Alcohol and Cancer Control

NOT-CA-20-034

Notice of Special Interest (NOSI) Webinar

Tanya Agurs-Collins (NCI), David Berrigan (NCI), Gary Murray (NIAAA), I-Jen Castle (NIAAA)

May 28, 2020
Using WebEx and Webinar Logistics

- All lines will be in listen-only mode
- Make sure icons are selected for them to appear as a drop-down option
- Submit questions at any time during the presentation by typing into the Q&A feature on the right-hand side of the WebEx interface.
  - Select Host and a moderator will ask the questions on your behalf
- Closed captioning available by selecting the Media Viewer Panel on the right-hand side of the screen
- This webinar is being recorded and will be posted at a later date
Webinar Presenters and NOSI Contacts

Tanya Agurs-Collins, Ph.D., R.D.
Program Director
National Cancer Institute
collinsta@mail.nih.gov

David Berrigan, Ph.D., M.P.H
Program Director
National Cancer Institute
berrigad@mail.nih.gov

Gary J. Murray, Ph.D.
Program Director
National Institute on Alcohol Abuse and Alcoholism
gary.murray@nih.gov

I-Jen Castle, Ph.D.
Program Officer
National Institute on Alcohol Abuse and Alcoholism
i-jen.castle@nih.gov
Webinar Overview

- Overview of NIH Notice of Special Interest (NOSI)
- Background and Purpose of NCI/NIAAA Alcohol and Cancer Control NOSI - NOT-CA-20-034
- NCI Research Priorities and Research Areas
- NIAAA Research Priorities and Research Areas
- Application and Submission Information
- Q & A
NIH Notice of Special Interest (NOSI)

- Notice posted in the NIH guide that institutes and centers can use to share and update research priorities.
- NOSIs briefly highlight a specific topic of research or programmatic interest.
- NOSIs direct applicants to relevant funding opportunities for grant, supplement or competitive revision submissions.
- NOSIs are not generally associated with set aside funds; gradually replacing Program announcements.
- Details on NIH NOSIs at [NOT-OD-19-107](#) and FAQs about grants.
Notice of Special Interest: Alcohol and Cancer Control (NOT-CA-20-034)

Release Date: March 18, 2020
First Available Due Date: June 05, 2020
Expiration Date: September 09, 2023

National Cancer Institute (NCI)
National Institute on Alcohol Abuse and Alcoholism (NIAAA)

Calls for R01s, R21s, R03s

Purpose: This Notice highlights interest in receiving investigator-initiate dressing the effects of alcohol on human health across the cancer control continuum.
Association Between Alcohol and Cancer Risk

- Alcohol is classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC).
- In the US, alcohol use causes 5.6% of cancer cases and 4.0% cancer deaths.
- “The overall absolute increase in cancer risk for one bottle of wine per week equals that of five (men) or ten cigarettes per week.”

### ALCOHOLIC DRINKS AND THE RISK OF CANCER

<table>
<thead>
<tr>
<th>WCRF/AICR GRADING</th>
<th>DECREASES RISK</th>
<th>INCREASES RISK</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STRONG EVIDENCE</strong></td>
<td>Convinced</td>
<td>Alcoholic drinks¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alcoholics drinks¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alcoholics drinks¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alcoholics drinks¹</td>
</tr>
<tr>
<td></td>
<td>Probable</td>
<td>Kidney 2015³</td>
</tr>
<tr>
<td><strong>LIMITED EVIDENCE</strong></td>
<td>Limited – suggestive</td>
<td>Alcoholics drinks¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None identified</td>
</tr>
<tr>
<td><strong>STRONG EVIDENCE</strong></td>
<td>Substantial effect on risk unlikely</td>
<td>None identified</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None identified</td>
</tr>
</tbody>
</table>

¹ Alcoholic drinks include beers, wines, spirits, fermented milks, mead and cider. The consumption of alcoholic drinks is graded by the International Agency for Research on Cancer as carcinogenic to humans (Group 1)[3].

² The conclusions for alcoholic drinks and cancers of the liver, stomach and pancreas were based on evidence for alcohol intakes above approximately 45 grams of ethanol per day (about three drinks a day). No conclusions were possible for these cancers based on intakes below 45 grams of ethanol per day.

