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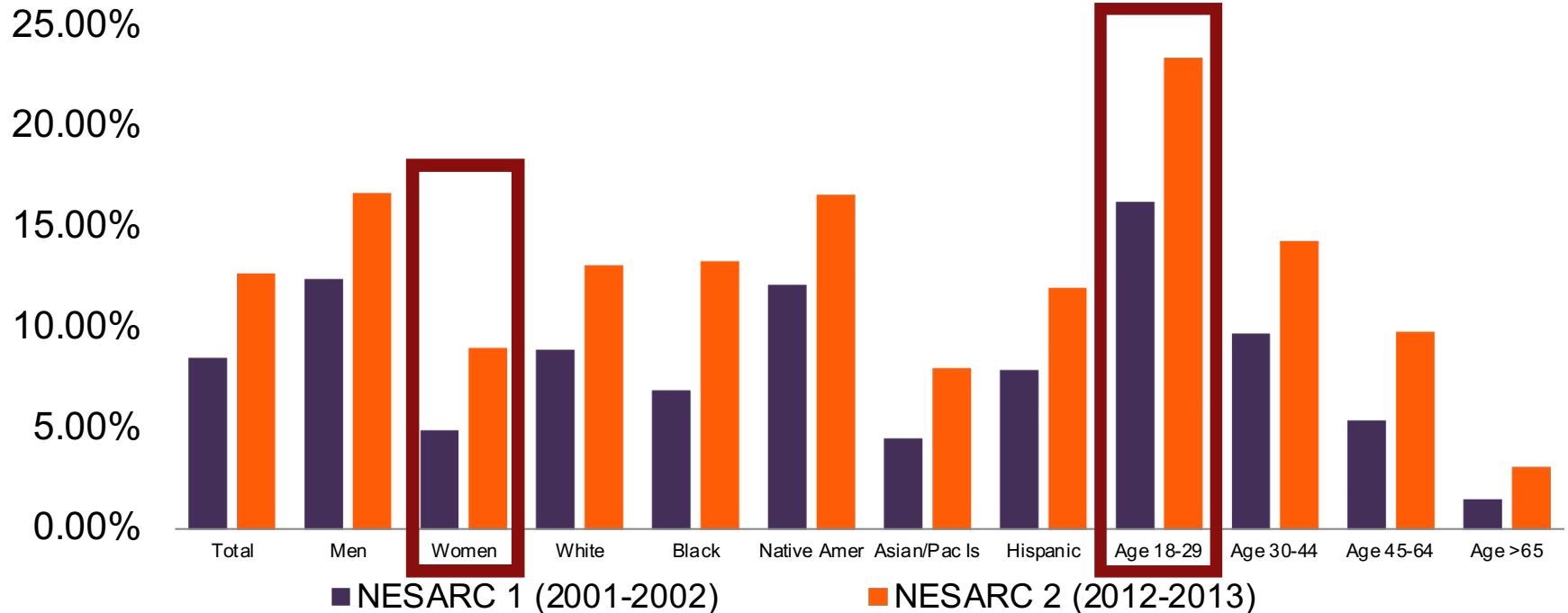
The Pinking of Drinking: Women and ALD

