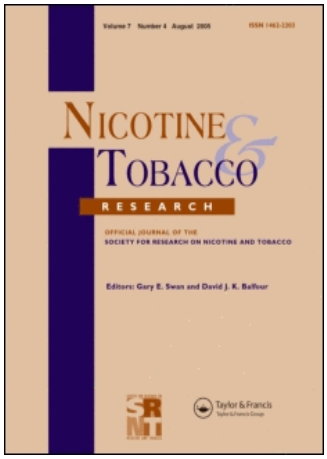

Nicotine & Tobacco Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713439766

International advances in nicotine and tobacco research

Suzanne M. Colby [a]; David J. Drobes [b]; Robert West [c]
[a] Center for Alcohol and Addiction Studies, Brown University,
[b] Departments of Interdisciplinary Oncology and Psychology, H. Lee Moffitt Cancer Center at the University of South Florida,
[c] Health Behavior Unit, Department of Epidemiology, University College London,

Online Publication Date: 01 August 2005
To cite this Article: Colby, Suzanne M., Drobes, David J. and West, Robert (2005) 'International advances in nicotine and tobacco research', Nicotine & Tobacco Research, 7:4, 667 - 709
To link to this article: DOI: 10.1080/14622200500186452
URL: http://dx.doi.org/10.1080/14622200500186452

Nicotine & Tobacco Research Volume 7, Number 4 (August 2005) 667–709

Conference summary and abstracts of selected presentations

International advances in nicotine and tobacco research

11th Annual Meeting
Society for Research on Nicotine and Tobacco
Prague, Czech Republic
20–23 March 2005

Suzanne M. Colby, David J. Drobes, Robert West

The 11th Annual Meeting of the Society for Research on Nicotine and Tobacco was held jointly with the Seventh Annual SRNT European Conference in Prague, Czech Republic, at the Hotel Hilton Prague, 20–23 March 2005. Following a 1-day preconference symposium that highlighted global issues in tobacco control, the formal scientific program covered preclinical, clinical, and public health/epidemiological research topics on nicotine and tobacco. Distinguished plenary "theme lecturers," symposia, and oral paper sessions were balanced across these themes, with a number of sessions emphasizing integration across levels of analysis.

On the first morning of the conference, opening remarks were provided by SRNT President Ken Warner, SRNT–Europe Chair Gay Sutherland, local meeting host Eva Kralikova, and special guests from the Czech Republic. The scientific program then began with the delivery of the keynote address.

Suzanne M. Colby, Center for Alcohol and Addiction Studies, Brown University; David J. Drobes, Departments of Interdisciplinary Oncology and Psychology, H. Lee Moffitt Cancer Center at the University of South Florida; Robert West, Health Behavior Unit, Department of Epidemiology, University College London.

Correspondence: Suzanne M. Colby, Brown University, Center for Alcohol and Addiction Studies, Box G-BH, Providence, RI 02912, USA. Tel: +1 (401) 444-1854; Fax: +1 (401) 444-1850; E-mail: Suzanne_Colby@brown.edu

Addresses

Keynote address: Injecting greater urgency into global tobacco control

Derek Yach of Yale University gave the keynote lecture at this year's meeting. Dr. Yach reviewed the substantial progress that has been made in moving to implementation of the World Health Organization (WHO) Framework Convention on Tobacco Control (FCTC). Sixty-one countries have ratified the treaty. However, the pace of progress has stalled and expected funding slowed. The results are that there has been no intellectual development of protocols and no development of specific targets. Protocols all require considerable legal expertise and scientific input. A protocol on illicit trade must include the problems of counterfeit products and new testing methods for them. Addressing cross-border advertising requires a review of Internet law and recent U.S. Supreme Court decisions on pornography. A product regulation protocol is needed. The speed of investment in new products by Philip Morris and British American Tobacco has increased. New product launches will confuse consumers. Developments should anticipate industry changes and consider fast-track ways to assess health impacts and shifts in consumer behavior. Absence of a regulatory framework could delay support of truly

ISSN 1462-2203 print/ISSN 1469-994X online
DOI: 10.1080/14622200500186452

safer products or allow new products with vague claims to increase harms. Dr. Yach recommended revisiting the pace of progress, developing targets, and mobilizing funding to support them. Smoking prevalence declines in New York City of 10% in a year show what is possible with almost full implementation of the best interventions. For even more rapid progress, research is needed to develop new ways of reducing tobacco marketing. Point of sale ad bans were endorsed by the Canadian Supreme Court. Saskatchewan's example should be evaluated and globalized. The time is right to test the legality and health consequences of plain packaging as the final step in "de-branding" and thereby removing the allure of brands. There will be potential threats by industry about infringements of World Intellectual Property Organization (WIPO) and Trade-Related Aspects of Intellectual Property Rights (TRIPS) agreements. These need to be tested against a backdrop of health gains.

Preclinical theme lecture: Molecular biology of learning and chronic drug-seeking behavior

This year, the preclinical theme lecture was presented by Nobel Laureate Eric Kandel of Columbia University. Dr. Kandel discussed his research on the molecular mechanisms that underpin memory, particularly in the hippocampus. He emphasized the way in which exposure to stimuli that we need to remember influences the expression of regulatory genes that control the synthesis of specific proteins involved in synaptic transmission. The changes in expression of these proteins, which he and his group have identified, facilitate the transmission of impulses between specific neurons involved in memory. He explained how these processes could be studied "in the test-tube" using cultured neurons derived from the hippocampus, and how the principles derived from these in vitro experiments could be used to explain changes evoked in vivo in experimental animals. He also showed how neurobiological results generated from learning studies with very simple animals, such as a sea snail (*Aplysia*), can be applied to our understanding of the mechanisms that mediate memory in higher animals. In the latter part of his talk, he turned his attention to the application of his theories to the neurobiology of addiction. He pointed out that addictive drugs have been shown to influence the molecular events within neurons that have been implicated in memory and suggested to us that these events may be fundamentally important to our understanding of the psychopathology of addiction. He closed the presentation by admitting that little attention had thus far been paid to the possibility that the addiction to tobacco involved similar mechanisms and encouraged those in the audience who were researching neurobiology underlying tobacco dependence to consider them.

Clinical theme lecture: The history of nicotine replacement and the present and future of treatment for tobacco dependence

Karl Fagerström, of Smoker's Information Centre in Sweden, delivered the Clinical Theme Lecture at this year's meeting. He began by providing a brief history on the use of nicotine replacement (NR). The conception of NR occurred when two scientists were working with submarine crews and discovered that many of the soldiers used smokeless tobacco. Smokeless tobacco was at the time very rare but, owing to the smoking ban in submarines, the soldiers sought this form of tobacco to get around the ban. The two scientists attributed this behavior to nicotine-seeking. They gave their idea to a small nearby pharmaceutical company, LEO, where Ove Fernö, the research director, developed the idea in the early 1970s. Dr. Russell and his colleagues in London were very instrumental in taking the first formulation, nicotine gum, through all the regulatory hurdles. Since then, there has been little innovation regarding efficacy and pharmacokinetics of NR products.

Dr. Fagerström suggested that NR should actually be initiated a few weeks prior to quitting to help the quitters get used to their product, cut down on smoking, and thereby increase the chance of success. Smoking while using some kind of pharmacotherapy is expected to become very common in the future, since bupropion and newer drugs under development (e.g., Rimonabant and Varenicline) require a period to build up effective concentrations. Immunization therapy for nicotine dependence would also require a "delayed" quit to allow antibodies time to build up.

Finally, not everyone can quit abruptly. An aided smoking-reduction approach could lead to quitting, particularly among the less motivated and more dependent smokers. While complete abstinence from both tobacco and nicotine is the ideal, Dr. Fagerström urged SRNT researchers not to let that ideal stand in the way of the possible. He asserted that NR and also low-nitrosamine smokeless tobacco is by several orders so much less harmful compared with smoking that such forms could be used to make cigarette smoking less prevalent in our societies. He pointed out, however, that nicotine carries significant negative connotations. It is perceived by consumers and to some degree by physicians to be a cause of cancer and addiction. Dr. Fagerström said that neither is probably true; there is little evidence that clean nicotine causes cancer or primary addiction. He blamed some SRNT members for misuse of the term "nicotine," which is too often used when the

appropriate term should be tobacco or cigarettes. Tobacco use delivers much more than nicotine.

Public health/epidemiology theme lecture: The regulation of nicotine and tobacco and its impact on public health

Ann McNeill, from the University College London, delivered this year's Public Health/Epidemiology Theme Lecture. Dr. McNeill started by analyzing early recommendations such as those in the first U.K. Royal College of Physicians (RCP) report on Smoking and Health published in 1962, which were based largely on common sense, because there was neither much evidence nor experience of tobacco control at that time. Since that time, many countries have successfully implemented similar interventions and are now in Stage 4 of the Lopez and colleagues stages of the cigarette epidemic model, but she queried what happens next. To hasten the decline of cigarette smoking, Dr. McNeill argued that we need to press on with current tobacco-control interventions but also give more focus now to nicotine and tobacco regulation. Tobacco use had been prevalent in societies long before cigarettes became popular and it was only with the advent of cigarettes that widespread death and disease resulted. Dr. McNeill believes it is negligent not to do everything within our powers to make nicotine use in society less harmful and that the time is right for this focus, realizing that a proliferation of new nicotine and tobacco products is being launched in some markets, and a consensus exists that all such products should be regulated.

However, Dr. McNeill cautioned that as we move forward we must not lose sight of the main goal—to reduce death and disease. Regulatory requirements should not be so onerous that they divert resources away from this goal nor appear so complex that countries do not take simple steps to bring products under regulatory oversight. She suggests that SRNT should be playing a prominent role in deliberations around these issues. We should be aiming to move smokers along the continuum of nicotine-delivery away from the most harmful delivery systems (cigarettes) primarily by encouraging as many smokers to quit, but failing that, then by encouraging them to use clean nicotine-delivery products, and failing that, regulated smokeless-tobacco products. Dr. McNeill stated that vigilance of the tobacco industry is required, and also the need to use common sense where evidence is lacking, as in the 1960s. Where we differ nowadays is that some innovative research projects are enabling quick feedback on smokers' and nonsmokers' responses to tobacco-control and product regulatory policies, such as the *International Tobacco Control Policy Evaluation Study*—research that needs much more widespread implementation.

Symposia

The Program Committee reviewed over 30 symposium submissions. Of these, 12 were selected for presentation at the meeting; selection was on the basis of scientific quality, innovation, and representation across the diverse interests of SRNT members. Three series of symposia were presented simultaneously across four disciplinary tracks. In many cases, content within symposia bridged two or more of these tracks. Consistent with prior meetings, symposia were classified according to their primary focus on preclinical, clinical, or public health/epidemiology research. Because of the growing number of outstanding proposals, the program offered a fourth track of symposia for the first time, which included one public health symposium and two symposia that highlighted issues in genetic research on tobacco dependence.

Preclinical symposia

The first preclinical symposium was entitled "Nicotinic receptor antagonism by antidepressants: Parsing the link between smoking and depression," and highlighted potential links between nicotinic acetylcholine receptors (nAChRs) and neural pathways involved in depression. This is significant because depression is potentially a critical factor in ongoing smoking and relapse to smoking, but these studies also have implications for normal brain function, the neural basis of depression, and development of novel antidepressant therapies. The panel focused on the idea that inactivating nAChRs, by nicotinic antagonists, genetic manipulation of nAChR subunits, smoking or classical antidepressants, is a mechanism involved in antidepressant action.

Ronald Lukas from the Barrow Neurological Institute presented evidence at the molecular level that a wide range of antidepressants act as noncompetitive antagonists of nAChRs. Marina Picciotto from Yale University showed work from animal studies demonstrating that mecamylamine, a nicotinic antagonist, can mimic the effects of classical antidepressants in behavioral models of depression-like behavior, and that amitriptyline, a tricyclic antidepressant, is ineffective in mice lacking high-affinity nAChRs. Finally, Tony George from Yale University presented results from a placebo-controlled clinical trial using mecamylamine (Inversine) to augment SSRI antidepressants in treatment-resistant patients.

Taken together, these studies provide further evidence that some smokers may use nicotine to self-treat depressive symptoms and provided a proof of concept for the idea that nAChR blockers could be clinically useful in treating depression. Understanding the mechanism underlying these effects of nicotinic agents may lead to more effective treatments for smoking cessation in the subpopulation of smokers with comorbid depression.

The second preclinical symposium was entitled "Revisiting the Role of Nicotine in Smoking Reinforcement." A central premise of nicotine and tobacco research is that nicotine drives tobacco use by acting as a primary reinforcer and by conferring secondary reinforcing properties on nicotine-associated stimuli. However, the data presented in this symposium support the hypothesis that nicotine also directly (i.e., nonassociatively) enhances the reinforcing properties of other stimuli. John Dani of Baylor College of Medicine presented in vivo research suggesting that nicotine alters the balance between glutamatergic and GABA-ergic influences on midbrain dopamine systems affecting synaptic plasticity. Stephanie Cragg of the University of Oxford presented in vitro research showing that desensitization of nAChRs amplifies the phasic release of dopamine in response to reward-related bursts of activity. Peter Olausson of Yale University presented behavioral research demonstrating that repeated nicotine—like cocaine and amphetamine—enhances reward-related learning, both in instrumental and Pavlovian learning paradigms, and increases the control over behavior by conditioned reward-associated cues. Anthony Caggiula of the University of Pittsburgh presented data from a rat self-administration paradigm demonstrating that the reinforcement-enhancing effects of nicotine occur with both unconditioned and conditioned reinforcers; are positively related to the reinforcing strength of the non-nicotine stimulus; and are observed across a wide range of doses and under multiple schedules of reinforcement (i.e., fixed and progressive ratio). Discussion was facilitated by Eric Donny of the University of Pittsburgh, who focused on how nicotine might act to make smoking stimuli (e.g., taste, smell, feel of a cigarette) more reinforcing both because of the association between these stimuli and the primary reinforcing effects of nicotine, and because of the ability of nicotine to directly enhance the value of these conditioned reinforcers.

The third preclinical symposium was entitled "Genetic Variation in Smoking Consumption and Cessation." Genetic variation has been shown to alter the amount smoked by individuals, as well as their ability to quit smoking. This symposium started with Dieter B. Wildenauer, of the University of Western Australia, Perth, who described an inbred mouse-strain study of nicotine consumption using the methodology of mapping quantitative trait loci, and indicated some of the genetic loci and candidate genes that were identified. One such linked locus contains the gene for *cyp2A5*, which codes for the enzyme that metabolizes nicotine in mice. The second presentation, by Rachel F. Tyndale (Centre for Addiction and Mental Health, University of Toronto), continued this theme, describing data suggesting that genetic variation in CYP2A-mediated nicotine inactivation in humans alters the amount smoked per day and how long people smoke for before stopping. Caryn Lerman (University of Pennsylvania) and Robert Walton (University of Oxford) focused on recent genetic findings from randomized smoking cessation trials using nicotine replacement therapies or bupropion. For example, Dr. Lerman showed data indicating that a functional variant in the dopamine receptor (DRD2) gene may increase the success rates of bupropion treatment, while those without this variant may be more successfully treated with NRT. Dr. Walton described data from a number of studies where genetic variation has altered quitting outcomes. He also demonstrated some of the integration of the genetic data with imaging techniques as one path forward in this research area. Overall, the goals of the symposium were to describe some geneticv-ariants from mouse and human data that altered rates of nicotine consumption and efficacy of treatment with the future goal of personalizing medicine by optimizing treatment according to the genetics of each individual. Gary Swan of SRI International, the discussant, summarized the findings and put them in the context of future directions in genetic research on nicotine dependence and translation to practice.

Clinical symposia

The first clinical symposium was "Adolescent smokers and smoking cessation studies: Issues in eligibility, enrollment, recruitment and retention." Paul McDonald, University of Waterloo, emphasized that improving utilization is as important as improving effectiveness. Utilization is a product of reach, access, and adoption; adoption is determined by how well a communication campaign can compel the intended adopters to try an intervention. Dr. McDonald analyzed 48 smoking cessation trials aimed at 12–24-year-olds and found that recruitment can be improved by increasing campaign length, using adult spokespersons, and offering comprehensive programs through schools, workplaces, and community centers. In a clinical trial of nicotine replacement therapy, Eric Moolchan (U.S. National Institute on Drug Abuse) found that

eligible adolescents were younger, more likely to be female, more likely to be European American, and had shorter prior quit-attempts than excluded adolescents. Adolescents were excluded because of insufficient tobacco use, lack of parental support, medical and psychiatric reasons, outside age range, and recent NRT use. Dr. Moolchan concluded that studies need to include lighter smokers and those with medical/psychiatric comorbidity. He encouraged wider use of waivers and emancipated-minor status to increase adolescents' access to treatment studies. Cathy Backinger, U.S. National Cancer Institute, analyzed predictors of recruitment and retention in 57 adolescent smoking-cessation studies. Among numerous factors (recruitment methods; type of site; study sample size; minimal level of smoking included; and length of follow-up), only inclusion of lighter smokers ($\leqslant 5$ cigarettes/day) significantly predicted higher recruitment and retention. Scott McIntosh, University of Rochester, reported on two large-scale adolescent smoking-cessation studies recruiting from physician offices. He emphasized that the quality and consistency of the relationship between the research team and medical practice site affects recruitment. Other lessons learned include the need to enhance recruitment of low SES adolescents, and that the consent form is a barrier to recruiting adolescents. The discussant, Myra Muramoto (University of Arizona), called for future adolescent smoking-cessation studies to systematically report recruitment and retention data, include lighter smokers, use less stringent inclusion criteria and more innovative settings, reduce parental barriers to providing consent, and increase use of consent waivers.

The second clinical symposium was "What is the role of smoking reduction in the clinical management of smoking?" Presenters included Karl Fagerström, John Hughes (University of Vermont), Matthew Carpenter (Medical University of South Carolina), and Steve Rennard (University of Nebraska Medical Centre). Michael Kunze (Medical University of Vienna) served as the discussant. This symposium discussed smoking reduction in smokers unable to quit or not interested in quitting. Four questions were posed: (a) Can reduced smoking (RS) yield any substantial reduction in harm; (b) Are pharmacological and behavioral methods effective in aiding reduced smoking; (c) What effect does RS have on motivation to quit altogether; and (d) Does RS produce quitting that would otherwise not have occurred.

The following observations and conclusions were made during the session. To date, no impressive scientific body of data shows reduced harm to individuals who reduce smoking, although it remains a largely untested issue. It is plausible that studies showing reduced harm can be done but they are likely to be time-consuming and require large sample sizes. Another barrier is that no valid surrogate markers exist yet. Both pharmacological (NRT) and behavioral methods to aid RS seem effective, although more and better-controlled behavioral studies would be welcomed. Participating in an RS study does not reduce the motivation to stop entirely. In most intervention studies, an increase in motivation to quit is actually seen. Consistent with this, when smokers not interested in quitting are helped to reduce smoking, twice as many go on to quit than smokers who have not been asked to reduce. Offering RS in a medical setting to those not interested in quitting seems to be a good strategy to bring more smokers into active treatment.

The third clinical symposium was "New medications for smoking cessation: Beyond NRT and buproprion." Despite the availability of nicotine replacement therapy, bupropion, and effective behavioral therapies, millions of smokers fail to successfully quit smoking each year. Even with the existing therapies, it is estimated that one billion people will die from smoking-related illnesses during this century. It follows that more effective medications, or medications that are effective in subpopulations that are refractory to current treatments, may save the lives of millions.

Attendees received an update on the development of new medications for smoking cessation at this symposium, organized and chaired by David McCann of the U.S. National Institute on Drug Abuse (NIDA). Speakers presented the latest available research findings on four new medications under clinical evaluation for smoking cessation; Tony George of Yale University presented on selegiline (a MAO-B inhibitor); Bernard Le Foll, also from NIDA, presented on BP 897 (a D3 receptor partial agonist); Steven Sands (Pfizer Global Research and Development) presented on varenicline (a nicotine receptor partial agonist); and Raymond Niaura (Brown University and Butler Hospital) presented on rimonabant (a CB-1 receptor blocker). The symposium discussant, John Cryan (Novartis Institutes for Biomedical Research), reviewed other biological targets (other receptors, enzymes, and ion channels) that hold promise for discovery and development efforts of future medications related to smoking cessation, giving meeting attendees a glimpse of what may be further back in the drug-development pipeline. From the presentations, it was clear that multiple targets exist for potential new therapeutic agents and that essential studies are under way to evaluate several novel medication candidates.

Public health/epidemiology symposia

The first public health/epidemiology symposium, "Women, tobacco, and cancer: An agenda for the 21st Century" was co-chaired by Ellen Gritz of the M. D. Anderson Cancer Center and C. Tracy Orleans of the Robert Wood Johnson Foundation. Presenters discussed the key recommendations of the July 2004 Report of the Women, Tobacco and Cancer Working Group, a public-private partnership supported by the U.S. National Cancer Institute (NCI) and other federal and private funders. The Working Group, made up of prominent members of the scientific, medical, public health, and advocacy communities from across the United States and around the globe, provided recommendations for research and action to more effectively address tobacco use as a "women's issue" and to reduce the rising burden of tobacco-related cancer among women around the world.

Presentations spanned the NCI's full "discovery-development-delivery" research-to-practice continuum, charting a promising course for the next decade of research and action to prevent tobacco use and its harms to women and girls. Carolyn Dresler, of the International Agency for Research on Cancer, began by summarizing current knowledge of the genetic, molecular, cellular, and hormonal factors contributing to sex differences in the biological processes underlying the development and treatment of lung cancer, highlighting many areas where sex differences are not fully understood. Gary Swan (SRI International) focused on basic science progress and gaps in understanding women's unique biological and behavioral responses to tobacco use, cessation, and relapse, with attention both to hormonal modulation of nicotine's effects and to broader biopsychosocial "gender" differences in those processes. Susan Curry (University of Illinois at Chicago) gave a presentation built on recommendations from the 2001 Surgeon General's Report, *Women and Smoking*, to "act now: we know more than enough" with a focus on promising strategies for improving the delivery of effective tobacco-control programs and policies, especially to women and girls in high-risk and underserved populations (e.g., pregnant smokers, low-income women, and minority populations). Kay Kahler-Vose, of Porter Novelli, summarized what we have learned over the past decade about the role of communication and social marketing campaigns, highlighting the need to develop and disseminate effective gender-tailored prevention and cessation campaigns. Mira Aghi, a consultant from New Delhi, India, presented a paper developed by Judy Wilkenfeld of Campaign for Tobacco-Free Kids on the importance of gender issues in international tobacco control, emphasizing that women around the world are a prime target of tobacco-industry marketing, and urging better surveillance of the impact of special tobacco-control policies on women's tobacco use and tobacco-related disease.

The second public health/epidemiology symposium was "Tobacco industry funding of scientific research: Policies, practices, and the integrity of public health research." SRNT members and other interested scientists debated the potential promises and pitfalls of accepting research funding from the tobacco industry.

