ACTIVE Workgroup Meeting
November 16 – 17, 2023
Virtual Live Meeting

Minutes

Participants:

Maryam Afshar
Arnie Aldridge
Ray Anton
Henri Jean Aubin
Summer Barlow, FDA Guest
Emmanuel de Rivoire
Zachary Dezman, FDA Guest
Dan Falk
John Hanrahan, Day One
Michaela Hoffman
Terry Horton
Zachary Illg, FDA Guest
Bruce Imbert, Day Two
Raye Litten, Day Two
Sarah Maggio, NIAAA Guest
Karl Mann
Patrick O'Connor, Day One
Stephanie O'Malley
Alain Puech
Lara Ray
Chamindi Seneviratne, FDA guest
Bernard Silverman, Day One
Celia Winchell
Katie Witkiewitz
Gary Zarkin
Laura Reynolds, staff

Thursday, November 16, 2023

1. ***Welcome:*** R. Anton welcomed the group and new workgroup members introduced themselves including L. Ray, T. Horton from Indivior which is the newest company to join ACTIVE, as well as guest representatives from NIAAA and the FDA. R. Anton gave an overview of the agenda and how the two-day meeting would be formatted, as well as reiterated the information sharing and confidentiality agreement.

Celia Winchell, Maryam Afshar, Zachary Dezman, Zachary Illg, Summer Barlow, and Chamindi Seneviratne, recused themselves from the meeting before the discussion of the FDA response letter.

2. ***Overview of FDA Response Letter on WHO RDL Qualification Plan:*** R. Anton provided a brief history of the ACTIVE group's work towards the clinical validation of the WHO reduction in drinking metric by the ACTIVE group, explained the submission process and timeline, as well as highlighted the major elements of the WHO-RDL. Additionally, D. Falk and K. Witkiewitz were acknowledged as significant participants in helping with the submission.
    a. ***Timeline:*** He also shared the more recent timeline of the various submissions to the FDA, including the following:
        i. May 2022: Preliminary reviewability memorandum was submitted.
        ii. March 2023: Modifications requested by FDA in the required format were submitted.
        iii. November 2023: The FDA announced that the FQP was complete, it would be reviewed, and a response can be expected within 10 months.
    b. ***Overview of the Qualification Plan:*** He concluded by sharing the following highlights from the qualification plan's executive summary:
        i. AUD is a ubiquitous and carries high morbidity and mortality.
        ii. AUD is undertreated with few medications approved for use.
        iii. AUD patients often want to reduce drinking rather than full abstinence.
        iv. The TLFB calendar method can validly quantify drinking in clinical trials and serve as the instrument from which WHO-RDL categories are derived.

v. The WHO-RDL is related to how individuals feel and function across a range of physical and socio-behavioral measures.
vi. A WHO-RDL reduction is related to patient improvement in RCT AUD clinical trials.
vii. The WHO-RDL change is equal to, or more, sensitive to medication effects than traditional drinking outcome measures and it endures up to a year after treatment.
viii. A "reduction in drinking" goal (as measured by the WHO-RDL change) should be more acceptable to patients and clinicians thereby encouraging more treatment seeking and success.

