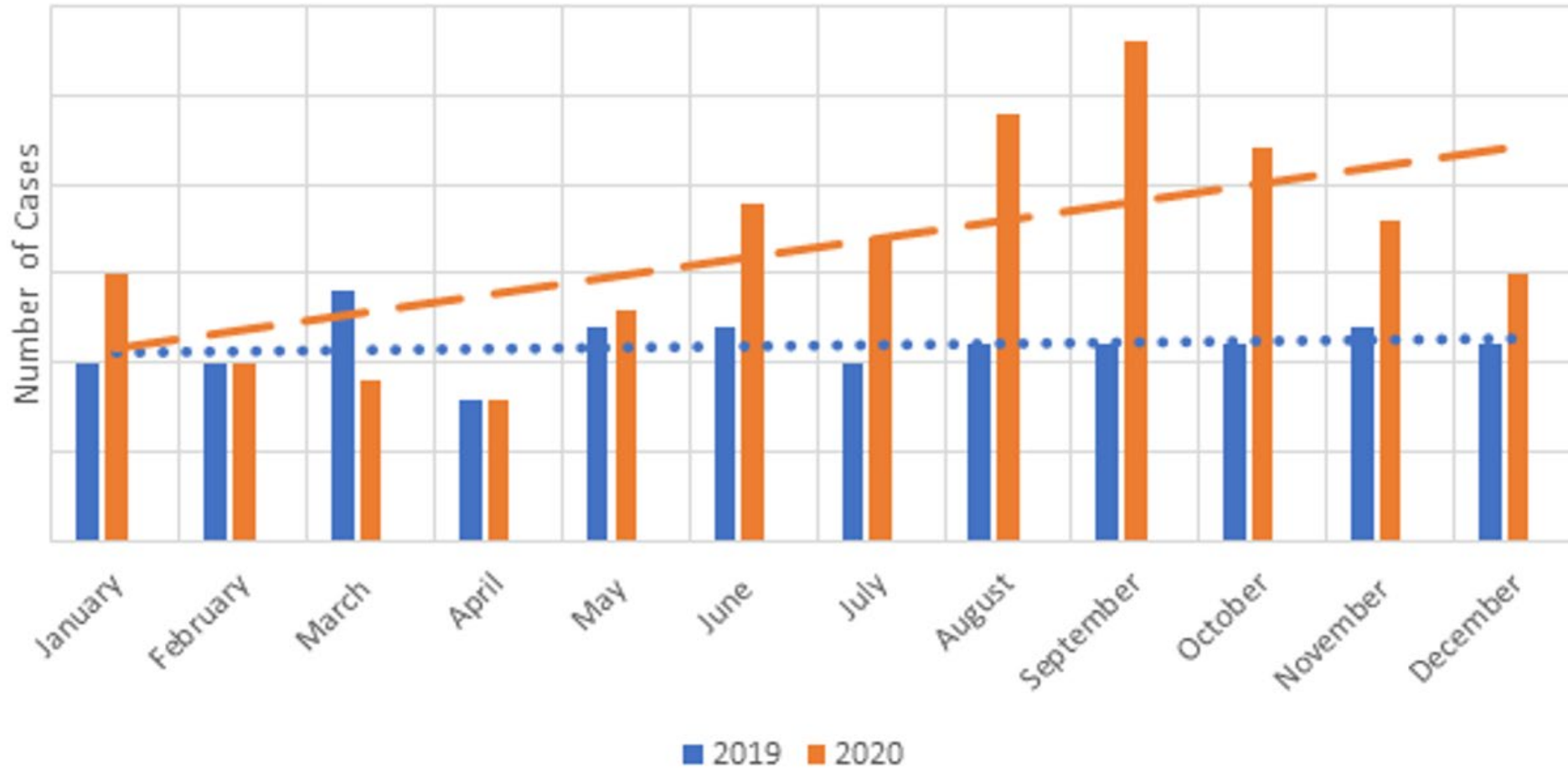
- Retrospective chart review

**329
patients**

- Inclusion criteria

- Alcohol-associated hepatitis
 - K70.10, K70.11
- Alcohol-associated hepatic failure
 - K70.40, K70.41
- Alcohol misuse within 3 months prior to admission
- WBC >10, AST/ALT ratio \geq 2:1, total bilirubin >1.2 mg/dL

