NIAAA Director's Report
on Institute Activities to the 162nd Meeting of the National Advisory Council on Alcohol Abuse and Alcoholism

February 9, 2023
Virtual Meeting

George F. Koob, Ph.D.
Director
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health

https://www.niaaa.nih.gov/about-niaaa/advisory-council

NIAAA Budget

- On December 29th, 2022, the President signed the Consolidated Appropriations Act of 2023.
  - NIH received a total of $47.7 billion, which is a $2.5 billion (or 5.5%) increase above the fiscal year 2022 enacted level.
  - NIAAA received $595.3 million. This represents a $21.66 million (or 3.8%) increase over fiscal year 2022. NIAAA estimates it will support 728 Research Project Grants this fiscal year.
- The preparation of the fiscal year 2024 President's Budget is under way.

Thank You, Abe Bautista

Dr. Abraham Bautista retired from his position as the Director of the Office of Extramural Activities (OEA) after 20 years of Federal Service.

Abe was responsible for extramural grant and contract review, the management of chartered initial review groups and special emphasis panels, and all grants management activities.

Abe served as the Executive Secretary of NIAAA's Advisory Council and was responsible for overseeing and coordinating committee management activities, including federal advisory committees.

In his retirement Abe looks forward to expanding his travels and finding other exciting ways to fill his days. He will be missed!

Philippe Marmillot is the Acting OEA Director

NIAAA Leadership Recruitment

- **Director, Office of Extramural Activities:** We are in the early stages of the recruitment process and anticipate completing the process within the next few months.

- **Scientific Director, Intramural Research Program:** The search committee recommended three candidates for consideration. Each candidate gave a talk about their research as well as their vision for the intramural program. We have solicited feedback from all NIAAA staff. After a final interview stage, we hope to have a selection made over the next few weeks.

- **Scientific Diversity Officer:** We are conducting pre-recruitment outreach efforts for this position and anticipate that the official announcement will open in the next few weeks.

For more information, visit:
https://www.niaaa.nih.gov/about-niaaa/career-and-training-opportunities

NIAAA Funding Opportunities

(See Director's Report for Complete Listing)

- **Research Opportunities for New and "At-Risk" Investigators to Promote Workforce Diversity:** NIAAA is participating in a funding opportunity announcement to support R01 grant applications from New Investigators and At-Risk Investigators from diverse backgrounds, including those from groups underrepresented in the health-related sciences (PAR-22-181)

  NIAAA Contact: Dr. Laura Kwako, laura.Kwako@nih.gov

NIH Data Management & Sharing Policy in Effect

- In January 2023, the final NIH Policy for Data Management and Sharing went into effect (NOT-OD-21-013). The policy promotes transparency and accountability in research by setting a minimum set of expectations for data management and sharing.
- Some notable changes:
  - Most applications are required to include a Data Management and Sharing Plan.
  - Data should be shared no later than the time of an associated publication, or the end of the award period, whichever comes first.
  - Awards will no longer have a 2-year embargo period before data are shared with the public.
- NIAAA has published two related Notices that:
  - Describe information to be included in the Data Management and Sharing Plan (NOT-AA-23-001), Contact: Dr. Elizabeth Powell (elizabeth.powell3@nih.gov)
  - Update the NIAAA Data Archive sharing requirements for human subjects research (NOT-AA-23-002), Contact Dr. Dan Falk (falkde@mail.nih.gov)
- More information can be found at sharing.nih.gov

National Conference on Alcohol and Other Substance Use in Women and Girls

- In October 2022, NIAAA and the Interagency Work Group on Drinking and Drug Use in Women and Girls hosted the "National Conference on Alcohol and Other Substance Use in Women and Girls: Advances in Prevention, Treatment, and Recovery."