³ The conclusion for alcoholic drinks and colorectal cancer was based on alcohol intakes above approximately 30 grams of ethanol per day (about two drinks a day). No conclusion was possible based on intakes below 30 grams of ethanol per day.

4 No threshold level of alcohol intake was identified in the evidence for alcoholic drinks and breast cancer (pre and postmenopause).

5 The conclusion for alcoholic drinks and kidney cancer was based on alcohol intakes up to approximately 30 grams of ethanol per day (about two drinks a day). There was insufficient evidence to draw a conclusion for intakes above 30 grams of ethanol per day.

*GBD, Lancet 2018; 392: 1015–35*
*Hydes et al. 2019 BMC Public Health 19: 316*
Which cancers?

- Mouth
- Throat (pharynx)
- Voice box (larynx)
- Esophagus
- Liver
- Colon and rectum
- Breast
- Alcohol may also increase the risk of cancers of the pancreas and stomach.
- Protective Effects: Kidney, Non-Hodgkins Lymphoma

Alcohol in comparison to other modifiable risk factors

Estimated Proportion and Number of Incident Cancer Cases Attributable to Evaluated Risk Factors in Adults 30+ Years, US, 2014

Islami, et al., 2018.
Renewed focus on Alcohol and Cancer Risk at NCI and Cancer Focused Organizations

Viewpoint

December 13, 2019

Alcohol and Cancer Risk
Clinical and Research Implications

William M. P. Klein, PhD; Paul B. Jacobsen, PhD; Kathy J. Helzlsouer, MD, MHS

Author Affiliations | Article Information


Alcohol and Cancer: A Statement of the American Society of Clinical Oncology

Noelle K. LoConte, Abenaa M. Brewster, Judith S. Kaur, Janette K. Merrill, and Anthony J. Alberg
Relative Ignorance Concerning Alcohol as a Cancer Risk Factor

“In general, although awareness appears to be increasing in many countries, at least half or more of the population does not consider alcohol to be a risk factor for cancer.”
Conceptual model of the effects of alcohol consumption on chronic diseases/cancer and societal and demographic factors

Purpose: To enhance research on alcohol and cancer control

- Investigator initiated research across the entire Cancer Control Continuum from mechanistic and epidemiological studies through prevention, diagnosis, treatment and survivorship

- A preponderance of past research has focused on heavy drinkers and alcohol use disorder; this Notice encourages research addressing light and moderate alcohol consumption
NCI’s Research Priorities and Research Areas

- Communication and awareness of alcohol as a risk factor for cancer
- Interactions between alcohol use and other health risk behaviors relevant to cancer
- Alcohol consumption and outcomes in cancer patients and survivors
- Alcohol-related policy and its influence on cancer and the cancer burden
- Addressing light and moderate alcohol consumption,
<table>
<thead>
<tr>
<th>Topics</th>
<th>Examples of NOSI Research Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Communication</td>
<td>Address communicating uncertainty and complexity in relation to alcohol, cancer, and health outcomes</td>
</tr>
<tr>
<td></td>
<td>Understand and improve patient-provider communication</td>
</tr>
<tr>
<td>Effects</td>
<td>Develop and improve measures of alcohol-related behaviors as they relate to cancer</td>
</tr>
<tr>
<td></td>
<td>Examine effects of light &amp; moderate alcohol consumption and cancer risk</td>
</tr>
<tr>
<td>Disparities</td>
<td>Examine disparities in alcohol consumption patterns and the relationship to cancer by race/ethnicity, socioeconomic factors, and sexual and gender minority status.</td>
</tr>
<tr>
<td>Prevention</td>
<td>Explore decision-making processes regarding alcohol consumption by patients and caregivers</td>
</tr>
<tr>
<td></td>
<td>Understanding of mechanisms linking alcohol consumption, cancer treatment effectiveness, and risk of recurrence or second cancers to identify targets for intervention.</td>
</tr>
</tbody>
</table>
Cancer-related Research Interests of the National Institute on Alcohol Abuse and Alcoholism (NIAAA)

NIAAA Contacts:

Gary J. Murray, PhD  
Division of Metabolism and Health Effects  

I-Jen Castle, PhD  
Division of Epidemiology and Prevention Research
Mission of NIAAA

To support and conduct research on the impact of alcohol use on human health and well-being.

