OVERVIEW: UW-CTRI releases a research update in January and July of each year. This report summarizes published and in-press manuscripts, presentations, grants, contracts and other research projects. The most recent reports are available online at: http://www.ctri.wisc.edu/Researchers/researchers.htm

SUMMARY: In 2015, the UW-CTRI research team produced:

- 26 published papers (p. 1)
- 6 papers in press (p. 7)
- 35 presentations or posters (p. 7)
- 2 new studies (p. 10)
- 8 active studies (p. 11)
- 6 studies recently completed (p. 15)
- Financials (p.18)

THANK YOU: UW-CTRI is grateful to its partners, Centers for Disease Control (CDC), Centers for Medicare and Medicaid Services (CMS), ClearWay Minnesota, Food and Drug Administration (FDA), Health Resources and Services Administration, National Institutes of Health (NIH), UW Department of Medicine, UW School of Medicine and Public Health, UW Department of Family Medicine, Veterans Affairs (VA), Wisconsin Department of Health Services (DHS), and the Wisconsin Partnership Program.

Published Papers

Note: Names in bold are current UW-CTRI employees.


Summary: Researchers found that a new, synthesized research approach efficiently evaluates multiple intervention components to identify promising components for every phase of smoking treatment. Many intervention components interact with one another, supporting the use of factorial experiments in smoking treatment development.

**Summary:** The authors suggest assessing each smoker’s quitting goal; if a smoker is willing to make a quit attempt, he or she would receive evidence-based cessation treatment. “Unwilling” smokers, however, would be urged to enter a “motivation” treatment designed to reduce smoking and prepare them to quit. Such treatment appears to be reliably efficacious and differs markedly from current cessation treatment practices.


**Summary:** For most smokers, alcohol use decreased following smoking cessation. These results suggest that the expectation should be of decreased alcohol use post-cessation. However, attention may be warranted for those who drink higher amounts of alcohol pre-cessation because they may be more likely to drink more in the post-quit period, which may influence smoking-cessation success.


**Summary:** The Nicotine Metabolite Ratio (NMR, ratio of trans-3'-hydroxycotinine and cotinine), has previously been associated with CYP2A6 activity, response to quit-smoking treatments, and cigarette consumption. Enhanced knowledge of the genes that influence nicotine metabolism, smoking behaviors, and clinical outcomes will help to characterize the risks from gene variants on smoking behaviors and smoking- attributable disease. Based on this analysis and additional studies cited, CYP2A6SNPs account for large fractions of the variance of the NMR, smaller fractions of the variance of cigarette consumption, and influence risk for lung cancer, but do not account for other nicotine-dependence factors.


**Summary:** Primary-care patients in a quit-smoking study periodically reported smoking status. Of 894 patients who relapsed, 83% renewed quitting for at least 24 hours, and 34% of these were abstinent at follow-up. The average latency to renewed quitting was 106 days and longer latencies predicted greater success. Renewed quitting was more likely for older, male, less dependent smokers, and later abstinence was predicted by fewer depressive symptoms and longer past abstinence. Renewed quitting is common and produces meaningful levels of cessation.


**Summary:** In this study, researchers created anxiety in smokers using minor electrical shocks. They found that, among smokers deprived of nicotine, anticipation of smoking significantly weakened both their physiological stress reaction and their self-reported anxiety (relative to smokers not deprived of nicotine). Smokers’ stress reactivity was not reduced by smoking beyond the prior effect of anticipation. These results
suggest that anticipation, rather than actual drug consumption, may drive the primary reinforcing effect of reduced stress-reactivity in smoking.


*Summary:* People with risk factors on the CHRNA5 gene are more likely to develop lung cancer at a younger age, and this research suggests that the reason is they are less likely to quit smoking early in life. So rather than directly affecting the susceptibility to lung cancer, researchers found this gene appears to operate through dependence on smoking.


*Summary:* The authors found no evidence of a significant association between the variant and successful smoking cessation. The authors conclude that the alleles of rs1051730 and rs16969968 are not associated with smoking cessation.


*Summary:* In two randomized trials examining smoking and genetics, researchers compared combination nicotine-replacement medication vs. placebo, and varenicline vs. placebo. Results demonstrate inconsistent genetic results in the placebo arms. This evidence highlights the need to compare the most effective quit-smoking medications with the same placebo control to aid decisions on medication choice for patients trying to quit smoking.

Christiansen B, Reeder K, TerBeek E, Fiore MC, Baker TB. Motivating Low SES Smokers to Accept Evidence-Based Smoking Cessation Treatment: A Brief Intervention for the Community Agency Setting. *Nicotine & Tobacco Research*. August 2015. 17(8):1002-1011.