Mitch Zeller of Pinney Associates provided evidence from tobacco-industry documents about the tobacco industry's motivations behind forming links with academic institutions and how these links add legitimacy to the tobacco industry at the risk of public health. Mark Parascandola of the U.S. National Cancer Institute reviewed data from a survey of U.S. academic institutions regarding their policies and practices related to acceptance of tobacco-industry funding. Institutions that have implemented policies restricting acceptance of tobacco-industry funding cite a fundamental clash of values as the primary justification, while institutions that do not have a policy cite concerns about academic freedom as a major obstacle to such policies. Jed Rose of Duke University described the procedures used by the Center for Nicotine and Smoking Cessation Research to address potential conflicts of interest and other concerns regarding the Center's funding from a major tobacco company. Jean King of Cancer Research UK discussed that organization's process of developing a policy to prohibit funds going to researchers that receive funding from the tobacco industry. Jeff Collin (London School of Hygiene and Tropical Medicine) used tobacco-industry documents to illustrate how tobacco companies have sought out connections with health leaders and academic institutions in the developing world to further their business interests.

Ken Warner chaired the symposium and moderated the lively discussion that followed. A number of members of the audience relayed additional concerns about how tobacco companies may take advantage of links to medical and public-health institutions to improve their tarnished public image. Although stringent conflict-of-interest rules may protect against bias in industry-funded research, these rules do not protect against how tobacco companies may use such affiliations to serve their own interests in ways that are counter to public health.

The third public health/epidemiology symposium was presented by The International Tobacco Control Policy Evaluation Project. Included were recent findings entitled "Evaluating tobacco control policies of the Framework Convention on Tobacco

Control.'' The ITC Project is designed to evaluate the psychosocial and behavioral effects of national-level tobacco-control policies of the Framework Convention on Tobacco Control (FCTC).

Geoffrey Fong, University of Waterloo, provided a brief introduction of the design and goals of the ITC 4-Country Survey, a random-digit–dialed phone survey of a cohort of more than 8,000 adult smokers across four countries—Canada, United States, United Kingdom, and Australia. David Hammond, University of Waterloo, presented findings demonstrating the effects of warning labels in enhancing knowledge of the health harms of smoking across the four countries. Fiona Harris and Gerard Hastings of the University of Stirling and Open University presented findings on the February 2003 U.K. tobacco-promotion ban, which led to significant declines of awareness of tobacco promotion among U.K smokers in controlled channels, but continued awareness in still-open channels. Andrew Hyland, Roswell Park Cancer Institute, presented findings on the relationship between price/taxation and purchase patterns, with particular focus on how the impact of taxation might be attenuated by price-avoidance behavior (e.g., buying from Indian reservations in the United States). Geoffrey Fong presented findings from the ITC-Ireland/UK survey showing that Ireland's 2004 smoke-free workplace law led to substantial reductions in tobacco smoke in key public venues and significant increases in support among smokers for the ban. Andrew Hyland and Ron Borland, The Cancer Council Victoria, presented findings on smoke-free homes suggestive of the possibility that establishing smoke-free homes is a precursor to cessation. Scott Leischow, U.S. Department of Health and Human Services, was the discussant and highlighted the importance of international cohort studies in providing the evidence base for the FCTC.

The fourth public health/epidemiology symposium, ''Barriers to cessation and treatment—underestimating tobacco harm and overestimating medicinal nicotine harm,'' was chaired by Martin Jarvis of University College, London. This symposium examined some of the barriers that may deter smokers from trying to quit smoking and from adopting nicotine medications to assist them.

Using recent data from the United States and from European countries, the presenters documented smokers' misperceptions of the risks of smoking and the risks of using nicotine medications, and how these misperceptions affect quitting behavior. Using data from the U.K. smokers, Dr. Jarvis described how older smokers misconstrue the data on the risks of smoking in order to rationalize continued smoking. Michael Cummings, Ph.D., of Roswell Park Cancer Institute, presented U.S. data showing that smokers misunderstand the risks of smoking, particularly misperceiving the contributions of nicotine (vs. other components) to the risks of smoking, and hold misperceptions about the risks of nicotine medications. Karl Fagerström presented data from a survey of EU countries showing that smokers believe nicotine is responsible for most of the diseases related to smoking; differences among countries were also discussed. The countries whose respondents best differentiated the effects of smoking versus nicotine were Denmark, Sweden, and the Netherlands, while respondents from Spain, Portugal, and Poland were least able to differentiate. Saul Shiffman (Pinney Associates) presented United States data showing that misperceptions about the risks of nicotine influence both the adoption of nicotine medications and compliance with medications if they are used. Finally, Mitchell Zeller (Pinney Associates) discussed communication and policy strategies for educating smokers about the risks of smoking and nicotine medications.

Symposia on genetic issues in tobacco dependence

The first of these two symposia was entitled ''Genetic studies of nicotine dependence: It's all about the phenotype.'' Presenters in this symposium proposed that one reason there have been few, if any, replications of results either from candidate gene or linkage studies may be imprecision in the assessment of nicotine dependence.

Gary Swan, SRI International, described a framework with which to classify nicotine dependence phenotypes; reviewed evidence for their reliability, validity, and heritability; and presented recently published evidence involving nicotine metabolism measures as examples of well-characterized endophenotypes that can, in turn, shed light on the amount of variation accounted for by the *CYP2A6* genotype. Jeanne McCaffery, Brown Medical School and The Miriam Hospital, reviewed new methods for incorporating environmental variables into a twin design and showed the importance of incorporating measured environmental phenotypes into genetically informative designs to determine the extent to which they moderate genetic effects. Christina Lessov, SRI International, provided evidence for the dimensionality of adult nicotine dependence and showed that some dimensions are associated with cigarette-use trajectories assessed prospectively when study participants were adolescents. Janet Brigham, SRI International, reviewed evidence pertaining to the reliable and valid assessment of lifetime tobacco-use trajectories and milestones and described progress being made with a new measurement strategy involving the use of Web-based survey methodology. Caryn Lerman, University of Pennsylvania Medical

School, reviewed new evidence supporting the use of a measure of the relative reinforcing value of nicotine (RRVN) in genetics research. This endophenotype determines nicotine reward from smoking or other delivery methods using a novel nicotine-choice paradigm adapted by Ken Perkins. Dr. Lerman showed that RRVN is lower in obese smokers and smokers with the *OPRM1 A118G* allele. Kirk Wilhelmsen, University of North Carolina at Chapel Hill, discussed the above papers as evidence of the wide range of phenotypic options that can be incorporated into future genotypic studies of nicotine dependence.

The second symposium was entitled "Psychiatric comorbidity and the nicotine dependence phenotype." It treated the rationale for interest in comorbidity with smoking behavior, particularly the underlying genetic and environmental effects on comorbidity.

In introductory comments, Jeanne McCaffery argued that psychiatric comorbidity may provide a unique window on understanding the causes of smoking in given individuals and may help identify subgroups of individuals in which different gene variation may impact smoking. Karestan Koenen (Harvard School of Public Health) presented data suggesting that both trauma and active PTSD symptoms increased the risk of onset of daily smoking but that this effect was stronger among those with a low level of genetic risk for smoking. Brian Hitsman (Brown Medical School) provided evidence that both dysthymia and double depression increased risk for onset of smoking, in addition to MDD. George Papandonatos of Brown University presented evidence that common genetic factors influence depressive symptoms and stage of smoking initiation among adolescent twins. Marcus Munafò (University of Bristol) explored genetic pleiotropy of a common variant in the promoter region of the serotonin transporter gene in the context of psychiatric comorbidity with smoking behavior. Lastly, Michael Lyons (Boston University) ended with some serious and comical thoughts on just how many psychiatric disorders predicted an increased risk of smoking behavior and postulated that a study of the few psychiatric disorders not showing comorbidity with smoking may also be of interest.

Oral paper and poster sessions

The plenary lectures and symposia were complemented by 12 oral paper sessions. Presentations are selected for paper sessions from among the highest-rated peer-reviewed abstracts submitted to the Program Committee, using criteria similar to those for symposia. The aim is for paper sessions to provide a forum in which a topic may be explored in-depth, drawing upon different perspectives and methodological approaches. Titles and cochairs of the paper sessions were:

- "Cue reactivity: Implicit and explicit paradigms" (Damaris J. Rohsenow, Ph.D., and F. Joseph McClernon, Ph.D.);
- "Smoking cessation in medical populations" (Nancy Rigotti and Ann Joseph);
- "Role of health care professionals in tobacco control" (Peter Hajek and Belinda Borelli);
- "Examining the tobacco industry: Strategies and documents" (Ken Warner and Pamela Ling);
- "Nicotine metabolism: CYP and beyond" (Rachel Tyndale and Robert Walton);
- "Role of nicotinic and other brain receptors" (Marina Picciotto and Ming Li);
- "Substance use and psychiatric comorbidity: Treatment issues" (Suzy Bird Gulliver and Robyn Richmond);
- "International tobacco research: Trends and treatment" (Eva Kralikova and Jacques Cornuz);
- "Studies of nicotine reward and neuroimaging" (Sakire Pogun and Anthony Caggiula);
- "Pharmacotherapy: New developments and evaluations" (Jean-Francois Etter);
- "Smoking in adolescence and youth: Trends and trajectories" (Denise Kandel and Johanna Lewis-Esquerre);
- "Alternative forms of tobacco: Evaluating effects and comparing risk" (Ari Haukkala and Thomas Eissenberg).

There were also three poster sessions, with more than 500 presentations that spanned the breadth of nicotine and tobacco research. The poster sessions provided an excellent format for discussing research in a less formal setting, with increased opportunity for interaction and professional networking. Posters were arranged in a manner designed to increase interaction across disciplinary boundaries at the conference. A selection of the top-rated paper and poster abstracts is reprinted in this issue.

SRNT awards

Research awards

Outstanding accomplishments of several SRNT members were recognized at the meeting. This year's awards include the Doll/Wynder Award for Research in Epidemiology and Public Health, the John Slade Prize, the New Investigator Award, and the New Investigator Travel Awards. Awards were announced in plenary session by Neal Benowitz of the University of California, San Francisco, Chair of SRNT's Awards Committee.

University of Wisconsin Professor of Medicine Michael Fiore became the third researcher to receive

the prestigious Doll/Wynder Award. This award honors scientists for making groundbreaking advances in helping people quit smoking. Dr. Fiore is the Director of the University of Wisconsin Center for Tobacco Research and Intervention and led the development of the U.S. clinical practice guideline to help doctors assist their patients with quitting. After accepting the award, Dr. Fiore gave an award address entitled "Investing in tobacco control research: We can move the mountain." Dr. Fiore described reductions in U.S. smoking rates as a historic public-health achievement. In 2005, for the first time in our history, more than half of Americans who ever smoked cigarettes had successfully quit. Drs. Fiore described some of the factors contributing to this accomplishment and spoke of the challenges that lie ahead to achieve even greater success. He elaborated on four critical leverage points—the smoker, the clinician, the health-care delivery system, and policy changes. It is at each of these levels that this battle for public health will be won both in the United States and worldwide. Dr. John Pierce and Gary Giovino are the past recipients of the award.

Jack Henningfield of Pinney Associates received the John Slade Prize, which recognizes outstanding contributions to public health and tobacco control through science-based public policy and policy advocacy. This prize is awarded annually by SRNT as a means of honoring individuals whose work is consistent with the vision of Drs. John Slade, which is to pursue science that directly contributes to the improvement of public health.

Darlene Brunzell of Yale University received the New Investigator Award for her early career contributions towards understanding the role of nicotinic receptors within animal models of nicotine dependence. Selection of Dr. Brunzell was based on the exceptional quality of her research, the level of her scholarly productivity, and the quality of the research abstract she submitted for presentation at the annual meeting. The New Investigator Paper Session was chaired by Marcus Munafò (Oxford University), last year's recipient of the New Investigator Award.

Four recipients of the New Investigator Paper Travel Awards each presented a 15-min oral presentation in plenary session. The recipients and their paper titles were:

- F. Joseph McClernon, Duke University Medical Center: "Abstinence-induced changes in self-reported craving are correlated with changes in brain responses to smoking cues: An event-related fMRI study."
- Christina N. Lessov, SRI International: "Cigarette smoking in Chinese male twins: The Qingdao Twin Registry."
- Jonathan B. Bricker, Fred Hutchinson Cancer Research Center: "Role of close friends' versus parents' and older siblings' smoking in children's 12th grade smoking: A prospective study."
- Stacey J. Anderson, University of California, San Francisco: "An evolution in low tar advertising: Lessons for the future."

Travel awards

In an effort to promote global participation in this year's meeting, a number of travel scholarships were provided to international participants. SRNT provided travel scholarships to: Maisara Abdelrazig (Sudan), Mira Agha (India), Taghrid Asfar (Syria), O.A. Ayo-Yusof (South Africa), Habiba Ben Romdhane (Tunisia), Naowarut Charoenca (Thailand), Marine Gambaryan (Russia), Monsurul Haque (Bangladesh), Shahadat Hossain (Bangladesh), Rama Kant (India), Nipapun Kungskulniti (Thailand), Vladimir Levshin (Russia), Abdullah Malami (Nigeria), Haniki Nik Mohamed (Malaysia), Neo Morojele (South Africa), Chizo Ngoka (Nigeria), Melike Sahiner (Turkey), Mamadou Thione (Senegal), Florante Trinidad (Philippines), Raydel Valdes-Salgado (Mexico), Olga Vikhireva (Russia), Gorken Yararbas (Turkey), and Alma Zhylkaidarova (Kazakhstan).

2006 Award recipients

Several 2006 award recipients were also named at this year's meeting. The Langley Award for basic science research will be awarded to William Corrigall. The John Slade Prize for impact on policy and public health will be awarded to Judith Wilkenfeld of the Campaign for Tobacco Free Kids. The recipient of the 2006 New Investigator Award will be Bernard Le Foll of the U.S. National Institute on Drug Abuse. The impressive contributions of these individuals will be recognized at the 2006 annual meeting in Orlando, Florida.

Other meeting events

Besides the formal scientific program described above, the annual meeting included seven lunchtime workshops, a members' meeting, and a special meeting on disclosure and competing interests.

Workshop 1: Career development in nicotine and tobacco research: International perspectives

Approximately 50 graduate students, postdoctoral fellows, and new faculty members from around the globe attended this workshop sponsored by the

Training Committee. Participants were able to enjoy a free lunch and hear from—and pose questions to—an international panel of respected researchers. Panelists included David Balfour (University of Dundee School of Medicine, U.K., and President of SRNT); Susan Curry (University of Illinois at Chicago, USA); Jean-Francois Etter (University of Geneva, Switzerland); John Hughes (University of Vermont, USA); Eva Kralikova (Charles University of Prague, Czech Republic); and Sakire Pogun (Ege University School of Medicine, Turkey).

Each panelist gave a brief overview of their own career development, including the role that mentorship has played in their own careers. The floor was then opened for questions, and a lively discussion ensued, touching on such topics as how to find a good mentor (and *be* a good mentor), obtaining funding, changing career focus, and balancing career and family. Based on evaluations submitted, attendees found the workshop to be very helpful.

Workshop 2: European smoke-free hospitals

This workshop, organized by Stephano Nardini, described the European Network for Smoke-Free Hospitals (ENSH). Bertrand Dautzenberg (Groupe Hospitalier Pitie-Salpetriere, France) first provided introductory comments and a general overview of the ENSH Network. Dr. Nardini then described the use of a self-audit questionnaire in the ENSH network. The importance of the audit process was highlighted; self-audits help to identify areas needing attention, provide a guide for policy development and, when administered periodically, ensure that progress in implementing smoke-free hospital policies is kept on track. Elvira Mendez (Catalan Institute of Oncology, Spain) described the maternity network, and Jacques Le Houezec (Amzer Glas, France) reflected on the challenges involved in implementing smoke-free policies in psychiatric services. Additional information about ENSH can be found at ensh.aphp.fr

Workshop 3: Training physicians in smoking cessation interventions

This workshop was organized by Jean-Paul Humair of Geneva University Hospital, Geneva, Switzerland, and Jacques Cornuz of University Hospital, Lausanne, Switzerland.

The presenters first emphasized the need to provide smoking-cessation interventions in medical care that are adapted to the health-care system and the setting. Programs must promote brief counseling tailored to the patient's context and motivation, and the use of pharmacological therapy for patients who are ready to quit. Training programs should teach these basic counseling skills in different modules of variable duration and content according to physicians' interest. Active learning methods with case studies, role-plays, and practice with standardized patients will be more effective to improve physicians' practices. This effect will be enhanced by organizational strategies facilitating smoking-cessation interventions such as reminders and involvement of other members of the primary-care team. In addition to learning from didactic presentations, workshop participants worked together in small groups to actively apply new knowledge by generating proposals and strategies in response to various real-world training situations.

Workshop 4: Publishing in Nicotine & Tobacco Research

The workshop was designed to encourage new authors to submit articles to SRNT's journal, to help them navigate successfully through the submission and publication process, and to address their questions. Editor-in-Chief Gary E. Swan outlined the mission of the journal and noted that the journal has nearly tripled in number of articles and pages printed since it was first published in 1999. The journal will receive an impact factor rating in 2006, following several years of evaluation. Submissions are climbing; the current rejection rate for original articles and brief reports is 65%. Dr. Swan and David J. K. Balfour, corresponding editor, explained that an acceptable manuscript is one that reports on well-designed research; provides authoritative reviews; has appropriate scientific design, with appropriate controls, valid measures, appropriate statistical analysis, and ample power; provides new information; and reports methodology in detail. Dr. Balfour advised authors to design studies for which they have adequate resources, to refer to previous studies for comparison, and to seek mentoring if needed. Coordinating Editor Janet Brigham, SRI International, encouraged potential authors to review the journal's contents before submitting a paper, and to tailor the approach to the journal's mission and worldwide readership. Dr. Brigham explained that the journal will assist authors for whom English is not a primary language, and indicated that reviewers and editors are instructed not to evaluate the acceptability of a manuscript on the basis of language. She demonstrated the journal's new online system, linked from the journal Web site at www.ntrjournal.org, and explained the need for rapid turnaround of reviews and revisions. Dr. Brigham also detailed the need for responding promptly to queries and checking page-proofs promptly once an article is accepted. Susannah Douch, editorial director at Taylor & Francis, the journal's publisher, outlined how the publisher

extends the reach of the journal to developing countries, and noted that the journal has grown quickly in size and interest relative to other journals in its portfolio. A set of frequently asked questions (FAQ) was provided to participants and is now available on the journal Web site at www.ntrjournal.org/faq.html. Associate Editors Ivan Berlin, Naomi Breslau, and Ray Niaura addressed specific questions from those in attendance, as did SRNT Publications Committee Chair Ed Lichtenstein.

Workshop 5: Lessons learned from the evaluation of the English smoking-cessation treatment services

In this workshop, organized by Martin Raw (University of London and Universidade Federal de Sao Paulo), the results of the evaluation of the English smoking cessation treatment services were presented. Subsequent presentations described the lessons learned during this process and proposed a minimum data set for monitoring outcome in similar services.

The speakers were Tim Coleman (University of Nottingham, U.K.), Gay Sutherland (Institute of Psychiatry in London), Jenny Wheeler (South Essex Stop Smoking Service), Martin Raw, and Robert West (University College London), and the session was chaired by Ann McNeill. Findings from the evaluation suggest that the effectiveness of these real-life smoking cessation services is in line with the research evidence. Moreover, they have done surprisingly well in reaching disadvantaged smokers. Government advice on service configuration (including that they should follow the evidence base) and sensible throughput targets had a positive effect in the first few years of this initiative. However, current throughput targets are so demanding and unrealistic that they risk demoralizing staff and provoking target-reaching behavior at the expense of quality.

Workshop 6: Smoking cessation and reduction with NRT during pregnancy: Regulatory barriers and current practice

This popular workshop was organized by Jacques Le Houezec of Amzer Glas in France, and Richard A. Windsor of George Washington University. More than 100 attendees were in the room, and the workshop attracted many questions from the floor at the end of the presentations.

The prevalence of smoking during pregnancy is still high in France despite a favorable regulatory environment; NRT contra-indication for pregnant smokers was removed in 1997, and clinical guidelines for smoking cessation have included the potential use of NRT during pregnancy since 1998. One possible explanation for this situation is the fear, both from physicians and pregnant smokers, to use NRT. This situation led us to the conclusion that specific guidelines (for gynecologists, obstetricians and midwives) might be needed.

The French Consensus Conference on Pregnancy and Tobacco was held in Lille in October 2004. Five hundred people, coming from 18 countries, participated in this consensus conference. The conference was organized by Michel Delcroix from APPRI (Perinatality Prevention Research Information Association) together with the French Alliance against tobacco, the European Smoke-free Hospital and Maternity Networks, the French Cancer league, and many other organizations including SRNT Europe. This conference was directed in compliance with the methodological rules recommended by ANAES (Agence Nationale d'accréditation et d'évaluation en Santé—National Agency of Health Accreditation and Assessment). Forty-six experts presented a review on topics that were selected by the Program Committee, and a literature search group assisted the Jury with another report. The conclusions and recommendations, drafted by the Jury of the conference in total independence, were presented by Michel Delcroix at Workshop 6. An English translation of the short version of the recommendations, with a foreword from Ann McNeill and Gay Sutherland, is available as a PDF file at www.treatobacco.net.

Conchita Gomez, a smoking-cessation specialist midwife, presented the results of a study on the use of CO measurements in follow-up of pregnant smokers. Marion Adler, a smoking-cessation specialist, talked about her experience of smoking cessation and smoking reduction during pregnancy, showing that smoking cessation can be obtained in pregnant women if the NRT dose is tailored to the needs of the women. Richard Windsor presented the rationale and design of an ongoing study on behavioral counseling and NRT during pregnancy, which should improve the scarcity of data in this field. Finally, Jacques Le Houezec presented an overview of the regulatory barriers concerning the use of NRT during pregnancy, showing the regulatory situation in different countries, and trying to understand why France, despite a good regulatory environment, is unable to significantly reduce tobacco smoking in pregnant women.

Workshop 7: "Have lunch at a smoke-free Irish Pub," and other good policy outcomes from research

This final workshop addressed the contribution of science to developing and implementing sound public policy and programs on tobacco and the need to ensure that science is translated into policy and

practice. C. Tracy Orleans from the Robert Wood Johnson Foundation discussed the role of a funder in facilitating collaboration between researchers, advocates, and practitioners. Danny McGoldrick, Director of Research for the Campaign for Tobacco-Free Kids, described how the Campaign uses research in media and policy advocacy. A case study on smoke-free Ireland then demonstrated the key role of science in the policy process. Shane Allwright from the Dublin Office of Tobacco Control presented the research her office conducted that served as the basis for the formulation of the smoke-free law in Ireland, and Fenton Howell from ASH Ireland told the story of how this research was used in the campaign to make Ireland smoke-free.

Special meeting on disclosure and competing interests

Ken Warner and Harry Lando chaired an open meeting to solicit feedback and discussion of a recent report by an SRNT ad-hoc Committee on Disclosure and Competing Interests. Approximately 15 members engaged in a lively discussion regarding the implications of various levels of disclosure that could be required for SRNT membership, officership, and committee membership. These issues will continue to be discussed by the SRNT Executive Committee and Board prior to implementing a policy change.

Members' meeting

All members are encouraged to attend the annual SRNT Members' Meeting in order to stay informed with respect to the status of the organization, and to contribute to important societal decisions. This year's meeting included a Presidential Report by Ken Warner, as well as reports from SRNT Executive Director Bruce Wheeler and Secretary/Treasurer Cindy Pomerleau (University of Michigan).

It was reported that the SRNT budget contains a surplus, and several comments from the floor suggested ways to utilize these funds in keeping with the SRNT mission. It was also suggested that the budget be posted on the SRNT Web site to provide a level of membership oversight. Service awards were given to several outgoing committee chairs and board members. Finally, it was announced that the incoming president-elect will be Ellen Gritz (M.D. Anderson Cancer Center) and the incoming Secretary/Treasurer will be Laura Klein (Pennsylvania State University).

