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 for calendar year 2016. Archived reports are available online at: http://www.ctri.wisc.edu/researchers-uw-ctri-research-reports.htm

Summary

In 2016, the UW-CTRI research team produced:

- 24 published papers (p. 1)
- 8 papers in press (p. 7)
- 38 presentations and posters (p. 7)
- 2 new studies (p. 10)
- 9 active studies (p. 12)
- 4 studies recently completed (p. 16)

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 Family Medicine, UW Institute for Clinical and Translational Research (UW-ICTR), UW Department of Medicine, UW School of Medicine and Public Health, Veterans Affairs (VA), Wisconsin Department of Health Services (DHS), and the Wisconsin Partnership Program.

Published Papers

Note: Names in bold are current UW-CTRI staff and faculty.

Summary: Fifteen clinics responded to the survey and 11 agreed to onsite academic detailing. Most clinics reported that they identify tobacco users, but fewer advised smokers to quit or provided evidence-based tobacco cessation treatments. Less than half of Wisconsin cancer clinics consistently seize the oncology visit to address tobacco use, and the majority of cancer clinics are receptive to onsite academic detailing to increase the frequency and effectiveness of their tobacco cessation interventions.


Summary: Research shows three medications combined with coaching to quit smoking—a pill called varenicline (Chantix), the nicotine patch alone, and a combination of nicotine-replacement medications—helped about the same percentage of participants to quit smoking. The research showed that about 1 out of 4 of the WSHE 2 patients had quit smoking 6 months after the quit date. Other studies have found that the average quit rate for those who try to quit without coaching or medication is only about 1 out of 20.


Summary: Only 24 percent of women Veteran smokers were referred to the tobacco cessation clinic at the Veterans Hospital, and these smokers tended to be older, heavier smokers who were in need of more services. Of that subset, just 54 percent of referred women actually enrolled in treatment, and again these patients tended to have more medical needs. The women Veterans who were referred were a much different subset than those who were not. More research is needed on why there is a discrepancy.


Summary: Prior smoking, higher distress, and recent alcohol use predicted smoking versus resisting temptation, and momentary impulsiveness was related to smoking for individuals with higher baseline impulsiveness. The risk factors, and combinations of those factors, associated with temptations and smoking lapses differ, suggesting a need for separate models of temptation and lapse.


Summary: In an examination of negative emotions related to quitting smoking, researchers found evidence supporting a 2-factor model with correlated but distinct agitation and distress factors. The agitation factor was indicated by these items: impatient, tense/anxious, restless. The distress factor was indicated by these items: sad/depressed, upset, distressed. The 2-factor model held true across 3 separate cessation phases: prequit, postquit with recent smoking, and postquit without recent smoking.

Summary: A common fear of many smokers who want to quit is that they will lose many people in their social network—family, friends or co-workers—when they quit smoking. In fact, the opposite is true. Smokers who quit were more likely to transition to larger social networks, especially amongst participants who had the highest levels of exposure to other smokers before quitting. In other words, quitting was associated with an increase in the number of people, especially non-smokers, in people’s social circles.


Summary: This paper demonstrates that quitting smoking is highly beneficial in reducing lung cancer risks for smokers regardless of their CHRNA5 rs16969968 genetic risk status. Smokers with high-risk CHRNA5 genotypes, on average, can largely eliminate their elevated genetic risk for lung cancer by quitting smoking—cutting their risk of lung cancer in half and delaying its onset by 7 years for those who develop it. These results suggest that the CHRNA5 rs16969968 genotype affects lung cancer diagnosis through its effects on smoking, and have potential value for framing preventive interventions for those who smoke.


Summary: A 65-item Internet survey measuring integration of tobacco treatment into behavioral health care garnered a response rate of 27.1%. Programs, on average, were 40% integrated. A significant proportion of programs (20%) were less than 20% integrated. A few programs (4.3%) exceeded 80% integration. Integration of tobacco policies and treatment into the behavioral-health-care delivery system remains limited and there is a need for ongoing education, technical assistance and training.


Summary: Since President Barack Obama took office in 2009, the U.S. age-adjusted prevalence of adult cigarette smoking has fallen markedly—from 20.6% in 2009 to 15.3% today. That’s a decrease of about 0.78 percentage points per year, more than double the annual rates of decline during the George W. Bush (.36 percentage points per year) and Bill Clinton (.28 percentage points per year) administrations. At the pace set during the Obama era, adult smoking in the US would end in about 20 years.


