E-Cigarette Use Among Youth and Young Adults

A Report of the Surgeon General

U.S. Department of Health and Human Services

E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General

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Message from Sylvia Burwell

Secretary, U.S. Department of Health and Human Services

The mission of the Department of Health and Human Services is to enhance and protect the health and well-being of all Americans. This report confirms that the use of electronic cigarettes (or e-cigarettes) is growing rapidly among American youth and young adults. While these products are novel, we know they contain harmful ingredients that are dangerous to youth. Important strides have been made over the past several decades in reducing conventional cigarette smoking among youth and young adults. We must make sure this progress is not compromised by the initiation and use of new tobacco products, such as e-cigarettes. That work is already underway.

To protect young people from initiating or continuing the use of e-cigarettes, actions must be taken at the federal, state, and local levels. At the federal level, the U.S. Food and Drug Administration (FDA)—under authority granted to it by Congress under the *Family Smoking Prevention and Tobacco Control Act of 2009*—took a historic step to protect America's youth from the harmful effects of using e-cigarettes by extending its regulatory authority over the manufacturing, distribution, and marketing of e-cigarettes. Through such action, FDA now requires minimum age restrictions to prevent sales to minors and prohibits sales through vending machines (in any facility that admits youth), and will require products to carry a nicotine warning.

We have more to do to help protect Americans from the dangers of tobacco and nicotine, especially our youth. As cigarette smoking among those under 18 has fallen, the use of other nicotine products, including e-cigarettes, has taken a drastic leap. All of this is creating a new generation of Americans who are at risk of nicotine addiction.

The findings from this report reinforce the need to support evidence-based programs to prevent youth and young adults from using tobacco in any form, including e-cigarettes. The health and well-being of our nation's young people depend on it.

Foreword

Tobacco use among youth and young adults in any form, including e-cigarettes, is not safe. In recent years, e-cigarette use by youth and young adults has increased at an alarming rate. E-cigarettes are now the most commonly used tobacco product among youth in the United States. This timely report highlights the rapidly changing patterns of e-cigarette use among youth and young adults, assesses what we know about the health effects of using these products, and describes strategies that tobacco companies use to recruit our nation's youth and young adults to try and continue using e-cigarettes. The report also outlines interventions that can be adopted to minimize the harm these products cause to our nation's youth.

E-cigarettes are tobacco products that deliver nicotine. Nicotine is a highly addictive substance, and many of today's youth who are using e-cigarettes could become tomorrow's cigarette smokers. Nicotine exposure can also harm brain development in ways that may affect the health and mental health of our kids.

E-cigarette use among youth and young adults is associated with the use of other tobacco products, including conventional cigarettes. Because most tobacco use is established during adolescence, actions to prevent our nation's young people from the potential of a lifetime of nicotine addiction are critical.

E-cigarette companies appear to be using many of the advertising tactics the tobacco industry used to persuade a new generation of young people to use their products. Companies are promoting their products through television and radio advertisements that use celebrities, sexual content, and claims of independence to glamorize these addictive products and make them appealing to young people.

Comprehensive tobacco control and prevention strategies for youth and young adults should address all tobacco products, including e-cigarettes. Further reductions in tobacco use and initiation among youth and young adults are achievable by regulating the manufacturing, distribution, marketing, and sales of all tobacco products—including e-cigarettes, and particularly to children—and combining those approaches with other proven strategies. These strategies include funding tobacco control programs at levels recommended by the Centers for Disease Control and Prevention (CDC); increasing prices of tobacco products; implementing and enforcing comprehensive smokefree laws; and sustaining hard-hitting media campaigns, such as CDC's *Tips from Former Smokers* that encourages smokers to quit for good, and FDA's *Real Cost* that is aimed at preventing youth from trying tobacco and reducing the number of youth who move from experimenting to regular use. We can implement these cost-effective, evidence-based, life-saving strategies now. Together with additional effort and support, we can protect the health of our nation's young people.

Thomas R. Frieden, M.D., M.P.H.
Director
Centers for Disease Control and Prevention

Preface

from the Surgeon General

E-cigarette use among U.S. youth and young adults is now a major public health concern. E-cigarette use has increased considerably in recent years, growing an astounding 900% among high school students from 2011 to 2015. These products are now the most commonly used form of tobacco among youth in the United States, surpassing conventional tobacco products, including cigarettes, cigars, chewing tobacco, and hookahs. Most e-cigarettes contain nicotine, which can cause addiction and can harm the developing adolescent brain.

