**ACTIVE Workgroup Meeting Minutes**
**March 27 – 28, 2024**
**Sheraton Rockville**
***920 King Farm Blvd. | Rockville, MD 20850***
**Meeting Room:** King Farm AB

**Participants:**
*Ray Anton*
*Maryam Afshar*
*Arnie Aldridge*
*Henri-Jean Aubin*
*Bartholt Bloomfield-Clagett (Day One, on Zoom)*
*Dan Falk (on Zoom)*
*Michaela Hoffman*
*Terry Horton*
*Zachary Illg, (Day Two)*
*Bruce Imbert*
*Raye Litten, (Day Two)*
*Alain Puech (on Zoom)*
*Lara Ray (Day Two, on Zoom)*
*Chamindi Seneviratne*
*Bernie Silverman*
*Celia Winchell*
*Katie Witkiewitz*
*Amy Thornburg (Staff on Zoom)*
*Laura Reynolds, staff*

***Minutes:***

1. ***Introduction of Members, Status Update, and Agenda Overview:*** R. Anton welcomed the group and provided an overview of the program. He reiterated the importance of annual "in person" meetings where people can freely exchange ideas formally and informally, get to know each other more personally, and develop comradery around our mission. He also mentioned continued progress on the FDA review of the WHO Risk Drinking Measure, having addressed a few extra queries and provided a few additional analyses. He also mentioned that the work on that project and few others was being coordinated and produced by a smaller ACTIVE group which he has called the ACTION subcommittee whose members include in addition to himself, Drs. O'Malley, Witkiewitz, Aldridge, Hoffman, and more recently Raye. Drs. Falk and Litten of NIAAA is acting as consultants to the group. The group meets once or twice a month on a continual basis coordinated through PMG. Dr. Anton also wanted to thank the Pharma companies for their continued interest and support and welcomed their involvement and ideas.

2. ***Methodological Considerations for The Alcohol Clinical Trial Simulation (ACTS) Project*:** M. Hoffman provided an overview of the clinical trials simulation project, as well as shared an update as to the progress made thus far. She began by sharing the

need for the simulation project, stating that pharmaceutical companies have limited experience designing and conducting AUD clinical trials and relatively few trials have been successfully completed. There is a critical mass of clinical trial data now available to take combined data from multiple trials which should provide improved information that would inform AUD clinical study design. M. Hoffman discussed the clinical trial design choices and the five studies that were used to collect data. She went into further detail discussing the project aims, stating the following:

1. Working towards the long-term goals, initial analyses will establish the foundations for building viable models of AUD clinical trials.
2. To analyze the individual specific clinical trial design variables and their impact on the study outcomes (drinking amounts and effect sizes). The initial variables of focus include sample size variables: number of sites, subjects per site, and missing data; length of study variables: titration time, length of treatment, and length of data collection (i.e. follow-up).
3. Include variables relating to the study population and inclusion/exclusion criteria: age, sex, and race distributions as well as other demographics, baseline drinking severity (drinks per day, drinks per drinking day, percent days abstinent, percent heavy drinking days, world health organization (WHO) category), and comorbidities.

In closing, she requested feedback from the group on ways the project could be improved, what study period should be utilized (taper, titration, etc.), and whether or not more multi-site studies should be incorporated or if single-site studies should be included. No definitive suggestions were made and the group will continue to discuss.

3. ***Study Site Variability Influence on Effect-Estimation and Statistical Power In Multi-Site AUD Pharmacotherapy RCT's*:** A. Aldridge provided an overview of why 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). He used an example of "the number of study sites and subject per site" to illustrate how variability in sites and subject numbers might interact in various ways to improve, or reduce, the probability of a clinical trial being successful under certain treatment effectiveness (a prior effect size) conditions.