Summary: In this editorial, the authors discuss their optimism that more hospital staff will seize the opportunity to help inpatients quit tobacco use. Approximately 20% of 3,705 hospitals are now reporting their performance on the tobacco cessation measure set, according to The Joint Commission. A binding rule that incentivizes compliance would likely dramatically improve the percentage of inpatients who get help to
quit smoking. A new measure set and the Affordable Care Act guidance to insurers to cover tobacco-use
counseling and medications offer hope more hospitals will treat tobacco dependence.

149(3):617-8.

Summary: Patients with COPD tend to be offered help to quit tobacco use at higher rates than other
patients. This editorial calls on clinicians not to wait until COPD to treat tobacco use.

Hendricks PS, Hall SM, Tyus LR, Thorne CB, Lappan SN, McMurray MV, Bailey WC, Cropsey KL, Baker TB.
Withdrawal Exposure and Withdrawal Regulation Training for Smoking Cessation: A Randomized Controlled Pilot

Summary: Smokers were randomized to one of two conditions: 1) Withdrawal Exposure with Withdrawal
Regulation Training (WT) over four separate sessions; or 2) Relaxation Control (RC) training, which
controlled for the therapeutic contact of WT. All sessions occurred before the quit date. Twenty-two percent
of participants in the WT condition were abstinent at both time points, whereas 0% and 4.2% of
participants in the RC condition were abstinent at Months 2 and 3. This suggests WT promotes abstinence
by enhancing withdrawal regulation.

Success in Real World Use: A Comparison of Cigarette Smokers and Dual Users of Both Cigarettes and E-

Summary: Among a group of experienced dual users, e-cigarettes helped maintain smoking reduction and
reduced some withdrawal symptoms, although both withdrawal symptoms and nicotine levels varied as a
function of gender. Compared to those who only smoked cigarettes, dual users of cigarettes and e-cigarettes
did not smoke significantly fewer cigarettes during either periods of ab lib use or during periods of smoking
restriction, nor did they produce lower CO levels. Thus, this research yielded a mixed pattern of how
effective e-cigarettes might be at displacing cigarette use.

King CC, Piper ME, Gepner AD, Fiore MC, Baker TB, Stein JH. The Longitudinal Impact of Smoking and
Smoking Cessation on Inflammatory Markers of Cardiovascular Disease Risk. Arteriosclerosis, Thrombosis, and

Summary: Researchers collected blood and urine samples and examined them for signs of inflammation,
which is the body’s way of protecting itself. Inflammation affects not only how quickly injuries heal but also
how healthy one’s heart and arteries are. The more inflammation a patient has, the harder it is on that
patient’s heart. Researchers found that certain inflammation markers, such as the number of white blood
cells, worsened the more people smoked. When people quit smoking, the number of white blood cells was
much lower. This seemed to be one more way quitting can improve cardiovascular health.

Krug J, O’Halloran A, Rosenthal AC, Babb SD and Fiore MC. Receipt of Evidence-Based Brief Cessation
Interventions by Health Professionals and Use of Cessation Assisted Treatments Among Current Adult Cigarette-
Summary: Among 10,000 smokers, 6% reported use of both counseling and medication for smoking cessation within the past year, medication-only (20%), a class or program (4%); one-on-one counseling (4%); and a telephone quitline (3%). Current cigarette-only smokers who reported receiving all 5 A’s during a recent clinic visit were more likely to use counseling, medication, or a combination of counseling and medication compared to smokers who received one or none of the 5 A’s components.


Summary: A cognitive interview study was conducted with 30 cancer patients at the NIH Clinical Center to evaluate and improve tobacco measurement. The resulting Cancer Patient Tobacco Use Questionnaire (C-TUQ) includes cigarette and other tobacco use status, intensity, and past use; use relative to cancer diagnosis and treatment; cessation approaches and history; and secondhand smoke exposure. The Task Force recommends that assessment occur at study entry and, at a minimum, at the end of protocol therapy in clinical trials. Broad adoption is recommended.


Summary: Adult daily smokers were randomly assigned to standard treatment with nicotine patch and individual counseling or to standard treatment plus “practice quitting.” Treatment manipulation increased the interval between cigarettes across practice quitting sessions on average by 400%. The primary endpoint, seven-day point-prevalence abstinence at four weeks post-quit, was not significantly affected by practice quitting (31.9% in the standard treatment condition, 37.0% in the practice quitting condition). Practice quitting increased latency to a first lapse and prevented progression from a first lapse to relapse.


