

Accomplishments for the UCSF TCORS 1.0 (2013-2018)
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The overarching theme of the UCSF Tobacco Center of Regulatory Science, "Improved Models to Inform Tobacco Product Regulation," was to develop models that integrated 1) economic impacts of tobacco use on healthcare costs, 2) risk perceptions, perceived acceptability, consumer responses to pro-tobacco marketing and anti-tobacco messages and other social determinants of tobacco use, and 3) rapid changes in risk due to tobacco use and secondhand smoke exposure as manifest in cardiovascular and pulmonary dysfunction. We had a particular focus on immediate effects of tobacco use and effects on susceptible populations (such as people exposed to infection) because these immediate effects have not been given adequate attention in the regulatory process.

Highlights of the results, published 100 peer reviewed papers and 81 public comments (as of October 2018), include:

- We developed the first national estimates of the cost of smokeless tobacco use and cigar smoking, estimating that annual excess health care expenditures totaled over \$3.4 billion for smokeless use and \$1.8 billion for cigar smoking (in 2014 dollars).
- Even after controlling for the number of cigarettes smoked per day, adults who had higher spending on e-cigarettes were more likely to report chest pain, blood on their toothbrush, a sore mouth, and more colds than those with lower spending on e-cigarettes.
- E-cigarettes are associated with increased odds of having had a heart attack, independent of the effects of cigarette smoking; dual use of both products is associated with higher risk than using either product alone.
- While some smokers successfully quit smoking with e-cigarettes, overall smokers who use e-cigarettes are less likely to stop smoking than smokers who do not use e-cigarettes.
- Flavors in e-cigarettes affect nicotine absorption, vaping topography, and rewarding effects of e-cigarettes, indicating that flavors can influence the addictiveness of e-cigarettes.
- Adolescents' and young adults' perceptions of risks and benefits of tobacco products varies significantly by product and tobacco use experience; and that perceptions of cigarette risks, benefits, and social norms have changed over the past 14 years, with adolescents perceiving greater risk and fewer benefits and viewing cigarettes as less socially normative.
- Youth believe that, contrary to industry arguments, ads for e-cigarettes depicting implicit and explicit cessation claims are interpreted by youth as conveying cessation and that flavored products are for them.
- Youth who used Juul e-cigarettes in 2018 do so more frequently than other tobacco products and they harbor misperceptions about the risks associated with Juuls or other e-cigarettes and that do not understand the addictive potential of Juuls.
- Believing that smokeless tobacco (ST) was socially normative, especially among family members, peers, and professional athletes, was positively associated with ST susceptibility and later initiation, as was believing that ST was substantively different from cigarettes in its risk profile, suggesting that modified harm messaging for ST is likely to increase ST use among youth.
- ST flavors stimulated adolescents' interest in trying ST, and time-limited promotional flavors and packaging also enhanced product appeal; youth who viewed flavored ST as "easier" to use than unflavored ST were more susceptible to use, suggesting that restricting availability of flavors and promotional packages would reduce the appeal of smokeless tobacco products.

- Youth who used any form of non-cigarette tobacco (including e-cigarettes) are at greater risk of subsequent cigarette smoking, with highest risk among poly-users of multiple non-cigarette products, a behavior increasing in prevalence among U.S. youth.
- Youth who use e-cigarettes have toxicants in their urine, showing that they are absorbing more than “harmless water vapor.”
- There is a large group of adolescent e-cigarette-only users (i.e., not using e-cigarettes); these youth have risk profiles that make them unlikely to initiate nicotine addiction with cigarettes.
- We identified the need for novel measures for e-cigarette perceptions and developed a new measure of e-cigarette dependence focused on sensory experiences.
- Cigarette smoke-exposed mice have more severe lung injury and more pulmonary edema than control mice following inhaled lipopolysaccharide; short-term smoke exposure at levels that cause no overt lung damage still prime the lung for acute inflammatory damage from a second insult, a finding that mirrors the increased risk of developing lung injury in patients who smoke.
- Cigarette smoke exposure increases lung injury in antibiotic-treated pneumococcal pneumonia in mice, a highly clinically relevant model of live bacterial pneumonia treated with antibiotics, highlighting the need to consider indirect effects of changes in smoking behavior when assessing policies that reduce smoking.
- Passive and active cigarette smoke exposure are associated with an increased risk of developing infection-related acute lung injury, which has significant implications for public health and healthcare associated costs.
- Primary human bronchial cells exposed to e-cigarette aerosol have increased cell death and inflammation, which may help explain clinical studies that have found that e-cigarette users have higher rates of pulmonary symptoms.
- Primary human alveolar cells exposed to e-cigarette aerosol have increased cell death and inflammation, suggesting that exposures to e-cigarette aerosol may place users at risk for enhanced susceptibility to inflammatory lung injury during respiratory infections.
- Mice exposed to 9 days of nicotine-containing e-cigarette aerosol have impaired clearance of influenza virus, suggesting that, like cigarettes, e-cigarette use exerts potent immunosuppressive effects against common and potentially lethal respiratory viruses.
- Two-thirds of homeless cigarette smokers also use other forms of non-cigarette tobacco products, with cigars, blunts, and e-cigarettes being the most commonly used products.
- Heated tobacco products being introduced around the world (but not yet authorized for sale in the US as of October 2019) likely deliver comparable risks to users as cigarettes and their marketing is likely to mislead consumers and attract youth.
- The Biomarker Core developed new methods that allow measurement of for several minor tobacco alkaloids (nicotelline, anathelline, beta nicotyrine and 3-ethenylpyridine) in a range of tobacco products, some of which are likely to have pharmacologic activity, both in tobacco and in emissions (including thermal degradation products), that will be of direct regulatory value.