Compared with older adults, the brain of youth and young adults is more vulnerable to the negative consequences of nicotine exposure. The effects include addiction, priming for use of other addictive substances, reduced impulse control, deficits in attention and cognition, and mood disorders. Furthermore, fetal exposure to nicotine during pregnancy can result in multiple adverse consequences, including sudden infant death syndrome, altered corpus callosum, auditory processing deficits, effects on behaviors and obesity, and deficits in attention and cognition. Ingestion of e-cigarette liquids containing nicotine can also cause acute toxicity and possibly death if the contents of refill cartridges or bottles containing nicotine are consumed.

This report highlights what we know and do not know about e-cigarettes. Gaps in scientific evidence do exist, and this report is being issued while these products and their patterns of use continue to change quickly. For example, the health effects and potentially harmful doses of heated and aerosolized constituents of e-cigarette liquids—including solvents, flavorants, and toxicants—are not completely understood. However, although e-cigarettes generally emit fewer toxicants than combustible tobacco products, we know that aerosol from e-cigarettes is not harmless.

Although we continue to learn more about e-cigarettes with each passing day, we currently know enough to take action to protect our nation's young people from being harmed by these products. Previous reports of the Surgeon General have established that nearly all habitual tobacco use begins during youth and young adulthood. To prevent and reduce the use of e-cigarettes by youth and young adults, we must work together as a society. We must implement proven prevention and education strategies. Health care providers, parents, teachers, and other caregivers should advise youth about the dangers of nicotine and discourage tobacco use in any form, including e-cigarettes. They can set a positive example by being tobacco-free and encouraging those who already use these products to quit. Free help is available at 1-800-QUIT-NOW or http://www.smokefree.gov. Preventing tobacco use in any form among youth and young adults is critical to ending the tobacco epidemic in the United States.

Vivek H. Murthy, M.D., M.B.A.
U.S. Surgeon General

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Vice Admiral (VADM) Vivek H. Murthy, M.D., M.B.A., Surgeon General, Office of the Surgeon General, Office of the Secretary, U.S. Department of Health and Human Services, Washington, D.C.

Thomas R. Frieden, M.D., M.P.H., Director, Centers for Disease Control and Prevention, Atlanta, Georgia.

Ursula E. Bauer, Ph.D., M.P.H., Director, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Dana Shelton, M.P.H., Deputy Director, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Peter A. Briss, M.D., M.P.H., Medical Director, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Rachel Kaufmann, Ph.D., M.P.H., Associate Director for Science, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Corinne Graffunder, Dr.P.H., M.P.H., Director, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Editors of the report were

Cheryl L. Perry, Ph.D., Senior Scientific Editor, Professor and Regional Dean, The Rockwell Distinguished Chair in Society and Health, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

Melissa Harrell, Ph.D., M.P.H., Senior Scientific Editor, Associate Professor, Department of Health Promotion and Behavioral Sciences and the Michael & Susan Dell Center for Healthy Living, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

MeLisa R. Creamer, Ph.D., M.P.H., Senior Scientific Editor, Faculty Associate, Department of Health Promotion and Behavioral Sciences and the Michael & Susan Dell Center for Healthy Living, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

Steven Kelder, Ph.D., Senior Scientific Editor, Beth Toby Grossman Distinguished Professor of Spirituality and Healing; Associate Regional Dean; Co-Director, Michael & Susan Dell Center for Healthy Living; Professor, Division of Epidemiology, Human Genetics, and Environmental Sciences, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

Brian King, Ph.D., Senior Associate Editor, Deputy Director for Research Translation, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Leslie A. Norman, M.B.A., Managing Editor, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Peter L. Taylor, M.B.A., Technical Editor, Fairfax, Virginia.

Contributing editors were

Thomas Eissenberg, Ph.D., Director, Center for the Study of Tobacco Products; Professor of Psychology (Health Program), College of Humanities and Sciences and Member Scientist, Massey Cancer Center, Virginia Commonwealth University, Richmond, Virginia.

Rachel A. Grana, Ph.D., M.P.H., Program Director, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Pamela Ling, M.D., M.P.H., Professor, Division of General Internal Medicine, Department of Medicine, Center for Tobacco Control Research and Education, University of California, San Francisco, California.

Mark Parascandola, Ph.D., M.P.H., Epidemiologist, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Jennifer L. Pearson, Ph.D., M.P.H., Research Investigator, The Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, D.C.; Adjunct Assistant Professor, Department of Health, Behavior, and Society, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland.