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University of Michigan

CLDF 3rd Annual Liver Connect Conference

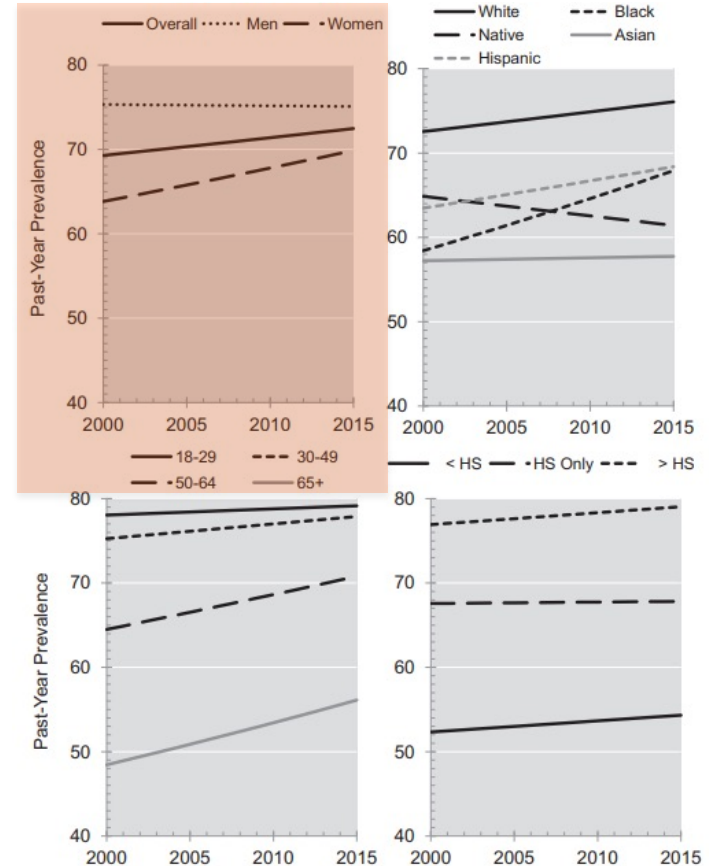
Alcohol Use Disorder in the US is Rising



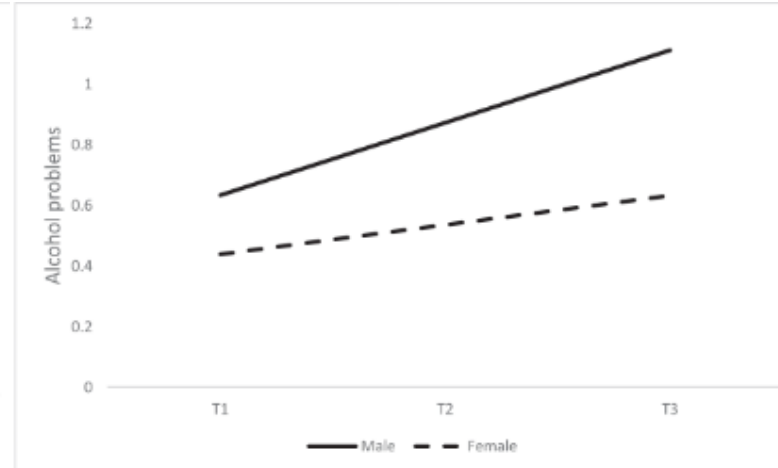
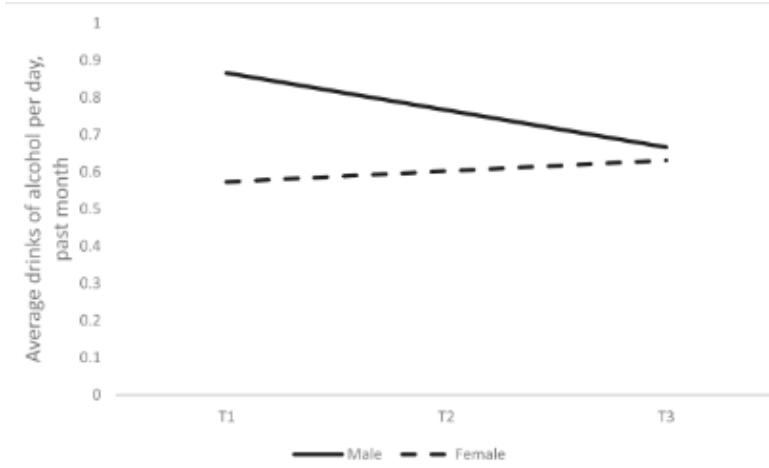
Data from National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

Alcohol Use Trends Across Large Population Surveys

- Meta-analysis of 6 large national surveys (NSDUH, NESARC, NAS, BRFSS, NHANES, NHIS)
- To the right: past-year prevalence of any alcohol use



Pandemic Effects on Drinking: Why So Much Use?