*Summary:* A brief, targeted, motivational intervention at 5 Wisconsin Salvation Army sites focused on cessation goals and beliefs among smokers of low socioeconomic status. Unmotivated participants in the intervention condition used the Wisconsin Tobacco Quit Line at a significantly higher rate (12.2%) than did those in the 2 control conditions (2.2% and 1.4%) and approached the rate of calling by participants who were initially motivated to quit (15.7%). Intervention condition participants also showed improved motivation to quit and stage of change.

Summary: Motivation-phase nicotine gum and behavioral-reduction counseling are promising intervention components for smokers who are initially unwilling to quit.


Summary: After quitting, many smokers suffer from anhedonia, a pervasive inability to experience pleasure during life activities that one normally enjoys. This paper is one of the first to show that anhedonia is a symptom of nicotine withdrawal in humans, and may be a key reason smokers who want to break their addiction to tobacco struggle to do so—especially during the first week after quitting smoking, when anhedonia spikes before eventually falling back to baseline levels. The good news is that researchers found that quit-smoking medications decreased the rise in anhedonia.


Summary: Results suggest that Mindfulness Training for Smokers can be provided via web-based video instruction with phone support and yield reasonable participant engagement on intervention practices and that intervention efficacy and mechanism of effect deserve further study.


Summary: While the FDA has the authority to regulate nicotine levels in cigarettes to below addictive levels, there has been debate about whether doing so would help reduce or eliminate smoking across America. In a perspective piece in the New England Journal of Medicine (NEJM), UW-CTRI leaders Dr. Michael Fiore and Dr. Tim Baker discuss a study also published in NEJM which found that reducing nicotine levels in cigarettes led to less smoking and more quit attempts. They call for the FDA to use its regulatory powers to reduce nicotine levels in conventional cigarettes to below addictive levels.


Summary: Smokers were randomized in a 2 (expectancy: told patch contains nicotine versus told placebo patch) × 2 (drug: receive 21-mg transdermal nicotine patch versus receive placebo patch) × 2 (sensorimotor: smoke very low nicotine content cigarettes versus no smoking) full factorial between-subjects design. Receiving nicotine (versus placebo) increased positive affect and anticipated pleasure from—and desire for—reward. Expecting nicotine (versus placebo) reduced negative affect and increased smoking delay. Sensorimotor stimulation from smoking (versus no smoking) reduced smoking urge and behavior.

Summary: In this study of genetic samples from 17,074 ever smokers, rs2273500-C was associated with increased lung cancer risk, likely through its effect on smoking, as rs2273500-C was no longer associated with lung cancer after adjustment for smoking. Using criteria for smoking behavior that encompass more than the single “cigarettes-per-day” item, researchers identified a common genetic variant with important regulatory properties that contributes to nicotine dependence and smoking-related consequences.


Summary: In multivariable models, patients had higher adjusted odds of wanting to quit if they had indications of severe mental illness and lower odds if they had health insurance. Patients had higher odds of receiving counseling if they had 2 or more chronic conditions and lower odds if they were Hispanic. Cigarette smoking prevalence is substantially higher among patients at health centers than among US adults in general. However, most smokers at health centers desire to quit. Continued efforts are warranted to reduce tobacco use in this vulnerable group.


Summary: Overall, PTSD symptom severity was significantly associated with negative-reinforcement smoking motives. It was not significantly associated with positive-reinforcement smoking motives. Emotional numbing was the only PTSD sub-factor associated with smoking rate. Therefore, anxiety sensitivity may be an important feature associated with PTSD that enhances motivation to smoke for negative-reinforcement purposes. Smoking-cessation interventions that alleviate anxiety sensitivity and enhance coping with negative affect may be useful for smokers with elevated PTSD symptoms.


Summary: The authors call on insurers across the country to comply with the Affordable Care Act (ACA) and do the right thing—cover tobacco-dependence treatments. This would reduce health-care costs and improve enrollee health.


Summary: In this secondary analysis of a clinical trial (N=1,433) of 5 smoking-cessation medications, patterns of smoking during the first 4 weeks of quitting emerged. Active treatment (compared to placebo), and particularly the patch and lozenge combination, was related to smoking pattern and promoted early quitting. The pattern of smoking in the first month of quitting was related to several baseline variables, including nicotine dependence, quitting history, self-efficacy, sleep disturbance, and minority status. Interestingly, smokers who recovered from initial smoking to achieve abstinence a few weeks after trying to quit had the second-highest 6-month quit rates, after those who abstained consistently for the first month.
Minami H, Tran LT, McCarthy DE. (This paper uses data from a UW-CTRI study, and McCarthy is a former UW-CTRI graduate student.) Using Ecological Measures of Smoking Trigger Exposure to Predict Smoking Cessation Milestones. *Psychology of Addictive Behaviors*. March 2015. 29(1):122-8.