3. ***Can Clinical Laboratory Paradigms Inform Efficacy Potential for AUD Medication Development? Populations and Design:*** L. Ray focused on the programmatic work evaluating the phases and medication development and shared her research on whether or not the human laboratory models can predict clinical trial outcomes. It was noted that the focus of the presentation would center around the transition from the human proof of concept to early efficacy in the laboratory to the more confirmatory phases where one establishes the efficacy through a randomized controlled trial. She discussed ways to bridge the gap between human lab studies and clinical trials, as well as shared the approaches that were taken as well as the data collected from the studies. It was foundational for L. Ray's research team to have the proof-of-concept study demonstrate that behavioral pharmacology endpoints of alcohol-induced stimulation, sedation, and craving track medication effects from the human laboratory to clinical trial outcomes. In a subsequent study, cue-induced craving in the laboratory did not track medication effects from the human laboratory to clinical trials. It's a null effect. There is no evidence to say that cue would track with clinical trial outcomes. It was noted that there is a relationship between alcohol-induced sedation and cue-induced alcohol craving. Medications that increased alcohol-induced sedation were more likely to reduce cue-induced alcohol craving. It is plausible that medication effects on subjective response and cue-induced craving models were well-suited for medications targeting the rewarding effects of alcohol; yet may not apply across a broad range of novel therapies. It was also noted that biomarkers are an important aspect for her group. The novel methods discussed are being applied to the preclinical literature with ongoing coding of over 300 animal studies. The data generated with the intensive coding and effect size estimation efforts advance the field through (a) literature synthesis, (b) informing use of early efficacy paradigms, (c) data sharing/publishing, (d) meta-regressions, and (e) systematic review of methods. A systematic review of cue-reactivity studies (n=36) identified many sources of variability in the application of this paradigm. This leads to opportunities for the development and refinement of standardized methods for trial design and reporting. A systematic review of AUD RCTs (n=139) indicated that percent days abstinent was the most frequently reported outcome. Considering alternative endpoints (e.g., WHO risk drinking levels) for AUD RCTs may increase sensitivity for detecting treatment effects. ***ACTION ITEM:*** L. Ray will send the paper that is under review regarding machine-learning analysis and models for both the Gabapentin trial. It was noted that the first split in the tree was by race. ***ACTION ITEM:*** It was suggested to plan a talk for a future meeting focused on some of the issues discussed including the new neuroimaging paradigm that are picking up a neural signal related to the craving experience. There is a lot of variation as to how people report craving but if you see how the brain reacts to cues, it may cut through some of the variation. It was suggested to invite Joe Schacht from the University of Colorado Health Sciences Center, who has published extensively on alcohol cue induced brain activation and medication/genetic effects, to present at the next ACTIVE meeting.

4. ***Strategic Perspectives to Improve AUD Care:*** T. Horton provided a presentation on Indivior's strategic perspectives to improve AUD care. He began by sharing his background and perspectives. Indivior is a longstanding innovation leader in the addition medicine and is broaden its scope to include developing medications for AUD and CUD. He discussed two assets from Indivior's pipeline:

a. ***Indivior 1000****:* a selective GABA-B positive allosteric modulator and is in preclinical development.
b. ***Indivior 4002****:* a Naltrexone Hydrochloride Nasal Spray in phase 2a of development

Also highlighted during the presentation were Indivior's related areas of interest related to AUD including the need for regulatory adoption of WHO endpoints for health benefits, patient segmentation (its challenging to blend in comorbidities along with AUD), and craving metrics, the role of digital therapeutics, genetics/epigenetics, understanding the impact of and addressing polysubstance use, comorbid mental and physical health, and social determinants of health; the adoption of a Cascade of Care Framework, recovery capital metrics, and methods to address stigma. ***ACTION ITEM:*** T. Horton will connect K. Witkiewitz with Phil Skolnik regarding the sequential parallel design of the clinical trial and how to handle placebo responders.

5. ***Update on the Utility of the Promise and New Craving Measures in AUD Trials:*** S. O'Malley discussed the PROMIS negative alcohol consequences measure, as well as work surrounding craving.
    a. ***PROMIS Discussion:*** S. O'Malley explained that PROMIS was originally an NIH roadmap initiative to improve self-report outcomes by using state-of-the art psychometric methods. She shared the FDA requirements for PRO (patient rated outcomes), the development of the PROMIS Alcohol Item Banks of which the negative consequences is one of five, the negative consequences measure in which she shared the item content, scale properties, and data regarding sensitivity to improvement in the intended patient population.
        i. ***Key Findings:*** It was noted that they key findings included:
            1. PROMIS Negative Consequences associated with expected measures were AUDIT, CAGE, PROMIS-Alcohol, PROMIS-Positive Consequences
            2. PROMIS Negative Consequences shows expected decrease over time after treatment.
            3. Time-varying covariates of alcohol use and mental health can predict PROMIS Negative Consequences across time.
            4. PROMIS Negative Consequences are sensitive to medication effects in treatment seeking patients with AUD.
        ii. ***Conclusion:*** The PROMIS Negative Consequences meets the FDA criteria for a patient rated outcome. It is an efficient, psychometrically sound measure of negative consequences of drinking rated from the patient's perspective that is sensitive to change and treatment effects. Additionally, it warrants inclusion in clinical trials of treatments for AUD.
    b. ***Craving Discussion:*** S. O'Malley shared that her team have begun to look at the possibility of developing a patient-rated outcome measuring alcohol and drug craving. They are hopeful that they will find a core set of measures that apply across drugs of misuse, which would allow them to do a better job of enrolling patients with multiple drug use comorbidities. S. O'Malley shared the progress her team has made thus far, which included:
        i. Performing a Systematic Review
        ii. Developing an Alcohol and Drug Craving PRO
            1. This yielded a final item pool with 98 craving items.
        iii. The next phase is to field test the final item pool in a calibration sample, as well as determine a plan for funding.