4. ***Prazosin and Cyproheptadine in Combination in the Treatment of AUD: A Phase 2 RCT:*** HJ. Aubin discussed the recently completed study examining prazosin and cyproheptadine in combination in the treatment of AUD. He presented the data from the phase 2 trial (whose results were expected to be published soon), in which the purpose was to test a concept advanced by Kinnov Therapeutics. He began by sharing the preclinical rationale of the concept, followed by the objective, design, participants, and measurements used for the clinical trial.
    1. ***Preclinical Rationale:***

i. Noradrenergic and serotonergic neurons activate dopaminergic neurons via cortical alpha1b-adrenergic receptors and VTA-5-HT2A receptors.
ii. Mutual regulation between noradrenergic and serotonergic neurons: the amplitude of the activation of one set of neurons induced by peripheral stimuli is limited by the other group.
iii. Uncoupling of noradrenergic and serotonergic neurons occurs following repeating stimulations of alpha1b-adrenergic and 5-HT2A receptors by drugs of abuse.
iv. Hypothesis: AUD subjects lose control of their drinking behavior in part because of the NE/5-HT uncoupling.
v. Simultaneous blockade of 5-HT2A and alpha1b-adrenergic receptors may restore the coupling of noradrenergic and serotonergic neurons, and thus restore some control of the drinking behavior.

2. ***Objective:*** The objective was to demonstrate the superiority of the combination of cyproheptadine (5-HT2A blocker) and prazosin (alpha1b blocker) extended-release (ER) formulation (high dose, low dose) over placebo on the reduction of the total alcohol consumption (TAC), in patients with severe AUD.
3. ***Design***: The primary outcome criterion was Total Alcohol Consumption (TAC) change from baseline to W9-12
4. ***Participants:*** The main inclusion criteria were individuals 18-65, with severe AUD (DSM-5), and who had at least a WHO high risk drinking level in the 2 weeks preceding the screening and the 2 weeks preceding randomization. HJ. Aubin also shared with the group the criteria that excluded someone from the trial.

He concluded by summarizing the findings in different ways, such as in terms of effect size, dose by baseline severity, effect of time and finally shared the summary of the safety profile. In general the positive results of this phase 2 study were supportive of further development of this drug combination for the treatment of AUD.

***ACTION ITEMS:*** HJ. Aubin will follow up on the following:

- Determine the Cohen's h, that might help compare the WHO RDL change to the continuous endpoints
- Look at other endpoints such as abstinence and no heavy drinking to see if the WHO RDL is similar or superior to those endpoints.

5. ***Imputation Approaches for the Categorical WHO Risk Levels: A Comparison of Estimates across Missing Data Approaches:*** K. Witkiewitz focused on the idea she recently had for a new paper in which she revisited an analysis she completed in 2017 on missing drinking data in clinical trials that was never published. She shared the missing data that would be examined as well as shared new analyses addressing the question of how to treat missing data in the context of the categorical WHO risk drinking level (RDL) variable and single imputation method of "worst case scenario" . She began by discussing how to treat missing data for binary and categorical WHO

RDL , followed by discussing treatment withdrawals versus completers analysis. She concluded by summarizing her findings which include:

1. 2-level reduction less impacted by single imputation methods than 1-level reduction, i.e., more robust to a variety of missing data methods.
2. Type of missingness.
    - If data are missing completely at random then all methods are acceptable
    - If evidence of systematic missingness then use multiple imputation, last observation carry forward (LOCF), or complete case (subjects with all drinking data only).
    - Missing=no change in WHO RDL is often the most biased approach, especially for a 1-level RDL reduction.

For the categorical WHO RDL variable, the type of imputation may not matter too much, but "no change" is a more reasonable imputation method that will not bias the data toward making "increasers" appear to have better outcomes.