Preconference meeting

The all-day preconference symposium on Global Tobacco Research was organized by Harry Lando (Chair), Ken Ward (Co-chair), and a planning committee of 25 SRNT members from around the globe. Several organizations provided funding, including SRNT, the U.S. National Cancer Institute, the U.S. National Institute on Drug Abuse, the American Cancer Society, GlaxoSmithKline, Pfizer, and Sanofi-Aventis. To encourage participation by individuals from developing countries, SRNT provided travel scholarships for 23 attendees (see Awards section). The overarching purpose of the meeting was to explore means of networking and increasing capacity for global tobacco research.

Occurring just 3 weeks after the landmark Framework Convention on Tobacco Control (FCTC) went into effect, the preconference provided a timely opportunity for more than 300 global tobacco researchers to meet, share information, and strategize for the future. The morning featured an introductory session that set the stage for the day's discussions by focusing on innovative adult and youth tobacco reduction initiatives from several regions.

Speakers included Abu Abdullah (Hong Kong), Taghrid Asfar (Syria), Wara Alderete (Argentina), Neo Morojele (South Africa), and Alex Prokhorov (United States). The morning's second session focused on national capacity-building in the context of the FCTC, with talks from Fran Stillman (United States), Tom Glynn (United States), Linda Waverly, Mira Aghi (India), and Derek Yach (United States). After a lunchtime poster session, attendees reconvened for a session on networking that featured several innovative projects from different areas of the world from speakers Heather Wipfli, Konstantin Krasovsky (Ukraine), Wasim Maziak (Syria), Mahmoud Eyad Bachir (Syria), Jean-Francois Etter (Switzerland), and Ruben Israel.

The day was capped off with a final session that addressed the role of research in the implementation of the FCTC. Challenges and demonstrated successes in implementing the FCTC were described for several regions of the world by Mostafa Mohamed (Egypt), Michael Kunze (European Union), Naowarut Charoenca (Southeast Asia), and Geoffrey Fong (Western hemisphere), with Samira Asma from the U.S. Centers for Disease Control and Prevention describing the latest results from global tobacco surveillance efforts. The full day of discussion and brainstorming was wrapped up by Harry Lando, who called for continued efforts to ''internationalize'' SRNT and increased collaborative efforts to raise awareness and resources to expand global tobacco control initiatives.

Conclusion of 11th Annual Meeting

The 11th Annual Meeting of the Society for Research on Nicotine and Tobacco, held in conjunction with SRNT–Europe, and held for the first time outside of

North America, was a success. The major aims of achieving truly international participation, fostering discussion and promoting collaboration among scientists across geographical and disciplinary boundaries, and providing a state-of-the-art update on research advances across a broad spectrum of nicotine and tobacco research were all attained. The beautiful city of Prague in the Czech Republic proved to be an outstanding setting for this exciting meeting.

Plans for 12th Annual Meeting

The 12th Annual Meeting of SRNT will be held in Orlando, Florida, at Disney's Coronado Springs Resort February 15–18, 2006. The Program Committee (Suzanne Colby, program chair; and Eric Donny and Jennifer Tidey, program co-chairs) look forward to providing a productive meeting for all participants.

One priority for the upcoming meeting is to build upon past success and further increase discussion across the three major areas (preclinical, clinical, and public health/epidemiology) of nicotine and tobacco research. To that end, symposia submissions that address a substantive research area in depth by presentations drawing upon these three themes will be prioritized. The Call for Abstracts submission deadline for the Orlando meeting is September 16, 2005. Meeting and abstract submission information will be available on SRNT's Web site (www.srnt.org).

Acknowledgments

We wish to acknowledge gratefully that many conference presenters and event organizers contributed symposia and/or event summaries for this manuscript. We are also grateful for the generous financial support for conference events provided by the American Cancer Society, the American Legacy Foundation, GlaxoSmithKline, Pfizer, the Robert Wood Johnson Foundation, Sanofi-Aventis, Taylor and Francis Publishing, the U.S. National Cancer Institute, and the U.S. National Institute on Drug Abuse.

We appreciate the valuable assistance provided by Sheila Kirschbaum (Meeting Planner) and her team, as well as Bruce Wheeler (SRNT executive director) of The Rees Group, Inc., who provided extensive planning assistance and logistical support before and during the conference. We also thank SRNT President Ken Warner for his support and helpful advice throughout the meeting planning process.

The 2005 Program Committee included Mustafa al'Absi, Paul Aveyard, Ivan Berlin, Ron Borland, Jacques Cornuz, Pebbles Fagan, Geoffrey Fong, John Hughes, Laura Juliano, Jacques Le Houezec, Laura Cousino Klein (2004 Program Chair), Pamela Ling, Athina Markou, Marcus Munafò, Christi Patten, Sakire Pogun, Hana Ross, Stevens Smith, Serena Tonstad, David Vandenbergh, and Sue Wonnacott.

The efforts of these Program Committee members, along with those of 140 abstract reviewers, were essential to organizing the Annual Meeting. We sincerely appreciate the time they devoted to the scientific review process and the contributions they made to this program.

For the first time, the Annual Meeting had the benefit of a Local Organizing Committee, which was essential to coordinating events "on the ground" in Prague and helping meeting participants to make the most of their stay in the Czech Republic. We wish to express our heartfelt appreciation to Eva Kralikova, the chair of this committee, along with the committee members: Michael Ascherman, Petr Bartunek, Jaroslav Blahos, Richard Ceska, Renata Cifkova, Eva Havrdova, Jaromir Hradec, Drahoslava Hruba, Jan Klozar, Stanislav Kos, Karel Nespor, Michal Miovsky, Jaromir Musil, Daniela Pelcova, Jan Pirk, Petr Popov, Hana Rosolova, Bohumil Seifert, Jan Skrha, Vaclav Spicak, Alena Steflova, Petr Sucharda, Stepan Svacina, Petr Widimsky, Jan Zaloudik, Petr Zatloukal, and Tomas Zima.

Preparation of this manuscript was supplied by grants and institutional support to each of the authors. This includes grants from the National Institute on Drug Abuse awarded to Dr. Colby (DA16737-02) and Dr. Drobes (DA017906-02). Robert West is funded by Cancer Research UK.

SELECTED ABSTRACTS

PREDICTORS OF SMOKING CESSATION IN PATIENTS WITH SCHIZOPHRENIA

A. Eden Evins, Cori Cather, Melissa Culhane, Don Goff, Nancy A. Rigotti

The smoking-cessation rate among schizophrenics is low. This analysis aimed to create a model that will identify factors associated with tobacco abstinence in patients with schizophrenia. We hope that this information will be useful to clinicians who are attempting to optimize clinical treatment prior to recommending a smoking-cessation attempt. We used a dataset of 114 patients with schizophrenia who participated one of two trials of bupropion for smoking cessation. A univariate screen was used to select variables strongly associated with smoking cessation in this sample. A stepwise forward selection was run on the variables significantly associated with outcome on univariate screen using a cutoff of significance of $p=.01$ for selection. A bootstrap analysis was then used to validate the analysis. Positive and Negative Symptom Scale total score; Cognitive Symptom Subscale and Positive Symptom Subscale scores; and Schedule for Assessment of Negative Symptoms alogia subscale score were significantly associated with abstinence on univariate analysis. Controlling for bupropion treatment in the multivariable model, the cognitive side was significantly associated with abstinence; for every one-point increase (worsening) in the score, the odds-ratio for achieving abstinence was 0.6 (95% *CI* 0.42–0.86), $p=.005$. Controlling for the cognitive symptom subscale score compared to those on placebo, the odds-ratio of abstinence for those on bupropion was 5.8 (0.94–36.4), $p=.056$. We concluded that cognitive disorganization decreased the odds of abstinence controlling for bupropion treatment. Treatments that reduce cognitive symptoms in patients with schizophrenia may improve smoking-cessation rates.

Funding: NARSAD Young Investigator Award NIDA K23.

Correspondence: A. Eden Evins, Massachusetts General Hospital, 25 Staniford Street, Boston, MA 02114, USA; E-mail: a_eden_evins@hms.harvard.edu

MENTAL HEALTH AND ENVIRONMENTAL FACTORS ASSOCIATED WITH TOBACCO USE AMONG AMERICAN INDIAN YOUTH

ManSoo Yu, Arlene R. Stiffman

American Indian and Alaska Native adolescents have the highest lifetime tobacco use rates among all ethnic groups in the United States. Our study merged theories on problem behavior and social ecology to examine how mental health and environmental factors, including culture, were associated with American Indian youth tobacco use. We interviewed a stratified random sample of 205 reservation and 196 urban American Indian youth (13–19 years), living in a Southwestern state in 2001. Data were from the American Indian Multisector Help Inquiry (AIM-HI), a NIDA-funded study. The instrument consisted of scales measuring the following: (a) Mental-health problems (conduct disorder, depression, alcohol, and substance abuse/dependence); (b) familial environment (family mental-health problems and stressful events in family life); (c) social environment (peer misbehavior and neighborhood/school problems); (d) cultural environment (cultural activities and cultural pride/spirituality); and (e) tobacco use. Two-thirds of the reservation youth and half of the urban youth in this sample reported lifetime tobacco use. Multiple logistic regression showed that, when controlling for age and location, a mental-health factor (substance abuse/dependence) and environmental factors (e.g., family members' mental health problems and peer misbehavior) were significant predictors of American Indian adolescent tobacco use. Cultural factors and location (reservation vs. urban) were not significant predictors of their tobacco use. Environmental and mental health factors should be assessed for and incorporated into tobacco use intervention and prevention plans for American Indian youth in both reservation and urban areas.

Funding: U.S. National Institutes of Health (NIH) grant R01 DA13227.

Correspondence: ManSoo Yu, GWB School of Social Work, Washington University, CB 1196, One Brookings Drive, St. Louis, MO 63130, USA

COMPARING NICOTINE INHALER, BUPROPION, AND NICOTINE INHALER PLUS BUPROPION IN TREATING TOBACCO DEPENDENCE

Ivana T. Croghan, Richard D. Hurt, Gary A. Croghan, Jeff A. Sloan, Shaker Dakhil

This study had two purposes: (a) To determine whether combined use of nicotine inhaler and bupropion will improve smoking abstinence compared to either alone; and (b) to examine relapse prevention after abstinence is achieved. This study recruited 1,700 smokers in 19 sites throughout the United States. In phase I, smokers were randomized to nicotine inhaler, bupropion, or combination for 12 weeks. In phase II, those who were abstinent were randomized to bupropion, nicotine inhaler, combination, or placebo for 40 weeks, and were followed

for 12 weeks postmedication (phase III). Those smoking at the end of the phase I entered phase II for continued treatment on alternative therapy. At the end of phase I, 14%, 26%, and 34% (nicotine inhaler, bupropion, and combination, respectively) were abstinent. Of the 432 smokers at the end of phase I, zero–7% were abstinent at week 24. Of the 430 who were abstinent at the end of phase I, 23%–54% were abstinent at the end of phase II; 7%–29% were abstinent at the end of phase III. We concluded that smokers on combined therapy have a higher probability of abstinence than either alone. Those failing to be abstinent at the end of 12 weeks of tobacco-dependence therapy should seek alternate therapy. Finally, although combined therapy can help smokers achieve abstinence, continued therapy on the same combined medication does not appear to prevent relapse.

Funding: NIH National Cancer Institute, North Central Cancer Treatment Group; medication supplied by GlaxoSmithKline and Pharmacia Pharmaceuticals.

Correspondence: Ivana Croghan, Ph.D., Mayo Clinic, Nicotine Research Program, 200 First Street SW, Rochester, MN 55905, USA; E-mail: croghan.ivana@mayo.edu

INTERVENTION FOR TOBACCO DEPENDENCE AMONG PEOPLE WITH A PSYCHOTIC ILLNESS: RANDOMIZED CONTROLLED TRIAL WITH ONE-YEAR OUTCOME

R. L. Richmond, A. Baker, M. Haile, V. Carr, T. Lewin, K. Wilhelm, R. Taylor, S. Jansons

Prevalence of smoking among people with schizophrenia is much greater than in the general population (90% vs. 23%). Smoking related diseases rate second in frequency to suicide as the greatest contributor to early mortality among people with schizophrenia. Our goal was to evaluate the effectiveness of Cognitive Behavior Therapy (CBT) and nicotine replacement therapy (NRT) on the course of smoking and psychiatric symptomatology. We performed a multi-center study Sydney and Newcastle, Australia including people with a psychotic illness dependent on tobacco. We randomly assigned 298 participants to an eight-session intervention (CBT+NRT) or usual treatment. Blind post-treatment and follow-up assessments were conducted at 3, 6, and 12 months. Self-reports of abstinence were biochemically validated using expired CO. The project yielded strong follow-up rates of 85%, 82%, and 83%. Significantly more people in the treatment group were abstinent at 3 months compared to control group (point prevalence [PP], 15% vs. 6%, $p<.05$; continuous abstinence [CA], 12.2% vs. 4%, $p<.01$). There were no significant effects at 6 and 12 months. Among continuing smokers at 3 months, there was a significant decline in nicotine dependence scores in the treatment group compared to placebo. Data for participants who completed all treatment sessions were: At 3 months follow-up: (PP) OR 6.76, $p<.001$; at 6 months follow-up: OR 5.51, $p<.001$; and at 12 months follow-up: OR 3.22, $p<.01$. Participants were significantly more likely to be abstinent at follow-ups compared to those in the control group. Participants in the intervention group who attended all therapy sessions of CBT combined with NRT were significantly more likely to remain abstinent for 1 year compared to the control group. It is difficult for people with a comorbid psychotic condition to quit smoking, but if they remain in the smoking-cessation intervention program, they are likely to quit and remain abstinent for a year.

Funding: National Health and Medical Research Council, Rotary, CHATA.

Correspondence: Professor Robyn L. Richmond, Ph.D., School of Public Health and Community Medicine, University of New South Wales, Kensington, NSW 2052, Australia; E-mail: r.richmond@unsw.edu.au

EFFECTIVENESS AND COSTS OF DIFFERENT BENEFIT DESIGNS FOR TREATING TOBACCO DEPENDENCE: RESULTS FROM A RANDOMIZED TRIAL

Helen Ann Halpin, Sara B. McMenamin, Jeffrey Rideout, Gifford Boyce-Smith

This study assessed the costs and effects of adding coverage for proactive telephone counseling to pharmacotherapy benefits. The two research questions were (a) Is the effect of coverage for pharmacotherapy enhanced if counseling is also covered; (b) What is the effect of limiting access to pharmacotherapy to smokers who enroll in counseling? The study was an 8-month randomized trial conducted in 2001 comparing three benefit designs: (a) Drugs only—coverage for Zyban, NRT patch, and NRT nasal spray; (b) drugs and counseling—coverage for drugs and proactive telephone counseling; (c) drugs if counseling—coverage for drugs conditional on enrollment in covered proactive telephone counseling. The sample included 391 randomized adult smokers enrolled in Blue Shield of California's Preferred Provider Organization Plan. No statistically significant differences were observed across treatment groups for any of the quitting outcomes. Quit attempt rates averaged 59% ($p=.1$); quit rates during the study averaged 38% ($p=.2$); sustained quit rates averaged 20% ($p=.3$). The results of the logistic regression models find that neither of the treatment

groups with coverage for proactive telephone counseling reported higher rates for any quitting outcomes compared to the drugs-only group. Respective costs per sustained quit were: US$406 for the drugs-only group; US$689 for the drugs-and-counseling group; and US$770 for the drugs-if-counseling group. If pharmacotherapy (Zyban and NRT) for treating tobacco dependence is covered, we conclude that it is not cost-effective to also cover proactive telephone counseling, regardless of benefit design.

Funding: California Tobacco-Related Disease Research Program (TRDRP) grant 9RT-0096.

Correspondence: Helen Ann Halpin, Ph.D., Professor of Health Policy, University of California, Berkeley, School of Public Health, 140 Warren Hall, MC 7360, Berkeley, CA 94720-7360, USA; E-mail: helenhs@berkeley.edu

EFFECTS OF NICOTINE REPLACEMENT THERAPY ON POSTCESSATION MOOD STATES: FOCUS ON DEPRESSION AND GENDER

Tellervo Korhonen, Taru Mustonen, Arthur J. Garvey

We examined how nicotine replacement therapy (NRT) affects postcessation mood using Profile of Mood States (POMS) during the first 2 weeks among abstinent, depressed, and nondepressed female and male smokers. We recruited 608 smokers attempting to quit within a randomized controlled trial that included nicotine or placebo gum and brief counseling. Data were analyzed for 116 women and 126 men, of whom 32% (35 women, 28 men) met the criterion for depression at baseline (Center of Epidemiological Studies Depression Scale). At 1, 7, and 14 postcessation days we examined six self-reported mood states from the POMS, i.e., anxious, depressed, confused, angry, and energetic or fatigued. We conducted a series of mixed-design ANCOVA (Depression × NRT × Gender) on POMS variables using the corresponding baseline variable as a covariate as well as Tukey's HSD tests. No NRT effects were detected in the feeling-anxious symptoms. A significant NRT effect ($p=.04$) was found in feeling-depressed scores, wherein the NRT groups reported lower scores than the placebo groups, independent of depression and gender. Significant Depression × NRT interactions were found in feeling-confused ($p=.003$) and in feeling-angry ($p=.01$) scores, showing the NRT effect among the depressed but not among the nondepressed. These phenomena were more visible among women than among men. Depression × NRT × Gender interactions ($p=.05$) were found in the energy-related moods. Depressed women in the placebo condition had the lowest energy and the highest fatigue scores.

Funding: Academy of Finland grant 103650; NIH grants DA12503; DA06183.

Correspondence: Tellervo Korhonen, Tobacco Dependence Treatment and Research, Harvard School of Dental Medicine, 188 Longwood Avenue, Suite 30, Boston, MA 02115, USA; E-mail: tellervo_korhonen@hsdm.harvard.edu

SAFETY AND EFFICACY OF BUPROPION FOR SMOKERS HOSPITALIZED WITH ACUTE CARDIOVASCULAR DISEASE

Nancy A. Rigotti, Anne N. Thorndike, Susan Regan, Richard C. Pasternak, Yuchiao Chang, Kathleen McKool, Karen Emmons, Daniel E. Singer, Susan Swartz, Nancy Torres-Finnerty

Smokers who stop smoking after myocardial infarction (MI) reduce their mortality from acute cardiovascular disease (CVD) by 50%. Hospitalization for acute CVD (MI or unstable angina) provides an opportunity for smoking intervention. Cessation rates produced by counseling alone need improvement. Concern about safety has limited the use of nicotine replacement or bupropion in this setting. We tested bupropion's safety and efficacy in smokers hospitalized with acute CVD. We employed a randomized, double-blind, placebo-controlled trial of 12 weeks of bupropion SR (150 mg twice daily) with 248 smokers hospitalized with acute CVD. All subjects received validated smoking-cessation counseling in the hospital and five telephone calls postdischarge. Smoking status (verified by cotinine or CO measurement) and cardiac endpoints were assessed at 3 and 12 months. Analysis was intention-to-treat. Subjects lost to follow-up were considered smokers. Biochemically verified 7-day abstinence rates in bupropion and placebo groups were 37% versus 26% ($p=.06$) at 12 weeks (end of treatment); and 25% versus 21% ($p=.49$) at 12 months. There was no significant difference in the number of drug- and placebo-patients who reached a combined CV endpoint at 3 months ($n=20$ vs. 18; $p=.72$) or 12 months ($n=32$ vs. 22; $p=.13$). Hypertension incidence (>160 systolic or >100 diastolic) was similar in both groups ($n=10$ vs. 9; $p=.81$). We concluded that bupropion SR is safe to use in smokers hospitalized with acute CVD. The end-of-treatment results suggest a small benefit of bupropion plus counseling over counseling alone but this disappeared by 1 year. Further improvement in cessation strategies for high-risk CVD patients is needed.

Funding: NIH grant R01 HL61779; GlaxoSmithKline.

Correspondence: Nancy A. Rigotti, MGH Tobacco Research Center, Harvard Medical School, Boston, Massachusetts, USA; E-mail: nrigotti@partners.org

EPIDEMIOLOGY OF SMOKING AMONG ADULTS IN ALEPPO, SYRIA: FIRST POPULATION-BASED ESTIMATES

Wasim Maziak, Kenneth D. Ward, Thomas Eissenberg

Despite the spread of smoking in Syria, population-based estimates of popular forms of smoking are still lacking. The Aleppo Household Survey (AHS) was conducted in 2004 in Aleppo among a representative sample of adults (18–65 years). We applied a two-stage, stratified, cluster sampling with probability proportional to size used for the selection of residential neighborhoods (PPS), and random sampling for the selection of households and adults within households. Overall, 2,038 participated in the survey (45.2% men, mean age 35.3 years, response rate 94%). Participants were asked about tobacco use in the previous month, categorized into cigarettes, waterpipes, daily, and occasional. Participants reported cigarette smoking by 60% and 23.4% of men and women, respectively. Waterpipe smoking was reported by 19.7% and 6.0% of men and women, respectively. Other forms of smoking (cigar, pipe) were infrequent and reported by 1.1% of respondents. Frequency of smoking analysis shows the predominance of daily smoking for cigarettes (32.9% daily, 7.1% occasional), but the opposite for waterpipe (0.9% daily, 11.3% occasional). The age-gender stratified analysis (18–29 years; 30–45 years; 46–65 years) shows that cigarette smoking was most common among the middle-age group (65.3% and 32.3% for men and women, respectively). Waterpipe smoking was most common among the younger age group for men (28.3%) and younger and middle-age groups for women (6.6%). To guide intervention efforts, the findings point at the dramatic situation with smoking in Syria and highlight groups most likely affected.

Funding: U.S. Public Health Service (PHS) grants R01 TW05962 and R21 TW006545.

Correspondence: Wasim Maziak, Ph.D., Syrian Center for Tobacco Studies, P.O. Box 16542, Aleppo, Syria; E-mail: maziak@net.sy

RAT BRAIN CYP2B1: AN ENZYME THAT INACTIVATES NICOTINE AND ACTIVATES BUPROPION IS METABOLICALLY ACTIVE IN VIVO

Sharon Miksys, Rachel F. Tyndale

Cytochrome P450 enzyme CYP2B1 is the rat form of human CYP2B6, which inactivates nicotine and activates bupropion and tobacco-specific nitrosamines. CYP2B1/6 is induced in brains of rodents and monkeys chronically treated with nicotine, and is higher in brains of human smokers compared to nonsmokers. Induction is brain region- and cell-type-specific, e.g., in frontal cortex pyramidal neurons. CYPs are expressed in brain tissue, but as yet they have not been demonstrated to be functional in vivo. Mechanism-based inactivators (MBI) are enzyme substrates that are activated to metabolites that bind covalently to the CYP, rendering it inactive. We used radiolabeled 8-methoxypsoralen (8MOP), a potent MBI of CYP2B1, to demonstrate that brain CYP2B1 is metabolically functional in vivo. Male Wistar rats were injected subcutaneously with 1 mg/kg nicotine base or saline daily for 7 days, a dosing regime that induces brain but not liver CYP2B1. C8-xanthate (20 μg), a selective inhibitor of CYP2B1, was injected unilaterally into the frontal cortex. After 30 min, 3H-8MOP (10 μg) was injected bilaterally at the same bregma coordinates. After 1 hr, animals were sacrificed and membranes were prepared from frontal cortex. More 3H-metabolite was detected in frontal cortex tissue of nicotine-treated rats compared with controls (1.4-fold). This is consistent with nicotine induction of CYP2B1 in frontal cortex detected by immunoblotting and immunocytochemistry. Tissue pretreated with C8-xanthate showed a twofold reduction in 3H-metabolite, demonstrating the selectivity of 8-MOP for CYP2B1. This is the first demonstration that constitutive and induced brain CYPs are functional in vivo.