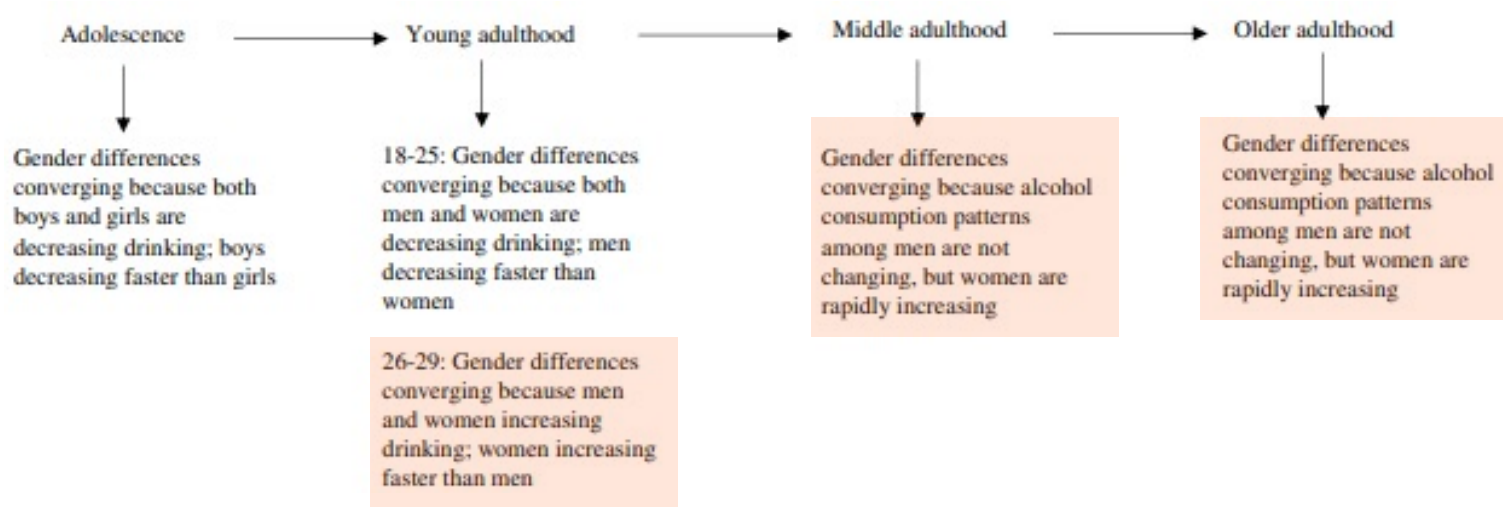


- Online survey of ~1770 adults, age 18 at three intervals (early, mid, late pandemic)
- Assessed **loneliness, social support satisfaction, social demands, social conflicts and social connectedness**
- Assessed **drinking motives** (coping motives: forget worries, improve self-confidence, help depression/anxiety, cheer up a bad mood; social motives: way to celebrate, what friends do together, be sociable, customary on social occasions, makes social gatherings more enjoyable)

Factors Influencing Alcohol Use Increases In the COVID Pandemic

- “Contextual factors”: solitary drinking/solitude/living alone, living with more people (and children) in household, income loss/financial stress, work-from-home, job loss, higher education, **greater intensity shut-downs**
- “Individual factors”: **women (greater % increase in consumption)**, men (inc risky drinking, greater consumption overall), age (<40-45 = greater increases), race (greater increase in quantity consumed among Black, non-White in US), **depression/anxiety/psych distress**, COVID fear/worry, coping motives, other substance use (MJ, tobacco, etc)

“Women are Drinking More Like Men”: Age/Sex Trends in Alcohol Consumption



Findings are heterogenous by **age cohort**. Suggest that closing the gap is occurring (pre-pandemic studies)

Why Are Women Drinking? Alcohol Social Media & Ad Environment

The “pinking” of drinking: Feminized representations of alcohol & drinking



Girl Power

Alcohol use as key to friendship & romantic relationships

Words like “besties”, “girlfriends”, sisters, bffs, queens used to promote solidarity, bonding, and encourage group drinking