6. ***Prediction of Naltrexone Efficacy from fMRI Cue-elicited Brain Activation: Background and Results from a Randomized Clinical Trial:*** R. Anton shared with the group work that his team from the Medical University of South Carolina worked on regarding brain imaging (particularly fMRI) as way to 1) identify the clinical potential of new medications and 2) to inform who might respond in clinical trials. He began by providing background as to how alcohol effects on the brain can be observed in humans from a translational neuroscience perspective, followed by explaining the basic principles of the Blood Oxygen Dependent (BOLD) functional magnetic resounce imaging (fMRI) . He shared early fMRI image data and how it correlates with real time craving ratings. He noted that fMRI can be used to predict pharmacotherapy efficacy in AUD individuals with the use of naltrexone. He then showed how naltrexone blunted/removed alcohol cue activation of salient brain areas (including the ventral striatal/nucleus accumbens). This led to its use in a RCT of naltrexone where his group showed that for those who had that reduction of alcohol induced VS/Nac activation during naltrexone treatment were the most successful in reducing their drinking through the study. He concluded by stating the ways fMRI neuroimaging can add value to pharmacotherapy development, which include:
    1. High translational value from neuroscience, through animal models, to humans.
    2. Craving is hard to measure, while brain imaging provides a direct, replicable, estimation of alcohol cue effects on the brain that are likely related to craving and relapse.
    3. The reduction of ventral striatal activation by naltrexone in early-stage AUD individuals is similar in later stage AUD individuals. This suggests that fMRI alcohol-cue study of early-stage AUD volunteers can potentially predict treatment efficacy of new drugs in clinical trials. Likely better than craving measurements alone.
    4. Caveat: this fMRI alcohol cue-based paradigm might work only for drugs that <u>reduce dopamine output</u> (directly or indirectly). Other mechanisms of

pharmacotherapeutic action, such as on alcohol withdrawal, stress, sleep, etc. might need different, or additional, imaging paradigms.

7. ***Parameter Space and Potential for Biomarker Development in 25 years of FMRI Drug Cue Reactivity: A Systematic Review:*** L. Ray reviewed the key points which included:
    1. The current status of functional magnetic resonance imaging drug cue reactivity (FDCR) research and how it could support the discovery of biomarkers to facilitate the intervention development and clinical care for substance use disorders.
    2. A systematic review including 415 FDCR studies results from 357 studies could potentially help develop diagnostic, prognostic, susceptibility, severity, monitoring, predictive, or response biomarkers. Substantial heterogeneity in task and study design was identified that can hinder biomarker development.
    3. A sizable literature supports the development of FDCR-derived biomarkers, but moving forward requires large scale collaboration, methodological harmonization and optimization, and clinical and analytical validation.

    The concluding points included:
    1. 25 years of research on FDCR supporting its utility across a range of substances, methods, and scientific purposes.
    2. For alcohol-specific FDCR, the typical study uses visual cues, a block design, RCT medical design, post medication vs. placebo design, sample of individuals with AUD, analyzed for a-priori brain Regions of Interest (like ventral striatum), subjective craving as a robust correlate.
    3. Chronic versus acute dosing matters and chronic dosing is recommended
    4. Biomarker development includes several steps including discover & definition, validation, regulatory qualification, and application. Additional work on validation may lead to regulatory qualification.
    5. Utilization of FDCR as a biomarker in drug development and discovery represents and area of opportunity, primed for clinical development.
    6. The ACTIVE workgroup may be well suited to advance clinical development in the space of AUD since the review focuses on both AUD and SUD.

A final discussion included a range of topics but importantly focused on reasons why medication treatment for AUD is not more widely accepted and utilized. In conclusion, it was felt it must be a combination of government support of education/knowledge initiatives and as well as industry-based commercialization (including educational material for patients and treatment providers) that should be fostered. Of course, successful development of effective new treatments should add to any forward momentum in this regard.

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

- Garcia, C. C., Richards, D. K., Tuchman, F. R., Hallgren, K. A., Kranzler, H. R., Audin, H. J., O'Malley, S. S., Mann, K., Aldridge, A., Hoffman, M., Anton, R. F., & Witkiewitz, K. (2024). Reductions in World Health Organization risk drinking levels are associated with

improvements in sleep problems among individuals with alcohol use disorder (AUD). Alcohol and Alcoholism. *Accepted*