6. ***AUD Treatment in Primary Care: "Challenges and Opportunities":*** P. O'Connor provided a brief introduction of himself and his program, Yale General Internal Medicine. Additionally, he shared an overview of roles for primary care regarding unhealthy alcohol use and concluded with an "Ask the Experts" segment in which he interviewed a panel of experts regarding AUD treatment in primary care.

a. ***Overall Challenges:*** P. O'Connor highlighted a few of the main challenges the experts identified for overall treating AUD and heavy drinking in primary care, which included the enigma of stigma, MDs being poorly trained in AUD screening, diagnosis, and treatment, as well as reimbursement concerns.

b. ***Challenges with Using Pharmacotherapy:*** The experts identified several challenges specifically related to using pharmacotherapy to treat AUD in primary care. Some of the challenges included, perceived lack of effectiveness, examples being naltrexone: need for opioid abstinence, gabapentin: potential abuse potential particularly in opiate abusers, and variable short-term benefits seen (vs Meds for OUD).

c. ***Opportunities for Improving Treatment:*** P. O'Connor highlighted a few of the opportunities that the experts identified for improving the treatment of treating AUD and heavy drinking in primary care, which include creating an "addiction educational thread" in every medical school and in GME, creating a tradition of determining AUD stage/severity so that proper referrals can happen, implementing federal "parity" mandates related to AUD care, and specifically requiring insurers to cover AUD pharmacology.

d. ***Acceptability of Reduced Drinking as an Outcome:*** The experts weighed in on the idea of including the acceptability of "reduced drinking" as an acceptable outcome in primary care and it was agreed it's a very positive change in perspective, avoids the "all or nothing" approach, and encourages ongoing participation in care.

D. Falk shared the NIAAA's Core Resource on Alcohol**:** https://www.niaaa.nih.gov/health-professionals-communities/core-resource-on-alcohol, which is designed for health care professionals and includes good resources for prescribing. P. O'Connor shared that they incorporate the resource guides in the resident training program.

ACTION ITEM: It was suggested to include the use of electronic medical records as a topic on a future meeting agenda.

Friday, November 17, 2023

7. ***Synopsis of the Previous Day:*** R. Anton welcomed everyone to the 2nd day of the 2023 Fall Workgroup Meeting, provided an overview of the day's sessions, as well as shared that the 2024 Spring ACTIVE Meeting will be held as an in-person meeting and a poll of meeting dates will be circulated to determine the date. Additionally, B. Imbert, Indivior's second representative joined and introduced himself. R. Anton also shared ideas for future meeting topics such as the following:
    a. The use of clinical laboratory studies that could inform clinical trials.
    b. What we know about clinical trials and medication development can be moved into primary care settings, such as engaging with the primary care specialists about treatment.
    c. How to approach dual diagnosis.
    d. Biomarkers and how they can be appropriately used, as well as neuroimaging.

8. ***Sleep Change as Related to WHO Shift in Extended-Release Gabapentin Trial:*** K. Witkiewitz began her presentation by sharing the World Health Organization's Risk Levels of drinks per day and drinks per week by sex. She shared that her new post doc, Christian Garcia led this study and why the current study on sleep was important and if the WHO risk level reductions were "reasonably predictive of clinical benefit (e.g., improvement in the way the patient feels and functions)", with respect to sleep quality. For the study, it was noted that they ran analyses from the Horizant (extended-release gabapentin NIAAA sponsored phase 2 study) dataset and the results were shared. It was stated that at least 1- and 2-level WHO RDL reductions are associated with greater sleep quality in a 6-month trial.