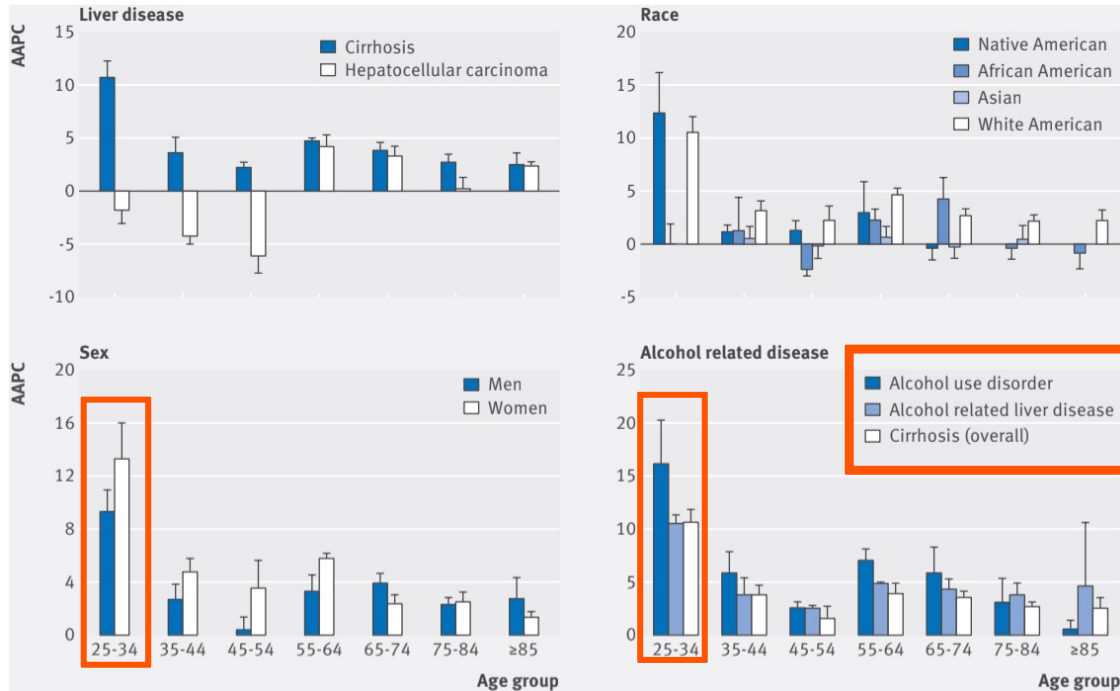
Alcohol use as Self-care

Alcohol use as a time out and reward from working and domestic duties

“Wine o’clock”
Wine down Wednesdays
Rose all day
“Mommy juice”

Draw on narratives of parenting (not seen in men’s alcohol adverts)

ALD is Not What it Used to be Annual Percent Change Highest in Ages 25-34, Native Americans, Women From 1999-2016



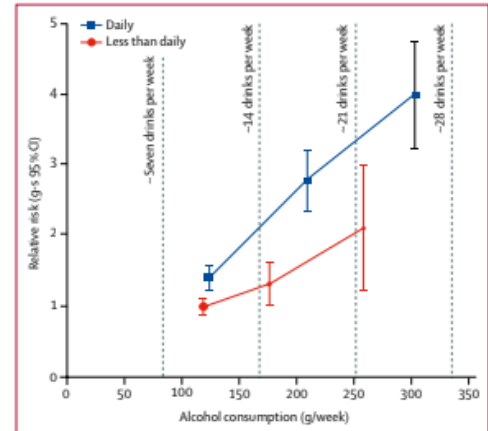
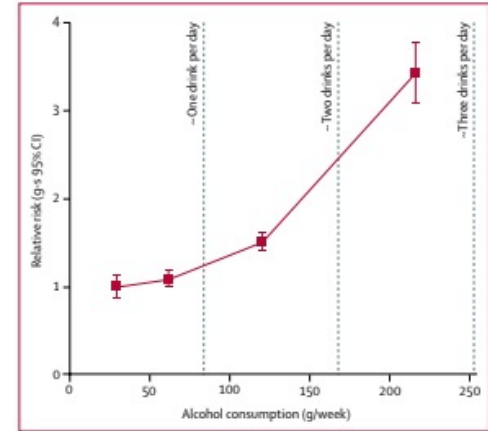
- Overall, annual deaths increased 65% for cirrhosis
- Deaths from hepatocellular carcinoma doubled
- 2009 saw cirrhosis deaths increase 3.4% annually
- Age-adjusted analysis