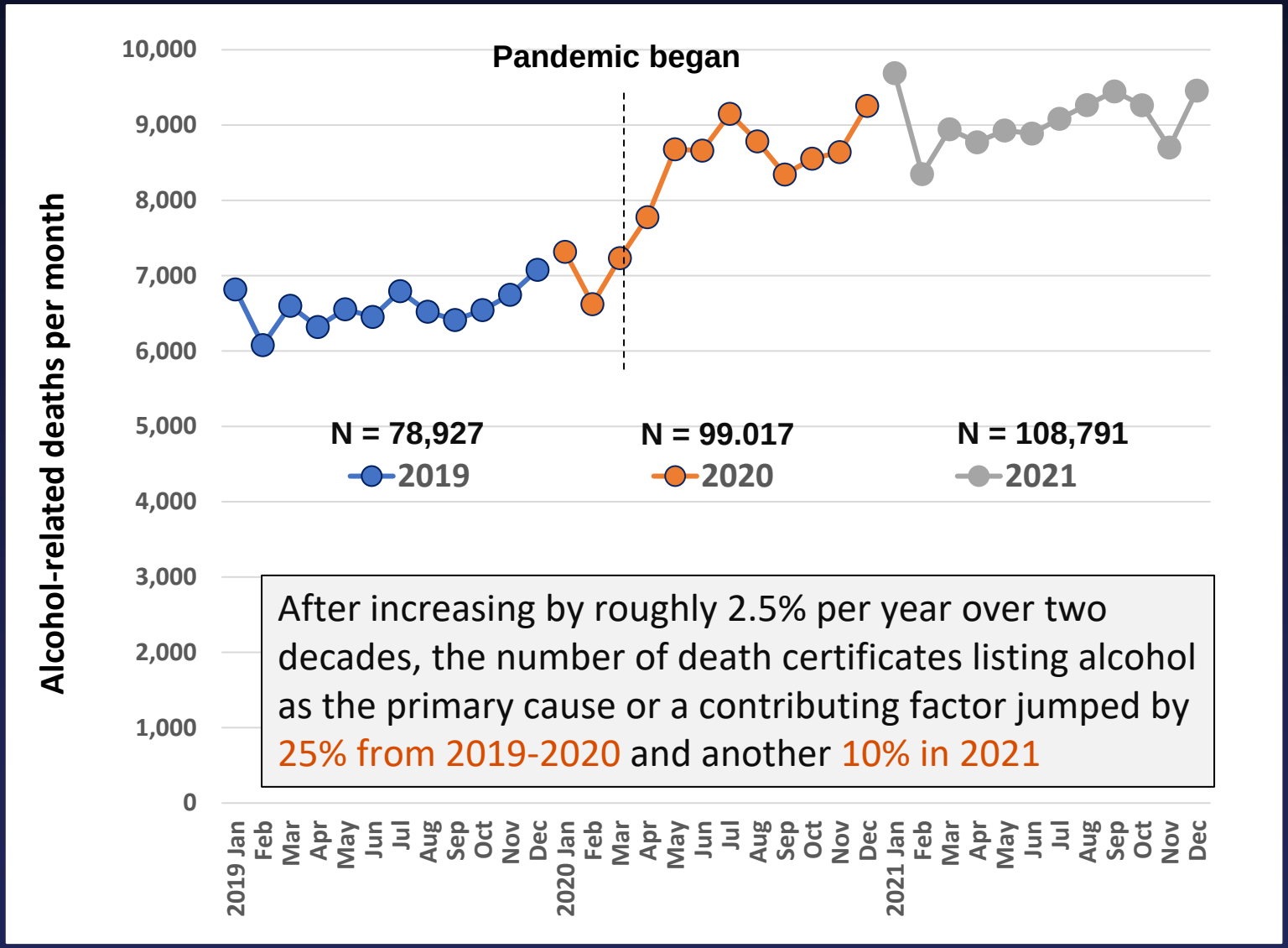
- More than 400 attendees participated in the virtual conference, which featured plenary lectures by NIAAA Director Dr. George F. Koob, National Institute on Drug Abuse Director Dr. Nora Volkow, and National Institute of Mental Health Director Dr. Joshua Gordon.