- 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, F.R., Hallgren, K.A., Richards, D.K., Aldridge, A., Anton, R.F., Aubin, H.-J. et al. (2024) Reductions in WHO risk drinking levels correlate with alcohol craving among individuals with alcohol use disorder. Alcohol: Clinical and Experimental Research, 48, 420–429. Available from: https://doi.org/10.1111/acer.15257
- 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.
- Witkiewitz K, Kranzler H, Hallgren K, Hasin D, Aldridge A, Zarkin G, Mann K, O'Malley S, and Anton RF. Stability of Drinking Reductions and Long-term Functioning Among Patients with Alcohol Use Disorder. Journal of General Internal Medicine. 2021 Feb; 36(2):404-412. PubMed PMID: 33180306; PubMed Central PMCID: PMC7878601.
- Shmulewitz D, Aharonovich E,Witkiewitz K, Raymond RF, Kranzler HR, Scodes J, Mann KF, Wall MM, Hasin D. The World Health Organization Risk Drinking Levels Measure of Alcohol Consumption: Prevalence and Health Correlates in US Adult Nationally Representative Surveys, 2001-2002 and 2012-2013. American Journal of Psychiatry. 2021 Jan 21. PubMed PMID: 33472388.
- Witkiewitz K, Heather N, Falk DE, Litten RZ, Hasin DS, Kranzler HR, Mann KF, O'Malley SS, Anton RF. World Health Organization risk drinking level reductions are associated with improved functioning and are sustained among patients with mild, moderate and severe alcohol dependence in clinical trials in the United States and United Kingdom. Addiction. 2020 Sep;115(9):1668-1680. doi: 10.1111/add.15011. Epub 2020 Mar 10. PMID: 32056311; PMCID: PMC7841874.
- Knox J, Scodes J, Witkiewitz K, Kranzler H, Mann K, O'Malley S, Wall M, Anton R, Hasin D, ACTIVE Group. Reduction in World Health Organization (WHO) Risk Drinking Levels and Cardiovascular Disease. Alcohol Clinical and Experimental Research. 2020 Aug; 44(8):1625-1635. PubMed PMID: 32619058; PubMed Central PMCID: PMC7484295.
- Anton RF, Witkiewitz K, Falk D, Litten R, Hasin D, Mann K, O'Malley SS., Response to Dr. Mark Litt Commentary. Alcohol Clinical and Experimental Research. 2019 Aug 5. PubMed PMID: 31381170.
- Witkiewitz K, Falk DE, Litten RZ, Hasin DS, Kranzler HR, Mann KF, O'Malley SS, Anton RF. Maintenance of World Health Organization Risk Drinking Level Reductions and Posttreatment Functioning Following a Large Alcohol Use Disorder Clinical Trial. Alcoholism: Clinical and Experimental Research. 2019 May; 43(5): 979-987. PubMed PMID: 30951210; PubMed Central PMCID: PMC6502682.
- Knox J, Wall M, Witkiewitz K, Kranzler HR, Falk DE, Litten R, Mann K, O'Malley SS, Scodes J, Anton R, Hasin DS. Reduction in Non-abstinent World Health Organization

(WHO) Drinking risk Levels and Drug Use Disorders: 3-year Follow-up Results in the US General Population. Drug Alcohol Depend. 2019 Apr 1; 197: 228-235. PubMed PMID: 30852375; PubMed Central PMCID: PMC440807.