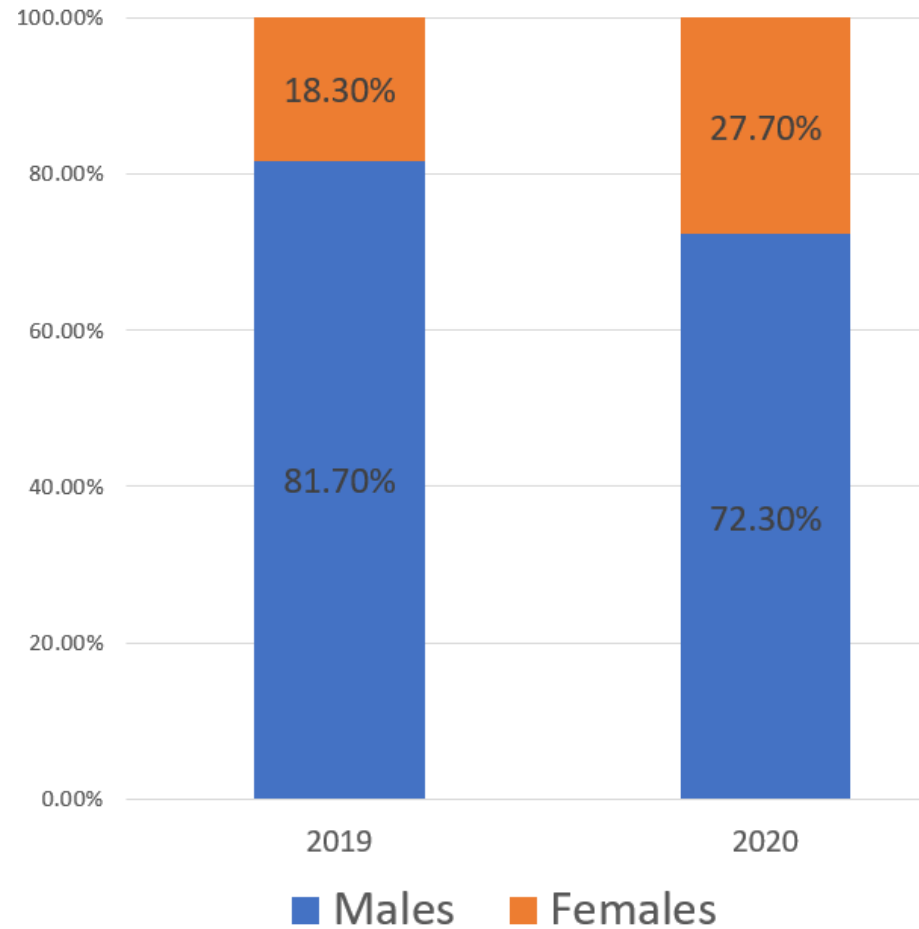
Alcohol-related hepatitis at CMC during COVID-19 pandemic