- In addition to highlighting the importance of reducing stigma and other health barriers, the conference featured panel sessions covering a wide range of topics, including:
  - Overview of Harmful Alcohol and Other Substance Use in Women and Adolescent Girls
  - Model Programs for Mothers with Alcohol Use Disorder and Other Substance Use Disorders
  - Children with Prenatal Substance Exposure

Virtual Forum on COVID-19 Research

- In January 2023, NIAAA held a virtual forum featuring NIAAA-supported grantees conducting COVID-19 related research.
- The purpose of the forum was to share progress on COVID-19 supplements and grants that NIAAA supported during the pandemic.
- There were 36 presentations across 6 scientific sessions focused on:
  - Effects of the COVID-19 pandemic on alcohol use
  - Pathophysiological impact of alcohol on COVID-19 outcomes
  - Impacts of COVID-19 stress on alcohol consumption, neural vulnerabilities, and mental health
  - Effects of COVID-19 and alcohol-related health outcomes
  - HIV/AIDS and other factors
  - Health services

Alcohol-Related Deaths Increased During the Pandemic



Source: Centers for Disease Control and Prevention, WONDER Online Database, Multiple Cause of Death 1999-2021, https://wonder.cdc.gov/controller/saved/D157/D324F825

Public Awareness: Dry January

- **NIAAA participated in more than 60 media interviews and a 'Dry January' Satellite Media tour, which discussed behaviors during the holidays that may be signs of a problem with alcohol and the benefits of Dry January. The Satellite Media Tour included interviews with 17 media outlets with a reach of more than 1.8 million people.**

The Washington Post

The benefits of 'Dry January' last longer than a month, studies show

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Is 'Dry January' Getting Drier?

The New York Times

Even a Little Alcohol Can Harm Your Health

Recent research makes it clear that any amount of drinking can be detrimental. Here's why you may want to cut down on your consumption beyond Dry January.

Provider Awareness: Healthcare Professional's Core Resource on Alcohol

- NIAAA continues to promote the HPCR through multiple efforts, including outreach to organizations, academic leaders, and health plans
- HPCR is now designated an:
  - American College of Academic Addiction Medicine Recommended Educational Activity
  - American Board of Addiction Medicine Recognized Activity for Certification of Diplomates

