VOLUME 2 ISSUE 1

Center for Studies of Addiction Newsletter

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Continuum of Care Staff
Front row (left to right): Max Stern, Megan Ivey, Jessica Hemmons, Sarah Rosenbach
Back row (left to right): Dr. Brenda Curtis, Dr. James McKay, Tyrone Thomas, Jason Freeman, Jamil Lane
Not pictured: Dr. Deborah Van Horn, Dan Summers, Casey Hamilton, April Howard, Alexandra Schepens

HIGHLIGHTING DR. JAMES MCKAY'S RESEARCH GROUP

Center on the Continuum of Care in the Addictions

Our unit is focused on identifying ways to better tailor interventions for substance use disorders across the continuum of care to improve retention and outcomes. Much of this work has been done in the continuing care phase of treatment. However, more recently we have also conducted studies on prevention interventions and during the initial phase of treatment. All of our studies are done in "real world" treatment programs such as community behavioral health (CBH)-funded intensive outpatient programs (IOPs) in Philadelphia and the VA. The unit is directed by Jim McKay. Other investigators are Debbie Van Horn, Brenda Curtis, Marcel Bonn-Miller, and Alexandra Wimberly. Other staff members are project coordinators Megan Ivey and Jessie Hemmons; counselors Tyrone Thomas and April Howard; and research techs Sarah Rosenbach, Max Stern, Jamil Lane, Jason Freeman, Casey Hamilton, and Dan Summers.

Our work on tailoring treatments has involved the development and evaluation of adaptive interventions. These interventions are adjusted during the course of treatment on the basis of patient response, according to clearly operationalized decision rules. Adaptive treatment algorithms can be developed through existing research results and expert consensus, or through experimental designs, such as Sequential Multiple Assignment Randomized Trials (SMART). We have used both of these approaches in our work.

We have also examined the efficacy of mobile communication technology in the delivery of these adaptive treatments. Findings from our early studies showed that for graduates of 4-week intensive outpatient programs (IOPs), continuing care provided via the telephone was at least as effective as standard clinic-based group counseling. Later research showed that adding extended telephone continuing care improved outcomes of standard IOPs, especially for patients who made poor progress toward meeting treatment goals while in IOP (e.g., failure to stop using cocaine or alcohol, poor social support, low motivation). Two of our studies also indicated that extended telephone continuing care was more effective for women than for men. We are currently conducting two clinical trials. The first, funded by NIAAA, is using a 2x2 design to test the efficacy and cost-effectiveness of novel continuing care interventions. The study features four conditions: standard IOP care only, standard care plus an automated smartphone recovery app that provides support 24/7, standard care plus our counselor delivered telephone continuing care intervention, and standard care plus the combination of the smartphone program and telephone continuing care. Participants are being recruited from two IOPs in the city. Each continuing care intervention is provided for 12 months, and participants are followed for a total of 18 months.

The second study is funded by the DoD, and is testing an adaptive prevention intervention designed to reduce rates of hazardous alcohol use in veterans receiving opioid medications for pain. The intervention follows vets for 12 months, and is tailored on the basis of response to initial prevention efforts. Vets who reduce drinking go into a monitoring track, which provides periodic assessment and supportive test messages. Those who do not reduce drinking initially instead receive stepped up prevention interventions and more frequent text messages. During the 12 month intervention period, vets can move from one track to the other, based on their drinking behavior. The veterans are followed for research for 18 months.

In an observational study funded by the National Institute of Health's Collaborative Research on Addiction (CRAN) and NIDA, we are examining how well social media language can predict relapse and outpatient treatment completion among patients who have recently entered Philadelphia area community outpatient treatment programs. Research staff members are recruiting 1,000 patients entering drug-free outpatient alcohol and other drug problem (AOD) treatment from community based substance abuse treatment programs. Participants will complete an intake battery and survey of their social media use, report weekly on their alcohol and drug use, give permission to extract treatment entry and discharge data from their clinic records, and to extract data from their Facebook and Twitter accounts for 26 weeks. We will be using linguistic analysis of naturally-occurring social media communications to gain a better understanding of the risk factors, attitudes, and behaviors associated with treatment entry, relapse and dropout. Social media monitoring could be used to generate algorithms in the development of relatively inexpensive applications (apps) that would monitor a patient's daily behaviors to help prevent the need for more expensive treatment, significantly curtailing healthcare costs.

Our unit is also participating in collaborative NIH funded research projects with investigators at Dartmouth, University of Michigan, and North Shore Long Island Jewish Hospital; conducting evaluations of new continuing care programs at Caron Treatment Centers; and working with investigators at Stavanger University Hospital in Norway on a longitudinal treatment outcome study and on mobile health communication technology. In addition, member Marcel Bonn-Miller, who is based at the Palo Alto VA, is the PI of two new cannabis grants funded by Colorado.