Additionally, it was found that there were no interactions with medication or age. Addressing sleep problems as part of AUD treatment plans could enhance overall treatment outcomes. Interventions that target both alcohol use and sleep disturbances could prove more effective in promoting recovery from both. K. Witkiewitz shared with the group that there is a need for more data with Timeline Follow-back and AUDIT-C repeated at least twice, ideally from pre-to post treatment to further validate. ***ACTION ITEM:*** K. Witkiewitz will run a repeat of the analysis, with just selecting people at baseline that have clinical level sleep problems, to evaluate if Cohen's d (effect size) of the relationship between drinking and the WHO Shift Reduction would increase. ***Update:*** If data is limited to those that have problems at baseline, we see a doubling effect size meaning the sleep improved more in those with more significant sleep problems as they reduced their drinking.

9. ***Sleep Change as Related to WHO Shift in Single Site Gabapentin Trial:*** M. Hoffman presented on the relationship between AUD, Gabapentin, and sleep. The data included 90 individuals who had 82.7% of the days pre-study as heavy drinking days and substantial insomnia. The outcome variables used were the insomnia severity index (ISI) and drinking variables assessed via the timeline follow-back. M. Hoffman shared the findings through a variety of graphs including baseline ISI by medication group and end of study insomnia severity index. The greatest significance found was that there is a correlation in difficulty staying asleep. WHO RDL Category (drinking level) is significantly related to ISI (perceived sleep difficulties) both pre-study and during the study. WHO RDL improvement (Shift to lower level) was related to ISI improvement. WHO 2+ Shift is particularly related to improvement in the interference of sleep problems in daily functioning and difficulty staying asleep. ***ACTION ITEM:*** It was suggested to use multiple imputation to improve efficiency of estimate of the p-value in the 3-way interaction of the ISI throughout study by medication group and the WHO 2+ shift.

10. ***Role of Sleep in AUD Treatment and Relapse- Should This Be a Target for Pharmacotherapy?:*** The group further discussed the role of sleep in AUD treatment and relapse. The group further discussed whether or not sleep assessment/measures should be a potential covariate for medication effects or even a main outcome variable in the development of AUD medications. Sleep might be a secondary outcome. For instance, it was noted that Gabapentin is largely working on drinking independent of its effect on sleep. It was also noted that it's possible that sleep quality at baseline could be a stratification variable in clinical trials, especially if a medication is known to affect sleep.

    ACTION ITEM: C. Winchell find out what the FDA's Division that reviews sleep medications uses/requires as a validate and effective sleep measure/scale.

11. ***Review of the Relationship of Drinking Reduction (WHO RDL Shift) and Labor Parameters in the COMBINE Study – Paper Status:*** A. Aldridge provided an update on the relationship between reductions in WHO drinking risk levels during treatment and labor market outcomes. The objective of the analyses is to evaluate the relationship between reductions in WHO risk drinking levels from baseline (pre-COMBINE treatment) to the treatment period and subsequent labor market outcomes. The group analyzed outcomes over a 12 – 32-month period following the end of the trial. A. Aldridge discussed the dependent variables, the independent variables of interest, and the covariates. He shared the statistical models that were used such as Logit for binary outcomes, OLS for hours worked, negative binomial for workdays missed due to drinking, Gamma GLM for earnings, and heteroskedasticity-robust standard errors in all models. It was noted that most people were employed and were a high-functioning group of individuals. Sustaining a two-level WHO risk drinking reduction over the COMBINE treatment period was associated with higher odds of being in the labor force, lower odds of being unemployed, more hours worked, higher earnings, and fewer days missed due to drinking in the year following COMBINE treatment ($p<0.05$). Associations did not vary considerably by whether subjects that were abstinent during the last month of treatment were excluded from the analysis. Risk drinking level shifts

based on the last month of treatment had weaker associations with unemployment and earnings over 12 months. Most relationships persist into the 32-month analysis, but the association between WHO risk drinking level shifts (reductions) from baseline to end of treatment and unemployment at 32 months was not significant.