This study suggests that post-quit environmental risk factors—such as cigarette availability and increased lapse risk—and stable risk factors—such as living with smokers and higher baseline carbon-monoxide levels or depressive symptoms—remain potent predictors of progression to relapse. Real-time contextual risk assessments post-quit predict lapse above and beyond stable, baseline risk factors.


*Summary:* This paper expands the current understanding of tobacco withdrawal by examining: 1) withdrawal variability; 2) underlying causes of withdrawal variability; 3) new withdrawal symptoms that allow for enhanced characterization of the withdrawal experience; and 4) withdrawal-related cognitive processes. These topics provide guidance regarding the optimal assessment of withdrawal and illustrate the potential impact modern withdrawal conceptualization and assessment could have on identifying treatment targets.


*Summary:* Preparation counseling and the combination of intensive in-person quit-smoking counseling with preparation nicotine gum or patch were promising intervention components and combinations for smoking cessation. These should be evaluated as an integrated treatment package.


*Summary:* 26 weeks of nicotine patch + nicotine gum (versus 8 weeks), and maintenance counseling provided by phone, are promising intervention components for the “Cessation Phase” and “Maintenance Phase” of quit-smoking treatment.


*Summary:* Implementation of a brief tobacco-treatment referral system within an existing EHR increased cessation counseling on a vascular-surgery unit. One potential limitation of the study was the modest sample size. Not being able to make quit-smoking treatment a mandatory component in discharge orders may also have contributed to the modest effect.

**Summary**: The research needs identified by the workshop participants included the following: Standards to measure the contents and emissions of e-cigarettes; biomarkers of exposure; physiological effects of e-cigarettes on tissues and organ systems, including pulmonary and cardiovascular; information on e-cigarette users, how the devices are used, and identification of the best tools to assess these measures; factors that drive use and influence patterns of use; and appropriate methods for evaluating a potential role for e-cigarettes in smoking or nicotine cessation.

**In Press**


Baker TB, Piper ME, Stein JH, Smith SS, Bolt DM, Fraser DL, Fiore MC. The Effects of the Nicotine Patch vs. Varenicline vs. Combination Nicotine Replacement Therapy on Smoking Cessation at 26 Weeks: A Randomized Controlled Trial. *JAMA*.


Fiore MC, Jorenby DE, Baker TB. Don’t Wait for COPD to Treat Tobacco Use and Dependence. *Chest*.


**Posters and Presentations**


Christiansen B. Reaching, Motivating, and Treating Low SES Smokers Webinar for the Central East Addiction Technology Transfer Center. Presentation. Silver Spring, Maryland. August 2015.


Piper ME. The Electronic Medical Record in Tobacco Dependence Treatment. Mayo Clinic Nicotine Dependence Conference. April 2015.


Piper ME. Electronic Cigarettes: What We Know and What We Need to Know About This Emerging Tobacco Product. Marshfield Clinic Grand Rounds. Marshfield, Wisconsin. September 2015.


New Studies

R35 Outstanding Investigator Award (OIA). The National Cancer Institute (NCI) has selected UW-CTRI Director Dr. Michael Fiore as an inaugural recipient of a 7-year R35 OIA, which supports investigators with excellent records of productivity in cancer research. The OIA allows funded investigators the flexibility to embark on long-term, transformative projects of unusual potential in cancer research; the opportunity to take greater risks and be more adventurous in their lines of inquiry; and sufficient time to develop new techniques. Thanks to this R35 award, Dr. Fiore will lead a partnership between UW-CTRI, Epic, and several Wisconsin health systems to use the latest innovations, including electronic health records, to help patients who smoke to successfully quit and avoid cancer. August 2015-July 2022, $6.1 Million. Funded by NCI of the National Institutes of Health. Dr. Michael Fiore, PI.

Exhale Study. (Status: Recruiting and seeing patients) As the federal government considers how to regulate electronic cigarettes (e-cigs), the University of Wisconsin has been awarded a $3.7 million, 5-year R01 grant from National Cancer Institute (NCI) and FDA to study them over the next five years. This research will provide in-
depth, longitudinal information, based on real-time reports, which will address key priorities that may inform regulatory and health concerns, including understanding the relations between vaping and nicotine dependence; changes in rates of smoking conventional cigarettes; health outcomes such as evidence of exposure to carcinogens, as well as acute and long-term pulmonary health; attempts to quit smoking and the success of those attempts. Specifically, researchers will identify and follow over time 150 participants who exclusively smoke cigarettes and 250 participants who both smoke and vape. Researchers will use smart phones and other tools to collect information on patterns of use of these products, levels of addiction, withdrawal symptoms, success quitting versus relapse, lifestyle factors, carcinogen exposure, and how one group of participants compares to the other over time. This research will provide essential information to inform regulatory bodies, as well as researchers, clinicians, and tobacco users, about the patterns of real-world e-cig use and how such use is related to conventional smoking and the health risks caused by it. March 2015–February 2020, $3.7 million. Funded by NCI of NIH, and FDA. Dr. Megan Piper and Dr. Douglas Jorenby, PIs.