With respect to cancer NIAAA supports studies directed toward a better understanding of the risks associated with alcohol use and basic studies to identify plausible mechanisms for the development or exacerbation of cancer.

http://www.niaaa.nih.gov/about-niaaa
Epidemiology - Risk of Cancer for Heavy Drinkers

Heavy drinking is an important modifier of risk for a variety of cancers.

*Data are from Bagnardi et al., 2001

Upper aerodigestive tract (UADT) (esophagus, pharynx, larynx, oral cavity)

(RR: 3.5-6.0)

Liver

(RR: 2.7)

Breast

(RR: 1.9)

Colorectal cancer

(RR: 1.4)

Other possible sites:

- Lung
- Pancreas

Risk Ratios are calculated at 100g ethanol per day which is equivalent to about 7 standard drinks
Epidemiology - Risk of Cancer for Heavy Drinkers

Heavy drinking is an important modifier of risk for a variety of cancers.

*Data are from Bagnardi et al., 2001

The strongest association between alcohol use and cancer has been demonstrated for Cancer of the UADT. Epidemiological studies have shown that individuals with one of the naturally occurring mutations in the enzyme ALDH2 that result in accumulation of acetaldehyde have a much higher incidence of this form of cancer \(\text{RR}: 3.5-6.0\)

**Epidemiology must be paired with basic studies that demonstrate plausible mechanisms at defensible (physiologically relevant) concentrations.**
Program Announcements

NIMHD/NCI/NIAAA
PAR-17-150 and PAR-17-151:
Mechanisms of Disparities in Chronic Liver Diseases and Cancer (R01, R21)

NIAAA
PA-17-219 and PA-17-220
Mechanisms of Alcohol-associated Cancers (R01, R21)
NIAAA Sponsored Research

✓ **Basic studies on metabolism** of alcohol, acetaldehyde, retinoic acid and other retinoids -- Oxidative Stress, DNA adduct formation, epigenetics, cell damage, the microbiome

✓ **Alcohol and Breast Cancer** - Enhanced aggressiveness of breast cancer

✓ **Alcohol and colorectal cancer**
  • Alcohol increased the expression of Monocyte chemoattractant protein-1 (MCP-1) and its receptor CCR2
  • Alcohol-altered CEA processing in liver → liver metastasis
  • ALDH polymorphisms and colorectal cancer

✓ **Alcohol and hepatocellular carcinoma**
  • Lipid metabolism, alcoholic fatty liver and links to HCC and other cancers
  • Epigenetics, miRNA signaling, NF-κB, TGFβ pathway, TNFα, IL-17

✓ **Alcohol and pancreatic cancer**
✓ **Alcohol-induced immunosuppression and cancer**
✓ **Alcohol and Non-Hodgkin's lymphoma** (reduction in risk)
Epigenetic signatures of alcohol abuse and hepatitis infection during human hepatocarcinogenesis

Ryan A. Hlady¹, Rochelle L. Tiedemann¹,², William Puszyk³, Ivan Zendejas⁴, Lewis R. Roberts⁵, Jeong-Hyeon Choi², Chen Liu³ and Keith D. Robertson¹

First published November 25, 2019; doi:10.1152/ajpgi.00218.2019.

Moderate alcohol intake promotes pancreatic ductal adenocarcinoma development in mice expressing oncogenic Kras

Kinji Asahina,¹ Steven Bolog,¹ Edward Hwang,¹ Eugene Moon,¹ Emily Wan,¹ Kaitlin Skrypek,¹ Yibu Chen,² Jay Fernandez,¹ Janet Romo,¹ Qihong Yang,¹ Keane Lat,¹ Samuel W. French,³ and Hidekazu Tsukamoto¹,⁴

http://www.niaaa.nih.gov
Of interest to NIAAA

- Understand the **cellular** and **molecular mechanisms** underlying the carcinogenic effects of alcohol especially in minorities and women.