Funding: CIHR MT-14173, CAMH, Canadian Research Chair.

Correspondence: Sharon Miksys, Ph.D., Department of Pharmacology, University of Toronto, 1 Kings College Circle, Toronto, Ontario, Canada M5S 1A8; E-mail: s.miksys@utoronto.ca

EFFICACY OF BUPROPION AND NORTRIPTYLINE FOR SMOKING CESSATION AMONG PEOPLE WHO ARE AT RISK FOR OR HAVE CHRONIC OBSTRUCTIVE PULMONARY DISEASE: RESULTS FROM A RANDOMIZED, PLACEBO-CONTROLLED TRIAL

E. J. Wagena, P. G. Knipschild, M. J. H. Huibers, E. F. M. Wouters, C. P. van Schayck

Cigarette smoking is an important risk factor and prognostic factor for chronic obstructive pulmonary disease (COPD). Yet, few clinical trials for smoking cessation in people at risk for COPD or with existing COPD have been conducted. We studied the effects of bupropion SR and nortriptyline in a randomized, double-blind, double-dummy, placebo-controlled trial. We randomly assigned 255 adults to receive bupropion SR (150 mg twice daily), nortriptyline (75 mg once daily), or placebo for 12 weeks.

Prolonged abstinence rates from week 4 to 26 were: Bupropion SR group, 28%; nortriptyline group, 25%; and placebo group, 15%. The difference between bupropion SR and placebo: 13.1%; 95% *PI* 1.2–25.1; between nortriptyline and placebo: 10.2%, 95% *PI* −1.7 to 22.2). Especially in participants with existing COPD, the use of bupropion SR or nortriptyline resulted in higher prolonged abstinence rates compared to placebo (27%, 21%, and 8%, respectively). The estimated risk of relapse in participants with existing COPD was 1.4 compared to that in participants at risk for COPD (hazard ratio: 1.44; 95% *PI* 1.08–1.93). We concluded that bupropion SR and nortriptyline seem useful medications for smoking cessation, especially in people with existing COPD.

Funding: Dutch Asthma Foundation (NAF grant 3.2.00.21), Health Research and Development Council (ZorgOnderzoek Nederland grant 2200.0111), The Netherlands; Lundbeck B.V. provided active nortriptyline free of charge, but played no role in the design or conduct of the study, nor in the interpretation and analysis of data.

Correspondence: Edwin J. Wagena, Pulmonary Rehabilitation Centre Hornerheide, P.O. Box 4080, 6080 AB Haelen, The Netherlands; Tel: +31 (0) 475 587469; Fax: +31 (0) 475 587592; E-mail: edwinwagena@proteion.nl

EVALUATING POTENTIAL REDUCED EXPOSURE PRODUCTS (PREPS) FOR SMOKERS

Alison B. Breland, Bethea A. Kleykamp, Amy J. Opilla, Thomas Eissenberg

In the United States, the tobacco industry markets potential reduced-exposure products (PREPs) to smokers. For example, Eclipse® primarily heats tobacco and is marketed to reduce polycyclic aromatic hydrocarbons (PAHs), whereas Advance®, made with specially cured tobacco, is marketed to reduce nitrosamines such as NNK. There are few accepted methods for determining if PREPS methods reduce exposure to these and other smoke toxicants. This study's purpose is to examine if clinical laboratory methods can be used to measure PREP users' toxicant exposure. Twenty-four smokers (18 men; >15 cigarettes/day) have completed this four-condition, within-subject outpatient study (anticipated n=36). Participants complete four, Latin-square ordered, 5-day conditions in which they smoke only Advance, Eclipse, own-brand, or no cigarettes. Compliance is reinforced monetarily and monitored daily. Preliminary analyses reveal that mean urine NNK metabolite levels (i.e., NNAL) were reduced significantly after 5 days of no smoking (0.56 pmol/ml); smoking Advance (0.72 pmol/ml); or smoking Eclipse (0.82 pmol/ml), relative to own-brand cigarettes (1.26 pmol/ml). Mean expired-air carbon monoxide levels were reduced significantly after 5 days of no smoking (2 ppm) or smoking Advance (14 ppm), but increased after smoking Eclipse (24 ppm), compared to own-brand (19 ppm). Mean PAH metabolite levels were significantly reduced only in the no-smoking condition. On average, participants used significantly fewer Eclipse (15 cigarettes/day), but not Advance (21 cigarettes/day), compared to their own brand (21 cigarettes/day). These findings suggest that PREP evaluation is complex, and highlight the need for continued objective and comprehensive PREP testing strategies that include clinical laboratory methods.

Funding: U.S. PHS grants R01CA103827 and F31DA015570.

Correspondence: Alison Breland, Virginia Commonwealth University, Box 980205, Richmond, VA 23298-0205, USA; E-mail: abbrelan@vcu.edu

PERFORMANCE OF α_7 NICOTINIC NULL MUTANTS IS IMPAIRED IN APPETITIVE LEARNING

Jeanne M. Wehner, Jason Keller, Ashleigh Keller, Barbara J. Bowers

Nicotine enhances learning and memory as measured in a variety of paradigms across a number of species. Little is known concerning which nicotinic cholinergic receptors (nAChRs) participate in the regulation of learning and memory. The most highly expressed nAChRs in mammalian brain are $\alpha_4\beta_2$ and α_7 receptors. A role has been identified for β_2-containing nAChRs in regulating some forms of learning in the laboratories of Changeaux, Picciotto, and Stolerman using null mutants. The role for α_7-containing nAChRs in some forms of learning has been less clear. Our previous work indicated that α_7 receptors were not necessary for contextual learning, but there are multiple forms of memory. We examined appetitive learning using a signaled nose-poke task in α_5, α_7, β_2, β_3, or β_4 null mutant mouse lines. All mutant mice performed normally in early stages of training. As task complexity increased, the α_7 mutants were impaired compared to wild types when the auditory cue was delivered on a variable schedule. Mutants lacking α_5, β_2, β_3, or β_4 subunit expression performed normally. Although α_7-mutant performance eventually equaled that of wild types, by 10 days of training, mutants continued to show increased impulsivity: They were less efficient than wild types in learning to withhold their responses until the presentation of the auditory cue to receive a

reward. These results agree with the recent results of Young et al. (2004, *Neuropsychopharmacology, 29*, 891–900) and demonstrate that α_7 receptors are important in learning tasks that have a large attentional component.

Funding: Colorado Tobacco Research Program grant 2R-033.

Correspondence: Jeanne M. Wehner, Institute for Behavioral Genetics, University of Colorado, 447 UCB, Boulder, CO 80309, USA; E-mail: wehner@ibg.Colorado.edu

ABSTINENCE-INDUCED CHANGES IN SELF-REPORTED CRAVING ARE CORRELATED WITH CHANGES IN BRAIN RESPONSES TO SMOKING CUES: AN EVENT-RELATED FMRI STUDY

F. Joseph McClernon, F. Berry Hiott, Scott A. Huettel, Jed E. Rose

Correlations between self-reported craving and brain responses to drug cues have been observed across addiction types and imaging modalities in many brain regions. These include the prefrontal cortex, anterior cingulate gyrus (ACG), insular cortex, and amygdala regions. These regions subserve processes related to emotion, motivation, attention, and response-inhibition/initiation. We investigated how the relation between craving and brain responses in these regions is influenced by overnight abstinence and smoking satiation in a sample (n=13) of dependent smokers. During each fMRI scanning session, participants viewed 60 pictorial smoking cues (e.g., lit cigarettes, people smoking) and 60 control cues (e.g., keys, people using the phone), and reported their craving for cigarettes. Averaged event-related hemodynamic responses (HDRs) were calculated for cortical and subcortical regions of interest (ROIs). Pearsons correlation coefficients were calculated between abstinence-induced changes in craving (abstinent day/satiated day) and changes in HDR amplitudes in response to smoking and control cues. The following significant positive correlations (two-tailed p values) between changes in craving and HDRs for smoking (but not control) cues were observed: (a) $p<.05$: Left-hemisphere inferior frontal gyrus (0.611); superior frontal gyrus (0.577); thalamus (0.575); right-hemisphere dorsal ACG (0.638); (b) $p<.01$: Ventral ACG (0.719); right bilateral middle-frontal gyrus (0.858); (c) $p<.001$: Left bilateral middle-frontal gyrus (0.818). These results indicate that frontal cortical circuits—particularly those in the left hemisphere—mediate relations between drug craving and cue reactivity.

Funding: NIH grant R03 DA016212-01.

Correspondence: F. Joseph McClernon, Ph.D., Tobacco Neuroscience Research Laboratory, Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Box 3516, Durham, NC 27710, USA; E-mail: mccle011@mc.duke.edu.

EXAMINATION OF A PROCESS MODEL OF ADOLESCENT SMOKING-CESSATION EFFORTS IN RELATION TO GENDER

Laura MacPherson, Mark G. Myers

Little is known regarding adolescent efforts to change smoking behavior, especially in regard to gender. This study investigated the role of gender in the relationship of motivation and cognitive variables with adolescent-smoking quit efforts. Baseline smoking-cessation motives, cessation self-efficacy, intentions to quit, and smoking outcome expectancies were modeled in relation to volitional quit attempts. These were assessed at a 6-month follow-up separately by gender. Cognitive variables were expected to partially mediate and moderate the relationship between motives and quit attempts. Social influence motives were expected to be stronger predictors of change efforts for girls and short-term consequence motives to be stronger predictors for boys. Participants were 98 adolescent smokers, on average 16.8 (1.0) years old, 55% female, and 71% White. Of these participants, 86% were daily smokers and 44% made at least one quit attempt between baseline and follow-up. Logistic regressions and multigroup path analyses were conducted. Patterns of predictors to prospective quit attempts differed by gender, with (a) intention to quit (OR=7.06) predictive of quit attempts for males; and (b) social-influence motives related to intentions to quit (OR=2.31) and to quit-attempts (OR=1.93) among females. Hypothesized mediating and moderating relationships were not supported within gender. However, intention-to-quit mediated the relationship between social-influence motives and quit attempts for the full sample. These results highlight the importance of social influences in motivating quit efforts among adolescent girl smokers. Further elucidation of adolescent smoking-cessation processes can serve to inform intervention design.

Funding: TRDRP grant 10IT-0280.

Correspondence: Laura MacPherson, Brown University Addictions Research, Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906, USA; E-mail: laura_macpherson@brown.edu

BRIEF SMOKING-CESSATION INTERVENTION WITH TUBERCULOSIS PATIENTS IN SUDAN

Mohamed Salieh, Hussein Elhaj, Khadija Adam, Amar Hassan, Karen Slama, Donald A. Enarson

Tuberculosis kills about half of those infected who go untreated. Tobacco use may play a role in unfavorable treatment outcomes and subsequent recurrence of disease even after treatment, but tobacco control is not systematically included in the comprehensive care of tuberculosis patients—particularly in low-income countries where the greatest majority of tuberculosis patients live. A controlled trial of brief smoking cessation was included as part of a feasibility study of adding tobacco cessation advice to tuberculosis case-management in health care facilities in Sudan. A sample of 531 newly diagnosed male tuberculosis patients in 24 healthcare centers was recruited into the trial. More than 80% of the intervention patients used either cigarettes or toombak (oral snuff). The smoking-cessation intervention consisted of four brief sessions over the 8 months of tuberculosis treatment. Final 12-month self-reported results indicated that a significantly greater number of patients in the intervention group (54%) than in the control group (10.6%) had stopped tobacco use during tuberculosis treatment and maintained abstinence from all tobacco use. Baseline motivation and confidence scores were significantly higher among those who had stopped by the second visit, as were second visit scores on later cessation. The TB patients enrolled in the study had lower default rates and lower death rates than the total population of newly detected male TB patients receiving treatment during the intervention trial period.

Funding: International Union Against Tuberculosis and Lung Disease.

Correspondence: Karen Slama, International Union Against Tuberculosis and Lung Disease, 68 Boulevard Saint-Michel, 75006 Paris, France; E-mail: kslama@iuatld.org

RANDOMIZED PLACEBO-CONTROLLED TRIAL OF NICOTINE NASAL SPRAY IN GENERAL PRACTICE

Gay Sutherland, John A. Stapleton, Michael A. H. Russell

To date, nicotine nasal spray has been tested in specialist smokers' clinic settings combined with intensive behavioral support. Twenty-four percent of active patients were continuously abstinent for 12 months compared to 12% of placebos. We aimed to evaluate if the nicotine spray is also effective when given with only brief advice and support by general practitioners and nurses in primary care. We conducted a randomized, placebo-controlled trial in 27 general practices (761 smokers) in England with 12 weeks follow-up. All participants received GP advice, a booklet, and either active nicotine nasal spray or placebo for up to 12 weeks, with brief support and follow-up at 1, 2, 3, 6, and 12 weeks after stopping. Nicotine spray compared to placebo more than doubled the number who were continuously abstinent between week 3 and week 12 (15.4% vs. 6.7%; odds ratio=2.6; 95% *CI*=1.5–4.4). Of those participants who had not stopped by the end of the first week (417), only one (0.2%) was classified as abstinent during weeks 3 to 12. We concluded that, when given with brief GP or nurse advice and support, nicotine nasal spray is an effective aid to stopping smoking. In this setting the effectiveness of the spray was similar to that previously demonstrated for the nicotine patch, but overall success rates were lower than with specialist support. There was no evidence that continued treatment of those initially failing was effective.

Funding: Medical Research Council; additional support and medication provided by Pharmacia UK.

Correspondence: Gay Sutherland, BA, M.Phil., Research Clinical Psychologist, Tobacco Research Unit, Addiction Sciences Building, Institute of Psychiatry, 4 Windsor Walk, London SE5 8AF, UK; E-mail: g.sutherland@iop.kcl.ac.uk

ROLE OF CLOSE FRIENDS' VS. PARENTS' AND OLDER SIBLINGS' SMOKING IN CHILDREN'S 12TH GRADE SMOKING: A PROSPECTIVE STUDY

Jonathan B. Bricker, Arthur V. Peterson, K. Bharat Rajan, Brian G. Leroux, M. Robyn Andersen

Our study aimed to use a novel "social epidemic" probability model to conduct one of the few longitudinal studies of the relative influence of smoking habits of close friends versus those of parents and older siblings in the prediction of youth smoking. We assessed the smoking status of close friends when the subjects were in 5th grade. We assessed the smoking status of parents and older siblings when the subjects were in 3rd grade. Children's daily smoking status was assessed in 12th grade of schools in 40 Washington State school districts, which participated in the long-term Hutchinson Smoking Prevention Project. Participants were the 4,689 families for whom the smoking status of friends, parents, older siblings—as well as that of the children subjects—was available. Questionnaire data were gathered on friends, parents, older siblings, and children, who were 49% female and 91% Caucasian. Results from this new social-epidemic statistical model show that:

(a) The probability that one close friend's smoking influenced the child to smoke daily was 9% (95% *CI* 6%–12%); (b) the probability that one parent's smoking influenced the child to smoke daily was 11% (95% *CI* 9%–14%); and (c) the probability that one older sibling's smoking influenced the child to smoke daily was 7% (95% *CI* 1%–12%). These results suggest that early exposure to a close friend's smoking has a similar influence as that of parents or older siblings. Thus, the role of early exposure to a close friend's smoking may not be as strong as previously thought. Public health interventions targeting family smoking, in addition to that of close friends, would be valuable.

Funding: NIH grants CA77581 and CA38269.

Correspondence: Jonathan B. Bricker, Ph.D., Fred Hutchinson Cancer Research Center, 1100 Fairview Avenue North, PO Box 19024, M2-C826, Seattle, WA 98109, USA; E-mail: jbricker@u.washington.edu

A RANDOMIZED, CONTROLLED TRIAL OF SMOKING REDUCTION IN HEART-DISEASE PATIENTS

A. Joseph, S. Hecht, S. Murphy, M. Gross, H. Lando, R. Bliss, C Le, D. Hatsukami

The Reduction of Smoking in Cardiac Patients (ROSCAP) Study is a randomized, controlled trial in heart-disease patients to test the effect of a smoking reduction intervention on cigarettes per day (CPD) and biochemical and clinical indicators of tobacco exposure. We randomly assigned 152 subjects with heart disease who did not intend to stop smoking to smoking reduction (SR) or usual care (UC). The SR group received counseling and nicotine replacement therapy to encourage at least 50% reduction in CPD. Subjects smoked an average of 27.4 CPD at baseline. At 6 months, SR participants reduced CPD by 39%, compared with 25% in UC (difference NS). Of the participants, 6/78 SR participants quit smoking, compared to 5/74 UC participants. There were no significant differences between treatment groups in changes in levels of nicotine; cotinine; carbon monoxide (CO); F2-isoprostane; hs-C-reactive protein (hs-CRP); or 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol and its glucuronides (total NNAL). The 6-min walk-test distance decreased by 138 feet in the SR group compared to 249 feet in UC (difference NS). Ten SR participants sustained serious adverse events (seven cardiac) compared to 13 UC participants (nine cardiac). Because there was significant reduction in both groups, we compared all subjects' biomarker levels at 6 months to baseline. There was no significant change in total NNAL, nicotine, cotinine, or F2-isoprostanes, and hs-CRP CO decreased by 6.0 ppm ($p=.0007$). We concluded that the SR intervention did not significantly reduce CPD or toxin exposure, or improve smoking cessation or clinical outcomes compared to UC. There was some evidence of compensation in the SR group as total NNAL levels increased.

Funding: NIH grant DA13333-02.

Correspondence: Anne Joseph, M.D., M.P.H., Minneapolis Veteran's Administration Medical Center and University of Minnesota, Section of General Internal Medicine (111-0), One Veterans Drive, Minneapolis, MN 55417, USA; E-mail: anne.m.joseph@med.va.gov

CIGARETTE SMOKING IN CHINESE MALE TWINS: THE QINGDAO TWIN REGISTRY

Christina N. Lessov, Gary E. Swan, Zengchang Pang, Qian Guo, Shaojie Wang, Liming Lee, Weihua Cao, C. Anderson Johnson

The world's largest concentration of tobacco users (300 million) is found in China but the extent to which genetic factors play a role in tobacco use etiology is unknown. Cigarette smoking was assessed in Chinese twins aged 24 or older from Qingdao City. Nearly all female twins were nonsmokers (99.2%; $n=524$ twins), whereas 58% of the male twins ($n=486$) were current smokers, and 8.4% reported having quit for 1 month or more. Among male lifetime smokers, 46.4% smoked 20 or more cigarettes per day. Because of low smoking prevalence in females, analysis of the relative contribution of genetic and environmental influences on cigarette smoking was limited to male data as follows: Current smoking, 120 monozygotic (MZ) and 72 dizygotic (DZ) complete pairs; heavy smoking, 103 MZ and 62 DZ complete pairs. The best-fitting univariate model for current smoking indicated that 75.1% (95% *CI* 56.7–87.5) of the phenotypic variance was explained by genetic effects, with no evidence for a significant contribution from shared environment. For heavy smoking, there was a relatively larger contribution from genes (66.2%, 95% *CI* 0.0–88.4) than from shared environment (8.7%, 95% *CI* 0.0–71.0). These results support findings from twins of Western origin and encourage further work in tobacco use in Chinese twins.

Funding: NIH grant P50 CA8473; Sidney Garfield Endowment; China Medical Board, New York (CMB01); School of Public Health, Beijing University.

Correspondence: Christina N. Lessov, SRI International, Center for Health Sciences, 333 Ravenswood Ave, Menlo Park, CA 94025, USA; E-mail: christina.lessov@sri.com

EFFECTS OF WEIGHT-RELATED CUES ON SMOKING MOTIVATION

Elena Lopez, David Drobes, Thomas Brandon

Previous research has established that among women smokers, weight concerns and negative body image are associated with tobacco smoking, smoking cessation, and relapse. Existing research has been correlational and quasi-experimental. A causal relationship between body image and smoking motivation has not yet been demonstrated. The aim of this study was to examine this relationship using a cue-reactivity paradigm, and to test whether an experimental manipulation designed to challenge women's body image produces changes in their motivation to smoke. The study employed a 2×2 crossed, factorial within-subjects design (body image cues $\times$ smoking cues) with 62 female college smokers. The body image manipulation included a photo of a thin model or a neutral object; the smoking manipulation displayed a photo of a smoking cue or a neutral object. Both factors were displayed simultaneously. Dependent measures were self-reported urge to smoke, heart rate response, and skin conductance response. As hypothesized, both smoking and thin model images increased reported urges to smoke. Additionally, as expected, trait-body dissatisfaction moderated the effect of the body image manipulation such that those women with greater body dissatisfaction produced greater reactivity to the thin model image (when smoking cues were not present). Preliminary analyses of the psychophysiological data appear consistent with the urge findings. In summary, the results indicate that among young women, the viewing of images of thin women can increase smoking urges, which is consistent with a causal influence of state body satisfaction. Clinical implications will be discussed.

Funding: University of South Florida and NIH grant R01 CA94256.

Correspondence: Elena Lopez, M.A., University of South Florida, H. Lee Moffitt Cancer Center and Research Institute, 4115 E. Fowler Avenue, Tampa, FL 33617, USA; E-mail: lopezen@moffitt.usf.edu

THE KNOWLEDGE AND UTILIZATION GAP: OPPORTUNITIES TO MARKET TELEPHONE QUIT LINES TO OLDER YOUTH

Dianne C. Barker, Gary A. Giovino, Cindy Tworek, Julia Gable, C. T. Orleans

Although 37 states manage telephone quit lines; few have tailored marketing or quit-line protocols for youth. We used weighted data from the 2003 baseline wave of the National Youth Smoking Cessation Survey, a 2-year longitudinal telephone survey of 2,582 randomly selected U.S. smokers aged 16–24 years, to study youth's awareness of, preference for, and use of telephone quit lines relative to other quitting approaches. Seventy-seven percent of young smokers had tried to quit at some time. Awareness of quit lines was higher among quit-attempters living in states with a quit line (49%), than among those in states without a quit line (30%; $p<.001$). Only 2% of quit attempters had ever called a quit line, compared to more than one-fifth of quit-attempters who had ever tried NRT or talked with a health professional about quitting. Less than a majority of all smokers (40%) believed that telephone support from a counselor would help them quit, compared to 81% for financial incentives; 57% for NRT; and approximately 50% for smoking-cessation support groups. Females (44%) were more likely than males (37%; $p<.01$) to believe telephone counseling would be helpful. Of those smokers who indicated that telephone counseling would be very helpful, characteristics of the counselor were important: 70% preferred an ex-smoker; 33% preferred one of the same age; and 17% wanted a counselor of the same gender. Implications of these findings will be discussed in the context of how quit line services should be designed and marketed to young smokers.

Funding: Robert Wood Johnson Foundation (RWJF); NIH; Centers for Disease Control and Prevention (CDC) Office on Smoking and Health (OSH).