Active Studies

Breaking Addiction to Tobacco for Health (BREATHE). (Status: Recruiting and seeing patients) UW-CTRI has received a $12 million 5-year P01 Center grant from NCI of NIH. The grant will fund research designed to test new phased-based treatments to help patients in the Milwaukee and Madison areas quit smoking. Partners in this research include colleagues from Penn State University and the University of Illinois-Chicago, as well as Aurora Health Care, Dean Health System, and Epic. Under the BREATHE project, any smoker who visits a participating clinic, regardless of the initial reason for the visit, is invited to get treatment through BREATHE. This study implements both an EHR system that increases smokers’ recruitment into treatment as well as a highly effective chronic-care treatment with intervention components for all smokers. First, the EHR system will be implemented in 18 clinics in 2 health-care systems and experimentally evaluated on its ability to increase the recruitment of smokers into chronic-care treatment (Project 1). Then, using highly efficient research methods, researchers will experimentally compare multiple intervention components and identify especially effective interventions for every phase of smoking treatment. This package of components will: increase quitting motivation amongst smokers initially unwilling to quit and prepare them for cessation (Project 2), enhance quitting success and prevent relapse when smokers are ready to quit (Project 3), and re-engage relapsed smokers in treatment and restore their abstinence (Project 4). Our highly integrated research projects will thus implement a powerful new EHR strategy to efficiently recruit primary-care patients who smoke into chronic-care treatment. BREATHE researchers will combine data from all projects and produce an optimized comprehensive chronic-care treatment for smoking that can be readily implemented in primary-care settings by project end. Thus, this research will simultaneously advance both smoking treatment and treatment research methods. June 2014-July 2019, $12 million. Funded by NCI. Dr. Michael Fiore and Dr. Tim Baker, PIs.

PTSD and Veterans Merit Award. (Status: Recruiting and seeing patients) UW-CTRI Researcher Dr. Jessica Cook has reached a major career milestone, receiving a Merit Award from the VA. The primary objective of her research is to produce an empirically validated treatment that increases smoking cessation in veterans with posttraumatic stress disorder (PTSD), one that can be easily integrated into smoking cessation clinics and/or mental health clinics within VA facilities. PTSD is highly prevalent in the VA patient population and is associated with a rate of smoking (53% - 66%) that far exceeds that of VA enrollees in general (22%). PTSD is also associated with unusually high rates of smoking-cessation-treatment failure. The disparity in smoking cessation outcomes amongst veterans with PTSD may occur because standard smoking cessation treatment does not address PTSD-specific
vulnerabilities. Veterans with smoking-PTSD comorbidity may respond better to treatment that addresses their PTSD and associated affective symptoms, because such symptoms can both reinforce smoking and undermine quit attempts. Recent evidence shows that behavioral activation therapy (BA), a behavioral treatment that increases engagement in reinforcing activities, significantly reduces PTSD symptoms. BA may improve smoking cessation outcomes amongst veterans with PTSD because it reduces overall PTSD symptom severity and affective distress (low positive affect, high negative affect), which can cause smoking relapse. The funded research will determine whether BA, as an adjunct to standard smoking cessation treatment, (ST+BA) is superior to a comparably intense combination of standard smoking cessation treatment + health and smoking education (ST+HSE) in improving smoking cessation outcomes among veterans with PTSD. The HSE intervention is intended to constitute a credible intervention that controls for contact time. Secondary objectives are to determine if BA improves PTSD symptomatology and associated affective distress, and to identify potential mediators of BA on smoking outcomes. A total of 120 veterans with PTSD who are motivated to quit smoking will attend an initial diagnostic and baseline assessment session. Those who are interested, eligible, and who provide consent will be randomly assigned to receive ST+BA or ST+HSE and will be contacted by their individual study therapist to schedule the first treatment session. Participants will be stratified into treatment groups based on: 1) Major depressive disorder (MDD: present versus absent), and 2) PTSD symptom severity. All participants will receive eight individual sessions of ST+BA or ST+HSE. All participants will receive 20 minutes of identical standard smoking cessation treatment in each of the eight sessions. Those in the ST+BA condition will receive an additional 30 minutes of behavioral activation therapy; those in the ST+HSE condition will receive an additional 30 minutes of health education and information about smoking. All participants will receive 8 weeks of the nicotine patch. Smoking cessation outcomes will be assessed 2, 4, 8, 16, and 26 weeks after the quit date. This research has important clinical and public health significance because smoking is especially common among veterans with PTSD, and it is the leading preventable cause of disease and disability. Reducing smoking rates among veterans with PTSD would result in substantially lower smoking-related illness and death in this vulnerable group of smokers. It would also reduce tobacco-related health-care costs charged to the VA. The grant will support a researcher and a study counselor. Jan. 2014-Sept. 2019, $770,500. Funded by the VA. Dr. Jessica Cook, PI.