IMPORTANT NEWS

In February, the Obama Administration proposed $1.1 billion in additional spending to address the growing prescription painkiller and heroin abuse epidemic. The money would be spent to expand and improve treatment facilities and prevention strategies, support targeted enforcement activities, and increase access to naloxone (Narcan), a medication that blocks the effects of opioids and most importantly, in an overdose situation, blocks the respiratory depressant effects of the opioids. Included in the budget proposal, is a pilot project that would allow nurse practitioners and physician assistants to prescribe buprenorphine for treatment when allowed by state law.

Check out the full article:

https://www.whitehouse.gov/the-press-office/2016/02/02/president-obama-proposes-11-billion-new-funding-address-prescription

Extended-Release Naltrexone to Prevent Relapse in Probationers

Opioid dependence is a public health problem with devastating consequences that affects criminal justice system populations disproportionately. These individuals have high rates of relapse and overdose deaths after release from incarceration. Dr. Charles O'Brien, Penn Professor of Psychiatry, is the senior author of a large, multisite, randomized clinical trial of extended-release naltrexone treatment of opioid dependent adult criminal justice offenders. Study participants were randomly assigned to receive six monthly injections of naltrexone or usual treatment consisting of brief counseling and referral to community treatment programs. During the 24-week treatment phase, participants receiving extended release naltrexone had a lower relapse rate than those that received usual treatment. Extended-release naltrexone was also associated with a lower rate of opioid relapse than usual treatment during 52-week and 78-week follow-up visits.

Check out the full article here:
http://www.nejm.org/doi/full/10.1056/NEJMoa1505409

HIGHLIGHTS OF OTHER CURRENT CENTER STUDIES

OPIOID TREATMENT STUDIES

The abuse of prescription painkillers and heroin has become a serious public health concern. In the United States, overdose deaths from painkillers and heroin account for more than 60% of overdose deaths. Dr. Kyle Kampman at the University of Pennsylvania's Treatment Research Center is conducting two studies examining treatment options for individuals with opioid use disorder.

A Phase 3 Study to Evaluate the Safety, Tolerability, and Efficacy of Naltrexone for use in Conjunction with Buprenorphine in Adults with Opioid Use Disorder Prior to First Dose of VIVITROL®

Vivitrol, also known as depot naltrexone, is a highly effective, yet underutilized, once a month injection for opioid use disorder. Because Vivitrol is an opioid antagonist, a patient must first be abstinent from opioids and no longer physically dependent before initiating therapy. Abstinence occurs through the process of detoxification, and this is one of the biggest obstacles in expanding the use of Vivitrol. Most detoxification programs involve either an extended, expensive inpatient stay or an uncomfortable, ineffective outpatient stay. This Phase 3 study aims to find a solution to the problem of detoxification by testing a new 7-day process of outpatient detoxification using low doses of buprenorphine and oral naltrexone. This study is a double-blind, placebo-controlled trial in which all patients will receive non-narcotic ancillary medications to assist the detoxification process. After detoxification patients will receive three monthly injections of Vivitrol. This trial is sponsored by Alkermes Pharmaceuticals and is actively recruiting.

***An Open-Label, Long-Term Safety and Tolerability Study of Depot Buprenorphine (RBP-6000) in Treatment-Seeking Subjects with Opioid Use Disorder*:**

Buprenorphine, a partial opioid agonist, is a highly effective treatment for opioid use disorder. Currently, it is available as sublingual or orally dissolving tablets or strips that are taken daily. However, a growing problem with buprenorphine treatment is non-adherence to treatment and medication diversion. One solution to this problem is the development of a long acting injectable formulation of buprenorphine. This trial is an open-label safety and tolerability follow up to a successful Phase III trial, where patients received RBP-6000 monthly for six months. Thus far, patients have tolerated the injections well and report decreased opiate use. This trial, sponsored by Indivior Pharmaceuticals, is no longer recruiting new subjects.

ALCOHOL TREATMENT STUDIES

A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 2 Pharmacogenetic Study of Ondansetron in Alcohol Use Disorder

Alcohol Use Disorder (AUD) is a heterogeneous and chronic relapsing disorder. Recently, studies of medications to treat AUD have used a personalized approach to therapy. Initial findings in pharmacogenetics have made it possible to identify discrete subgroups of individuals with an AUD to target those who are most likely to respond to treatment with a particular medication. Taking a personalized approach to AUD, Henry Kranzler, MD is conducting a study of ondansetron to treat AUD to determine the medication's efficacy and safety and to identify individuals that are most responsive to the medication. Comparable, but not identical, studies are being conducted at two sites: the University of Pennsylvania Treatment Research Center (TRC) and at the University of Maryland at Baltimore (where Dr. David Gorelick is the Principal Investigator). The 24–week study includes screening, 16 weeks of treatment with ondansetron or placebo and a 4-week follow-up period. Within each medication group, subjects are stratified based on pre-specified genotypes. The primary hypothesis is that both African Americans and European Americans receiving ondansetron will consume fewer drinks per drinking day and that the medication will be most effective in individuals with "responsive" genotypes. Here at the TRC, we are recruiting African Americans with AUD who want to reduce or stop drinking. The research group at the University of Maryland is conducting a parallel study in European Americans.