Correspondence: Dianne C. Barker, M.H.S., Principal, Barker Bi-Coastal Health, 3556 Elm Drive, Calabasas, CA 91302, USA; E-mail: dcbarker @earthlink.net

SMOKING PREVALENCE AND TOBACCO USE DETERMINANTS AMONG STUDENTS FROM 10 MEXICAN CITIES

Raydel Valdés-Salgado, I. Hernández-Ramos, J. Thrasher, E. Lazcano-Ponce, F. Meneses-González, M. Hernández-Ávila

Our goal was to use cross-sectional data from the Global Youth Tobacco Survey Mexico 2003 (19,502 students enrolled in 225 schools) to estimate the prevalence and determinants of tobacco use among adolescents enrolled in Mexican secondary schools. We used a school-based survey with a two-stage cluster sampling design. Estimates adjusted for the study design and sampling weights. We found that one-fifth of students (19.9%) had smoked in the last month, 90% of whom thought they could quit smoking if they wanted to. One-fourth (25.2%) of never-smokers were susceptible to initiating smoking the following year. Smokers mostly bought their own cigarettes (37%) or borrowed them from friends

(32.2%). Multivariable analysis showed that factors significantly associated with current student smoking included the following (adjusted by gender, parents smoking, and discussion with a family member about the harmful effects of smoking): Having pocket money to spend per month; friends smoking (*OR* 1.81, 95% *CI* 1.50–2.18); age (*OR* 1.40, 95% *CI* 1.31–1.50); belief that it is safe to smoke for 1–2 years if they quit after that (*OR* 1.72, 95% *CI* 1.34–2.21); knowledge that cigarette smoking is harmful to their health (*OR* 0.47, 95% *CI* 0.34–0.64); knowledge that tobacco is a drug (*OR* 0.56, 95% *CI* 0.47–0.67); belief that he/she is too young to smoke (*OR* 0.61, 95% *CI* 0.45–0.82); and ownership of an item with a cigarette brand logo on it (*OR* 1.85, 95% *CI* 1.48–2.32). We concluded that tobacco-control activities in Mexico need to be strengthened to combat tobacco use among adolescents.

Funding: Pan American Health Organization; National Institute of Public Health, Mexico.

Correspondence: Raydel Valdes-Salgado, National Institute of Public Health, Avenida Universidad 655, Cuernavaca, Morelos 62508, Mexico; E-mail: rayvs@insp.mx

TELESTOP: A RANDOMIZED TRIAL OF INCREASED ACCESS TO BEHAVIORAL AND PHARMACOLOGICAL THERAPY FOR SMOKING CESSATION

Lawrence An, Shu-Hong Zhu, David Nelson, Nancy Arikian, Sean Nugent, Melissa Partin, Anne Joseph

Brief health-care provider intervention is recommended for all tobacco users. The U.S. National Action Plan for Tobacco Cessation also endorses telephone counseling that includes access to pharmacological therapy. The benefit of telephone care compared to primary-care–initiated intervention has not been examined previously. We performed a randomized, controlled trial of telephone versus standard care at five Veterans Administration medical centers. We recruited 838 smokers via direct mail. Of these, 420 were randomized to standard care (tobacco treatment as part of routine health care); 418 were randomized to telephone care and received counseling (adapted from the California Helpline protocol). Pharmacological therapy (NRT and/or bupropion SR) was mailed directly to appropriate subjects. There were no baseline differences between study groups on demographic or smoking characteristics (91% male; age 57+11 years; 26+12 cigarettes per day). During the study, 90% of standard-care subjects visited their health-care provider, and 98% discussed tobacco (92% advised to quit; 50% offered pharmacological therapy). Standard-care discussions were brief (75% reporting <5 min). Telephone-care subjects completed a median of seven calls (total phone contact 123+71 min). Telephone care increased use of any behavioral counseling programs (85% vs. 24%, $p<.001$) and pharmacological therapy (90% vs. 52%, $p<.001$). At the 12-month follow-up, telephone care was superior to standard care in terms of 30-day abstinence (19.2% vs. 13.3%, $OR=1.55$ [1.06–2.25], $p=.03$) and 6-month sustained abstinence (13.1% vs. 4.1%, $OR=3.50$ [1.99–6.15], $p<.001$). Telephone care increases the use of behavioral counseling and pharmacological therapy and leads to substantially higher rates of sustained abstinence compared to standard care.

Funding: Veterans Administration Health Services Research and Development Service grant SUI99101.

Correspondence: Larry An, M.D., Internal Medicine, University of Minnesota, MMC741, 420 Delaware Street SE, Minneapolis, MN 55455, USA; E-mail: lcan@umn.edu

NICOTINE ENHANCES RESPONSE TO A VISUAL REINFORCER IN A NOVEL SELF-ADMINISTRATION PARADIGM

Matthew Palmatier, F. Fay Evans-Martin, Alycia Hoffman, Anthony R. Caggiula, Nadia Chaudhri, Alan F. Sved

Previous studies from our laboratory have demonstrated that nicotine (NIC) enhances responses to a discrete visual stimulus (VS). One shortcoming of these studies is that delivery of both the VS and NIC depends on the same behavior (i.e., pressing a single, active lever). The experiments we report here examined whether making each outcome contingent on separate levers would alter the reinforcing efficacy of NIC, VS, or both. Four groups of rats (2-Lever; NIC+VS; NIC-Only; or VS-Only) were surgically implanted with jugular catheters. Self-administration training began after a short recovery period (4–7 days). For the 2-Lever group, pressing one lever resulted in VS presentation, whereas pressing the other lever produced a NIC infusion (0.06 mg/kg, free-base). For the remaining groups, the appropriate outcome (NIC+VS; NIC-only; or VS-only) was delivered as a result of responding on the randomly assigned active lever. Across daily 1-hr self-administration sessions, the NIC+VS group received more NIC relative to the NIC-Only group. In contrast, the 2-Lever and NIC-Only groups self-administered similar amounts of NIC. Notably, VS presentations for the 2-Lever and NIC+VS groups did not differ across training. However, both of these groups received more VS-deliveries than the VS-Only group. For the NIC+VS group, this pattern replicates the previously described synergistic increase in response induced by co-delivery of NIC and VS.

The results from the 2-Lever condition suggest that high rates of response normally seen for NIC self-administration reflect increased motivation for the VS, which is engendered by a relatively small amount of NIC that is sufficient to sustain both the primary reinforcing and reinforcement-enhancing effects of the drug.

Funding: NIH grant DA10464.

Correspondence: Anthony R. Caggiula, Department of Psychology, University of Pittsburgh, 3131 Sennott Square, 210 South Bouquet Street, Pittsburgh, PA 15260, USA; Tel: (412)-624-4501; Fax: (412)-624-4428; E-mail: tonypsy@pitt.edu

BRITISH AMERICAN TOBACCO'S STRATEGY TO MARKET TO YOUNG PEOPLE WITH "LIGHT" CIGARETTES

Richard D. Hurt, Monique E. Muggli, Jon Ebbert

New internal corporate documents produced by British American Tobacco (BAT) in ongoing litigation in the United States reveal that, despite BAT's public pronouncement of adult choice and its development of Youth Smoking Prevention (YSP) programs, it remains committed to reaching young people through light cigarettes. BAT's marketing department found that the consumer psychology of the term "lights" was far superior to that of "low tar." BAT's corporate marketing vision of globalizing its low-delivery brands targeting young people is in direct conflict with the company's YSP programs and its public support for eliminating underage smoking worldwide through the WHO's Framework Convention on Tobacco Control. To increase profits and compete with the globalization of Philip Morris's Marlboro, BAT's marketing department pushed for additional market research and development of low-delivery cigarettes in 1998. Through its light-cigarettes segment, the company sought to attract younger smokers. It recognized that there is a higher likelihood to induce younger smokers to start smoking with light cigarette offerings; that young people saw lights as a separation from the adult world; and that peer-pressure among young people plays a very important spur to use light cigarettes. BAT's consumer research concentrated on sensory and behavioral aspects of smoking so-called light and ultra-light products. Reported findings included that behavioral adjustment is a per-stick rather than per-day phenomenon, and that smoking is to optimum not maximum delivery. Also noted was that switching adjustment takes up to 1 month and that physiological intolerance of full flavor develops.

Funding: NIH grant R01 CA90791.

Correspondence: Monique E. Muggli, MPH, Nicotine Research Program (contracted researcher); St. Paul, MN 55105, USA; E-mail: mmuggli@comcast.net

HOW THE FDA MIGHT APPLY PRINCIPLES OF RISK MANAGEMENT PRIOR TO PERMITTING HEALTH CLAIMS FOR SMOKELESS TOBACCO AS PART OF A HARM-REDUCTION STRATEGY

Jack Henningfield, Reginald Fant, Mitch Zeller, Joe Gitchell, John Pinney

Health claims for smokeless tobacco (SLT) raise profound public health concerns. Given the historical marketing practices of SLT manufacturers, new health claims should be disallowed prior to regulatory scrutiny of the science behind such claims, as well as the risks and benefits of permitting claims. One precedent is the Food and Drug Administration's (FDA's) evaluation of over-the-counter (OTC) marketing for nicotine gum and patches in the mid 1990s, in which the concerns included the following: Abuse by youth, leading to the development of addiction in nontobacco users; inappropriate use, such as for weight control; and use to enable smoking and delay cessation by addressing nonsmoking situations. The FDA's approval required the sponsors to study the risks and how they would be minimized; conduct real world simulation trials; commit to marketing and packaging to minimize the risks; and implement postmarketing surveillance to detect youth abuse. Since the 1990s, the FDA has devised a systematic approach termed Risk Management to guide the evaluation of products that pose credible risks: (www.fda.gov/cder/guidance/5766dft.pdf). Risk Management has been applied to medications with high risk of birth defects, addiction, and other unintended consequences. Key components include the following: (a) Thorough evaluation of potential risks and benefits; (b) provision of relevant epidemiological and survey data, and (c) development of a risk-minimization action plan (RiskMAP) to enable realization of anticipated benefits. In some cases, postmarketing surveillance is required to detect potential unintended consequences and guide corrective actions by the Sponsor and Agency. Strategic application of FDA Risk Management principles provides a basis for determining approvability by evaluating the risk/benefit ratio and a strategy for minimizing risk. This presentation will discuss the rationale and elements of Risk Management and describe how the strategy might be applied to an evaluation of new health claims for SLT products prior to marketing.

Funding: Travel support for JH, JG, RF, and MZ provided by Pinney Associates, which receives support from GlaxoSmithKline Consumer HealthCare; additional support to JH provided by Innovators Awards program of the Johns Hopkins University School of Medicine and RWJF; JH, JG, and JP have an interest in a smoking-cessation product under development.

Correspondence: Jack Henningfield, vice president, Research and Health Policy, Pinney Associates, 3 Bethesda Metro Center, Suite 1400, Bethesda, MD 20814, USA; E-mail: jhenning@pinneyassociates.com

AN EVOLUTION IN LOW-TAR ADVERTISING: LESSONS FOR THE FUTURE

Stacey J. Anderson, Pamela M. Ling

Our aim was to explore the evolution from cigarette product attributes to psychosocial needs unrelated to smoking in advertising campaigns for low-tar cigarettes. We analyzed previously secret tobacco-industry documents and public advertising collections. We found that Lorillard's "Kent," RJ Reynolds's "Vantage," and Philip Morris's "Merit" brands targeted smokers who were concerned about the health hazards of smoking; these brands competed in the moderation segment from the late 1950s through the 1980s. Their advertising first emphasized product characteristics (filtration, low tar) that implied health benefits. Over time, advertising emphasis shifted to salient psychosocial needs of the brands' target markets. Kent advertising presented its users sophistication and confidence; Vantage campaigns created images of upward-striving people who had achieved personal success; Merit ads depicted individualistic people enjoying leisurely sailing. The minimal product information retained in advertising for these brands was relegated to the small print. These examples illustrate one strategy to appeal to concerned smokers by not describing the product itself (which may remind smokers of the problems associated with smoking), but instead using evocative imagery to distract smokers from these problems. Current advertising for potential reduced emissions products (PREPs) emphasizes product characteristics, but these products have yet to deliver on the promise of a healthier alternative cigarette. Our results suggest that the public health community should be on the alert for a shift in PREPs advertising focus away from the cigarette to the image of the user. Advertising bans that prohibit all tobacco advertising user-imagery could preempt a psychosocial needs-based advertising strategy for PREPs and maintain public attention on the health hazards of smoking.

Funding: American Legacy Foundation; NIH grant CA87472.

Correspondence: Stacey J. Anderson, Ph.D., Center for Tobacco Control Research and Education, 530 Parnassus Avenue, Suite 366, Box 1390, University of California, San Francisco, CA 94143-1390, USA; E-mail: staceya@itsa.ucsf.edu

TOBACCO USE, ATTITUDES, AND EXPOSURES AMONG SMOKERS IN THE DOMINICAN REPUBLIC

Deborah J. Ossip-Klein, Sergio Díaz, Essie Sierra, Zahira Quiñones, LaToya Armstrong, Joseph Guido, Scott McIntosh, Omar Díaz, Ann Dozier, Susan Fisher, Tim Dye, Nancy Chin

Although the Dominican Republic (DR) has been ranked as having among the highest smoking rates in the region, little empirical data are available. Results from a survey of >600 smokers across six marginalized DR communities (two small urban, two peri-urban, two remote rural) will be reported. Preliminary results from the first community (n=97 smokers) indicate that 75% smoke daily, with 90% smoking <10 cigarettes/day. Further results: 68% had been asked as children to light adults' cigarettes; 24% had asked children to light adults' cigarettes; 76% of women had smoked during pregnancy; 64% were advised by a doctor to quit; 71% quit because of pregnancy; and 50% had often been exposed to ETS. Among the total sample, smokers were most often exposed to smoking images in convenience stores (93%), TV (81%), and billboards (71%). Exposure to smoking-risk information came from TV (91%); radio (90%); health facilities (89%); school (81%); printed materials (61%); and Internet (63%). Diseases most often associated with smoking were respiratory problems (64%) and cancer (50%); relatively few identified hypertension, asthma, heart disease, or ear infections in children. Health-care providers had given 65% of them the advice to quit, although 65% felt smoking is too enjoyable to quit, and 76% had no confidence that they could quit. Nevertheless, 77% indicated a past-year quit attempt; 91% indicated interest in quitting. Data support the need for tobacco intervention, and indicate challenges and opportunities. Complete data across a broad range of variables from six communities will be available for presentation.

Funding: NIH FIC grant R01 TWO5945.

Correspondence: Deborah Ossip-Klein, Ph.D., University of Rochester School of Medicine, 601 Elmwood Avenue, Box 704, Rochester, NY 14642, USA; E-mail: deborah_ossipklein@urmc.rochester.edu

THE EFFECTIVENESS OF A NURSE-DELIVERED SMOKING-CESSATION INTERVENTION FOR CARDIAC PATIENTS: A RANDOMIZED, CONTROLLED TRIAL

Sophia SC Chan, Tai-Hing Lam, Chu-Pak Lau

Our objective was to study the effectiveness of the stage-matched intervention provided by nurses in motivating Chinese cardiac patients to quit smoking. Our method was to conduct a multisite, randomized, controlled trial among Chinese cardiac patients at the cardiac outpatient clinics of six major hospitals in Hong Kong. The intervention group received a stage-matched smoking-cessation intervention by trained nurse counselors and a telephone reminder at 1 week and 1 month. The control group received usual care and a placebo educational intervention about healthy diet. Telephone follow-up was carried out on all subjects at 3 months and 6 months to measure the quit-rate, cigarette consumption, and stages of readiness to quit. A total of 1,039 completed 6-month follow-up by August 2004. About 91.1% were males, 48.2% over 60 years of age, and 50.4% suffered from coronary heart disease. We randomized 52.2% (542/1,039) into the intervention group and 47.8% (497/1,039) into the control group. At baseline, 40.4% smoked over 10 cigarettes daily in the past 30 days and 31.5% had moderate-to-severe nicotine dependence (FTND). At 6 months, 21.4% (116/542) of the intervention group versus 15.1% (75/497) of the control group had not smoked in the past 3 months ($p<.01$). For those who had not quit, 46.9% (200/426) of the intervention group versus 32.9% of the control group ($p<.001$) had reduced their daily cigarette intake by 50%. More contemplators and preparators in the intervention group (49.5%) moved into the action stage as compared with the control group (34.9%) ($p<.01$). We concluded that the nurse-delivered stage-matched smoking-cessation intervention is effective in helping cardiac patients stop smoking. Patients who received the intervention achieved a significantly higher quit rate and smoking reduction rate than the controls. The intervention also motivated patients to reach a higher stage of readiness to quit.

Funding: The Research Grants Council, Hong Kong, grant HKU7224/01M.

Correspondence: Sophia SC Chan, Ph.D., 4/F Academic and Administrative Block, Faculty of Medicine Building, 21 Sassoon Road, Pokfulam, Hong Kong; E-mail: nssophia@hkucc.hku.hk

THE EFFECTS OF NICOTINE ON BRAIN ACTIVITY AND NEUROCOGNITION IN SCHIZOPHRENIC SMOKERS

Kirsten Fleming, Crystal Holbert, Christian Caceres, James Fallon, Steven Potkin

Approximately 90% of schizophrenics (SC) smoke, compared with rates of under 25% in the general population in the United States. The rate of smoking in SC is much higher than in other severe mental illnesses, and neither substance abuse, institutionalism, nor antipsychotic use can account for this high rate. We hypothesize that nicotine compensates for a defect in frontal-lobe function and hypometabolism in SC. In this study we examined the neuronal circuitry involved in the effects of nicotine and of nicotine withdrawal via fluorodeoxyglucose (FDG) positron emission tomography (PET). Comprehensive neurocognitive evaluations and mood ratings were also obtained. Subjects were scanned twice following overnight abstinence from nicotine—once while wearing a 21-mg nicotine patch, and once while wearing a placebo patch. The continuous performance test (CPT) was used as the activation task. Thus far, 10 SC smokers and 19 normal controls (NC) smokers have been assessed. In the withdrawal condition, the SCs demonstrated broad bilateral reductions as compared to the NCs, consistent with the well-established pattern of hypoactivity in SC. Following nicotine administration, there were no significant changes in brain activity for the NCs. Conversely, SCs reacted dramatically to the nicotine with overall bilateral activations. Most significant were increases in the dorsal stream and the left nucleus accumbens and thalamus ($p<.001$). Further, nicotine significantly enhanced memory in the SCs. By elucidating the specific brain mechanisms involved in nicotine and schizophrenia, we hope that new treatments may be developed to aid smoking cessation in schizophrenics.

Funding: TRDRP.

Correspondence: Kirsten Fleming, Ph.D., University of California, Irvine, 101 The City Drive South, Orange, CA 92868, USA; E-mail: kfleming@uci.edu

DISSEMINATION OF TOBACCO DEPENDENCE COUNSELING THROUGH PUBLIC HEALTH MATERNITY CLINICS

Lesa L. Woodby, Myra A. Crawford, Toya V. Russell, J. Michael Hardin, Thomas M. Miller, Richard A. Windsor

This presentation will focus on the translation of effectiveness research into public health policy and

practice. A research collaboration spanning 20 years between the University of Alabama at Birmingham and the Alabama Department of Public Health has resulted in the establishment of an infrastructure to sustain a tobacco-dependence patient education protocol within public health maternity care services. More than 30,000 pregnant women receive care annually through this public health service, of which approximately 30% are smokers. Using the health planning model, PRECEDE-PROCEED, a best-practices program to disseminate tobacco-dependence counseling through public health maternity clinics across the State of Alabama will be described. Process and outcome indicators will be summarized.

Funding: NIH grants RO1 CA86311and RO1 HL56010.

Correspondence: Lesa L. Woodby, Ph.D., UAB Family Medicine Research, 930 South 20th Street, Room 304, Birmingham, AL 35205, USA; E-mail: lwoodby@uab.edu

GENETIC AND ENVIRONMENTAL INFLUENCES ON MULTIPLE SMOKING OUTCOMES: FINDINGS FROM VIETNAM-ERA TWINS

Michael Lyons, Matthew Panizzon, Michael Grant, Seth Eisen, Ming Tsuang

Smoking is not a unitary construct; rather, it is a multifaceted phenomenon. To capture this complexity, we examined data on a range of smoking behaviors: (a) Ever a regular smoker; (b) age of smoking initiation; (c) number of cigarettes smoked during heaviest regular use; (d) lifetime DSM-III-R nicotine dependence; and (e) current smoking (circa age 42). Participants were members of the Vietnam Era Twin Registry, a national sample of male twin pairs in which both served in the military during the Vietnam era (1965–1975). The mean age of the 6,744 participating twins was 42 (range 33–53). Information about smoking was derived from a telephone administration of the Diagnostic Interview Schedule. Data were analyzed using biometrical modeling. Regular smoking was the only outcome significantly influenced by the family environment. All five smoking variables reflected a moderate degree of genetic influence, with heritabilities ranging from 0.43 to 0.61. We also fitted a multivariate model that included regular smoking, lifetime nicotine dependence, and current smoking. We found that 67% of the genetic variance in regular smoking is shared with nicotine dependence and 31% is shared with current smoking, while 29% of the genetic variance in nicotine dependence is shared with current smoking. The extent to which environmental variance was shared among these variables was considerably less. Our results indicate that there is substantial overlap among these smoking variables in terms of genetic influences, while aspects of the environment that influence each outcome tend to be specific to that outcome.

Funding: NIH.

Correspondence: Michael J. Lyons, Ph.D., Psychology Department, 648 Beacon Street, 2nd Floor, Boston University, Boston, MA 02215, USA; E-mail: mlyons@bu.edu

A STUDY OF NICOTINE DEPENDENCE IN TWINS BASED ON THE NDSS SCALE

Jaakko Kaprio, Ulla Broms, Saul Shiffman, Pamela A. F. Madden

Twin and family studies have indicated a major contribution of genetic factors to interindividual differences in degree of nicotine dependence among smokers. Estimates of heritability may vary with operationalization of the phenotype. DSM and Fagerström-based measures yield ranges of heritability in adult twin samples from 60 to 75%. The Nicotine Dependence Syndrome Scale (NDSS; *Nicotine and Tobacco Research* [2004], *6*, 327–348) is a multidimensional measure of nicotine dependence. Earlier twin studies of the NDSS have not been published. Twin pairs concordant for smoking were identified in the Finnish Twin Cohort Study and recruited to an international, multicenter family study of the genetics of nicotine dependence. Subjects were interviewed by telephone using a structured interview that assessed smoking habits and nicotine dependence based on FTND-related criteria. Subjects filled out a questionnaire with the NDSS scale (33 items) soon after the interview. In this ongoing study, we identified 223 pairs of smokers with NDSS T-scores (a summary measure of dependence). NDSS-T scores correlations among the 51 monozygotic (MZ), 85 same-sex dizygotic (DZ), and 97 opposite-sex DZ pairs were: (a) 0.32 in MZ pairs; (b) 0.14 in same-sex DZ pairs; and (c) −0.09 in opposite-sex pairs. The corresponding correlations for FTND scores were 0.47, 0.23, and 0.06. The pattern of correlations suggests modest-to-moderate genetic influences with sex-specific effects. Initial estimates of heritability based on the correlations are 36% for NDSS-T scores and 48% for the FTND measure of dependence, but further genetic modeling is needed to investigate the underlying genetic architecture.

Funding: NIH grant DA12854.