Clinical Relevance of Stress Neuroadaptation in Tobacco Dependence. (Recruiting and seeing patients) The broad goals of this research are to identify the origin of biomarkers related to how the body compensates for the presence of cigarette chemicals so that it can continue to function. Dr. John Curtin of UW Psychology is the principal investigator, while Dr. Megan Piper of UW-CTRI is a co-investigator on this RO1 grant. It examines stress neuroadaptation in the laboratory via startle potentiation during uncertain threats among nicotine-deprived smokers versus non-deprived smokers and non-smokers. Smokers are subsequently assigned to one of three smoking-cessation treatment conditions and reported on episodic stressors, negative feelings, smoking urge, and tobacco consumption in real time from their regular environments via smart phones or other digital devices that prompted them to enter data. Treatment outcomes are assessed at four weeks and end of treatment. Researchers evaluate the impact of this stress neuroadaptation on smokers’ feelings, urge, and tobacco consumption during smoking-cessation treatment. They examine whether first-line pharmacotherapies could dilute the influence of this stress neuroadaptation on smoking-cessation outcomes. August 2012-June 2017, $180,000. Funded by National Institute on Drug Abuse (NIDA) of NIH. Dr. John Curtin, PI. Dr. Tim Baker and Dr. Megan Piper, Co-I’s.

Genetically Informed Smoking Cessation Trial. (Status: Recruiting patients) This randomized clinical trial is the first genetic study to look at nicotine replacement therapy (NRT) vs. varenicline head-to-head, and how participants with different genetics respond to the medications. Led by Li-Shiun Chen with collaboration from UW-CTRI Research Director Dr. Tim Baker and UW-CTRI Director of Clinical Services Dr. Doug Jorenby, the researchers
hope to determine whether genetic markers can be used to optimize smoking cessation pharmacotherapy to enhance efficacy, medication adherence, and reduce side effects. The researchers’ recent work, which suggests that the nicotinic receptor gene CHRNA5 alters the response to NRT, has been replicated in a meta-analysis. New preliminary data suggest that CHRNA5 may be a useful marker for medication choice, because patients with CHRNA5 variant rs16969968 AA/GA genotypes may benefit from NRT and those with GG genotypes (conferring poor response to NRT) may benefit from varenicline, a medication with higher cost and use restrictions. Similarly, other genetic variation such as the nicotine metabolism gene CYP2A6 also alters response to NRT. Currently, there is insufficient evidence to support the clinical use of genotype-based smoking-cessation treatment, because these findings are based on retrospective pharmacogenetic analyses of different trials with markedly different placebo and counseling effect sizes and dissimilar designs. For clinical translation, we need head to head comparison of state-of-the-art interventions, use of key genotypes implicated by current research, and valid assessments of side effects and adherence. This study of 720 smokers uses a stratified randomization trial design based on a subject’s pertinent genotype for smoking cessation. Specifically, in Aim 1, researchers will determine if CHRNA5 genotype moderates the effect of medication (combination NRT, varenicline, vs. placebo) on abstinence. In Aim 2, researchers will determine if CHRNA5 genotype predicts medication adherence and side effects. In Aim 3, researchers will incorporate multiple genotypes and other predictors in order to develop a clinical treatment assignment algorithm for cessation success. This work could result in improved physician care of patients who smoke, overall smoking cessation success, and prevention of cancer, heart, and lung disease. Sept. 2014-July 2019, $90,000. Funded by NIH. Li-Shiun Chen, PI. Douglas Jorenby, co-PI.

Can Smartphone Games Help Smokers Quit? (Status: Recruiting patients) Most smokers who try to quit do not succeed. Even if they use evidence-based treatment, only approximately 10% to 30% achieve long-term abstinence. It is known that strong craving for cigarettes is a powerful reason many smokers fail in their quit attempts. Unfortunately, medication and cessation counseling are only modestly successful in quelling craving. The objective of the proposed research is to determine whether smartphone games can help smokers distract themselves, suppress their cravings, and increase their chances of quitting. Dr. Schlam will use the findings from this research as pilot data in a grant application for a NIH K23 Career Development Award. Sept. 2013-June 2016. The $20,000 grant from a UW-CTRI Developmental Pilot Grant was part of UW-CTRI’s NIH P50 Center Grant. The $6,000 grant is from a UW Department of Family Medicine Small Grant. Dr. Tanya Schlam, PI.