51% overall increase in incidence

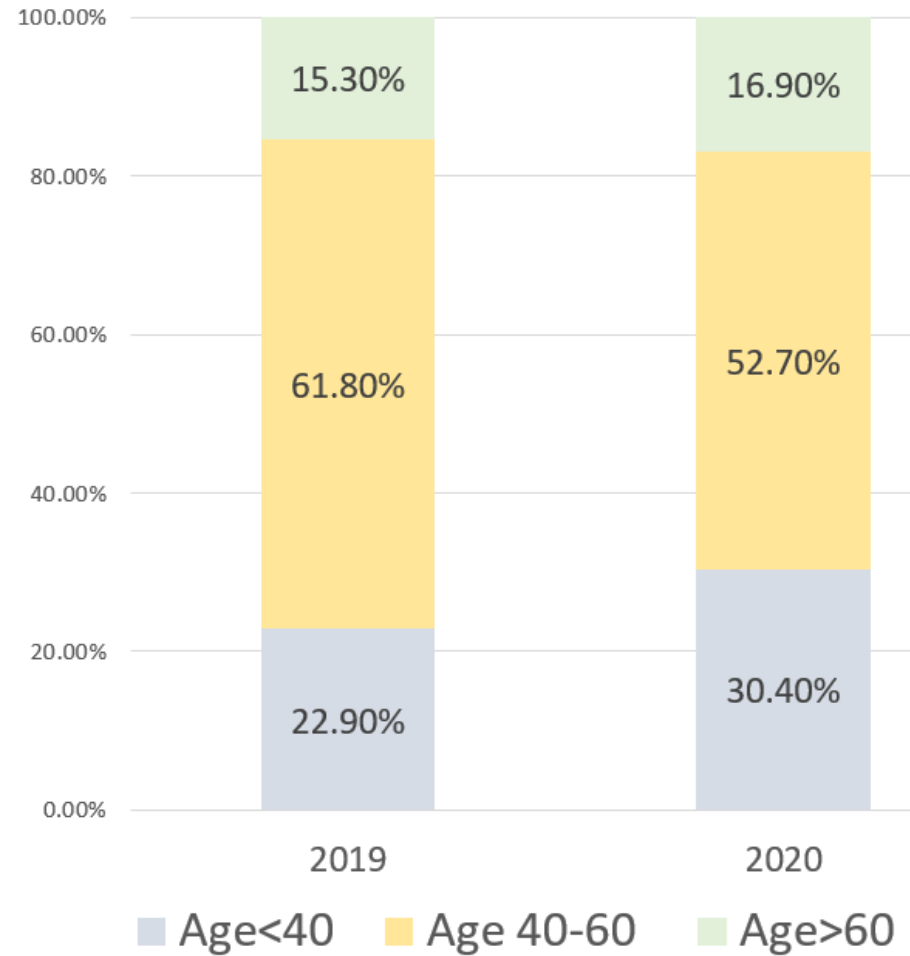
69% increase since Stay-at-home orders

Increase in women with severe alcoholic hepatitis during COVID-19



125%
increase in
women

Increase in younger patients with severe alcoholic hepatitis during COVID-19



100 %
increase
in
patients
under 40

Why did this happen?

- Many states relaxed alcohol laws
- Early pandemic timeline: 54% increase in sales (stores), 262% (online)
- 60% reported increased drinking compared to pre-COVID-19
 - 46% = increased stress
 - 34% = increased availability of alcohol
 - 30% = boredom
 - 64% = combination of above three reasons.



Smoking and Liver Disease

- Smoking affects the liver via 3 separate mechanisms:
 - **Toxic:**
 - **Direct:** Oxidative stress caused by substances in cigarettes with cytotoxic properties.-activation of stellate cell leading to fibrosis. Increase proinflammatory cytokines causing inflammation leading to hepatocytes injury.
 - **Indirect:** Secondary polycythemia increased carboxyhemoglobin causing tissue hypoxia.
 - **Immunologic:** Cell-mediated and humoral effects.
 - **Oncogenic:** Multifold, direct oncogenic effects and viral infection such as HBV and HBV.

Cannabinoid and Hepatic Fibrosis

- Reports of increased hepatic fibrosis in patients with chronic hepatitis C
 - Ishida JH, *et al.* (2008) **Influence of cannabis use on severity of hepatitis C disease.** *Clin. Gastroenterol.Hepatol.* 6:69–75.
 - Hezode C, *et al.* (2005) **Daily cannabis smoking as a risk factor for progression of fibrosis in chronic hepatitis C.** *Hepatology.* 42:63–71.
 - Hezode C, *et al.* (2008) **Daily cannabis use: a novel risk factor of steatosis severity in patients with chronic hepatitis C.** *Gastroenterology.* 134:432–9..
- The difference psychiatric effects between Cannabinoid and Delta THC.

Serious Cocaine effects on liver include:

- Concurrent Chronic Liver Diseases.
- Acute and prolonged Arterial hypotension
- Hyperpyrexia.
- Rhabdomyolysis, acute renal failure.
- Severe liver injury in acute intoxication via IV usage.

Amphetamine causing liver injury

- Include Amphetamines, Meth. , Ecstasy (MDMA).
- Acute hepatitis leads to acute liver failure with hyperpyrexia, heat stroke syndrome, Shock, hepatic ischemia.
- Massive hepatic necrosis.
- High mortality.

Acetaminophen (Paracetamol)

- Daily drinkers were more than twice as likely as nondaily drinkers to be regular daily acetaminophen users and abusers.
- Alcoholic subjects with elevated GGT concentrations had significantly lower **plasma total glutathione concentrations**, and plasma total glutathione concentrations inversely correlated with GGT concentrations.
- **Glutathione depletion** is associated with Acetaminophen hepatic toxicity.

Drug Induced Liver Injury:

- Drugs that can cause hepatitis include Percocet, Vicodin, Acetaminophen, Ibuprofen, Naproxen, birth control pills, aspirin, and statins. People who combine these drugs with alcohol are at an even higher risk of developing hepatitis.
- Herbal supplement especially “energy enhancing agent”, Diet pills, Androgen products, contaminants.
- Hypervitaminosis A.

Management: A multispecialty Intergrated Approach

- Medical support : Health providers, Behavior medicine , Addiction medicine.
- Social economic support: Shelter and Food insecurity.
- Coordination support: Case manager, Navigator.
- Funding support: Governments. Insurance providers.

My take home messages

- Liver diseases in SUD population almost always are multifactorial and carry serious outcome.
- Harm reduction is the key.
- Multi-disciplinary integrated approach is needed.