Correspondence: Jaakko Kaprio, Professor of Genetic Epidemiology, Department of Public Health, PO Box 41, University of Helsinki FI-00014, Helsinki, Finland; Tel: +358 9 191 27595; Fax: +358 9 191 27 600; Mobile: +350 50 371 5419; E-mail: jaakko.kaprio@helsinki.fi

GENETIC VULNERABILITY TO NICOTINE DEPENDENCE

Pamela Madden, Arpana Agrawal, Michele Pergadia, Alexandre Todorov, Scott Saccone, Andrew Heath, John Rice, Alison Goate, Grant Montgomery, Richard Todd, Danielle Dick, Katherine Morley, Jaakko Kaprio, Nicholas Martin

Despite the public health significance of smoking and evidence from adult twin studies for a strong genetic influence on smoking behavior (heritability estimates as high as 70%), there has been limited research designed specifically to identify genes that contribute to risk of addiction to nicotine in humans. As part of an international consortium, families have been ascertained through panels of adult Australian and Finnish twins and a sample of spouses of Australian twins. These subjects were identified as having a history of heavy smoking in earlier surveys. We conducted diagnostic telephone interviews on index cases, full siblings, and parents to identify sibships with at least one affected sib-pair (ASP) concordant for heavy smoking (target: 400 Australian and 400 Finnish families with approximately 600 ASPs from each). A 10 cM genome-wide scan was conducted on samples of DNA obtained from 100 Australian families, including 493 individuals. Quantitative trait locus analyses were conducted for quantitative measures of nicotine dependence including the Fagerström Test for Nicotine Dependence (FTND: Heatherton et al., 1991) and the two-item Heavy Smoking Index (HSI: Heatherton et al., 1989). Results for the HSI were more significant than for the FTND. Suggestive linkage ($p<.001$) was found for HSI on chromosomes 15 (lod: 2.73). This finding is preliminary, being based on a small subset of families. Similar phenotypes are being examined in data obtained from families in Finland.

Funding: NIH grant DA12854.

Correspondence: Pamela Madden, Washington University, 40 North Kingshighway, St. Louis, MO 63108, USA

GENETIC VULNERABILITY TO *DSM-IV* NICOTINE WITHDRAWAL: AUSTRALIAN FAMILIES

Michele L. Pergadia, Alexandre A. Todorov, Scott Saccone, Arpana Agrawal, Andrew C. Heath, John Rice, Alison Goate, Grant Montgomery, Nicholas G. Martin, Jaakko Kaprio, Pamela A. F. Madden

Studies of twins suggest that genetic factors influence nicotine withdrawal. However, genetic linkage studies that focus on nicotine withdrawal have not been reported. As part of an international consortium, genome-wide scans are being conducted in a study of Australian families. These have been selected through heavy smoking index-cases, using 400 microsatellite markers. Samples of DNA and telephone diagnostic interview data were obtained from families ascertained from the Australian twin registry. For this project, sources were families with at least two adult offspring who reported a history of *DSM-IV* nicotine withdrawal. Linkage analyses were conducted on genome-scan data from 100 families, including 493 individuals. This study used an affected-sib-pair design and conducted the linkage analyses using GENEHUNTER. Significant linkage was found on seven chromosomes (in descending effect size): 11 (NPL score $Z=2.29$; $p=.001$); 19 ($Z=2.20$; $p=.002$); 1 ($Z=2.04$; $p=.004$); 21 ($Z=1.86$; $p=.007$); 6 ($Z=1.63$; $p=.016$); 7 ($Z=1.61$; $p=.018$); and 4 ($Z=1.40$; $p=.034$). The positions for at least two candidate genes—CYP2A6 and CHRNB2—lie within or near regions identified by linkage. These findings are preliminary, being based on a small subset of families.

Funding: NIH grants AA13321, DA12854, and AA07580; Australian National Health and Medical Research Council.

Correspondence: Michele Pergadia, Washington University School of Medicine, 40 North Kingshighway, St. Louis, MO 63108, USA; E-mail: michelep@matlock.wustl.edu

ALTERED STRESS RESPONSE AND VULNERABILITY FOR SMOKING RELAPSE

Mustafa al'Absi, Dorothy Hatsukami, Gary L. Davis

Research has demonstrated that psychosocial stressors increase smoking and risk for smoking relapse. Alterations in biological systems involved in the stress response related to chronic smoking may contribute to early relapse. This study was designed to examine the extent to which hypothalamic–pituitary–adrenocortical and cardiovascular responses to stress predict early relapse following the first 24 hr of a quit-attempt. Seventy-two smokers interested in cessation attended a laboratory stress session 24 hr after the beginning of their cessation attempt. Adrenocorticotropin (ACTH); plasma and salivary cortisol concentrations; systolic and diastolic blood pressure (BP); heart rate (HR); and mood reports were obtained during rest and in response to acute psychological stressors (public speaking and cognitive challenges). Participants attended four weekly follow-up sessions to measure smoking status and verify abstinence. Those who relapsed within 4 weeks showed attenuated hormonal and cardiovascular responses to stress; exaggerated withdrawal symptoms; and mood deterioration after quitting. A series of regression analyses to predict number of

days until relapse confirmed these results—with attenuated responses to stress predicting shorter time to relapse, especially in men. Among women, withdrawal symptoms and mood changes consistently predicted time-to-relapse. These results suggest that altered stress response may indicate increased vulnerability for smoking relapse.

Funding: NIH grants CA88272 and DA016351.

Correspondence: Mustafa al'Absi, Ph.D., Department of Behavioral Sciences, University of Minnesota Medical School, 1035 University Drive, Duluth, MN 55812, USA; Tel: (218) 726-7144; Fax: (218) 726-7559; E-mail: malabsi@umn.edu

DOSE-RELATED EFFECTS OF NICOTINE NASAL SPRAY ON COGNITIVE PROCESSING

Stephen J. Heishman, Carol S. Myers, Richard C. Taylor, Eric T. Moolchan

We examined the effect of nicotine nasal spray (Nicotrol) on three cognitive tests: Continuous performance (sustained attention), N-back (working memory), and arithmetic (computational skills). Participants were 20 (of 24 planned) adult smokers (13 men, 7 women). Participants took part in one training and two experimental sessions. At one experimental session, participants were tobacco deprived for 12 hr and smoked ad libitum before the other session; order of sessions was counterbalanced. In each experimental session, three doses of nicotine nasal spray (0, 1 and 2 mg) were administered 90 min apart in randomized order. A battery of physiological, subjective, and cognitive measures was assessed before each dose and was repeated for 40 min after dosing. (Physiological measures and nicotine plasma concentration will be reported elsewhere.) Nicotine dose-dependently increased subjective ratings of alert, head rush, and stimulated, and decreased ratings of relaxed, urge to smoke, and drowsy. Performance on the arithmetic test (single digit addition and subtraction) was enhanced by nicotine in a dose-related manner. Percent correct responding was increased and reaction time to all problems and correctly answered problems was decreased. Subjective data are consistent with previous reports and indicate that psychoactive doses of nicotine were delivered. To our knowledge, this is the first study to demonstrate the dose-related enhancing effect of nicotine on computational abilities.

Funding: U.S. National Institute on Drug Abuse, Intramural Research Program.

Correspondence: Stephen J. Heishman, Ph.D., Clinical Pharmacology and Therapeutics, National Institute on Drug Abuse/Intramural Research Program, 5500 Nathan Shock Drive, Baltimore, MD 21224, USA; E-mail: heishman@nih.gov

TRANSDERMAL NICOTINE-INDUCED WITHDRAWAL SUPPRESSION IN SMOKERS: A GENDER COMPARISON

Sarah E. Evans, Michael F. Weaver, Cynthia Sams, Kasha White, Jennifer Gray, Robert Collins, Thomas Eissenberg

Transdermal nicotine (TN) is a proven smoking-cessation pharmacotherapy, although there are suggestions of lower efficacy in women. TN is thought to work, at least in part, by suppressing withdrawal symptoms in abstinent smokers, and laboratory studies demonstrate this effect. Differential withdrawal suppression in men and women may underlie reports of differential efficacy. The purpose of this acute laboratory study is to examine if smokers' gender influences TN-induced withdrawal suppression. Overnight-abstinent smokers (50 women; 75 men) completed four double-blind, randomized, 6.5-hr laboratory sessions in which further cigarette abstinence was required. Sessions differed by TN dose (zero, 7, 21, or 42 mg). Plasma nicotine level and tobacco/nicotine withdrawal were assessed hourly and heart rate was recorded continuously. Results demonstrate TN-induced withdrawal symptom suppression on most measures (e.g., individual symptom ratings and both factors of the questionnaire of smoking urges (QSU), and suggest that on some measures this suppression is dose-related. For example, for QSU Factor 1, at 4 hr after TN administration (when peak nicotine blood-levels are expected), mean scores were 60.6 for placebo; 55.6 for 7 mg; 51.1 for 21 mg; and 47.7 for 42 mg. Heart rate increased in a TN dose-related manner. There was little evidence of a differential effect between men and women—i.e., a dose by time/by gender interaction was observed on two withdrawal measures: Irritability/frustration/anger and QSU Factor 2. Results from this laboratory study confirm TN-induced withdrawal suppression, and suggest that it does not depend upon smokers' gender.

Funding: U.S. PHS grants R01 DA11082 and T32 DA07027.

Correspondence: Thomas Eissenberg, Ph.D., Virginia Commonwealth University, Box 980205, Richmond, VA 23298-0205, USA

VARENICLINE (CP-526,555): A NOVEL, POTENT, SELECTIVE NICOTINIC RECEPTOR PARTIAL AGONIST (SNRPA) FOR THE TREATMENT OF SMOKING CESSATION

Jotham W. Coe, Paige R. Brooks, Michael G. Vetelino, Michael C. Wirtz, Brian T. O'Neill, Steven B. Sands, Lorraine A. Lebel, Carol B. Fox, F. David Tingley, Thomas I. Davis, Hans Rollema, Yi Lu, Eric L. Schaeffer, Janice P. Holland, Robert S. Mansbach, David W. Schulz

More effective therapeutic approaches for smoking cessation are needed. We hypothesized that a selective nicotinic receptor partial agonist (SNRPA) of the neuronal $\alpha_4\beta_2$ nicotinic acetylcholine receptor would provide sufficient dopaminergic tone to overcome craving and withdrawal while blocking the reinforcing actions of nicotine. Theoretically, this would prevent relapse in cases when the intent is to achieve greater reward via inhaled nicotine. Using as a structural starting point (-)-cytisine, a natural SNRPA with poor bioavailability and limited brain penetration, we sought to identify SNRPAs with improved physicochemical properties. Initial synthetic efforts revealed that substitutions at C-3 of cytisine were beneficial, prompting a study of pyridone replacements. Although these exhibited poor receptor affinity and weaker antagonist profiles, a key modification to this bicyclic architecture led to an extremely potent and selective series of compounds with excellent physicochemical profiles from which varenicline was identified (CP-526,555, IC50nM=0.1) as the most promising. In vivo studies examining dopamine turnover in the nucleus accumbens indicated that it had an oral ED50 of 0.05 mg/kg; a maximal efficacy of 40% relative to nicotine; and inhibition of the nicotine-mediated increase in dopamine turnover (ID50 of 0.07 mg/kg subcutaneous), consistent with SNRPA pharmacology. Based on the potential benefits of these agonist/antagonist properties, varenicline has been advanced to clinical trials for smoking cessation.

Funding: Pfizer Global Research and Development.

Correspondence: Jotham W. Coe, Pfizer Global Research and Development, Groton Laboratories, Eastern Point Road, MS8220-4115, Groton, CT 06340, USA; E-mail: jotham.w.coe@pfizer.com

SAFETY, TOLERABILITY, AND MULTIPLE-DOSE PHARMACOKINETICS OF VARENICLINE IN ELDERLY SMOKERS

Aaron Burstein, Terence Fullerton, David Clark, Helene Faessel

Varenicline is a selective nicotinic receptor partial agonist (SNRPA) that blocks smoking reward. It is currently in development as a novel treatment for smoking cessation. Our goal was to investigate the safety, tolerability, and multiple-dose pharmacokinetics of two varenicline doses, given once or twice daily to elderly (≥65 years) smokers. This phase 1, randomized, double-blind study included 24 male and female smokers aged 65–75 years (mean 69.4). Subjects received either (a) varenicline 1 mg (n=8) or placebo (n=4) once daily for 7 days; or (b) varenicline 1 mg (n=8) or placebo (n=4) twice daily for 6 days with a single dose on Day 7. Safety and tolerability of varenicline were assessed. Pharmacokinetic parameters (C_{max}, T_{max}, AUC_{0-t}) for varenicline were determined on Days 1 and 7. The terminal phase half-life was obtained following Day 7 dosing. Accumulation was evaluated using the ratios of AUC_{0-t} and C_{max} following repeat administration (Day 7) relative to single dosing (Day 1). At conclusion, no clinically significant changes in vital signs and no serious adverse events (AEs), or withdrawals because of AEs were reported. There was no evidence of concentration- or time-dependent changes in the pharmacokinetics of varenicline upon repeat dosing. Consistent with a mean half-life of approximately 28 hr, steady state appeared to be reached within 4 days of repeat administration. Once and twice daily dosing resulted, on average, in an approximate two- and threefold increase in systemic exposure, respectively. Following repeat administration of varenicline 1 mg once or twice daily, systemic exposure in elderly smokers was comparable to that previously observed in younger smokers. Varenicline was well tolerated, and may be administered without dose adjustment to elderly smokers.

Funding: Pfizer Global Research and Development.

Correspondence: Aaron Burstein, Pfizer Global Research and Development, Groton/New London Laboratories, Eastern Point Road, MS8260-2505, Groton, CT 06340, USA; E-mail: aaron_h_burstein @groton.pfizer.com

LONG-TERM TREATMENT WITH RIMONABANT FOR SMOKING CESSATION AND THE MAINTENANCE OF ABSTINENCE: RESULTS FROM STRATUS-WORLDWIDE TRIAL

Raymond Niaura

Smoking is currently the leading cause of death worldwide, with smokers experiencing a two- to threefold increased risk of death from cardiovascular and cancer-related diseases. The STRATUS-WORLDWIDE (WW) trial was designed to assess the long-term efficacy and safety of rimonabant, the first selective cannabinoid type 1 (CB1) receptor blocker, for maintenance of abstinence in successful

quitters. STRATUS-WW is a 2-year multiple-country, multicenter, randomized, double-blind, five-arm, placebo-controlled clinical trial. A total of 5,055 cigarette smokers (≥10 cigarettes/day) motivated to quit were randomized to two treatment groups: 5 mg or 20 mg rimonabant. At Week 10, 1,672 successful quitters were re-randomized to either placebo or 5 mg (for those already receiving 5 mg); and placebo, 5 mg, or 20 mg (for those already receiving 20 mg). Active treatment continued for 42 weeks, followed by a 50-week off-drug period. The primary endpoint was the efficacy of rimonabant in the maintenance of abstinence from cigarette smoking at Week 32 (6 months post–re-randomization). Secondary endpoints included body weight, tobacco craving, quality-of-life, safety, and tolerability. Rimonabant has been recently shown to enhance short-term cigarette smoking abstinence and reduce postcessation weight gain. The 6-month efficacy and safety data will be presented.

Funding: Sanofi-Aventis.

Correspondence: Raymond Niaura, Centers for Behavioral and Preventive Medicine, Coro Building, Suite 500, One Hoppin Street, Providence, Rhode Island 02903, USA; Tel: (401) 793-8002; Fax: (401) 793-8056 or (401) 793-8078; E-mail: Raymond_Niaura@brown.edu

STAGES OF CHANGE AND CESSATION OUTCOMES IN A TELEPHONE QUIT-LINE SETTING

Ken Wassum, Abigail Halperin, Terry Bush, Tim McAfee

Telephonic cessation programs have proven to be an effective means of treating tobacco dependence by providing an efficient and accessible format for delivering tailored services to smokers trying to quit. Because cessation resources are often modest, health plans and public tobacco-control programs attempt to limit service access to those who are most ready to quit. The most common tool used to determine readiness to quit is the Transtheoretical Model, which classifies smokers into stages of precontemplation, contemplation, preparation, action, and maintenance. However, little evidence exists to link stages of change to cessation outcomes in the context of telephonic cessation programs. Free & Clear is an intensive, telephonic cessation program serving health plans, employers, and state quit lines. In this study, quit rates of participants in Free & Clear were examined and correlated with readiness to quit at enrollment, as determined by a stated plan to quit within the next 30 days. The analysis included all enrollees who completed the Free & Clear program during a 12-month period. Participants (n=6,588) consisted of those covered through their health plan (60.2%); through an employer group (17.7%); or through a state tobacco quit line (22.1%). All groups were eligible for the same number of calls (e) and had access to NRT and/or bupropion at minimal or no cost. Sixty-four percent were female and the mean age was 44.4 years. Seven-day abstinence point prevalence was determined by self-report at the final call, 9 or 12 months after enrollment. We found that while those in the preparation stage had the highest abstinence rates (34.5%), more than a quarter of contemplators (25.5%) were also abstinent at follow-up. These results show that smokers seeking quit line services who are in the contemplation stage benefit from access to an intensive telephonic program; thus, eligibility for participation should not be limited to those who fall in the preparation or action stages.

Funding: None.

Correspondence: Ken Wassum, The Center for Health Promotion, Inc., 12401 East Marginal Way South, Tukwila, WA 98168, USA; E-mail: wassum.k@ghchp.org

SMOKERS OF LOW-YIELD CIGARETTES LESS LIKELY TO QUIT

Hilary Tindle, Nancy A. Rigotti, Roger Davis, Saul Shiffman, Ichiro Kawachi

Many smokers erroneously believe that low-nicotine/low-tar cigarettes, also called low yield cigarettes (LYC), reduce health risks and are a rational alternative to cessation. We determined the prevalence and characteristics of ever-smokers (current or past) who switched to LYC and assessed the association between switching to LYC and smoking cessation. We analyzed 32,374 respondents to the U.S. 2000 National Health Interview Survey, who provided information on sociodemographic factors and health conditions and behaviors. Ever-smokers were asked, "Did you ever switch to a lower tar and nicotine cigarette to reduce your health risk?"; and "Do you now smoke cigarettes every day, some days, or not at all?" Those answering not at all were considered currently abstinent. Multivariable logistic regression identified determinants of LYC use and cessation. All analyses used SUDAAN and were weighted to reflect national estimates. Of 12,285 ever-smokers, 37% (n=4,414) reported switching to LYC to reduce health risks. Independent correlates of switching to LYC included longer smoking history; white race; younger age; female gender; higher education level; and lung or vascular disease. Current abstinence was less frequent among ever-smokers who had previously switched to LYC than those who had never switched (37% vs. 53%; $p<.01$). Ever-smokers who had switched to LYC were

significantly less likely to have quit smoking than those who had never switched (*AOR*=0.60 [95% *CI* 0.53–0.67]). We found that over one-third of U.S. smokers report having switched to LYC to reduce their health risk. A history of switching to LYC was associated with lower odds of current tobacco abstinence, supporting the hypothesis that use of LYC may hinder cessation.

Funding: None.

Correspondence: Hilary Tindle, Harvard Medical School, 401 Park Drive, Suite 22A West, Boston, MA 02215, USA; E-mail: hilary_tindle@hms.harvard.edu

INTERNATIONAL BEST PRACTICES FOR COMPREHENSIVE TOBACCO CONTROL

Terry F. Pechacek, Samira Asma

The development of tobacco control program efforts around the world should be guided by efficacy and best practices data. In the United States, the 1999 CDC Best Practices for Comprehensive Tobacco Control provide programmatic and budgetary guidelines for states and territories based both on evidence-based reviews and on best-practice experience of multiple states. The application of these guidelines in the planning of new program efforts across the United States over the last 3 years has confirmed the overall utility of this recommendation format. Program evaluation data have continued to support both the importance of recommended funding levels and individual program components. Specifically, multivariate, time-series analyses of both per-capita cigarette consumption and adult prevalence trends (1990–2001, for all 50 states and the District of Columbia) have shown highly significant effects for level of annual state tobacco control investments. The analyses controlled for price and tax changes, demographic patterns, and other potential confounding factors. However, the 1999 CDC-recommended Best Practices funding levels of US$5–US$7 (U.S.) per capita per year greatly exceeds the available resources of many countries. Therefore, based upon the scientific foundations of the U.S. Best Practices recommendations, we will provide key recommendations for an International Best Practices for Comprehensive Tobacco Control. The scientific foundations and best-practice models for each of the nine component areas of the United States Best Practices will be reviewed from the international dissemination perspective. Components such as community-based and school programs likely can be implemented internationally with lower direct funding support. Other components such as counter-marketing and cessation pose greater challenges. Partnerships are a critical component when applying best practices in a global context. Available scientific data and international examples supportive of possible application of the U.S. comprehensive model at lower funding levels will be presented, along with cautions where such data are either lacking or suggestive of the importance of adequately funded interventions.

Correspondence: Terry F. Pechacek, Ph.D., Office on Smoking and Health, 4770 Buford Highway NE, Mail Stop K-50, Atlanta, GA 30316, USA; E-mail: tpechacek@cdc.gov

SMOKING TOPOGRAPHY, BRAND SWITCHING, AND NICOTINE DELIVERY: RESULTS FROM AN IN VIVO STUDY

David Hammond, Geoffrey T. Fong, K. Michael Cummings, Andrew Hyland

Exposure to toxins in tobacco smoke is influenced by how a cigarette is smoked. Cigarettes have been designed to allow a range of puffing behavior and to provide different, nonlinear tar and nicotine yields in response to different puffing profiles. However, puffing behavior and its influence on risk-exposure has yet to be assessed outside the laboratory, in smokers' natural environment. Fifty-nine adult smokers used a portable device to measure smoking topography over the course of three 1-week trials. Participants were asked to smoke their usual regular-yield brand through the device for Trial 1 and again, 6 weeks later, at Trial 2. Half the subjects were then randomly assigned to switch to a low-yield brand for Trial 3. The findings show a high degree of stability in puffing behavior within the same subject over time, but considerable variability between smokers. Smokers who were switched to a low-yield cigarette increased their total smoke intake per cigarette by 40% (p=.007), with no significant change in their in salivary cotinine levels. Cigarettes smoked per day and nicotine yield were only weakly associated with salivary cotinine levels; however, salivary cotinine was strongly associated with a composite measure that included cigarettes per day; brand elasticity; and puffing behavior (sr=0.61, p<.001). These findings provide strong evidence of behavioral compensation to low-yield cigarettes from in vivo measures of smoking behavior. The findings also demonstrate the importance of brand elasticity and smoking topography in predicting nicotine uptake and smoke exposure.

Funding: American Cancer Society; Health Canada; RWJF; NIH grant CA16056; Canadian Tobacco Control Research Initiative.