Wisconsin Smokers Health Study 2 (WSHS 2). (Status: Recruitment complete, still seeing patients) UW-CTRI was awarded a $10-million 5-year National Heart, Lung, and Blood Institute (NHLBI) R01 grant to discover the best ways to help Wisconsin residents stop smoking. The new study essentially extends the Wisconsin Smokers’ Health Study and is known as WSHS 2. It includes potentially life-saving tests—including artery scans that can signal impending risk of a stroke or heart attack—free of charge. Participants get free coaching and medications to help them quit smoking. Drs. Mike Fiore, Tim Baker, and James Stein (of UW Preventive Cardiology) are the lead researchers for this grant. The original Smoker’s Health Study (WSHS), launched in 2004, revealed how quitting smoking affects nearly every part of a person’s health, lifestyle, and well-being. Many patients from WSHS are continuing participation in WSHS 2, and their participation will culminate in health data spanning 10 years. The media announcement of WSHS 2 garnered 2,500 volunteers. The Center recruited smokers as new study participants for WSHS 2. In addition, everyone from the previous study—whether now smoking or not—was invited to continue their participation. In total, 1,500 individuals will participate in WSHS 2. Each participant gets assistance from a personal quit coach—something many former smokers say is essential because they felt that giving up cigarettes was like “losing my best friend.” The quit coach is a familiar face who ensures that the patient doesn’t feel like s/he is going through the process alone. All participants will be compensated for time and travel. Each
individual participant receives test results, such as cholesterol levels, artery scans, blood counts, and diabetes tests. These results could signal imminent trouble and save lives. The study employs medical tests—such as carotid artery ultrasound scans and arterial tonometry—to determine how quitting smoking improves health over time, and how continuing to smoke harms health. These tests concentrate on cardiovascular disease, but will also target conditions such as lung disease and diabetes mellitus. While it is well known that smoking is very dangerous, we know less about how quitting (versus continued smoking) affects health. Every participant gets state-of-the-art active medication: 1) varenicline or 2) nicotine patch + nicotine lozenge or 3) just nicotine patch. The first two medication treatments listed above have offered the highest quit rates of all quit-smoking medications. However, these two treatments have never been compared head-to-head. “We’ll not only determine which works better,” Dr. Baker said, “but also whether one approach works better with some types of smokers than does the other.” At the end of this study, the researchers hope to enhance knowledge of how to treat smoking optimally, as well as how quitting smoking helps participants to reduce their risk of heart disease, stroke, and cancer, and the mechanisms by which these health benefits occur. Sept. 2011-Nov. 2016, $10 million. Funded by NHLBI. Dr. Tim Baker, Dr. Michael Fiore, Dr. Jim Stein, PIs.

State Medicaid Grant: Striving to Quit. (Status: Data under analysis for dissemination) Wisconsin received a five-year, $9.2 million grant from the federal CMS to help Medicaid recipients quit smoking. The project, called Striving to Quit, is designed to test the effects of incentives on engagement in smoking cessation treatment and quitting behavior among adult BadgerCare (Medicaid) members who smoke. It includes two distinct evidence-based approaches to smoking cessation. The first focuses on linking adult BadgerCare Plus members to the Wisconsin Tobacco Quit Line (WTQL) where participants receive up to five proactive coaching calls (plus additional calls initiated by the participant). The second focuses on linking adult BadgerCare Plus members who are pregnant with intensive cessation counseling and support via First Breath (FB), a smoking cessation program of the Wisconsin Women’s Health Foundation (WWHF), and additional postpartum services. Postpartum services include four home visits and five support phone calls up to 6 months after delivery. In each of the focus areas, WTQL and FB, half of the enrolled members will receive financial incentives for participating in counseling services and for quitting. The WTQL component of Striving to Quit will serve up to 2,000 members who smoke. Members can enroll via WTQL referral from participating clinics in South Central and Northeastern Wisconsin. Additionally, members who reside in participant counties (Dane, Milwaukee, Racine, Kenosha, Brown, Winnebago, Portage, Marathon, Oneida, Vilas, Oconto, Forest, Fond du Lac and La Crosse) can also call the WTQL to enroll. FB will enroll 1,250 pregnant members who smoke and live in 17 counties throughout the state. This grant offers a tremendous opportunity to improve the health of thousands of Wisconsin residents with low incomes and discover whether financial incentives increase rates of smoking cessation among BadgerCare Plus members. Sept. 2011-Sept. 2016, $9.2 million. Funded by CMS in a grant to DHS. Dr. Tim Baker, PI.