- Clarify the role of alcohol in the development of **breast cancer**.

- Investigate the **synergy** between alcohol and multiple agents especially **viral hepatitis** in exacerbating **liver cancer** and **smoking** in **UADT cancers**.

- Characterize the effects of alcohol on **cancer stem cells**.

- Among others…
CANCER-RELATED RESEARCH INTERESTS OF THE NATIONAL INSTITUTE ON ALCOHOL ABUSE AND ALCOHOLISM (NIAAA)

NIAAA Contact:

Gary J. Murray, PhD | Division of Metabolism and Health Effects
National Institute on Alcohol Abuse and Alcoholism

gary.murray@nih.gov

(301) 443-9940

http://www.niaaa.nih.gov
Highlights of NIAAA Cancer-Related Research Interests

Prevention and Epidemiological Studies

I-Jen Castle, Ph.D.
i-jen.castle@nih.gov
Program Officer
Division of Epidemiology and Prevention Research

NOT-CA-20-034 Webinar, May 28, 2020
Epidemiological Studies

- Hypothesis driven and supported by biological mechanisms
- Considering life-course drinking patterns
- Disentangling the interplay of alcohol use and other risk and protective factors (e.g., smoking, drug use, BMI, physical activity, and diet)
- Methodological considerations:
  - e.g., measurement errors, recall bias, healthy drinker effects, survivor bias, effect modification, confounding, and generalizability
  - Analytical approaches, e.g., sensitivity analysis and quantitative bias analysis
LIFE-COURSE DRINKING PATTERNS

Hypothetical Examples

Baseline Average Alcohol Consumption Measured in Midlife (Drinks/Week)

Heavy drinkers
Moderate drinkers
Former drinkers
Lifetime abstainers

Windows of Susceptibility to Cancers?

Average Alcohol Consumption
(Dawson, 2003. PMID: 15301397)
Epidemiological Studies

- Hypothesis-driven and supported by biological mechanisms
- Considering life-course drinking patterns
- Disentangling the interplay of alcohol use and other risk and protective factors (e.g., smoking, drug use, BMI, physical activity, and diet)

Methodological considerations:
- e.g., measurement errors, recall bias, healthy drinker effects, survivor bias, effect modification, confounding, and generalizability
- Analytical approaches, e.g., sensitivity analysis and quantitative bias analysis
A Model of Breast Cancer Causation

Visualizing the many factors and relationships influencing breast cancer incidence in women.

Source: California Breast Cancer Research Program [http://www.cabreastcancer.org/causes/]
Reference: Hiatt et al., 2014 DOI: 10.1158/1055-9965.EPI-14-0403
Epidemiological Studies

- Hypothesis-driven and supported by biological mechanisms
- Considering life-course drinking patterns
- Disentangling the interplay of alcohol use and other risk and protective factors (e.g., smoking, drug use, BMI, physical activity, and diet)

Methodological considerations:
- e.g., measurement errors, recall bias, healthy drinker effects, survivor bias, effect modification, confounding, and generalizability
- Analytical approaches, e.g., sensitivity analysis and quantitative bias analysis
PREVENTION STUDIES

- Evidence-based guidelines
  - Does drinking reduction or cessation reduce risk of recurrence or second cancers, improve cancer prognosis, and improve aging trajectories during cancer survivorship?

- Innovative and integrative interventions which have low barriers to implementation and which can achieve sustained effects

- Alcohol-related policy and its influence on cancer prevention
  - Address effects of warning labels on all alcohol-containing products in relation to alcohol and cancer prevention (JSAD 2020;81(2):222–292)
WELCOME TO THE
Alcohol Policy Information System

The Alcohol Policy Information System (APIS) provides detailed information on a wide variety of Alcohol-Related Policies in the United States at both State and Federal levels, as well as policy information regarding the Recreational Use of Cannabis. The information and resources available on this site are geared toward alcohol and cannabis policy researchers and others interested in alcohol and cannabis policy issues.

Underage Drinking

APIS provides convenient access to policy topics that pertain to underage drinking, in order to encourage research, evaluation, and outreach efforts in this important area.