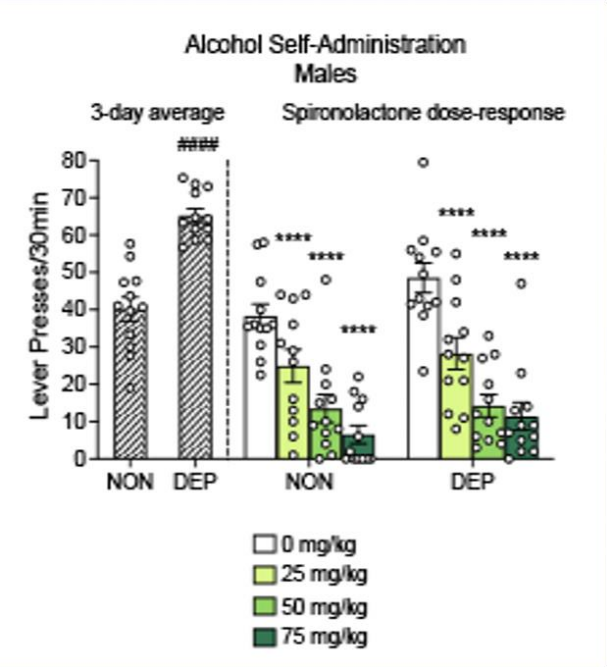
Ad for nursing schools

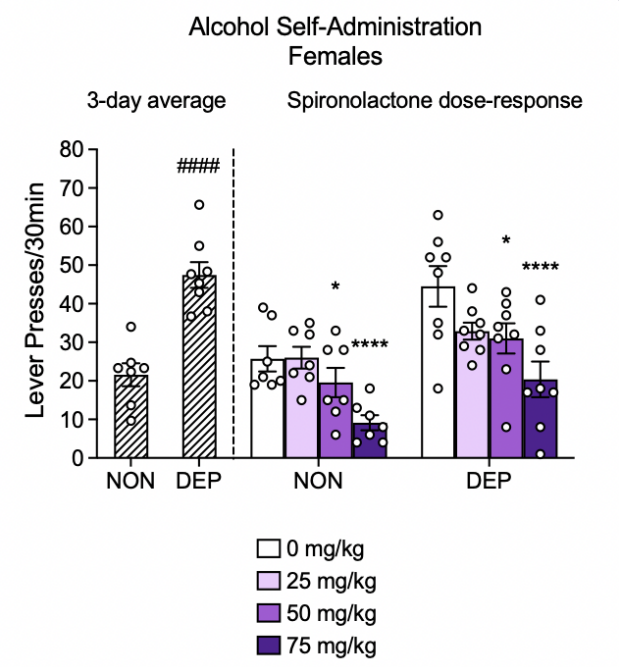
NIAAA hosted a webinar in December 2022 that included a discussion of how the HPCR can support people in recovery

Research Highlights

Spironolactone Decreased Alcohol Self-administration in Male and Female Rats

A set of mouse and rat experiments, combined with a human pharmacoepidemiology analysis (using VA EMR), provided convergent evidence supporting the overall hypothesis that the non-selective mineralocorticoid receptor antagonist spironolactone may represent a novel medication for AUD.





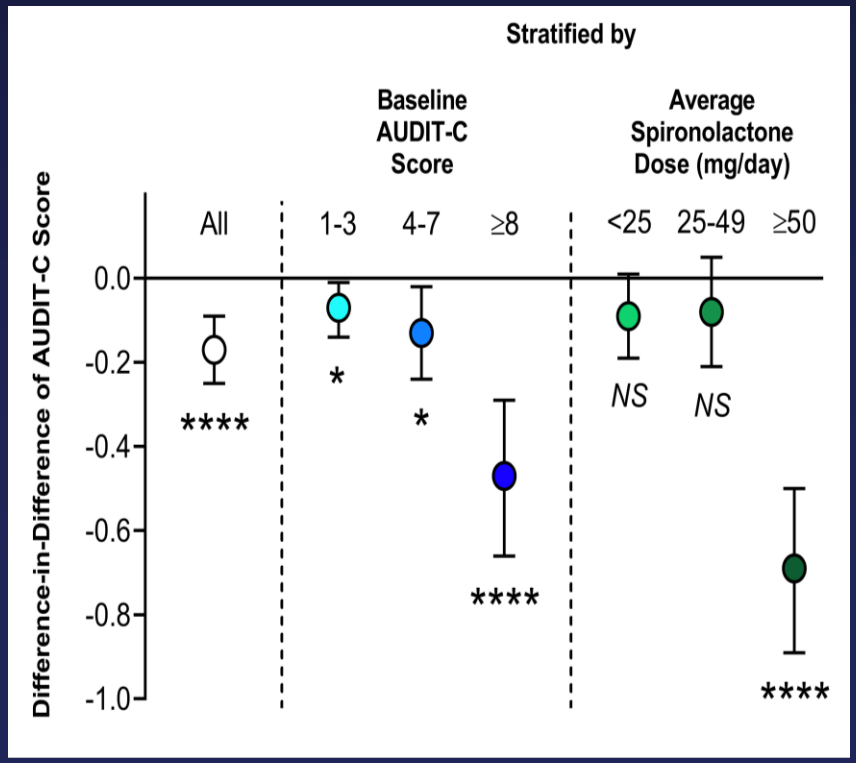
(Farokhnia M, Rentsch CT, Chuong V, McGinn A, Elvig SK, Douglass EA, Sanfilippo JE, Marchette RCN, Tunstall BJ, Fiellin DA, Koob GF, Justice AC, Leggio L, Vendruscolo LF. Spironolactone as a Potential New Pharmacotherapy for Alcohol Use Disorder: Convergent Evidence from Rodent and Human Studies. Molecular Psychiatry, https://doi.org/10.1038/s41380-022-01736-y)