A Randomized, Double-blind Placebo-Controlled Pharmacogenetic Study of Topiramate in European-American Heavy Drinkers:

Topiramate is an anticonvulsant medication that, in addition to being approved to prevent seizures, is also approved to prevent migraine headaches, and to promote weight loss (in combination with phentermine). Although not approved to treat alcohol use disorder (AUD), several studies have shown that topiramate reduces heavy drinking. In one study of topiramate, Dr. Henry Kranzler and colleagues found that the effects of topiramate on heavy drinking were greatest in European Americans with a specific genotype in the single nucleotide polymorphism rs2832407, which is in the gene encoding the kainate receptor. Dr. Kranzler is currently conducting a study entitled "A Randomized, Double-blind, Placebo-Controlled Pharmacogenetic Study of Topiramate in European-American Heavy Drinkers" to determine whether the effects of rs2832407 on the efficacy of Topiramate in reducing heavy drinking can be replicated in a new sample of participants. The 12-week treatment study involves weekly visits to the UPenn Treatment Research Center for the first 6 weeks, followed by visits every other week for the last 6 weeks. The medication dosage (topiramate or placebo) is gradually increased to limit side effects. At each treatment visit, a research nurse meets with participants to review the effects of the study medication and provide brief counseling. There are two follow-up visits at three and six months after the 12-week treatment period is completed.

NICOTINE TREATMENT STUDIES

Placebo Controlled Trial of Bupropion for Smoking Cessation in Pregnant Women

Smoking during pregnancy increases the risk of low-birth-weight babies, miscarriage, placental complications, preterm delivery, and fetal and neonatal death. Most women quit smoking when they learn that they are pregnant, but most of those still smoking at their first prenatal visit continue to smoke throughout pregnancy. Efforts to reduce smoking in this population through behavioral interventions are minimally effective. Bupropion, a medication approved for both smoking cessation and depression, is not approved for use in pregnant women, however, it is commonly prescribed during pregnancy. Bupropion is classified as FDA Pregnancy category C, meaning that although animal studies have shown an adverse effect on the fetus, there are no well-controlled studies in humans and the potential benefits of use in pregnancy may outweigh the risks. Dr. Henry Kranzler is conducting this study to improve smoking cessation treatment during pregnancy. Participants in the study receive bupropion or placebo in conjunction with behavioral counseling for 10 weeks. Visits are conducted in person or by phone.

A Randomized, Double-blind High/Low Dose Controlled trial of AZD8529 for Smoking Cessation in Women

Smoking among women is doubly problematic for women, as they both suffer more severe consequences from smoking and have more difficulty quitting than men. Dr. Teresa Franklin is investigating a novel glutamate receptor modulator, AZD8529 for smoking cessation. The molecule shows promise as an anti-craving medication. This 12-week treatment study involves weekly visits to the UPenn Treatment Research Center for the first 6 weeks, followed by visits every other week for the last 6 weeks. The medication regimen (high- or low-dose AZD8529) will begin following a one-week lead in period for women who are a good fit for the study. At each treatment visit, participants meet with a member of the medical staff to review the effects of the study medication and a counselor who provides brief counseling to help with smoking cessation. There are three follow-up visits over the next 5 weeks.

USING BRAIN IMAGING TOOLS TO IMPROVE ADDICTION AND PUBLIC HEALTH

Center investigators use a variety of brain imaging tools to improve addiction treatment outcomes. There are no FDA-approved medications for cocaine addiction, and even the FDA-approved medications for smoking cessation, alcohol use disorder, and opiate addiction do not help all individuals with these problems. *Thus, there are many individuals who do not yet have an effective medication for their drug, alcohol or smoking disorders*. As medications provide benefits through actions on the brain, brain imaging offers an important tool for understanding how the existing medications work, and for finding new medications. Brain imaging can determine whether an existing or candidate medication is reaching the brain, whether it is targeting the intended brain circuits, and – importantly -- whether the individual's brain response to the medication is linked to "real world" clinical outcomes such as smoking, drug use, or alcohol use.