ACTION ITEMS:

a. It was suggested for future discussion to have a shift that is stable for the whole study, not just the last month, at least for labor/employment outcomes.
b. Continued discussion within the ACTIVE Data Workgroup is needed in terms of which analyses should be included in the labor paper.
c. Dr. Aldridge said there was renewed interest and energy to publish this data as soon as possible.

12. Update on AI - Simulation Study Funding: Baseline Data Aggregation Results of NSIG AUD Trials: R. Anton provided a brief background as to how the simulation project began and he suggested the heightened interest in artificial intelligence (AI) and machine learning was quite germane to this project. M. Hoffman provided an update on the work done thus far on the project, and A. Aldridge concluded by sharing how the model can be used for the public good for AUD medication development in particular.

a. ***Status of Project:*** It was noted that pharma companies have little experience designing and conducting AUD clinical trials and this has been considered as an impediment for medications development as relatively few trials have been done successfully. With this lack of experience, little is known about what the ideal conditions are in designing and conducting AUD clinical trials since there are a number of factors that can impact the successful completion and statistical power of the studies. ACTIVE members have been involved in many clinical trials and have reexamined data from those trials (including those done under NIAAA contract phase 2 programs) and have published on methodologies and tested new analytic ideas. There is a critical mass of clinical trial data now available to take knowledge to the next level to inform the field on how "salient study variables" are likely to impact study outcome (e.g. NNT) and effect size estimates – allowing for better choices/tradeoffs on study design features. Combined data from multiple trials should provide improved information that would inform AUD clinical study design. Researchers/companies must make numerous concurrent decisions when developing the protocol for a clinical trial, all of which will impact the power. Design choices are subject to known information on study parameters, including uncertainty (anticipated variation around each parameter). The group focused on analyzing the five NIAAA sponsored studies that focus on AUD and M. Hoffman combined all data sets into various tables organized by treatment conditions, sample size by study site, demographics, study timelines, drinking data, and baseline drinking etc. The ACTIVE Data Workgroup is actively working on this project and will be determining how these factors impact trial outcomes, such as drop-out rates, adherence to treatment and study protocols, as well as the effect sizes of the treatments. Aggregate data and simulations of various predictive study variables can be modified to estimate their effects on important study outcome variables. This will lead to a variance matrix that can be employed in trial design choice and decisions, hence the same simulation project.
b. ***Utilization of AI-Simulation:*** A. Aldridge summarized the process and how the model can be used and stated that this is something that would always be worked on and constantly evolving as more data is available.
    i. Dr. Hoffman has officially requested and acquired data from five previously completed multisite alcohol studies from NIAAA.
    ii. The data will be combined into one large dataset containing the outcome drinking data as well as the relevant study design variables (number of sites, length of treatment, etc.).
    iii. Effect sizes for the study site variables will be examined.
    iv. Based on these effect sizes the data will be simulated.

v. The simulated data will be analyzed as though it were a study, producing effect sizes and p values for comparison between study design choices.

c. ***Funding:*** R. Anton discussed the challenges that the group has faced in terms of securing funding to proceed with the project. The group weighed in on suggestions for funding and it was suggested to investigate the possibility to apply for an investigator-sponsored grant through Indivior.

d. ***ACTION ITEMS:***

a. Dr. Mann suggested to compare data from the five studies and a study in Germany that used the same methodology as used in the COMBINE Study K. Witkiewitz and S. O'Malley have the data and would be interesting to see. Dr. Anton pointed out the German study population was more severe and recruited from inpatient facilities which could add another dimension to the outpatient less severe NIAAA sponsored US studies.

b. L. Ray has a similar, but less complex, paper under review and shared that the simulation project was exciting, as she could pull out the NSIG and NIAAA multisite studies and compare them in terms of their methodology to some of the single site studies. It was suggested for L. Ray to join the workgroup that is working on the simulation project.