Positive Association Between Spironolactone Treatment and Decreased Alcohol Consumption in Humans

Observational cohort study

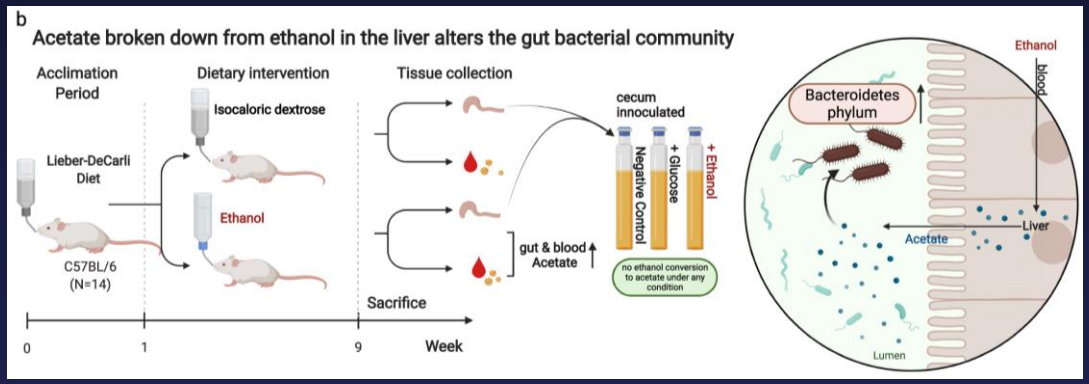
- US Dept of Veterans Affairs electronic health record data
- 10,726 – exposed to spironolactone
- 34,461 – unexposed matched controls
- Examined change in self-reported AUDIT-C scores at baseline and follow-up
- Significantly greater decrease in individuals exposed to spironolactone
- Subgroup analysis stratified by baseline AUDIT-C score and spironolactone dose
- Largest reductions in those with heavy alcohol consumption, highest dose of spironolactone

		Exposed	Unexposed
		n = 10,726	*n* = 34,461
All patients	Pre	3.07 (0.02)	2.96 (0.01)
	Post	2.16 (0.02)	2.22 (0.01)
	D^n	-0.91 (0.03)	-0.75 (0.02)
	Diff-in-Diff (95% CI)	-0.17 (-0.09, -0.25), $p < 0.0001$	