Increased Risk of Cirrhosis With Moderate Alcohol Consumption in Women

- Million Woman Study (1.3 million women in United Kingdom)
- Initial recruitment: 1996-2001, Prospective surveys every 3-5 years
- Ages at recruitment: 50-64 years
- Self-report alcohol consumption

Overall increasing amounts lead to increasing risk of cirrhosis

Daily drinkers had slightly higher risk than those who drank less than daily (but drank same amount)



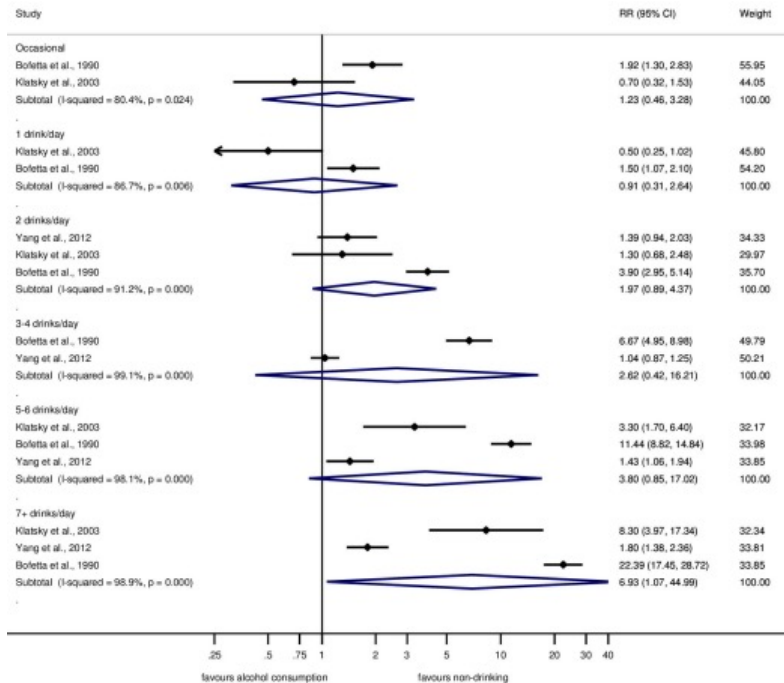
Cirrhosis Mortality Increases Dramatically With Any Drinking- Especially in Women

Alcohol consumption (pure alcohol g day ⁻¹)	RR	P-value	(95% CI)
Women			
>0–12 ^b	1.9	0.013	(1.1, 3.1)
>12–24 ^b	5.6	<0.001	(4.5, 6.9)
>24–36 ^b	7.7	<0.001	(6.3, 9.5)
>36–48 ^b	10.1	<0.001	(7.5, 13.5)
>48–60 ^b	14.7	<0.001	(11.0, 19.6)
>60 ^b	22.7	<0.001	(17.2, 30.1)
Men			
>0–12 ^c	1.0	0.991	(0.6, 1.6)
>12–24 ^c	1.6	<0.001	(1.4, 2.0)
>24–36 ^c	2.8	<0.001	(2.3, 3.4)
>36–48 ^c	5.6	<0.001	(4.5, 7.0)
>48–60 ^c	7.0	<0.001	(5.8, 8.5)
>60 ^c	14	<0.001	(11.7, 16.7)