Alcohol Policy Topics

- Alcohol Beverages Pricing
  - Drink Specials
  - Wholesale Pricing Practices and Restrictions
- Alcohol Beverages Taxes
  - Beer
  - Distilled Spirits
  - Wine
- Alcohol Control Systems
  - Retail Distribution Systems for Beer
  - Retail Distribution Systems for Spirits
  - Retail Distribution Systems for Wine
  - Wholesale Distribution Systems for Beer
- Pregnancy and Alcohol
  - Civil Commitment
  - Legal Significance for Child Abuse/Child Neglect
  - Limitations on Criminal Prosecution
  - Priority Treatment
  - Reporting Requirements
  - Warning Signs: Drinking During Pregnancy
- Retail Sales
  - Bans on Off-Premises Sunday Sales
  - Beverage Service Training and Related Practices
  - Registry Registration

Cannabis Policy Topics

- Advertising, Marketing and Mass Media
  - Advertising Restrictions – see Columns 10 and 11.
- Cannabis Product Control
  - Agency with Authority to Regulate – see Column 4.
  - Legalization of Recreational Use – see Volume 1, Column 2 and Volume 2, Column 3.
  - Local Authority – see Column 13.
  - Products Permitted – see Column 5.
- Cultivation and Distribution
  - Cultivation Restrictions – see Column 6.

COVID-19 is an emerging, rapidly evolving situation.

Get the latest public health information from CDC: https://www.coronavirus.gov
Get the latest research information from NIH: https://www.nih.gov/coronavirus

Special Coverage: State-by-State Alcohol-Related COVID-19 Policies (PDF, 1.6 MB)

KEY POINT

Address research gaps

& move the field forward
Submit applications for this initiative using one of the 10 funding opportunity announcements (FOAs) or any reissues of these announcements listed in the NOSI.

- Parent RO1s - PA-19-055; PA-19-056
- Specific RO1 PAs/PARs - PAR-19-348; PA-17-220 ; PA-17-135
- Specific R21 PAs/PARs - PAR-19-350; PA-17-219; PA-17-132; PA-19-053 PAR-20-052
- RO3 (NCI) - PAR-20-052

Applications referencing this NOSI should be submitted one of the FOAs listed above.
## Details on FOAs for Alcohol and Cancer Control NOSI - 1

<table>
<thead>
<tr>
<th>Activity Code</th>
<th>FOA Title</th>
<th>First Available Due Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>R01</td>
<td>NIH Research Project Grant (Parent R01 Clinical Trial Allowed)</td>
<td>June 5, 2020</td>
</tr>
<tr>
<td>R01</td>
<td>NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed)</td>
<td>June 5, 2020</td>
</tr>
<tr>
<td>R01</td>
<td>Innovative Approaches to Studying Cancer Communication in the New Media Environment (R01- Clinical Trial Optional)</td>
<td>June 10, 2020</td>
</tr>
<tr>
<td>R01</td>
<td>Mechanisms of Alcohol-associated Cancers (R01)</td>
<td>June 5, 2020</td>
</tr>
<tr>
<td>R01</td>
<td>Public Policy Effects on Alcohol-, Marijuana-, and Other Substance-Related Behaviors and Outcomes (R01)</td>
<td>June 5, 2020</td>
</tr>
</tbody>
</table>
### Details on FOAs for Alcohol and Cancer Control NOSI - 2

<table>
<thead>
<tr>
<th>Activity Code</th>
<th>FOA Title</th>
<th>First Available Due Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>R21</td>
<td><strong>PAR-19-350</strong> Innovative Approaches to Studying Cancer Communication in the New Media Environment (R21- Clinical Trial Optional)</td>
<td>June 10, 2020</td>
</tr>
<tr>
<td>R21</td>
<td><strong>PA-17-219</strong> Mechanisms of Alcohol-associated Cancers (R21)</td>
<td>June 16, 2020</td>
</tr>
<tr>
<td>R21</td>
<td><strong>PA-17-132</strong> Public Policy Effects on Alcohol-, Marijuana-, and Other Substance-Related Behaviors and Outcomes (R21)</td>
<td>June 16, 2020</td>
</tr>
<tr>
<td>R21</td>
<td><strong>PA-19-053</strong> NIH Exploratory/Developmental Research Grant Program (Parent R21 Clinical Trial Not Allowed)</td>
<td>June 16, 2020</td>
</tr>
<tr>
<td>R03</td>
<td><strong>PAR-20-052</strong> NCI Small Grants Program for Cancer Research for Years 2020, 2021, and 2022 (NCI Omnibus R03 Clinical Trial Optional)</td>
<td>June 24, 2020</td>
</tr>
</tbody>
</table>
Application Process **Important Dates**  
**NOT - CA-20-034**