Summary: Baseline behavioral measures of impulsive choice and impulsive action were used as predictors of smoking cessation success over 12 weeks. Facets of impulsiveness appear to function largely independently in adult smokers, as indicated by their lack of intercorrelation, differential stability, and differential relations with abstinence. Impulsive action may impede initial quitting, whereas impulsive choice may be an obstacle to maintaining lasting abstinence.


Summary: In this analysis, 3-month point-prevalence abstinence rates varied among the latent classes, with 38-55% abstinent among early quitters, 3-20% abstinent among those who smoked intermittently
throughout the first 27 days, and fewer than 5% abstinent in the classes marked by little or delayed change in smoking. High-dose nicotine patch and bupropion promoted abstinence.


*Summary:* Combination nicotine-replacement therapy (NRT), which includes a pairing of patches with gum or lozenges, reduced the number of participants classified in the group who experienced especially low pleasure, illustrating the importance of NRT to mitigate relapse risks. This was especially important because the group with high cravings and low pleasure levels had the lowest abstinence rates at 8 weeks and 6 months, as well as the fewest days until they relapsed.


*Summary:* Across comorbid conditions, smoking adversely affects treatment efficacy and promotes other adverse health conditions. People with comorbid conditions who smoke are motivated to quit and respond to evidence-based smoking cessation treatments. However, tobacco cessation is not regularly incorporated into the clinical care of many individuals with comorbidities. Further work is needed to disseminate evidence-based care into clinical practice for smokers with comorbid disease and addiction. Research should consider comorbid conditions as an important construct to explore.


*Summary:* This pilot examined the feasibility and acceptability of a tobacco-cessation intervention compared with usual care in inpatients. No subjects utilized free tobacco cessation services after discharge. After discharge, abstinence rates were 17% for the intervention group and 7% for the control group. Secondary outcomes with regard to infections showed that, at discharge, 12% of the intervention group (n=17) and 18% of the control group (n=22) tested positive for Staphylococcus aureus.


*Summary:* In this paper on research strategy, the authors discuss plans to study treatment strategies for smokers with panic attacks. Building upon emerging evidence supporting the efficacy of d-cycloserine (DCS) for augmenting exposure-based therapy, the authors are conducting an initial test of the efficacy of DCS for enhancing Panic and Smoking Reduction Treatment (PSRT) outcomes. Utilizing a randomized, double-blind trial comparing PSRT+DCS to PSRT+placebo, they’ll obtain short- and long-term smoking cessation outcomes and test mechanisms.

*Summary:* Smoke-free home rules are associated with lower current use of alternative tobacco products (ATP) such as smokeless tobacco products, regular and water pipes, and cigars. Future research should examine whether promoting smoke-free home rules could help to reduce ATP use and related diseases.

**In Press**


**Research Presentations and Posters**


Fiore MC. Health System Changes to Promote Tobacco Dependence Treatment. ClearWay Strategic Planning Committee Retreat. Bloomington, MN. October 2016.


Fiore MC, Skora A, Adsit R. Systems Integration of Evidence-Based Tobacco-Cessation-Treatment Interventions UW Health Primary Care Leadership Committee Meeting – Tobacco Integration. Madison, WI. November 2016.


New Studies

Disseminating and Implementing a Smoking Cessation Program for Pregnant and Postpartum Women. First Breath (FB) is a program administered by the Wisconsin Women’s Health Foundation (WWHF) to help pregnant women quit smoking. While FB is successful helping women quit during pregnancy, it is unable to provide support after a woman delivers. This is very unfortunate because about 85% of women relapse and resume smoking when...
they return home with their new infant. Recently, UW-CTRI partnered with WWHF on a new program, Striving to Quit (STQ), to address this gap in FB by extending the program to help the new mother stay quit after she returns home with her baby. STQ was conducted as a rigorous research study. Unknown is whether STQ will produce similarly positive outcomes when disseminated and implemented in more real-world contexts. This grant is designed to address these issues. Specifically, it will:

1. Evaluate STQ in more real-world settings.
2. See if STQ produces better outcomes than FB.
3. Identify barriers to expanding STQ throughout Wisconsin so more pregnant women who smoke can benefit.