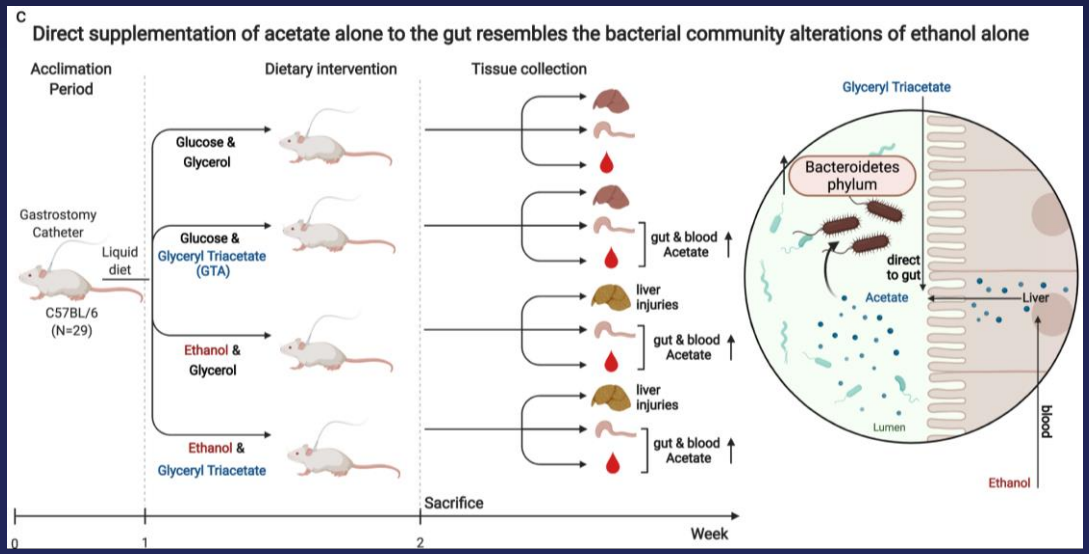


Acetate reprograms gut microbiota during alcohol consumption

Altered gut microbiota and intestinal bacterial overgrowth (dysbiosis) can be found in patients with alcohol-related liver disease. In this study, investigators found that acetate, a by-product of alcohol metabolism, diffused from circulation into the intestine where it provided a source of energy for bacterial growth.



In mice on Lieber-DeCarli diet, anaerobic gut bacteria did not break down ethanol to acetate but used acetate from the liver for gluconeogenesis

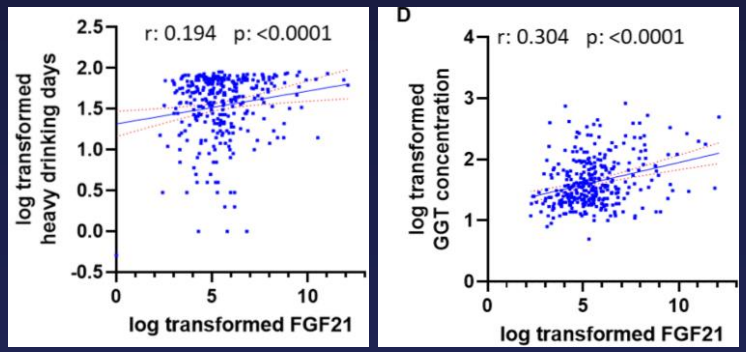


Intragastric infusion of glyceryl triacetate, which increased gut acetate levels directly, replicated alterations in gut microbiota found above

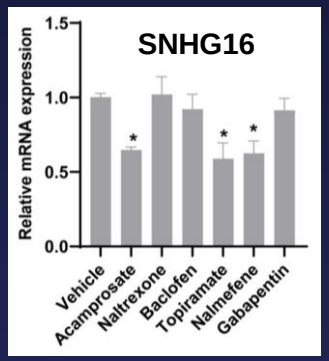
(Martino C, Zaramela LS, Gao B, Embree M, Tarasova J, Parker SJ, Wang Y, Chu H, Chen P, Lee KC, Galzerani DD, Gengatharan JM, Lekbua A, Neal M, Knight R, Tsukamoto H, Metallo CM, Schnabl B, Zengler K. Nat Commun. 2022 Aug 8;13(1):4630. doi: 10.1038/s41467-022-31973-2. PMID: 35941112)

Genome-wide association study for circulating FGF21 in patients with alcohol use disorder

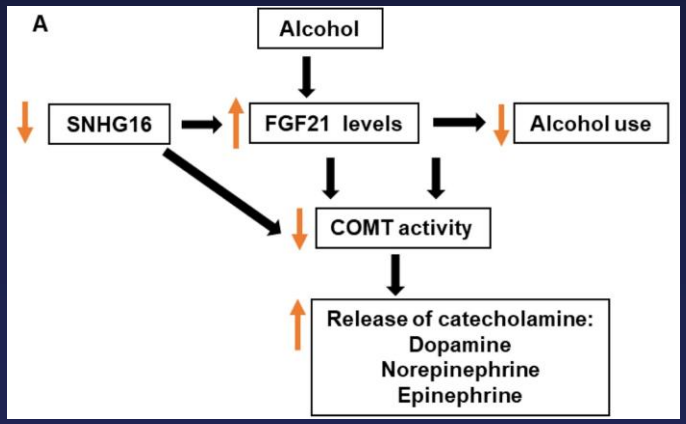
Circulating plasma levels of fibroblast growth factor 21 (FGF21) are associated with recent alcohol and chronic consumption and injection of FGF21 reduced alcohol intake in mice (Soberg et al., 2018). The present study identified genetic variants associated with FGF21 levels and evaluated their functional role in AUD. One variant, located 5' of the SNHG16 gene on chromosome 17, was associated with plasma FGF21 levels and with AUD risk. Knockdown of SNHG16 in HepG2 cells resulted in increased FGF21 levels and decreased expression and enzyme activity for COMT, an enzyme that is involved in catecholamine metabolism. Alcohol induced FGF21 production in iPSC-derived brain organoids, which was blocked by AUD treatments. These results suggest that theSNHG16-FGF21 axis could be a potential pharmaceutical target for the treatment of AUD.