Integrating Genetics, Adverse Events, and Adherence to Improve Smoking Cessation. (Status: Data under analysis for dissemination) Using data from the Wisconsin Smokers’ Health Study, the goal of this project is to identify genetic associations to adverse events arising from pharmacological treatments for smoking cessation and examine how genetics, adverse events, and medication adherence jointly impact the efficacy of pharmacological treatments for smoking cessation. The results could lead to individually tailored treatments that decrease adverse events and increase successful cessation. April 2015-March 2017, $34,000. Funded by NIH. Dr. Robert Culverhouse, PI. Dr. Megan Piper, co-I.
Recently Completed Studies

Advancing Tobacco Research by Integrating Systems Science and Mixture Models. This project advanced knowledge of how different smoking-cessation treatments worked, for whom, and when. Dr. Stephanie Lanza of Penn State was the lead investigator and Dr. Megan Piper, UW-CTRI associate director of research, was a co-investigator on this R01 grant from the National Cancer Institute. Researchers from The Methodology Center at Penn State integrated time-varying effect models and latent class analysis in order to identify subgroups of smokers who experienced the process of nicotine withdrawal differently. Latent class analysis allowed researchers to gauge the impact of exposure to patterns of multiple risks, as well as the antecedents and consequences of complex behaviors, so that interventions could be tailored to target the subgroups that will benefit most. Results from the project informed the construction of interventions that (1) are tailored to the individual and that (2) adapt to participant response over time. Importantly, the overall impact of this project extended far beyond the proposed analysis; the project’s full potential for accelerating the pace of smoking-cessation research was realized as a result of programmatic dissemination efforts of important new analytic methods to tobacco researchers. Sept. 2013-Aug 2015, $63,000. Funded by NCI. Dr. Stephanie Lanza, PI. Dr. Megan Piper, co-I.

Primary Care Research Fellowship. Dr. Schlum was a Primary Care Research Fellow, supported by a National Research Service Award (T32 Postdoctoral Training Grant) from the Health Resources and Services Administration to the University of Wisconsin Department of Family Medicine. July 2012-June 2015. Funded by the Health Resources and Services Administration. Dr. Bruce Barrett, PI.

Veterans and Smoking Studies. Dr. Jessica Cook led this study at the William S. Middleton Memorial VA Hospital in Madison. The study tested the hypothesis that smokers with posttraumatic stress disorder (PTSD) and depression smoked cigarettes to improve aversive mood states and other mental health symptoms. The effect Dr. Cook was most interested in was whether smoking regulates anhedonia, a common feature of both PTSD and depression characterized by an inability to respond to pleasurable events. The first part of the study examined how nicotine influenced mood responses to positive and negative stimuli. The second part of the study was done at a critical point, 24 and 48 hours after being deprived of nicotine, which can be the peak of withdrawal. The team explored whether veterans with PTSD and depression had a more difficult time experiencing pleasure in response to rewarding events and whether they experienced more withdrawal-related negative affect. 2007-2014, $640,000. Funded by NIDA. Dr. Jessica Cook, PI.

Tobacco Interventions Delivered by Community Agencies to Those Living in Poverty. UW-CTRI received a $332,000 NIH grant to train staff at four Salvation Army centers (in Green Bay, Appleton, La Crosse and Wausau) to provide a brief intervention with clients who smoked. UW-CTRI Researcher Dr. Bruce Christiansen led this project, which sprouted from pilot data collected via an ICTR grant awarded to Dr. Christiansen. More than 37 million Americans live in poverty, and they smoke at twice the rate of other Americans. As a result, they bear a disproportionate burden from tobacco-related diseases. Research also shows many people who are homeless or very poor have either mental-health or substance-abuse issues. Both of these groups tend to smoke at high rates and struggle to make quit attempts using evidence-based methods. This grant tested a brief intervention that challenged smokers’ beliefs that discouraged quit attempts. These beliefs included:

1) Smoking is both normal and acceptable.
2) Willpower is sufficient to quit, rendering outside help unnecessary and irrelevant.
3) Evidenced-based treatments are not more effective than other methods.
4) Stop-smoking medicines are ineffective, dangerous, addictive and/or too expensive.
5) Help in quitting is not available, hard to access and/or too expensive.

The goal of the intervention was to correct these misconceptions so they would consider quitting smoking. As a control, researchers randomized another 140 clients into a 15-minute intervention wherein a Salvation Army counselor read them a booklet on smoking and health, but without any behavioral or motivational interviewing. Another control group, consisting of 140 clients, received a booklet to peruse by themselves. All three groups were compared with 100 participants who were already set to quit smoking. Researchers made follow-up phone calls after three months. September 2011-September 2014, $332,000. Funded by NCI. Dr. Bruce Christiansen, PI.