Correspondence: David Hammond, Department of Psychology, University of Waterloo, 200 University Avenue West, Waterloo, Ontario, Canada N2L 3G1; E-mail: dhammond@uwaterloo.ca

PREDICTORS OF BRAND-SWITCHING AMONG SMOKERS IN THE UNITED STATES AND CANADA: FINDINGS FROM THE ITC 4-COUNTRY SURVEY

K. Michael Cummings, Andrew Hyland, Cheryl Higbee, Frank Chaloupka, Geoffrey T. Fong

Smokers can choose from hundreds of cigarette varieties, although little data exists on this behavior. We report data on 2,994 smokers who completed Waves 1 and 2 (8–10 months apart) of the International Tobacco Control Policy Evaluation 4-Country Survey (ITC-4) and who resided in the United States or Canada. Brand switchers were those who reported smoking their current brand in Wave 2 for less than 6 months. In the United States, 8% of smokers had quit by Wave 2, and 19% had switched to a different cigarette brand family; whereas in Canada, 11% had quit and 21% had switched brand families. Brand switchers were more likely to have lower incomes and to have plans to quit within the next 6 months. The most common reasons given for switching cigarette brands were: Lower price (U.S.=69%; Canada=53%); product quality (U.S.=57%; Canada=43%); and to help quit (U.S.=32%; Canada=22%). Brand switching was higher in the seven U.S. states that increased cigarette excise taxes between survey waves (28%) compared to those who lived in a state that did not increase taxes (18%). There appears to be a fair amount of volatility in the cigarette market in the United States and Canada, with between 20% to 30% of smokers either quitting or switching cigarette brands over an 18-month period. The increasing cost of cigarettes appears to be one of the main factors contributing to this volatility.

Funding: Canadian Institutes for Health Research; RWJF; Cancer Research UK; Canadian Tobacco Control Research Initiative; National Health and Medical Research Council of Australia; Australia Commonwealth Department of Health and Ageing.

Correspondence: Andrew Hyland, Ph.D., Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA; E-mail: andrew.hyland@roswellpark.org

NONRESPONSE BIAS IN A WEB-BASED SURVEY

Eric O. Johnson, Scott Crawford

Web-based survey administration is appealing owing to easy implementation and potential cost saving. However, response rates, which are continuing to fall for all survey forms, may be problematic. This study assessed nonresponse bias in a Web-based survey on smoking among college students and examined implications for generalizing results to this population and for characterizing smokers within it. Use of multiple imputation to address the effects of nonresponse bias is presented. These data come from a survey of undergraduates at a Midwestern urban university. After Web-based data collection, we attempted nonresponder recruitment by telephone. We used a regression-based multiple imputation method to reestimate smoking prevalence, adjusting for nonresponse bias. Of the 2,500 students, 913 responded to the Web survey (response rate=36.5%), and 434 of the 1,587 nonresponders responded by telephone (RR=27.3%): Overall RR=53.9%. Indicating potential nonresponse biases, we found statistically significant differences between nonresponders and responders, and between Web-based and telephone responders, on demographic and student-status characteristics. Prevalence estimates of current smoking and nicotine dependence based on multiple imputation of data missing among nonrespondents were higher than crude estimates (crude current smoking and nicotine dependence=20.9% and 4.5%; *MI* estimates=26.2%$\pm$3.8% and 5.9$\pm$2.2%, respectively). However, no differences in smoking characteristics between Web-based versus telephone-responding smokers was found (e.g., number of cigarettes smoked per day; number of quit attempts; family history). We concluded that nonresponse bias can be a significant problem for generalizing from surveys with the low response-rates typically achieved today. Use of multiple imputation is an important and accessible tool to address this problem. However, nonresponse bias effects on population estimates may not significantly bias analyses of subgroups identified through such surveys.

Funding: HFHS Grant Development Award.

Correspondence: Eric O. Johnson, Ph.D., Center for Health Promotion and Disease Prevention, Henry Ford Health Sciences Center, One Ford Place, Room 3A, Detroit, MI 48202, USA

HOW MUCH DOES SMOKING CONTRIBUTE TO SOCIOECONOMIC DISPARITIES IN HEALTH IN THE UNITED STATES?

Paula Lantz, James House, Richard Mero

Prior research demonstrates that health status over the life course differs significantly by socioeconomic status (SES). However, the degree to which higher rates of smoking among people of low SES contribute to health disparities needs further investigation. We analyzed data from the four waves of the Americans' Changing Lives survey (N=3,617, representative of U.S. adult population in 1986) to (a) investigate trajectories in smoking between 1986

and 2001; and (b) identify the degree to which smoking at baseline explained subsequent SES disparities in mortality and health-status change (measured as physical functioning and self-rated health). We used Cox proportional hazard models and multinomial logistic regression. As expected, smoking rates were significantly higher among people of low SES at all four survey waves. Among survivors at Wave 4, 41% of smokers were still smoking; 50% had quit; 9% had quit and resumed again, with SES differences in trajectories. Mortality was significantly higher among those with low income (response rate [RR]=2.33); smokers (RR=1.78); and former smokers (RR=1.45). Furthermore, both current and former smokers had significantly higher rates of health-status decline over the 15-year study period. The health risks of smoking were less than the risks of low income in all models; only a small proportion of the impact of low income and education on health outcomes was explained by smoking behavior. We concluded that Low SES has a greater negative impact on health change and mortality than tobacco use. Although reducing smoking in low SES populations is a critical public health goal, it will currently do little to reduce socioeconomic disparities in major health outcomes.

Funding: NIH.

Correspondence: Paula Lantz, University of Michigan SPH, 109 Observatory, Ann Arbor, MI 48109-2029, USA; E-mail: plantz@umich.edu

CHANGES IN QUALITY OF LIFE AFTER SMOKING CESSATION AMONG OLDER ADULTS

Kenneth D. Ward, George Relyea, Mark W. Vander Weg, Deborah Sherrill-Mittleman, Robert Klesges, Margaret DeBon, Marie Sell

Smoking cessation among older adults is thought to produce substantial quality-of-life (QOL) benefits, but little prospective data are available. A total of 296 adults at least 60 years of age, were randomized to receive one of three smoking-cessation interventions, consisting of usual care (MD advice plus one behavioral counseling session); standard behavioral counseling (four sessions)+nicotine patch; or four sessions of behavioral counseling targeted to older adults+patch. Health-related QOL was assessed at baseline and 6 and 12 months follow-up using the SF-36. Biochemically confirmed point-prevalent abstinence rates at 12 months were 26.6%; 21.6%; and 31.2% for the three groups, respectively. Using a mixed model approach, six of eight QOL indices (physical functioning; emotional well-being; social functioning; body pain; general health; energy/fatigue) worsened over 12 months, regardless of treatment condition or smoking outcome ($p<.05$). A significant time by smoking-status interaction was observed for energy/fatigue, indicating that nonquitters worsened substantially over time, while quitters experienced no change. Collapsing across assessment periods (baseline, 6 months, 12 months), QOL was greater in quitters compared to nonquitters for emotional well-being and role limitations arising from emotional problems. The results indicate that QOL generally worsens over the course of a year in older smokers, even after quitting. However, cessation may preserve QOL in terms of energy/fatigue level.

Funding: NIH grants HL56626 and HL68569.

Correspondence: Dr. Ken Ward, Center for Community Health, 5050 Poplar Ave, Suite 1800, Memphis, TN 38157, USA; E-mail: kdward@memphis.edu

CAN EXPECTANCIES ABOUT TAILORED SMOKING-CESSATION MATERIALS BE PRIMED TO ENHANCE OUTCOME?

Monica Webb, Peter Hendricks, Thomas Brandon

Designing effective tailored interventions for smokers has been the focus of stage-based research. Our previous research indicated that high levels of content personalization and individuals' trait expectancies about tailored interventions contribute to the impact of tailored messages. That is, smokers who held strong expectancies about the value of tailored materials showed the greatest change when they received a highly personalized intervention. This study attempted to replicate and extend this research by testing whether tailoring-related expectancies could be influenced via a brief priming intervention, and whether this would then enhance the impact of the cessation materials. A 2×2 factorial design manipulated personalization level and expectancy priming on evaluation of the intervention content; readiness to quit smoking; cessation self-efficacy; cognitive processing; and behavioral changes. We randomized 205 smokers to one of four cells. Participants in the priming conditions received a preintervention letter to enhance their expectations for either generic or tailored interventions. Postpriming expectancies were assessed 7–10 days later, and tobacco intervention booklets were subsequently mailed. Results replicated and extended previous work, finding main effects of personalization on content evaluation; readiness to quit; cognitive processing; and behavioral change. That is, smokers who received the personalized (placebo-tailored) booklets reported greater change than those who received the standard booklets. A priming by personalization interaction indicated that the

expectancy-manipulation was effective, and priming main effects were found for content evaluation and cognitive processing. Thus, enhancing smokers' expectancies about their materials improved outcomes. Theoretical and applied implications will be discussed.

Funding: University of South Florida.

Correspondence: Thomas Brandon, Ph.D., Tobacco Research Program, 4115 East Fowler Avenue, Tampa, FL 33617, USA; E-mail: brandont@moffitt.usf.edu

ADHD AND SMOKING IN A SAMPLE OF MIDDLE-AGED VETERANS

Mark Schultz, Karen Rabi, Michael Lyons, Stephen Faraone, William Kremen

Attention-deficit hyperactivity disorder (ADHD) is known to confer vulnerability to substance abuse. Among adults, it is strongly associated with earlier smoking initiation, higher risk of nicotine dependence, and longer persistence of smoking even when confounding factors like socioeconomic status, IQ, and psychiatric comorbidity are controlled. Data were collected from 346 pairs of dizygotic (DZ) and monozygotic (MZ) male twins from the Vietnam Era Twin Registry using the K-SADS-E that assessed 14 ADHD symptoms during childhood. Smoking information (initiation, duration) was collected via the Diagnostic Interview Schedule Version 3, Revised (DIS-3R). Lifetime nicotine dependence diagnoses were obtained by applying standard DSM-III-R algorithms. ADHD individuals: Initiated smoking earlier ($p=0.015$); were more likely to become nicotine-dependent ($p<.001$); had more lifetime symptoms of nicotine dependence ($p<.001$); smoked for a greater duration ($p<.001$). Genetic analysis of the data showed smoking initiation was primarily influenced by different genetic factors than ADHD and by the common family environment, whereas the same genetic factors that influenced ADHD also influenced nicotine dependence and duration of smoking. An ADHD diagnosis in childhood was highly predictive of several dimensions of adult smoking behavior. Because nicotine is an indirect dopamine agonist and shares its mechanism of action with current treatments for ADHD, this finding suggests smoking may be motivated by self-medication. Our results are consistent with data from clinical samples that indicate ADHD symptoms persist into adulthood and may cause a generalized liability for substance-use disorders. Potential limitations of our data include the fact that childhood symptoms were reported retrospectively by our middle-aged participants and our results may not generalize to females or nonveteran males.

Funding: NIH.

Correspondence: Mark Schultz, Boston University, 648 Beacon Street, Boston MA 02215, USA; E-mail: mschultz@bu.edu

HOUSEHOLD RULES AROUND REDUCING ENVIRONMENTAL TOBACCO SMOKE (ETS) EXPOSURE: A QUALITATIVE STUDY OF COUPLES WITH YOUNG CHILDREN

Kim Bercovitz, Joanna Cohen, Roberta Ferrance, Rebecca Haines, Blake Poland, Peter Selby, Donna Stewart, Saman Wickramasinghe

Our aim was to examine the household as a setting for establishing nonsmoking arrangements. We conducted semi-structured interviews in 21 households with male/female couples and newborn children. Interviews focused on exploring how couples negotiate nonsmoking household rules and how issues of gender, class, and power influence the establishment of and adherence to ETS control measures. We found that the establishment of nonsmoking arrangements within households is not an overt source of conflict between male and female partners who become parents. Couples expressed anticipatory concerns about social modeling of smoking in front of preschoolers; this provided an incentive to adhere to nonsmoking rules. ETS control measures vary depending on the smoking partner's history and level of tobacco use, and are influenced by the type of home, neighborhood location, and extended family arrangement in which the couple/family lives. There were also notable differences in the establishment of smoking rules in the home according to social class, cultural background, type of cohabitating relationship, and single versus extended family living arrangement. We concluded that tobacco-control in the home should be located within the context of family dynamics. Households vary in their norms and expectations about the control of ETS exposure. Broader issues of gender and power do come into play when negotiating nonsmoking rules within the context of the male/female partnership. Priority must be given to understanding how unique aspects of both the "couple" relationship and extended family dynamics inform ETS control and harm reduction practices. Overall, although there was support for increased public health information and education to reduce children's exposure to ETS, the majority of respondents were wary of policy approaches that would position ETS as a child-neglect or protection issue.

Funding: Canadian Tobacco Control Research Initiative.

Correspondence: Dr. Kim Bercovitz, Department of Public Health Sciences, University of Toronto, C/O 15 Wellwood Avenue, Toronto, Ontario, Canada M6C 1G8

PRENATAL NICOTINE EXPOSURE FEMINIZES MALE MOUSE GENITALIA

David J. Vandenbergh, Kate Anthony, Jennifer E. Foreman, Laura Cousino Klein

Among the consequences of nicotine exposure in utero to the offspring of smokers are such negative effects as low birth weight and increased prevalence of sudden infant death syndrome (SIDS). We show in mice that nicotine's toxic effects include endocrine disruption. Timed pregnant C57BL/6J mice were administered nicotine (50 µg/ml) with 2% saccharin in their drinking water for 24 hr/day starting on gestational day (GD) 9 through delivery (n=4). Control dams were given tap water with 2% saccharin (n=3). Pups were weighed the morning of birth, and their anogenital distance (AGD) was measured. The AGD is a sensitive indicator that is used to detect chemicals with endocrine-disrupting effects. Body weight and AGD were significantly reduced in nicotine-exposed male pups compared to controls, a finding that remained significant after adjusting the anogenital distance index for weight. None of these measures was significantly different in female pups. The range of prenatal nicotine exposure effects are not known, but nicotine has been shown to block the normal perinatal surge of testosterone in male rat pups, and cause a subsequent feminization of adult male saccharin preference (Lichtensteiger and Schlumpf, 1985). Additional studies are under way to explore the possible demasculinization of other male phenotypic traits by nicotine and its mechanism of action.

Funding: Tobacco Formula Funds, Commonwealth of Pennsylvania, Department of Health. The Department specifically disclaims responsibility for any analyses, interpretations, or conclusions.

Correspondence: David Vandenbergh, 101 Amy Gardner House, Pennsylvania State University, University Park, PA 16802, USA; E-mail: djv4@psu.edu

NICOTINE EXPOSURE IMPACTS SEVERITY OF NEONATAL ABSTINENCE SYNDROME OF NEONATES BORN TO METHADONE-STABILIZED WOMEN

Hendree Jones, Michelle Tuten, Heather Fitzsimons, Candice Evans, Renee Cieslak

Although methadone is beneficial for pregnant opioid-dependent women, many neonates undergo neonatal abstinence syndrome (NAS). NAS is characterized by signs and symptoms of gastrointestinal dysfunction, respiratory distress, and central and autonomic nervous system disruptions. Although it is presently unclear why some neonates exhibit a greater NAS than others, it has been recently shown that in-utero exposure to 20 or more cigarettes/day is associated with more severe NAS than in-utero exposure to 10 or fewer cigarettes/day (Choo et al, 2004, *Drug and Alcohol Dependence, 75*, 253–260). Our study extends past research by comparing the birth outcomes of methadone stabilized pregnant women who did not smoke during pregnancy to those who were heavy smokers (e.g., 20+cigarettes/day). Preliminary data show similar demographic (e.g., 34 vs. 29 years; p=0.118, respectively); and treatment outcomes (e.g., mean methadone dose 65 vs. 70 mg; p=0.733, respectively). Despite similarity in gestational age at delivery (38 vs. 40 weeks; p=0.279) and birth weights, fewer neonates of nonsmokers were treated for NAS relative to heavy smokers (16% vs. 67%; p=0.030). These results further support the role of smoking in the severity of NAS.

Funding: NIH grant R01 DA12403-06.

Correspondence: Hendree Jones, Ph.D., Associate Professor, Johns Hopkins University, Department of Psychiatry and Behavioral Sciences, JHBMC, 4940 Eastern Avenue, D-3, East Baltimore, MD 21224, USA; E-mail: hejones@jhmi.edu

PRENATAL NICOTINE EXPOSURE EXAGGERATES SYNAPTIC CARDIORESPIRATORY INTERACTIONS IN THE MEDULLA; IMPLICATIONS FOR SUDDEN INFANT DEATH SYNDROME

David Mendelowitz, Robert Neff, Kathleen Griffioen

Maternal cigarette smoking and prenatal nicotine exposure are the highest risk factors for sudden infant death syndrome (SIDS), the most common cause of death in infants between 1 and 12 months. During hypoxia, respiratory frequency and heart rate transiently increase and subsequently decrease. These biphasic cardiorespiratory responses normally serve to prolong survival during hypoxia by reducing the metabolic demands of cardiac and respiratory muscles. However, exaggerated responses to hypoxia may be life threatening and have been implicated in SIDS. Infants that succumb to SIDS have a severe centrally mediated slowing of the heart that precedes or accompanies apnea. Heart rate is primarily determined by the activity of brainstem preganglionic cardioinhibitory vagal neurons. We developed an in vitro rat brainstem slice preparation that maintains rhythmic inspiratory-related activity and contains

fluorescently labeled cardiac vagal neurons. Synaptic inputs to cardiac vagal neurons were examined using patch-clamp electrophysiological techniques. Hypoxia evoked a biphasic change in the frequency of both GABA-ergic and glycinergic respiratory-related inhibitory postsynaptic currents (IPSCs) in cardiac vagal neurons. These consisted of an initial increase, then a decrease, in IPSC frequency. Prenatal exposure to nicotine changed the GABA-ergic response to hypoxia from a biphasic response to a precipitous decrease in GABA-ergic IPSC frequency. Hypoxia also recruited an excitatory glutamatergic synaptic pathway to cardiac vagal neurons during gasp-like events in animals exposed to prenatal nicotine, but not in unexposed animals. These results establish a neurochemical link between prenatal nicotine exposure and an exaggerated bradycardia during hypoxia that may contribute to SIDS.

Funding: NIH grants HL72006 and HL59895.

Correspondence: Dr. David Mendelowitz, George Washington University, 2300 Eye Street N.W., Washington, DC 20037, USA; E-mail: dmendel@gwu.edu

EFFECTS OF REDUCED SMOKING DURING PREGNANCY ON TERM-INTRAUTERINE GROWTH RETARDATION

Dmitry Krupitsky, Shirley Thompson, Cheryl L. Addy

Our goal was to investigate the relationship between smoking, the reduction of smoking, and term-intrauterine growth retardation (IUGR). Methods: Population-based data from October 1992 to December 1995 were provided by the South Carolina (SC) Pregnancy Risk Assessment Monitoring System (PRAMS). Statistical analyses were performed with SUDAAN software for weighted data. The cohort consisted of 2,862 term births (weighted n=105,306). Term-IUGR, defined as less than the 10th percentile of birth weight for gestational age among infants of >37 gestational weeks, was based on race- and sex-specific standards for SC. After adjusting for confounders, we found that the odds of having a term-IUGR baby were 3.69 times (95% *CI* 2.39–5.68) greater among women who smoked prior to conception and during the 3rd trimester than among women who did not smoke either time. Among women who smoked prior to conception but quit smoking prior to the 3rd trimester of pregnancy, the risk of having a term-IUGR baby was similar to that of the nonsmoker. Among smokers, reduction by 10 cigarettes per day prior to the 3rd trimester decreased the risk of IUGR by 50% (*AOR*=0.50, 95% *CI* 0.31–0.81). Our findings indicate that smoking is a strong risk factor for IUGR; the effect of cigarette smoking on growth retardation is more pronounced during the last trimester of gestation and any reduction in smoking is likely to be beneficial. Interventions to reduce maternal smoking should begin prior to the 3rd trimester of pregnancy.

Correspondence: Dmitry Krupitsky, MSPH, University of Hawaii, Department of Public Health Science and Epidemiology, 1960 East-West Road D210, Honolulu, HI 96822, USA; E-mail: krupitsk@hawaii.edu.

GENETIC INFORMATION FOR ALPHA-1 ANTITRYPSIN DEFICIENCY MAY INDUCE CHANGES IN SMOKING BEHAVIOR

Matthew Carpenter, Ryan Dickson, Cindy Carter, Yonge Jones, Brian Holladay, Charlie Strange

As genetic testing becomes increasingly widespread, genetic information may result in behavior change if disease course is modifiable. Few studies have examined changes in behavioral health outcome as a function of genetic testing. Alpha-1 antitrypsin (AAT) deficiency (AATD) is a genetic condition that may lead to chronic obstructive pulmonary disease for some people. Thus, knowledge of AAT's genetic status may induce cessation among smokers who test positive for the deficiency, or undermine cessation among smokers who test negative. As part of a large study examining the psychosocial impact of AATD testing, individuals (N=1,495) completed a blood-test kit and were informed of their AAT genetic status. Of these, 356 who self-identified as current smokers at the time of testing were sent a follow-up questionnaire 3 months after receiving test results, and 130 (37%) responded (95% Caucasian; 53% female; mean age 41yrs), reflecting a genetic status representative of the larger population, which is: Nondeficient in AAT—59%; carrier of AAT—36%; severely deficient in AAT—5%. In the 3 months following testing, the following percentages of subjects by group expressed a plan to quit smoking (p>.05): Nondeficient in AAT—66%; carrier of AAT—65%; severely deficient in AAT—100%. Cigarettes per day decreased 7% versus 20% versus 53%, respectively (p<.001). Similarly, 40% versus 39% versus 71%, respectively, made a quit attempt (p>.05). Although limited by small sample-size, these preliminary trends suggest that knowledge of AATD genetic status, but perhaps not carrier status, may motivate smokers toward health change. An update, with larger sample size and additional cessation data, will be presented during conference proceedings.

Funding: Alpha-1 Foundation grant.

Correspondence: Matthew Carpenter, Medical University of South Carolina, Charleston, SC 29425, USA; Tel: (843) 792-3974; E-mail: carpente@musc.edu

DIFFERENCES IN SMOKING TOPOGRAPHY ASSOCIATED WITH CYP2A6 GENOTYPE

Andrew A. Strasser, Viba Malaiyandi, Caryn Lerman, Rachel F. Tyndale

Approximately 80% of nicotine is inactivated when metabolized to cotinine. Variations in CYP2A6 genotype alter the rate of nicotine metabolism. Previous research has demonstrated that smokers with variant alleles associated with slower metabolism smoked fewer cigarettes per day and per week compared to those smokers who were homozygous normal. Smokers can also control their nicotine administration on a per-cigarette basis by adjusting smoking topography measures, such as number of puffs, puff volume, puff velocity, and puff duration. Participants (N=119) smoked one of their preferred-brand cigarettes through a smoking topography device and provided a blood sample for genotyping as part of the baseline session of a large nicotine-replacement therapy study. Smokers with genotypes associated with slow or poor metabolism took significantly smaller puff volumes than those with genotypes associated with intermediate/normal nicotine metabolism. Analyses indicate no significant association with CYP2A6 genotype and number of puffs, puff velocity, puff duration, or time between puffs. These results suggest that besides smoking fewer cigarettes, those who metabolize nicotine slowly may also be taking smaller puff volumes on the cigarettes they smoke relative to those who metabolize nicotine normally.

Funding: NIH grant P50 CA84718; Canadian Institutes of Health Research grant MOP53248.