WWHF and UW-CTRI will continue their productive partnership for this project. In addition, four key stakeholder groups will be involved throughout the project:

1. Most importantly, women enrolled in STQ will serve in focus groups that will provide candid guidance and feedback regarding smoking cessation education materials, challenges to maintaining smoke-free homes, perceptions of the intervention, unmet needs, and barriers to staying quit.
2. Discussion groups with current FB Providers will identify key clinical barriers to dissemination. This will be followed by a statewide survey to all FB Providers.
3. Health Educators who will deliver STQ will be observed to ensure that the program is delivered as designed. Results of interviews with these Health Educators will be used to develop statewide training materials.
4. Stakeholders who set state policies and payment structures will form a “Sustainability Planning Committee” because their decisions are key to securing sustained statewide financial support of STQ.

This project aims to have a substantial impact on the greatest preventable cause of poor birth outcomes in Wisconsin. Researchers expect the findings to inform public policies regarding the need to embrace smoking-cessation programs that begin during pregnancy and extend them into the postnatal period. October 2016-March 2018. $150,000. Funded by University of Wisconsin Institute for Clinical and Translational Research (UW-ICTR). Dr. Michael Fiore, PI. Lisette Kablil, WWHF Community Partner Lead.

**Engaging Stakeholders in Integration of Preventive Care and Health Promotion in Rheumatology Clinics.**

This research is part of a collaborative effort to identify interventions to help patients with rheumatoid arthritis and systemic lupus erythematosus to reduce their cardiovascular disease risk. UW-CTRI Associate Director of Research Dr. Megan Piper is part of the team led by Dr. Christie Bartels, which is funded by a Patient-Centered Outcomes Research Award from the UW Institute for Clinical and Translational Research (ICTR). Piper will collaborate to create a patient advisory board and a mixed patient-clinical advisory board. These boards will provide insight into important patient-centered health outcomes and develop a plan for implementing an intervention that can serve diverse, hard to reach patients who have rheumatoid arthritis or lupus. Researchers from the UW and the Medical College of Wisconsin will conduct focus groups with patients, including current and former smokers, to help fill the gap regarding the patient perspective on addressing rheumatoid arthritis and lupus, both in outcomes and care processes. The creation of advisory boards will define the patient centered outcomes, its measures and implementation strategies for a PCORI grant application submission. Funded by UW ICTR. August 2016-July 2018. Dr. Megan Piper, co-investigator.
Active Studies

Transforming the Treatment of Tobacco Use in Health Care: Seizing the Potential of the Electronic Health Record to Deliver Comprehensive Chronic Care Treatment for Smoking. This study, funded by an R35 grant to Dr. Michael Fiore, is designed to overcome barriers to effective treatment of smokers in the primary care setting. One of the major obstacles to smoking cessation is the lack of treatment effectiveness. Researchers believe that this lack of effectiveness is largely due to two factors:

- First, most treatments delivered in the health-care setting are isolated applications of a single type of cessation treatment. Optimal chronic care for tobacco dependence requires multiple types of interventions that collectively target the different phase of quitting, are sustained over time, and are adaptive.
- A second factor contributing to the lack of treatment effectiveness is that translational science is not yet sufficiently powerful so as to make the most effective smoking interventions appropriate for, and effective in, real-world healthcare contexts.

This research is intended to address this deficit by developing and applying innovative, efficient, and powerful research methods to translate efficacious treatments into clinical use. This study will focus on the treatment effectiveness obstacle by piloting a potentially more powerful combination of two of the most effective pharmacotherapies: varenicline plus combination nicotine replacement therapy (NRT) treatment. Data from this pilot study will help inform the design of future studies that would use this combination treatment as a cessation tool within the chronic care arsenal of treatments. August 2015-July 2022. Funded by NCI of NIH. 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 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.

Breaking Addiction to Tobacco for Health (BREATHE). (Status: Recruiting and seeing patients) UW-CTRI has received a $12 million 5-year 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. Michael Fiore and 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. Jessica Cook, PI.