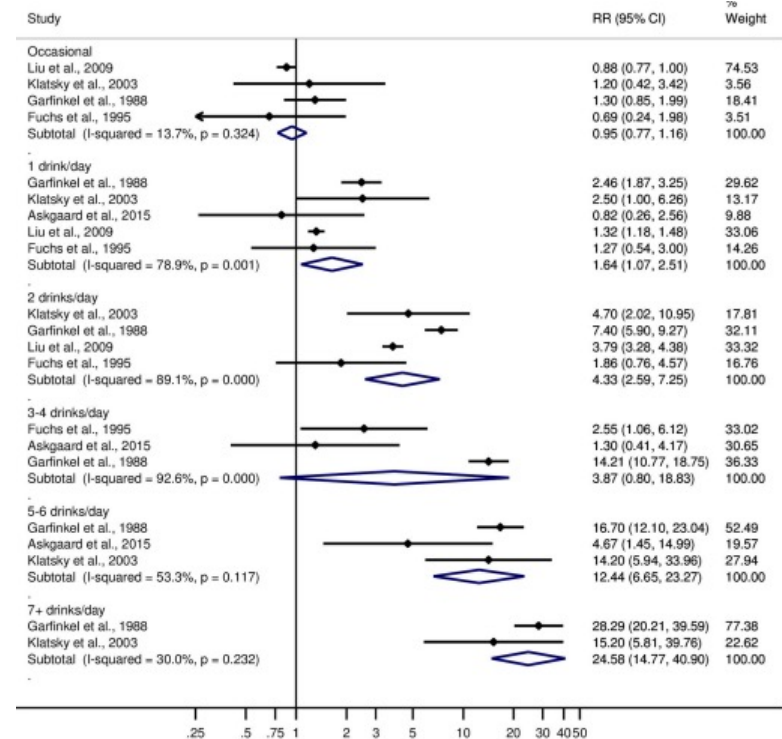


Risk of Cirrhosis by Amount of Drinking

Men



Women

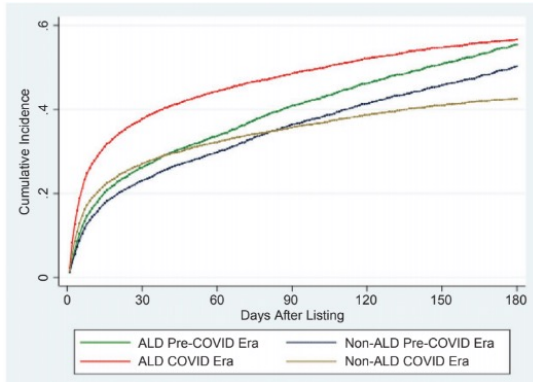


Potential Mechanisms for Sex Differences in ALD

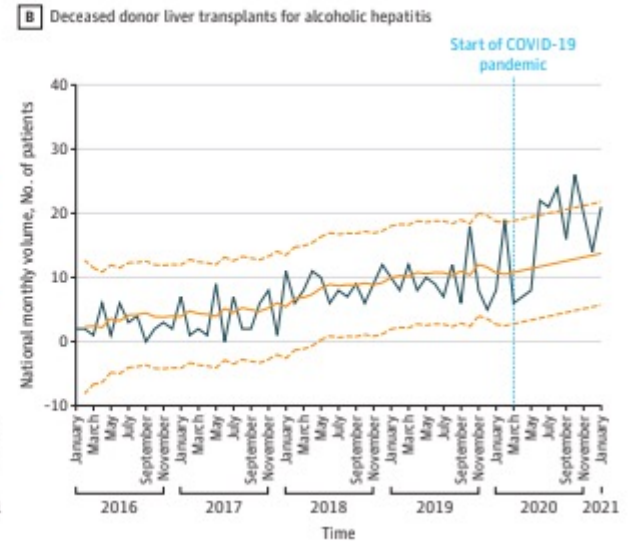
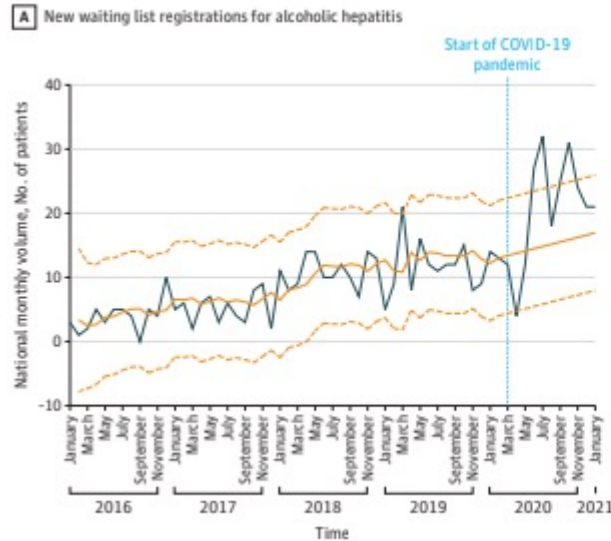
	Sex Differences	Outcome
Alcohol Metabolism	Women typically have decreased body weight, decreased body water	Decreased volume of distribution of alcohol in women
First-pass Metabolism	Women have decreased gastric ADH and slower gastric emptying of alcohol	Increased bioavailability of alcohol in women
Estrogen	Chronic alcohol consumption increases estrogen in male/female rodent models	Increased estrogen coincides with more liver injury in rodent models
Growth hormone	Female rodent models show continuous secretion of GH leading to increased hepatic ADH activity	Increased accumulation of toxic acetaldehyde
Endotoxin and Kupffer cell activation	Estrogen sensitizes Kupffer cells to LPS in rodent models	Increased accumulation of pro-inflammatory cytokines