- 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.
- Knox J, Scodes J, Wall M, Witkiewitz K, Kranzler HR, Falk DE, Litten RZ, Mann KF, O'Malley SS, Anton RF, Hasin DS; Alcohol Clinical Trials (ACTIVE) Workgroup. Reduction in non-abstinent WHO drinking risk levels and depression/anxiety disorders: 3-year follow-up results in the US general population. Drug Alcohol Depend. 2019 Feb 14; 197:228-235. PubMed PMID: 30852375.
- Witkiewitz K, Kranzler HR, Hallgren KA, Hasin DE, Mann KF, Falk DE, Litten RZ, O'Malley SS, & Anton RF. Drinking Risk Level Reductions Associated with Improvements in Physical Health and Quality of Life Among Individuals with Alcohol Use Disorder. Alcoholism: Clinical and Experimental Research. 2018 Dec; 42(12):2453-2465. PubMed PMID: 30395350; PubMed Central PMCID: PMC6286196.
- Knox J, Wall M, Witkiewitz K, Kranzler HR, Falk DE, Litten RZ, Mann KF, O'Malley SS, Scodes J, Anton RF, & Hasin DS. Reduction in Non-Abstinent WHO Drinking Risk Levels and Change in Risk for Liver Disease and Positive AUDIT-C Scores: Prospective 3-Year Follow-Up Results in the US General Population. Alcoholism: Clinical and Experimental Research. 2018 Nov; 42(11)2256-2265. PubMed PMID: 30204248; PubMed Central PMCID: PMC6263142.
- Mann K, Aubin HJ, Charlet K, & Witkiewitz K. Can Reduced Drinking be a Viable Goal for Alcohol Dependent Patients? World Psychiatry. 2017 Oct; 16(3):325-326. PubMed PMID: 28941117; PubMed Central PMCID: PMC5608854.
- Mann K, Aubin HJ, & Witkiewitz K. Reduced Drinking in Alcohol Dependence Treatment, What is the Evidence? European Addiction Research. 2017 Sep 22;23(5):219-230. PubMed PMID: 28934736.
- Litten RZ, Falk DE, O'Malley SS, Witkiewitz K, Mann KF, Anton RF. Letter to Editor in Response to Johnson's Commentary (2017) on the Witkiewitz et al. (2017) Article. Alcoholism: Clinical and Experimental Research. 2017 May 4. PubMed PMID: 28471501.
- Witkiewitz K, Wilson AD, Pearson MR, Hallgren KA, Falk DE, Litten RZ, Kranzler HR, Mann KR, Hasin DS, O'Malley SS, & Anton RF. Temporal Stability of Heavy Drinking Days and Drinking Reductions Among Heavy Drinkers in the COMBINE Study. Alcoholism: Clinical and Experimental Research. 2017 May;41(5):1054-1062. PubMed PMID: 28295414; PubMed Central PMCID: PMC5404970.
- Hasin DS, Wall M, Witkiewitz K, Kranzler HR, Falk D, Litten RZ, Mann K, O'Malley SS, Scodes J, Robinson RL, Anton RF. Change in Non-Abstinent World Health Organization Risk Drinking Levels and Alcohol Dependence: A 3-Year Follow-Up Study in the United States General Population. Lancet Psychiatry. 2017 Jun; 4(6):469-476. PubMed PMID: 28456501.
- Witkiewitz K, Hallgren KA, Kranzler HR, Mann KR, Hasin DS, Falk DE, Litten RZ, O'Malley SS, & Anton RF. Clinical Validation of Reduced Alcohol Consumption after

Treatment for Alcohol Dependence using the World Health Organization Risk Drinking Levels. Alcoholism: Clinical and Experimental Research. 2017 Jan;41(1):179-186. PubMed PMID: 28019652; PubMed Central PMCID: PMC5205540.

- Witkiewitz, K, Falk, DE, Kranzler HR, Litten RZ, Hallgren KA, O'Malley SS, & Anton RF. Missing Data in Alcohol Clinical Trials with Binary Outcomes. Alcoholism: Clinical and Experimental Research. 2016 Jul;40(7):1548-57. PubMed PMID: 27254113.
- Witkiewitz K, Falk DE, Kranzler HR, Litten RZ, Hallgren KA, O'Malley SS, & Anton RF. Methods to analyze treatment effects in the presence of missing data for a continuous heavy drinking outcome measure when participants drop out from treatment in alcohol clinical trials. Alcoholism: Clinical and Experimental Research. 2014 Nov;38(11):2826-34. PubMed PMID: 25421518; PubMed Central PMCID: PMC4244651.
- Stout RL, Braciszewski JM, Subbaraman MS, Kranzler HR, O'Malley SS, Falk D and ACTIVE group. What happens when people discontinue taking medications? Lessons from COMBINE. Addiction. 2014 Dec; 109(12):2044-52. PubMed PMID: 25098969 PubMed Central PMCID: PMC4254710.
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- Anton RF, Litten RZ, Falk DE, Palumbo JM, Bartus RT, Robinson RL, Kranzler HR, Kosten TR, Meyer RE, O'Brien CP, Mann K, Meulien D. The Alcohol Clinical Trials Initiative (ACTIVE): purpose and goals for assessing important and salient issues for medications development in alcohol use disorders. Neuropsychopharmacology. 2012 Jan;37(2):402-11. PubMed PMID: 21900883; PubMed Central PMCID: PMC3242301.

***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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