13. ***Meeting Recap:*** R. Anton shared closing remarks, stating the meeting was a success due to all of the members and guests that participated, especially to the new members and members from Europe. K. Mann shared an update regarding his last communication with the EMA in which he asked if they would be interested in receiving a copy of the WHO Qualification Plan. He did not receive a response, so there is a chance that they may already receive it from the FDA. However, it was noted that the EMA continues to be interested in ACTIVE and wants to remain informed.

a. ***ACTION ITEMS:***

i. ACTIVE will share the final response from the FDA with the EMA.

ii. L. Reynolds reminded the group to send ACTIVE papers to her so that they can be added to the ongoing document.

***Papers in Progress or to Be Considered*:**

Dr. Anton recognized Dr. Witkiewitz and her group for their particularly continuous, diligent, and meaningful efforts on publications involving the WHO RDL and and various AUD related outcomes and variables.

- S. O'Malley might consider coordinating a publication on the Promise or Craving Measures measure.
- Dr. Witkiewitz and her group plans to write up the data on the WHO RDL and sleep.
- Dr. Aldridge and his RTI colleagues plan to submit the labor/employment WHO RDL association paper ASAP.

ACTIVE Published/In-Press/Submitted Papers*:*

- Richards Dylan K, Tuchman Felicia R, Hallgren Kevin A, Kranzler Henry R, Aubin Henri-Jean, O'Malley Stephanie S, Mann Karl, Aldridge Arnie, Anton Raymond F, Witkiewitz Katie. Reductions in World Health Organization Risk Drinking Level are Associated with Reductions in Alcohol Use Disorder Diagnosis and Criteria: Evidence from an Alcohol Pharmacotherapy Trial. Journal of Addiction Medicine. *Accepted.*
- Tuchman Felicia R, Hallgren Kevin A, Richards Dylan K, Aldridge Arnie, Anton Raymond F, Aubin Henri-Jean, Kranzler Henry R, Mann Karl, O'Malley Stephanie S, Witkiewitz Katie. Reductions in WHO Risk Drinking Levels Correlate with Alcohol Craving Among Treatment-Seeking Individuals with Alcohol Use Disorder. *Accepted*
- Aldridge AP, Zarkin GA, Dowd WN, Witkiewitz K, Hasin DS, O'Malley SS, Isenberg K, Anton RF. The Relationship Between Reductions in WHO Risk Drinking Levels During Treatment and Subsequent

Healthcare Costs for the ACTIVE Workgroup. J Addict Med. 2021 Dec 3. doi: 10.1097/ADM.0000000000000925. Epub ahead of print. PMID: 34864785.

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- Falk DE, O'Malley SS, Witkiewitz K, Anton RF, Litten RZ, Slater M, Kranzler HR, Mann KF, Hasin DF, Johnson B, Meulien D, Ryan M, & Fertig J. Evaluation of Drinking Risk Levels as Outcomes in Alcohol Pharmacotherapy Trials: A Secondary Analysis of 3 Randomized Clinical Trials. JAMA Psychiatry. 2019 March 13. PubMed PMID: 30865232l; PubMed PMCID: PMC6450273.
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ACTIVE Posters:

- Wikiewitz K. (2023, June). Craving. Poster presented at the 46th Annual RSA Scientific Meeting, Bellevue, Washington.
- Wikiewitz K. (2023, June). AUD Remission. Poster presented at the 46th Annual RSA Scientific Meeting, Bellevue, Washington.
- Knox J. (2019, June). WHO Findings from the NESARC. Poster presented at the College on Problems of Drug Dependence 81st Annual Scientific Meeting, San Antonio, Texas.
- O'Malley SS. (2018, June). Response to Pharmacotherapy: A Comparison of Endpoints Based on Abstinence, No Heavy Drinking and Reductions in WHO Drinking Levels in Three Trials. Poster presented at the Research Society on Alcoholism Scientific Meeting, San Diego, CA.
- Hasin D. (2018, June). WHO-Defined Risk Drinking Levels and Drinking Consequences: Prospective Findings From the NESARC Waves 1 & 2 (2001-2005). Poster presented at the Research Society on Alcoholism Scientific Meeting, San Diego, CA.
- Falk DE. (2017, December). Novel Efficacy Endpoints Based on Shifts in the World Health Organization (WHO) Risk Levels of Drinking: Treatment Effects in Alcohol Pharmacotherapy Trials. Poster presented at the American College of Neuropsychopharmacology 56th Annual Meeting, Palm Springs, CA.