- NOSI expiration date: September 9, 2023
- Earliest submission date: June 5, 2020
- Importantly, application due dates differ for different FOAs with first dates ranging from June 5 – June 24 **Make sure you have the right one!**
- Applicants may submit to any of the reissuances of above announcements through NOSI expiration date.
Application Requirements

- All instructions in the SF424 (R&R) application guide and the FOA used for submission must be followed.

- Applicants must include “NOT-CA-20-034” (without quotation marks) in the Agency Routing Identifier field (box 4B) of the SF424 R&R form.

- Applications without the correct Agency Routing Identifier information will not be considered for the NOSI initiative.

- Applications nonresponsive to terms of this NOSI will not be considered for the NOSI initiative.
Review Criteria

- Standard review criteria as described in eligible R01 FOAs
- **Scored review criteria**: Significance, Innovation, Investigators, Approach, Environment
- **Additional review criteria**: Study timeline (for clinical trials), protections for human subjects, inclusion, vertebrate animals, biohazards
- **Additional review considerations**: Check FOA to see resource sharing plan requirements (e.g., data sharing plan) or other listed requirements
Additional Resources

- NCI Division of Cancer Control and Population Sciences -

- NCI Health Behaviors Research Program -
  [https://cancercontrol.cancer.gov/brp/hbrb/about.html](https://cancercontrol.cancer.gov/brp/hbrb/about.html)

- NIAAA Division of Metabolism and Health Effects -

- NIAAA Division of – Epidemiology and Prevention Research -

- Sample NCI grants -

- NIH RePORTER - [https://projectreporter.nih.gov/reporter.cfm](https://projectreporter.nih.gov/reporter.cfm)
Common Question #1

- Where can I find more information about NIH NOSIs?
  - **NIH NOSI FAQs** What is a NOSI? How does NIH distinguish applications submitted in direct response to an FOA from applications submitted in response to a NOSI that uses that FOA for submission? Can I include an assignment request when I submit my application to a NOSI?
Common Question #2

- Can I submit a grant about alcohol and cancer control to an FOA not listed in the NOSI?
  - Yes, but in these cases do not list the NOSI in Box 48 of the SF424
Submission Inquiries

Scientific/Research Contacts

- Tanya Agurs-Collins, Ph.D., R.D.
  National Cancer Institute (NCI)
  Telephone: 240-276-6956
  Email: collinsta@nih.gov

- David Berrigan Ph.D., M.P.H.
  National Cancer Institute (NCI)
  Telephone: 240-276-6752
  Email: berrigad@nih.gov

- Gary J. Murray, Ph.D.
  National Institute on Alcohol Abuse and Alcoholism (NIAAA)
  (for biological studies)
  Telephone: 301-443-9940
  Email: murrayg@mail.nih.gov

- I-Jen Castle, Ph.D.
  National Institute on Alcohol Abuse and Alcoholism (NIAAA)
  (for prevention and epidemiological studies)
  Telephone: 301-827-4406
  Email: i-jen.castle@nih.gov

Peer Review Contact(s)

- Examine your eRA Commons account for review assignment and contact information (information appears 2 weeks after the submission due date).

Financial/Grants Management Contact(s)

- Carol Perry
  National Cancer Institute (NCI)
  Telephone: 240-276-6282
  Email: perryc@mail.nih.gov

- Judy Fox
  National Institute on Alcohol Abuse and Alcoholism (NIAAA)
  Telephone: 301-443-4704
  Email: jfox@mail.nih.gov
Webinar Audience

Q & A

Please type your question in the Q&A section on WebEx.