In patients with AUD, plasma FGF21 levels were positively correlated with the number of heavy drinking days and blood levels of gamma-glutamyl transferase (GGT), a marker for heavy alcohol use



Drug treatment was associated with changes in mRNA expression of *SNHG16* in organoids



The data suggest that the genetic variant SNHG16 can regulate FGF21 concentrations and decrease COMT expression and enzyme activity

(Ho MF, Zhang C, Moon I, Wei L, Coombes B, Biernacka J, Skime M, Choi DS, Frye M, Schmidt K, Gliske K, Braughton J, Ngo Q, Skillon C, Seppala M, Oesterle T, Karpyak V, Li H, Weinshilboum R. Genome-wide association study for circulating FGF21 in patients with alcohol use disorder: Molecular links between the SNHG16 locus and catecholamine metabolism. Mol Metab. 2022 Sep;63:101534. doi: 10.1016/j.molmet.2022.101534. Epub 2022 Jun 22. PMID: 35752286.)

COVID-19 pandemic-related changes in utilization of telehealth and treatment overall for alcohol use problems

This study investigated the impact of the COVID-19 pandemic on alcohol treatment utilization and potential disparities. Investigators analyzed electronic health record and claims data from Kaiser Permanente Northern California for adults with alcohol use problems during pre-COVID-19 (March-December 2019) and COVID-19 onset (March- December 2020). The transition to telehealth may have attracted individuals who have historically underutilized care for alcohol use problems, particularly younger and healthier adults, without exacerbating pre-pandemic racial and ethnic disparities.

Outcome	Unadjusted % (95% CI)		COVID-19 onset vs pre-COVID-19, aOR (95% CI)	p-value	Interaction p-value
	Pre-COVID-19 (*n* = 32,806)	COVID-19 onset, (*n* = 26,763)			
Telehealth treatment initiation					
Overall	5.9 (5.7, 6.2)	20.3 (19.8, 20.7)	4.01 (3.79, 4.24)	<0.001	—
By age group (years)					
18–34	4.5 (4.2, 5.0)	18.9 (18.1, 19.8)	5.21 (4.67, 5.81)	<0.001	<0.001
35–49	8.2 (7.7, 8.9)	24.9 (23.9, 25.9)	3.74 (3.39, 4.12)	<0.001	
50–64	7.0 (6.4, 7.5)	21.4 (20.4, 22.4)	3.63 (3.27, 4.03)	<0.001	
65+	4.0 (3.6, 4.5)	12.4 (11.4, 13.5)	3.32 (2.83, 3.90)	<0.001	
Treatment engagement					
Overall	34.0 (32.9, 35.0)	41.4 (40.3, 42.4)	1.32 (1.23, 1.41)	<0.001	—
By age group (years)					
18–34	35.5 (33.4, 37.7)	40.8 (38.8, 42.8)	1.30 (1.14, 1.48)	<0.001	0.456
35–49	41.3 (39.2, 43.5)	49.8 (47.8, 51.8)	1.42 (1.25, 1.60)	<0.001	
50–64	36.5 (34.5, 38.6)	41.5 (39.6, 43.5)	1.23 (1.09, 1.40)	0.001	
65+	18.5 (16.6, 20.5)	24.1 (21.7, 26.6)	1.35 (1.12, 1.62)	0.002	