ACTIVE Data Presentations:

- Witkiewitz K. (2023, May). Beyond Abstinence: Reductions in Drinking as an Endpoint for Alcohol Clinical Trials. Panel presented at the International Congress on Alcoholism and Stress, Volterra, Italy.
- O'Malley S. (2021, June). WHO Risk Drinking Reduction A New Endpoint for Clinical Trials. Symposium presented at the Research Society on Alcoholism Scientific Meeting, Virtual.
- Anton, R. (2021, June). WHO Risk Drinking Level: A Harm Reduction Outcome For Clinical Trials For Alcohol Use Disorder. Symposium presented at the Research Society on Alcoholism Scientific Meeting, Virtual.
- Knox J. (presenter), Scodes J., Witkiewitz K., Kranzler H., Mann K., O'Malley S., Wall M., Anton R., Hasin D. (2021, June). Reduction in WHO Risk Drinking Levels and Cardiovascular Disease: 3-year Follow-up Results in the US General Population. Symposium presented at the Research Society on Alcoholism Scientific Meeting, Virtual.
- Schacht J., Anton R. (2019, June). Prediction Of Alcohol Harm Reduction (Who RDL) Outcomes From Cue-Elicited Brain Activation In A Randomized Trial Of Naltrexone. Symposium presented at the Research Society on Alcoholism Scientific Meeting, Minneapolis, Minnesota.
- Witkiewitz K. (2019, June). Beyond Abstinence: Reductions in Drinking as an Endpoint for Alcohol Clinical Trials. Symposium presented at the College on Problems of Drug Dependence 81st Annual Scientific Meeting, San Antonio, Texas.
- Hasin D. (2019, June). Validation of a Measure of Opioid Use Disorder Among Chronic Pain Patients Treated With Opioids. Workshop presented at the College on Problems of Drug Dependence 81st Annual Scientific Meeting, San Antonio, Texas.
- Anton RF. (2018, December) Harm Reduction as a Goal in AUD Pharmacotherapy– Role For the WHO Risk Drinking Category Change. Symposium presented at the AAAP Annual Meeting and Scientific Symposium, Bonita Springs, FL.
- O'Malley SS. (2018, June) 2018 RSA Distinguished Researcher Awardee: Beyond Abstinence: An Evolving Perspective on Naltrexone and Pharmacotherapy for Alcohol Use Disorder. Plenary presented at the Research Society on Alcoholism Scientific Meeting, San Diego, CA.
- Anton RF. (2018, June) Insights From The Design and Implementation of Medications Development Trials for Alcohol Use Disorder. Panel presented at the Research Society on Alcoholism Scientific Meeting, San Diego, CA.

- O'Malley SS. (2018, May) ACTIVE Update: Reduction in World Health Organization (WHO) Drinking Risks Level as a Primary Endpoint for Alcohol Treatment Trials. Panel presented at the ASCP Annual Meeting, Miami Beach, Florida.
- Witkiewitz K. (2017, August). Reduction in World Health Organization (WHO) Drinking Risk Level as an Endpoint for Alcohol Clinical Trials. Symposium presented at the APA Annual Meeting, Washington D.C.
- O'Malley SS. (2017, May). The Development and Selected Performance of Patient Reported Outcomes (PRO) in Psychopharmacotherapy Trials – is the Juice Worth the Squeeze? A Review of Initiatives by the FDA, NIH, and the Alcohol Clinical Trials Initiative (ACTIVE). Panel presented at the ASCP Annual Meeting, Miami Beach, Florida.

ACTIVE Press Coverage:

- O'Connor, A. (2021, July 12). Alcohol Abuse Is on the Rise, but Doctors Too Often Fail to Treat It. *The New York Times*, Retrieved from https://www.nytimes.com/2021/07/12/well/live/alcohol-abuse-drinking-treatment.html?referringSource=articleShare

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