Neuroimaging Studies of Cocaine Use Disorder

Dr. Anna Rose Childress has three neuroimaging projects (one ongoing and two upcoming) in cocaine addiction. The ongoing study examines whether the opiate antagonist **naloxone**, when taken as an intranasal spray, impacts brain circuits linked to cocaine relapse. Upcoming studies will measure the action of either **arbaclofen placarbil** (a long-acting formulation of the familiar and safe anti-

spasmodic medication baclofen) or a new medication acting at **dopamine D3 receptors,** on cocaine relapse-relevant brain circuits. The primary imaging tool in most of these studies is fMRI (functional magnetic resonance imaging), a technique that shows where the brain is more (or less) active, during various scans and tasks. In addition to fMRI, later in 2016, we are preparing to conduct imaging studies using PET (positron emission tomography) and a special tracer for dopamine D3 receptors – helping us to know whether our candidate D3 medications are binding to dopamine D3 receptors in the brain. The cocaine imaging studies generally involve an 8-10 day inpatient stay (imaging is done during this time) and several weeks of outpatient treatment with urine monitoring following discharge from the inpatient unit.

Neuroimaging Studies of Nicotine Addiction

Use of SPECT to Examine DAT Binding and Trafficking in Cigarette Dependence

Dr. Teresa Franklin has two ongoing studies that use neuroimaging to study nicotine addiction. The first study evaluates the hypothesis that individuals who smoke and are carriers of a specific allele (genetic variant) of the dopamine transporter (DAT) gene have an enhanced vulnerability to relapse to smoking in the presence of smoking cues, while those who are carriers of another allele of the DAT gene are more susceptible to nicotine withdrawal symptoms. However, the mechanisms underlying the different effects seen in the genotype groups are unknown. To test this hypothesis, we will use Single Photon Emission Computed Tomography (SPECT) and the DAT-specific radiotracer DaTscan to measure dopamine availability in genotyped subjects during two conditions: after recent smoking and after overnight smoking abstinence. This study is enrolling only men because DAT trafficking is influenced by sex hormones in women. As additional funding is acquired, the study will include women. Participants are genotyped at the initial visit. Individuals who participate in the screening process and are a good fit for the study will participate in two SPECT scanning sessions on separate days, one after recent smoking and one after overnight abstinence.

A Randomized, Double-blind Placebo-Controlled Treatment Trial of the Effects of Baclofen on Brain and Smoking Behavior in Cigarette Smokers

The second study by Dr. Franklin uses fMRI to observe the effects of the GABA-B agonist, baclofen, on the brain's response to craving. Relapses to smoking are often preceded by a strong desire for a cigarette when an individual is exposed to stimuli related to smoking. Knowledge of the mechanisms underlying smoking cue-induced nicotine craving may aid in the identification of new medications to help smokers remain free of tobacco. In the study, craving is induced in subjects by watching videos of smoking-related cues before and during medication. Individuals who participate in the screening process and are found to be a good fit for the study will participate in two neuroimaging sessions: one prior to receiving medication and one after 3 weeks of medication. Individuals will remain in the study for an additional 5 weeks to meet weekly with our study staff and receive study medication.

Neuroimaging Studies of Alcohol Addiction

Effectiveness of Topiramate: Characterizing Individual Differences

Dr. Reagan Wetherill is conducting a sub-study of Dr. Kranzler's topiramate trial (described on Page 4) that uses functional magnetic resonance imaging (fMRI) to evaluate the effects of topiramate on the brain's response to alcohol-related cues. Individuals who participate in the screening process and are found to be a good fit for the 12-week treatment trial and the sub-study participate in two neuroimaging sessions: one session prior to receiving topiramate or placebo and one session after 6 weeks of study medication in addition to the 12-week treatment.

UPCOMING EVENTS AT THE CENTER

April 11, 2016
Dr. Lyle Ungar, PhD
Social Media Language Analysis for Health Behaviors

April 18, 2016
Dr. Dennis Durbin, MD, MSCE
Being Intentional about Work/Life Integration

May 2, 2016
Dr. John Farrar, MD
Brain Imaging in Pain and Addiction

May 9, 2016
Mr. Marlow Kee
A Comptroller's-eye View of Funds Flow in the Perelman School of Medicine and the University of Pennsylvania

May 16, 2016
Dr. Marja Evenden, MD
On GABA-A Receptor Ligands in Clinical Psychiatry

Penn Behavioral Health
Penn Medicine

Treatment Research Center

Addiction Treatment
& Research

CONTACT US

Click below for a complete list of our clinical trials:

http://www.med.upenn.edu/csa/addiction_clinicaltrials.html

If you have any questions regarding one of our clinical trials, please call 215-243-9989 or email: addicted@med.upenn.edu