Kezer CA et al. *Mayo Clin Proc.* 2021; Edenberg HJ et al. *ACER.* 2018; Shimizu I et al. *Trends Alc Liver Dis Res.* 2012; Baraona E et al. *ACER.* 2001; Frezza M et al. *NEJM.* 1990; Eagon PK et al. *World Jnl Gastro.* 2010; Colantoni A et al. *Mol Cell Endo.* 2002; Mello NK et al. *Alc and Endocrin System.* 1993; Shapiro BH et al. 1995; Mezey E et al. *ACER.* 2000; Ikejima K et al. *Am J Physio.* 1998.

Waitlisting and Transplants for ALD Rose Dramatically During COVID-19

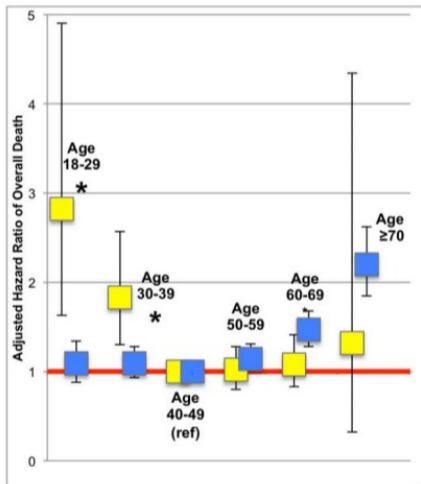


Incidence of overall ALD transplant increase in COVID era, outpacing non-ALD transplant

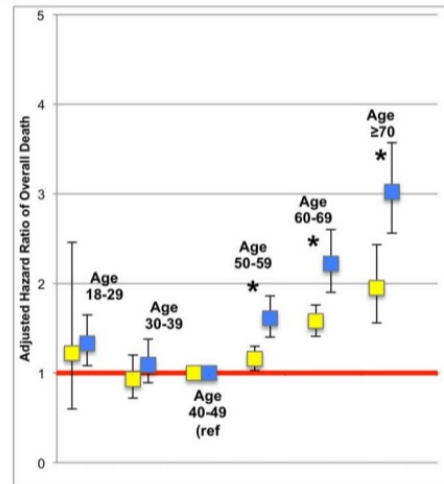


ALD increase in transplants is due to increases in alcoholic hepatitis waitlisting and transplant