UW Partnership to Assist and Serve Smokers (UW-PASS). A $9 million P-50 grant from the National Cancer Institute provided five years of funding for UW-CTRI to study various quit-smoking treatments in primary-care clinics throughout Wisconsin. In this study, led by Dr. Michael Fiore and Dr. Tim Baker, UW-CTRI delivered seamless, cutting-edge treatments for all smokers, including those who were ready to quit and those who weren’t. Beginning in the summer of 2010, UW-CTRI offered participation to patients who smoked and visited select primary-care clinics within two health-care systems—Dean Health System and Aurora Health Care. Medical assistants at partnering clinics identified smokers and asked if they were interested in being contacted about a study. They invited all smokers whether they were willing to quit or not. If the patient was interested, an e-mail was generated from the electronic medical record to UW-PASS staff, employed by UW-CTRI, who conducted screening, orientation, patient visits and follow up. The electronic medical records were supported by Epic Systems Corp. and Cerner. All participants have completed treatment. UW-PASS included three projects:

**Project 1** focused on increasing the smoker’s motivation to quit. This project offered treatment strategies for smokers who weren’t ready to quit now but were willing to participate in treatment to help them get ready to quit. The hope was to increase their motivation to quit smoking as well as to make actual quit attempts. Treatments included behavioral coaching, motivational interviewing, nicotine patches, and nicotine gum.

**Project 2** examined whether use of nicotine-replacement medication and behavioral coaching—before actually quitting smoking—helped the patient remain smoke-free. Typically, those who use nicotine-replacement medications (such as the nicotine patch or lozenge) quit smoking first, then use medications to stave off cravings and remain smoke free. Project 2 also tested coaching types and lengths, including in-person coaching vs. telephone coaching.

**Project 3** studied ways to increase the number of patients who take quit-smoking medication at the proper dosage for the prescribed duration. Most smokers don’t use enough medication or use it the right way. The goal was to see what happened when a patient took medication as prescribed vs. skipping doses or ceasing treatment prematurely. Adherence treatments included automated-adherence phone prompts, electronic monitoring/feedback and a cognitive-adherence intervention. Project 3 also examined the outcomes of long-term coaching and medication.

September 2009-August 2014, $9 million. NCI P-50 grant. Dr. Tim Baker and Dr. Michael Fiore, PIs.
Dual Use of E-Cigarettes and Traditional Cigarettes in Primary Care and Community Settings. The National Institutes of Health awarded UW-CTRI a $1.8 million supplement to its NCI-funded center grant. With this supplement, researchers investigated questions of importance to the FDA in its role of regulating tobacco products:

- How dual use of tobacco products (both smoking cigarettes and vaping e-cigarettes) is related to outcomes of public health importance, such as cessation attempts and success.

- Mechanisms by which dual use affects such outcomes, for instance showing how dual use affects cigarette withdrawal symptoms, smoking reward, and cigarette dependence.

In the NCI Center Grant Primary Care study, UW-CTRI researchers added new measures and analyses to the parent study to see how dual use may (or may not) affect the user’s dependence on cigarettes, withdrawal severity, perception of harm, treatment engagement, and smoking outcomes (smoking reduction and cessation). Participants in the parent grant were recruited through primary-care visits. Dr. Tanya Schlam led this primary care component.

In the Community Sample sub-study, researchers used measures and analyses that elucidated the mechanisms responsible for the associations observed in the Primary Care sub-study. Dr. Doug Jorenby led this community sample component, which recruited 150 daily smokers via advertisements (e.g., convenience stores, TV, social media) throughout the Milwaukee and Madison areas, half of whom also used e-cigarettes.

These participants generated real-time data (using an innovative smartphone app) to determine how dual users and exclusive smokers compared on hedonic ratings of cigarettes, cigarette use, daytime tobacco use, mood, suppression of cigarette withdrawal, contexts of use, and exposure. Moreover, data from dual users revealed how recent use of other tobacco products (OTP) affected cigarette use and reward, especially during periods of reduced cigarette intake. Researchers used the data to compare risk profiles and determine how to improve cessation. September 2012-August 2014, $1.8 million. Funded by NIH and FDA. Dr. Tim Baker and Dr. Michael Fiore, PIs.
UW-CTRI Financial Statistics

2015 Funding Sources
Total=$8.6 million

- Federal (79%)
- State (11%)
- UW (8%)
- Nonprofit/Other (2%)

Funding Sources Since Inception (1992)
Total=$120 million

- Funding Brought Into WI (79%)
- Wisconsin Funding (21%)

UW-CTRI Funding by Year

Note: Quitline funding was increased by $4 million one time only in 2008

Additional UW-CTRI financial information is available year-round at http://www.ctri.wisc.edu/funding.html