Clinical Relevance of Stress Neuroadaptation in Tobacco Dependence. (Recruiting and seeing patients) The broad goals of this research were 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 was the principal investigator, while Dr. Megan Piper of UW-CTRI was a co-investigator on this RO1 grant. It examined stress neuroadaptation in the laboratory via startle potentiation during uncertain threats among nicotine-deprived smokers versus non-deprived smokers and non-smokers. Smokers were 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 were assessed at four weeks and end of treatment. Researchers evaluated the impact of this stress neuroadaptation on smokers' feelings, urge, and tobacco consumption during smoking-cessation treatment. They examined whether first-line pharmacotherapies could dilute the influence of this stress neuroadaptation on smoking-cessation outcomes. August 1, 2012-June 30, 2017. Funded by National Institute on Drug Abuse (NIDA) of NIH. Dr. John Curtin, PI. Dr. Tim Baker and Dr. Megan Piper, Co-Is.

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 Dr. 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 rs16969668 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.
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. Robert Culverhouse, PI. Megan Piper, co-I.

Primary Care Research Fellowship. Dr. Kristin Berg is 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 and Community Health. July 2015–June 2017. Funded by the Health Resources and Services Administration. Dr. David Rabago, PI.

Wisconsin Smokers Health Study 2 (WSHS 2). (Status: Recruitment complete, year 1 outcome data analyses underway, participants are finishing up Year 3 final visits) UW-CTRI was awarded a $10-million 5-year National Heart, Lung, and Blood Institute (NHLBI) grant to discover the best ways to help Wisconsin residents stop smoking. The new study essentially extended the Wisconsin Smokers’ Health Study and is known as WSHS 2. It included potentially life-saving tests—including artery scans that can signal impending risk of a stroke or heart attack—free of charge. Participants got free coaching and medications to help them quit smoking. Drs. Mike Fiore, Tim Baker, and James Stein (of UW Preventive Cardiology) have been 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 continued 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 got 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 was a familiar face who ensures that the patient doesn’t feel like s/he is going through the process alone. All participants were compensated for time and travel. Each individual participant received test results, such as cholesterol levels, artery scans, blood counts, and diabetes tests. These results could signal imminent trouble and save lives. The study employed medical tests—such as carotid artery ultrasound scans and arterial tonometry—to determine how quitting smoking improved health over time, and how continuing to smoke harmed health. These tests concentrated on cardiovascular disease, but also targeted conditions such as lung disease and diabetes mellitus. While it was well known that smoking is very dangerous, researchers knew less about how quitting (versus continued smoking) affected health. Every participant received state-of-the-art active medication: 1) varenicline or 2) nicotine patch + nicotine lozenge or 3) just nicotine patch. WSHS 2 researchers have found that the three treatment options helped about the same percentage of participants (1 out of 4) to quit smoking 6 months after the quit date. These results were published in the Journal of the American Medical Association (JAMA). 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. 2017, $10 million. Funded by NHLBI. Dr. Tim Baker, Dr. Michael Fiore, Dr. Jim Stein, PIs.
Recently Completed Studies

**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 included two distinct evidence-based approaches to smoking cessation. The first focused on linking adult BadgerCare Plus members to the Wisconsin Tobacco Quit Line (WTQL), where participants received up to five proactive coaching calls (plus additional calls initiated by the participant). The second focused on linking adult BadgerCare Plus members who were 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 included 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 received financial incentives for participating in counseling services and for quitting. The WTQL component of Striving to Quit served up to 2,000 members who smoked. Members enrolled in Striving to Quit via a referral from participating clinics in South Central and Northeastern Wisconsin. Additionally, members who resided in participant counties (Dane, Milwaukee, Racine, Kenosha, Brown, Winnebago, Portage, Marathon, Oneida, Vilas, Oconto, Forest, Fond du Lac and La Crosse) could also call the WTQL to enroll. FB enrolled approximately 1,250 pregnant members who smoked and lived in 17 counties throughout the state. This grant offered 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.*

**Can Smartphone Games Help Smokers Quit?** (Status: Data under analysis for dissemination) 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 research was to determine whether smartphone games can help smokers distract themselves, suppress their cravings, and increase their chances of quitting. 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 was from a *UW Department of Family Medicine Small Grant*. Dr. Tanya Schlam, PI.

**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. Tanya Schlam 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.


**UW-CTRI Financial Statistics**

2016 Funding Sources
Total = $8.7 million

Funding Sources Since Inception (1992)
Total = $129 million

- **Federal (75%)**
- **State (11%)**
- **UW (11%)**
- **Nonprofit/Other (3%)**

- **$26 Million**
- **$103 Million**

**UW-CTRI Funding by Year**

2016 Funding = $8.7 Million

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.htm](http://www.ctri.wisc.edu/funding.htm).