Young Women Post-Transplant for ALD Have Higher Mortality



Women w/ ALD
Women w/o ALD

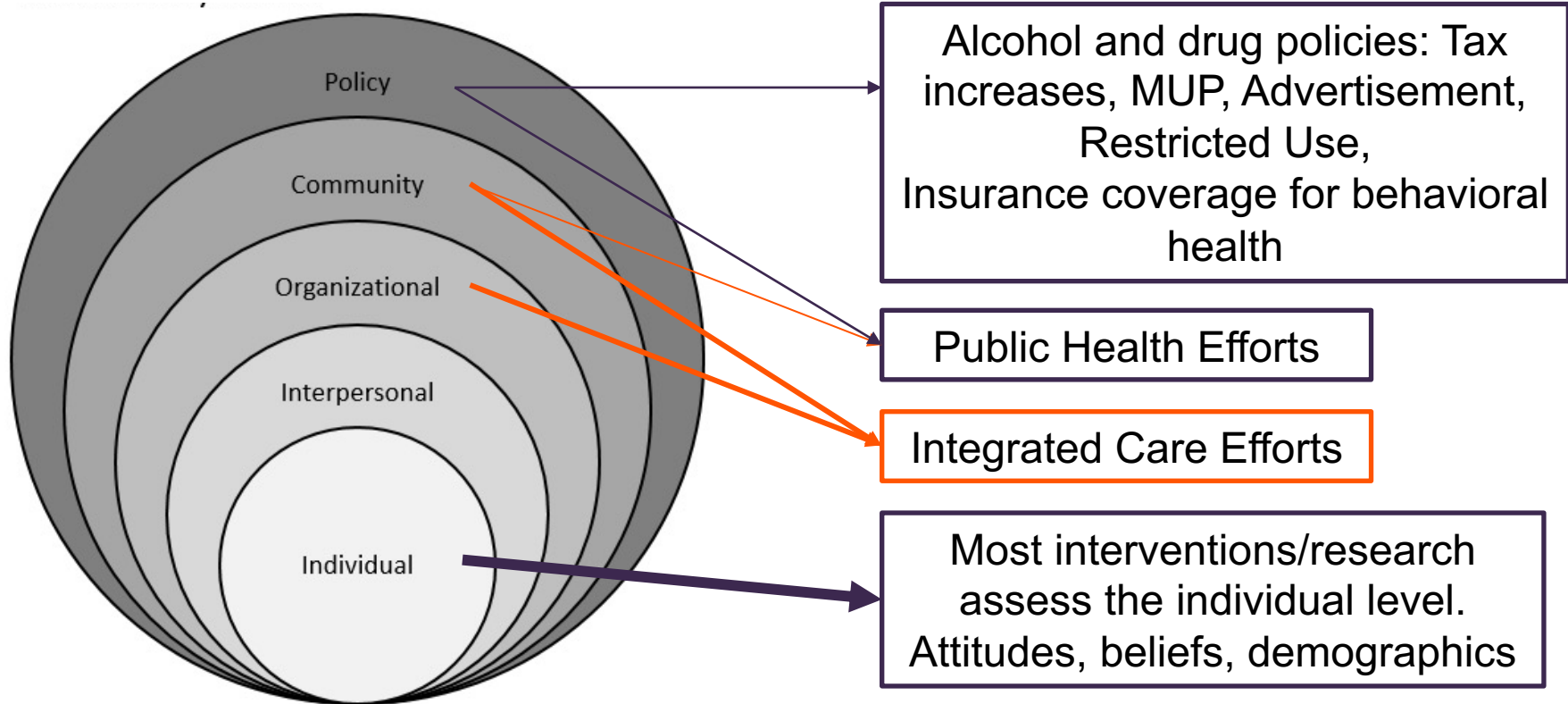


Men w/ ALD
Men w/o ALD

Age	Adjusted Hazard Ratio (95% CI)			
	Women		Men	
	ALD	Non-ALD	ALD	Non-ALD
18-29	2.82 (1.63-4.90)	1.09 (0.88-1.34)	1.22 (0.60-2.46)	1.33 (1.08-1.65)
30-39	1.83 (1.30-2.57)	1.09 (0.93-1.28)	0.93 (0.72-1.20)	1.09 (0.89-1.38)
40-49	Ref	Ref	Ref	Ref
50-59	1.02 (0.80-1.28)	1.14 (1.00-1.31)	1.16 (1.03-1.30)	1.61 (1.40-1.86)
60-69	1.08 (0.83-1.41)	1.47 (1.28-1.68)	1.58 (1.41-1.76)	2.22 (1.90-2.60)
≥70	1.32 (0.50-3.50)	2.20 (1.85-2.62)	1.95 (1.56-2.43)	3.02 (2.56-3.57)

Age	Adjusted 5-Year Survival (95% CI)			
	Women		Men	
	ALD	Non-ALD	ALD	Non-ALD
18-29	74% (63-88%)	92% (91-94%)	88% (81-96%)	92% (90-93%)
30-39	82% (78-87%)	92% (91-94%)	91% (89-92%)	93% (92-94%)
40-49	90% (88-92%)	93% (92-94%)	90% (89-91%)	94% (93-95%)
50-59	90% (89-91%)	92% (91-93%)	89% (88-90%)	90% (89-91%)
60-69	89% (87-91%)	90% (88-91%)	85% (84-86%)	86% (85-88%)
≥70	87% (76-100%)	85% (82-88%)	82% (79-85%)	82% (80-84%)

Potential Solutions Need to Incorporate Gender Considerations at Every Level





Thank You

Questions: email
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