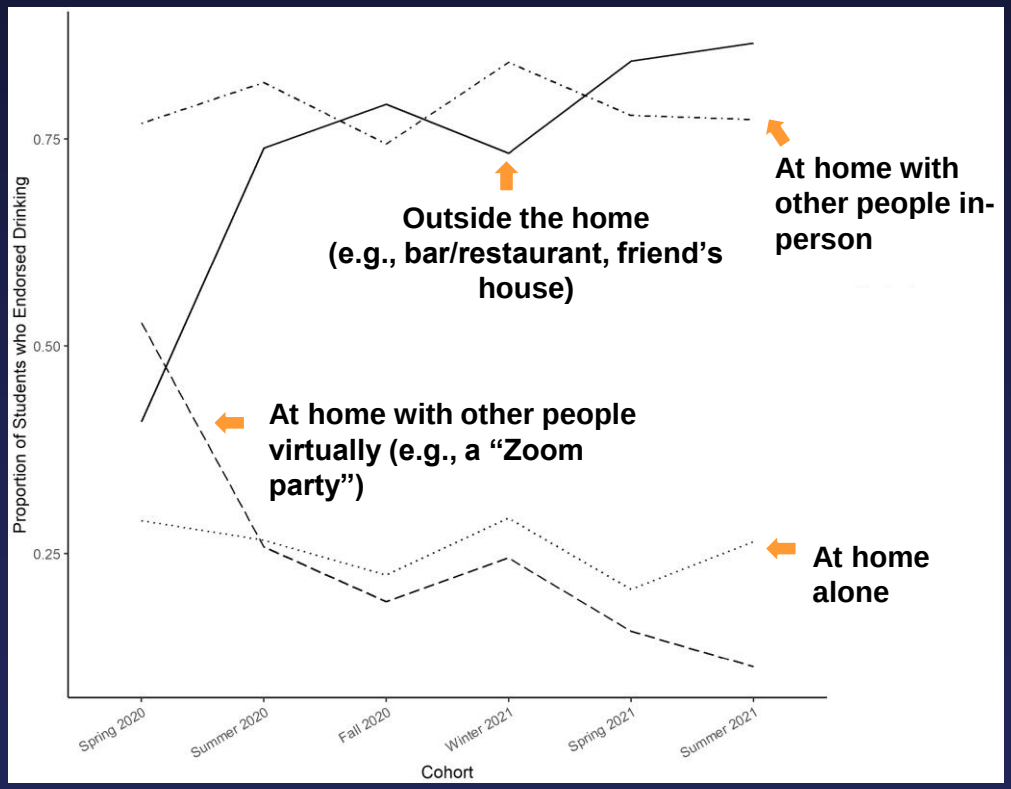
4-fold greater odds of telehealth treatment initiation during pandemic onset, and greater among young adults

Greater odds of treatment engagement was observed during pandemic onset and did not vary by age group, race, and ethnicity.

(Palzes VA, Chi FW, Metz VE, Campbell C, Corriveau C, Sterling S. Alcohol Clin Exp Res. 2022 Dec;46(12):2280-2291. doi: 10.1111/acer.14961. Epub 2022 Dec 17. PMID: 36527427)

College students virtual and in-person drinking contexts during the COVID-19 pandemic

Although college drinking decreased at the onset of the pandemic, this study sought to identify a more nuanced understanding of changes in drinking contexts and the risks conferred by each context. Secondary analyses were performed on screening data from a large clinical trial assessing a college student drinking intervention. Participants across six cohorts reported on the frequency of drinking.



The proportion and frequency of drinking outside the home increased and was most consistently associated with more alcohol-related consequences. However, drinking at home was not without risks.

Future prevention and intervention efforts may benefit from considering approaches specific to different drinking contexts.

(Hultgren BA, Smith-LeCavalier KN, Canning JR, Jaffe AE, Kim IS, Cegielski VI, Garcia TA, Larimer ME. Alcohol Clin Exp Res. 2022 Nov;46(11):2089-2102. doi: 10.1111/acer.14947. Epub 2022 Dec 1. PMID: 36454103)

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