Correspondence: Andrew A. Strasser, Ph.D., Transdisciplinary Tobacco Use Research Center, University of Pennsylvania, 3535 Market Street, Suite 4100, Philadelphia, PA 19104, USA; E-mail: strasse3@mail.med.upenn.edu

DRD2-TAQ1A GENOTYPIC MODERATION OF BUPROPION TREATMENT EFFICACY FOR SMOKING CESSATION AT SIX-MONTH FOLLOW-UP

Sean P. David, George D. Papandonatos, Marcus R Munafó, Jeanne M. McCaffery, Caryn Lerman, Elizabeth E. Lloyd-Richardson, Peter G. Shields, Richard A. Brown, Raymond Niaura

This randomized, placebo-controlled clinical trial examined the influence of candidate genes in the dopamine pathway and CYP2B6 on treatment response to bupropion for smoking cessation. Smokers of European ancestry (n=292) provided blood samples for genetic analysis and received bupropion or placebo (10 weeks) plus counseling. Assessments included the dopamine D2 receptor (DRD2 Taq1A) genotype; dopamine transporter (SLC6A3 3'VNTR) genotype; cytochrome P450 2B6 (CYP2B6 1459 C→T); and cotinine-verified 7-day point prevalence. Univariate association models with 6-month intent-to-treat analyses of smoking abstinence were fitted using logistic regression. Of the potential interaction effects examined, only that for DRD2 reached statistical significance (p=.03). Among smokers with the DRD2 Taq1-A2/A2 genotype there was a 21% difference in 6-month biochemically verified abstinence: Bupropion group—34%, 95% *CI* 0.24–0.35; placebo group—13%, 95% *CI* 0.07–0.22. However, there was absolutely no response to bupropion therapy among A1/A1 or A1/A2 subjects (23% abstinence rate on both arms). This study provides the first demonstration in a prospective clinical trial of a significant DRD2-by-bupropion interaction for smoking cessation.

Funding: NIH grants HL32318, P50CA84719, and K08 DA14276-03; GlaxoSmithKline, Inc.

Correspondence: Sean P. David, MD, SM, Brown University Center for Primary Care and Prevention and Primary Care Genetics Laboratory and Translational Research Center, 111 Brewster Street, Pawtucket, RI 02860, USA; (401) 729-2071; Fax: (401) 729-2494

SENSITIVITY AND SPECIFICITY OF QUANTITY/FREQUENCY DATA FOR IDENTIFYING NICOTINE DEPENDENCE

Lisa Dierker, Nicholas Perrine, Richard Clayton

To date, little is known about the level of smoking that is necessary or sufficient to achieve nicotine dependence. The relative lack of research attention is largely based on the fact that dependence criteria are typically evaluated if respondents meet a rather high level of smoking, thus artificially constraining the range of possibly quantity/frequency levels. Recent data collected by the Tobacco Etiology Research Network are ideal for addressing this topic owing to (a) planned over-sampling across the continuum of use; and (b) the markedly low threshold of use required for the evaluation of dependence criteria. Thus, our study examines cut-points for quantity and frequency of smoking that most accurately classify individuals with nicotine dependence. We analyzed a college-freshman sample that represented smoking behavior across the continuum of use, quantity, frequency of smoking, and dependence symptoms

based on DSM-IV criteria. We used ROC curves to determine cut-points for smoking quantity and frequency that maximize the sensitive and specific characterization of nicotine dependence. Smoking 3 or more cigarettes (quantity) or smoking on 2 or more days (frequency) during the preceding week emerged as the most meaningful cut-points. Corresponding sensitivity and specificity estimates were (Se 95%; Sp 94%) and (Se 93%; Sp 95%), respectively. The combination of quantity and frequency data did not improve accurate classification of nicotine-dependent individuals. Aside from the substantive implications of this study in terms of emerging dependence at nondaily smoking levels, these results may be used to inform a brief screen in studies that require a high concentration of dependent smokers.

Funding: RWJF Tobacco Etiology Research Network.

Correspondence: Lisa Dierker, Wesleyan University, 207High Street, Middletown, CT 06459, USA; E-mail: ldierker@wesleyan.edu

MEASUREMENT OF SMOKING OUTCOME EXPECTANCIES IN CHILDREN: THE SMOKING CONSEQUENCES QUESTIONNAIRE—CHILD

Amy L. Copeland, James M. Diefendorff, Donald A. Williamson

Based on evidence highlighting the importance of nicotine-related measures to be developmentally and age-appropriate, we developed a smoking outcome-expectancy measure. The Smoking Consequences Questionnaire—Child (SCQ—C) is for children aged 7–12 years who are enrolled in a tobacco-prevention program. We used the recommendations of Nichter et al. (2002) regarding development of nicotine-related surveys for youth. Items were derived from both qualitative and quantitative sources, including focus groups, pilot work, and content sampling of the Smoking Consequences Questionnaire (SCQ; Brandon and Baker, 1991). Children (N=743) responded using a dichotomous agree/disagree response format to 20 items describing possible consequences of smoking a cigarette. Confirmatory factor analysis (CFA) was used to compare four factor structures, implied by previous theory and empirical research: A four-factor model consisting of scales measuring positive reinforcement, negative reinforcement, negative consequences, and weight control; a three-factor model consisting of scales measuring positive reinforcement, negative consequences, and weight control; a two-factor model consisting of scales measuring positive reinforcement and negative consequences; and a one-factor model assessing a global measure of smoking attitudes. The three-factor model with 16 items was retained as the final model. All of the items had primary factor loadings greater than 0.35 and negligible cross-loadings. Reliability estimates of coefficient alpha for the three subscales ranged from 0.5 to 0.7. The SCQ-C Positive Reinforcement scale was associated with children's smoking behavior, and the SCQ-C Negative Consequences scale was inversely related to having a parent or other immediate family member who smoked. These tests provide initial evidence of construct validity.

Funding: NIH grant R01 DK063453.

Correspondence: Amy L. Copeland, Ph.D., Psychology Department, Louisiana State University, Baton Rouge, LA 70803, USA; E-mail: copeland@lsu.edu

USE OF MORE NICOTINE LOZENGES LEADS TO BETTER SUCCESS IN QUITTING

Saul Shiffman

Compliance with instructions to use adequate amounts of cessation medications such as nicotine gum or lozenge is considered important to achieving treatment success. Studies show that smokers who used more pieces of nicotine gum achieved better outcomes. However, these correlational data are subject to two alternative explanations: (a) A motivational hypothesis that those who use more pieces are more motivated to quit, and achieve better outcomes on that account; and (b) a reverse-causation hypothesis that smokers reduce their nicotine-replacement therapy because they have started smoking, rather than the converse. We tested these alternative explanations in the context of a large published placebo-controlled trial of a nicotine lozenge (2 and 4 mg; GlaxoSmithKline). The motivational hypothesis predicts that high lozenge use would be associated with improved outcomes, even in the placebo condition. In the whole sample (N=1,818), use of more lozenges was associated with success only among those on active lozenges, and not in the placebo group. This shows the effect is pharmacological, not motivational. To address the reverse-causation hypothesis, we analyzed lozenge use during the first 2 weeks of quitting in a subgroup of smokers (n=826) who were known and biochemically verified to be abstinent during this period. In this prospective analysis, use of more active lozenges (but not placebo) was again significantly associated with improved outcome at subsequent follow-up. The analyses rebut the alternative explanations, and suggest that use of more nicotine lozenges is causally associated with better quit rates.

Funding: GlaxoSmithKline Consumer Healthcare, for whom the author provides consulting and research services.

Correspondence: Saul Shiffman, Ph.D., Pinney Associates, 201 North Craig Street, Suite 320, Pittsburgh, PA 15213, USA; E-mail: shiffman@pinneyassociates.com

SAFETY OF NICOTINE LOZENGES AND GUM IN PATIENTS WITH LABEL-SPECIFIED UNDERLYING MEDICAL CONDITIONS

Carolyn M. Dresler, Jae H. Choi, Darren A. Targett, Howard S. Marsh, Michael L. Gamble, Kenneth R. Strahs

The current labels for nicotine-replacement therapy (NRT) products require the smokers with certain medical conditions to consult their physicians before starting to use NRT. Because the 4-mg nicotine lozenge delivers approximately 25% more nicotine compared to the 4-mg nicotine gum per piece, the safety of additional available nicotine was questioned. Our multicenter, randomized, open-label study was conducted to compare the safety profile of these two products among subjects with certain label-specified medical conditions (hypertension, diabetes, or cardiac diseases). A total of 901 subjects were randomized to receive lozenge or gum on a 1:1 ratio. The adverse events (AEs) were captured using a daily diary and clinic visits (five visits during the 12-week treatment). Treating physicians evaluated the clinical condition of the subjects by reviewing symptom-control and disease-specific parameters at each clinic visit. The mean age of the study population was 54 years of age and the subjects smoked on average 25 cigarettes per day (CPD) at baseline. In both groups, approximately 70% of subjects had hypertension; 30% had both diabetes and cardiac diseases; and 35% had more than two disease conditions. Subjects used 5–6 pieces per day of the assigned product on average during the first 6 weeks. Even though more than 90% of subjects admitted to have smoked during the study, CPD was reduced from 25 CPD at baseline to 5 CPD at week 6. Incidence of AEs reported; evaluation of the clinical conditions by the treating physicians; and measurements of disease-specific parameters (change in blood glucose, vital signs, and ECG) indicated comparable safety profiles between the two products. The analysis of AEs stratified by product usage and smoking levels did not reveal any increase in the incidence of AEs, even in the highest risk group (>median usage plus heaviest smokers). The findings from our study suggest that the 4-mg lozenges and 4-mg gum are comparable in safety and did not appear to worsen clinical conditions of the subjects with hypertension, diabetes, or cardiac diseases. Given the favorable safety profiles of nicotine lozenges and gum demonstrated in this study and the clear benefit of stopping smoking, clinicians should recommend the use of NRT in these patients.

Funding: GlaxoSmithKline Consumer Healthcare.

Correspondence: Jae H. Choi, Pharm.D., GlaxoSmithKline Consumer Healthcare, 1500 Littleton Road, Parsippany, NJ 07054, USA; E-mail: jae.h.choi@gsk.com

TOLERABILITY AND KINETICS OF ORAL NICOTINE TABLETS

Neal L. Benowitz, Delia Dempsey, Jae Choi, Rick S. Chan, Darren Targett

Oral dosing represents a potential route of administration of nicotine (Nic) for pharmacotherapy of nicotine addiction. Whether orally ingested Nic could achieve adequate Nic blood levels at tolerated doses has not been studied. Accordingly, the feasibility of oral Nic replacement tablets as a medication remains a question. We conducted a parallel-group, placebo-controlled, dose-escalation study of immediate-release Nic tablets. We randomly assigned 48 healthy smokers who smoked at least 15 cigarettes per day to active or placebo pills at each dose level (6:2 ratio). Doses were started at 4 mg and escalated by 4 mg as tolerated. Dosing was stopped at 24 mg because of development of nausea, vomiting, and/or abdominal pain in four subjects. Plasma Nic levels increased in proportion to dose, with maximal levels ranging from 5.3 to 23.2 ng/ml, occurring on average 2.3 hr after dosing. Heart rate and blood pressure increased with Nic, with an apparent plateau in response at the 8–12-mg dose level. A dose-related decrease in cigarette craving was observed. Our study demonstrates that oral Nic tablets are tolerated fairly well at doses up to 24 mg, achieving levels similar to or higher than those seen with other forms of NRT. The primary adverse effects at higher doses were gastrointestinal, with evidence of tolerance to cardiovascular effects at higher Nic doses. The clinical pharmacology of oral Nic tablets supports the feasibility of its investigation as an alternative form of NRT to aid smoking cessation.

Funding: GlaxoSmithKline Consumer Health Care; NIH grants DA02277 and DA12393.

Correspondence: Neal L. Benowitz, M.D., Box 1220, University of California, San Francisco, San Francisco, CA 94143, USA

EVALUATION OF EFFECTIVENESS OF A SCHOOL-BASED SMOKING-CESSATION PROGRAM FOR ADOLESCENTS

Connie Kohler, Yu-Mei Schoenberger, Martha Phillips

Unlike the extensive base of evidence regarding the efficacy and effectiveness of adult smoking-cessation strategies, the base of evidence regarding efficacy or effectiveness with youth cessation is scant. This project was funded to provide an effectiveness evaluation of a widely disseminated smoking-cessation program, the American Lung Association's Not-on-Tobacco (N-O-T) Program. Working with the ALA of Alabama, we recruited 48 high schools to implement the N-O-T Program over a 3-year period (n=252 students). Another 27 schools were recruited as comparison schools (n=251 students). Data were collected at baseline, end-of-program, 6, and 12 months. Students reported any smoking in the last 30 days. At end-of-program, 6.4% of N-O-T participants reported not smoking in the last 30 days, compared to 3.2% of comparison students. N-O-T participants were 2.5 times as likely to report not smoking as students in comparison schools when accounting for race (adjusted *OR*=2.5; 95% *CI* 1.01–6.2). There were substantial differences in the treatment effects noted for whites and nonwhites. Among whites, N-O-T participants were over 5 times as likely to report not smoking as nonparticipants (*OR*=5.3; 95% *CI* 1.1–24.1); among nonwhites, N-O-T participants were 1.2 times as likely as nonparticipants to report not smoking. Differences remained at 12 months (4.4% of N-O-T participants reported not smoking in the last 30 days, compared to 3.6% of comparison students). White students were 2.8 times as likely to report not smoking, but these differences were not statistically significant (*OR*=2.8; 95% *CI* 0.8–10.6). The difference in the *OR* at 12 months may reflect the 72% (65.4% in the comparison group vs. 78.6% in the intervention group) attrition in this intent-to-treat analysis.

Funding: American Legacy Foundation.

Correspondence: Connie Kohler, University of Alabama at Birmingham, School of Public Health, 1530 Third Avenue, South Birmingham, AL 35294-0022, USA; E-mail: ckohler@uab.edu

ACTIVE TOBACCO SMOKING IN EARLY ADOLESCENCE AND ADVERSE HEALTH EFFECTS TWO DECADES LATER: LONGITUDINAL EVIDENCE OF RISK

Karen M. Jennison, Kenneth A. Johnson

This study investigates the long-term health risks of tobacco smoking using data from the National Longitudinal Surveys of Youth (n=5,227) for the years 1982–2002. Questions on smoking behavior measured the age-at-onset of tobacco use as well as smoking history. After adjustment for confounding, the results of a multiple-logistic regression analysis indicated that, when compared to the typical person in the United States general population, active cigarette smoking before the teen years greatly increased the risk of lowered physical and mental-health scores among respondents aged 40–45 as measured on the Short-Form 12-Question (SF-12) Inventory. Lower scores were 2 to 4 times as common among males and 2 to 10 times among females. For males, smoking onset in childhood and early adolescence conjointly with continued tobacco use over the life course significantly predicted the severity of self-reported health problems as defined by the International Classification of Diseases (ICD-9) health codes, even if smokers reduced their smoking from daily to occasional during their 30s. Although the health problems of females were equally influenced by smoking initiation before the teen years, negative health consequences for them increased dramatically irrespective of subsequent smoking or nonsmoking history. Significant depressive symptomatology, measured using the Center for Epidemiologic Studies Depression scale, was predicted more among males by higher cigarette smoking rates (a pack or more a day) at ages 19 to 25 than in later years, whereas depression symptoms among females were nearly 4 times more likely if they began smoking before their teens. These findings underscore the important linkage between youthful cigarette smoking and long-term adverse health effects. Evidence is provided that the earlier the age at which one starts to smoke tobacco, the greater the risk of diminished health in middle age.

Funding: NSLY from the Bureau of Labor Statistics of the U.S. Department of Labor. *Data*: National Longitudinal Survey of Youth (NLSY79); Center for Human Resource Research, Ohio State University.

Correspondence: Karen M. Jennison, Ph.D., Department of Sociology, Box 142, University of Northern Colorado, 501 20th Street, Greeley, CO 80634, USA; E-mail: karen.jennison@unco.edu

DEPRESSION AND RELAPSE TO SMOKING IN PATIENTS HOSPITALIZED WITH ACUTE CARDIOVASCULAR DISEASE

Anne Thorndike, Nancy A. Rigotti, S. Regan, R. Pasternak, Kathleen McKool, Karen Emmons, DanielE. Singer, S. Swartz

Depression is common among cardiac patients and increases CV morbidity and mortality. The impact of depressive symptoms on relapse to smoking after

hospitalization for acute cardiovascular disease (CVD) is unknown. We analyzed data from a double-blind randomized, controlled trial of 12 weeks of bupropion SR in 248 adult smokers hospitalized with acute CVD. All smokers received smoking counseling in the hospital and at five follow-up telephone calls. Cotinine-verified 7-day tobacco abstinence was assessed at 3 and 12 months. The Beck Depression Inventory (BDI) assessed depressive symptoms at baseline, 3, and 12 months. We defined BDI $\geqslant$16 as current depression. Chi-square tests and logistic-regression models compared differences in quit rates. Time-to-relapse was analyzed with survival analysis. We found that at baseline, 53 (21%) of the smokers had a BDI score $\leqslant$16. Depressed smokers were less likely than nondepressed smokers to quit at 3 months (17% vs. 35%; $p=.01$); and 12 months (8% vs. 27%; $p=.004$). These differences remained significant when controlling for study arm, race, sex, age, cigarettes/day, and nicotine dependence. Depressed smokers relapsed very quickly after hospital discharge. Quit rates and days-to-relapse did not differ between drug and placebo groups among subgroups of patients who were depressed or nondepressed at baseline. We concluded that baseline depressed mood is a strong predictor of relapse to smoking after hospitalization for acute CVD. Bupropion does not improve cessation rates among these depressed smokers. Relapse occurs soon after discharge, often before outpatient follow-up, indicating the need for better hospital-initiated intervention.

Funding: NIH grant R01 HL61779; GlaxoSmithKline.

Correspondence: Nancy A. Rigotti, MGH Tobacco Research and Treatment Center, Harvard Medical School, Boston, Massachusetts, USA; E-mail: nrigotti@partners.org

A COMPUTER-SIMULATION MODEL FOR THE SURVEILLANCE OF TOBACCO CONTROL POLICIES IN CALIFORNIA

David T. Levy, Andrew Hyland

Debates over state and national tobacco legislation and the use of state funds demonstrate that there is a need for information on the likely effects of state-level tobacco-control policies. Well-developed, dynamic computer-simulation models that are based on empirical evidence and that account for the variety of influences on tobacco use can be useful tools for informing policymakers. They can identify the effects of different policies on all smokers and on specific demographic profiles of smokers. In so doing, the model can be used to convey the importance of comprehensive policy approaches to tobacco control and to improve the focus of tobacco-control policies. The SimSmoke tobacco-control policy simulation model may be used to track smoking and to evaluate tobacco-control policies. The model tracks cohorts of smokers by age, gender, and racial/ethnic group over time, and predicts trends in smoking and smoking-attributable deaths. Specific modules analyze how public policies—such as taxes, mass media, clean air laws, cessation treatment, and youth-access policies—affect smoking rates and smoking-related mortality. Modules also show how the effects depend on the manner in which a policy is implemented. SimSmoke was originally a national model. Because of its rich data sources, pioneering research, and policies in the field of tobacco control, California has been chosen as the first state in which to implement a state level model. California SimSmoke tracks smokers by age and gender and predicts smoking and smoking related deaths based on population subgroups and public policies in effect. The model includes the effects of policies such as taxes, mass media, clean-air laws, treatment to stop smoking, and youth access to tobacco. The model examines the effect of past policies and develops predictions on the effect of future policies. The California SimSmoke model estimates that tobacco-control policies reduced smoking rates in California by an additional 25% relative to the level that they would have been if policies were kept at their 1988 level. As of 2003, the model attributes over 60% of the reduction to price increases; over 25% of the overall effect to media policies; 10% to clean air laws; and only a small percent to youth-access policies. The model estimates that over 40,000 Californians die each year. Over 5,000 lives will be saved in the year 2010 alone as a result of the CTCP and industry-initiated price increases. Tobacco-control policies implemented as comprehensive strategies have significantly impacted smoking rates. Further tax increases should lead to additional lives saved. Additional policies may result in further impacts on smoking rates, and consequently on smoking-attributable health outcomes in the population. Policymakers will be able to use the model to monitor the value of each policy and demonstrate where past policies have been effective and ineffective. They could then use the model to shape future policies. They could discern which age groups and racial groups are currently being affected by tobacco-control policies in the state of California, and determine polices to improve the health of these groups. Developing this computer model will also help leaders understand about past policies and make better decisions about future policies. They could also see how the effect of policies depends on the way in which they are implemented, and on the other policies already in place.

Funding: NIH National Cancer Institute CISNET grant UO1-CA-097450; TRDRP.

Correspondence: David T. Levy, Ph.D., 14403 Sylvan Glade Drive, North Potomac, MD 20878, USA; E-mail: levy@pire.org

REDUCING INITIATION VS. INCREASING CESSATION: AN INVESTIGATION OF THE DIFFERENTIAL IMPACT OF SMOKING-CONTROL POLICIES ON SMOKING-RELATED DEATHS AND MEDICAL COSTS IN THE UNITED STATES

David Mendez, Kenneth E. Warner, Kristen M. Hassmiller

National targets for smoking-rate reduction in the United States usually focus on achieving a smoking prevalence level by a certain date without considering the specific dynamics of initiation and cessation necessary to achieve those targets. We hypothesize that different combinations of initiation and cessation efforts can achieve the same smoking prevalence level with a very different effect on mortality and medical costs. This paper examines the impact on mortality and medical costs of smoking-control policies that focus on reducing initiation versus those that center on smoking cessation. We first present a system-dynamics model that keeps track of smoking prevalence, medical costs by smoking status, and smoking-related mortality over time. We then introduce various combinations of smoking-cessation increase and initiation decline that will produce the same adult-smoking prevalence by the year 2020 in the United States. Finally, we evaluate the subsequent impact on mortality and medical costs of such policy combinations up to the year 2050. Our research highlights the importance of considering the dynamic nature of the smoking problem when formulating control policies.

Funding: RWJF grant 034909.

Correspondence: David Mendez, Ph.D., Assistant Professor, Department of Health Management and Policy, School of Public Health, University of Michigan M3232 SPH II, 109 Observatory, Ann Arbor, MI 48109-2029, USA; E-mail: dmendez@umich.edu

IS TOBACCO PUP ENFORCEMENT RELATED TO YOUTH SMOKING BEHAVIOR AND ATTITUDES?—A FOCUS GROUP STUDY

Cindy Tworek, Gary Giovino, K. Michael Cummings, Andrew Hyland

State and local youth-access legislation penalizing minors for possession, use, and/or purchase (PUP) of tobacco products has increased in recent years; however, evaluation of PUP legislation and its enforcement has been minimal. This study conducted focus groups among 25 young people in New Jersey towns with local tobacco-related PUP ordinances at varying levels of enforcement (moderate vs. high). Focus groups were conducted in school or town libraries, and all student participants received a brief health-behavior questionnaire, including demographic and tobacco-related questions. All participants were 15–17-year-old students and town residents. All participants followed informed-consent procedures, obtaining parental permission to participate. Within the context of varying PUP enforcement levels, this focus-group study explored youth awareness, knowledge, perceptions, opinions, and experiences related to local New Jersey tobacco PUP ordinances. The study also explored possible effects of school and community enforcement of these PUP ordinances on youth-smoking behavior and attitudes toward smoking. Students expressed a general sense of awareness concerning local PUP ordinances, but perceived greater school enforcement versus community enforcement in both moderate- and high-enforcement towns. PUP laws did not affect smoking behavior or attitudes toward smoking among participants. Students expressed an unmet need for tobacco prevention, education, and cessation classes, as opposed to ineffective penalties such as fines for tobacco PUP violations. Qualitative discussion group results and quantitative survey results will be presented within the context of varying PUP enforcement levels.

Funding: RWJF.

Correspondence: Cindy Tworek, MPH, MS, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA; E-mail: cindy.tworek@roswellpark.org