Jonathan M. Samet, M.D., M.S., Distinguished Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine; Director, Institute for Global Health, University of Southern California, Los Angeles, California.

Andrea C. Villanti, Ph.D., M.P.H., Director for Regulatory Science and Policy, The Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, D.C.; Adjunct Assistant Professor, Department of Health, Behavior, and Society, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland.

Contributing authors were

Melissa D. Blank, Ph.D., Assistant Professor, Department of Psychology, West Virginia University, Morgantown, West Virginia.

Frank J. Chaloupka, Ph.D., Director, Health Policy Center, Institute for Health Research and Policy, and Distinguished Professor, Department of Economics, University of Illinois at Chicago, Chicago, Illinois.

Shari P. Feirman, Ph.D., M.S., Project Director for Regulatory Science and Policy, The Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, D.C.

Jonathan Foulds, Ph.D., Professor, Departments of Public Health Sciences and Psychiatry, College of Medicine, Penn State University, Hershey, Pennsylvania.

Allison M. Glasser, M.P.H., Senior Project Manager, The Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, D.C.

Maciej L. Goniewicz, Ph.D., Pharm.D., Assistant Professor of Oncology, Department of Health Behavior, Roswell Park Cancer Institute, Buffalo, New York.

Rachel A. Grana, Ph.D., M.P.H., Program Director, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Lisa Henriksen, Ph.D., Senior Research Scientist, Stanford Prevention Research Center, Department of Medicine, School of Medicine, Stanford University, Palo Alto, California.

Jidong Huang, Ph.D., Senior Research Scientist, Institute for Health Research and Policy, University of Illinois at Chicago, Chicago, Illinois.

Lauren K. Katz, M.P.H., Research Associate I, The Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, D.C.

Frances Leslie, Ph.D., Vice Provost for Graduate Education; Dean of the Graduate Division; Professor of Pharmacology and Anatomy and Neurobiology, University of California, Irvine, California.

M. Jane Lewis, Dr.Ph., Associate Professor, Health Education and Behavioral Science and Center for Tobacco Studies, School of Public Health, Rutgers University, New Brunswick, New Jersey.

Kristy Marynak, M.P.P., Public Health Analyst, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Mark Parascandola, Ph.D., M.P.H., Epidemiologist, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Terry F. Pechacek, Ph.D., Professor and Interim Division Director of Health Management and Policy, School of Public Health, Georgia State University, Atlanta, Georgia.

Gabbi Promoff, M.A., Associate Director for Policy, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Kurt M. Ribisl, Ph.D., Professor, Department of Health Behavior, University of North Carolina Gillings School of Global Public Health; Program Leader in Cancer Prevention and Control, University of North Carolina Lineberger Comprehensive Cancer Center, Chapel Hill, North Carolina.

April Roeseler, B.S.N., M.S.P.H., Chief, California Tobacco Control Program, California Department of Public Health, Sacramento, California.

Jonathan M. Samet, M.D., M.S., Distinguished Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine; Director, Institute for Global Health, University of Southern California, Los Angeles, California.

Laura R. Stroud, Ph.D., Senior Research Scientist, Centers for Behavioral and Preventive Medicine, The Miriam Hospital; Associate Professor, Department of Psychiatry and Human Behavior, Alpert Medical School, and Department of Behavioral and Social Sciences, School of Public Health, Brown University, Providence, Rhode Island.

Prue Talbot, Ph.D., Director, University of California, Riverside Stem Cell Center and Core; Professor of Cell Biology, Department of Cell Biology and Neuroscience, University of California, Riverside, California.

Mark Travers, Ph.D., M.S., Assistant Professor of Oncology, Department of Health Behavior and Air Pollution Exposure Research Laboratory, Roswell Park Cancer Institute, Buffalo, New York.

Scott Weaver, Ph.D., M.A., Assistant Professor, Division of Epidemiology and Biostatistics, School of Public Health, Georgia State University, Atlanta, Georgia.

Reviewers were

David B. Abrams Ph.D., Executive Director, The Schroeder Institute for Tobacco Research and Policy Studies at Truth Initiative, Washington, D.C.; Professor, Department of Health, Behavior, and Society, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland; Professor of Oncology, Georgetown University Medical Center, Lombardi Comprehensive Cancer Center (adjunct), Washington, D.C.

Heather Rubino Althouse, Senior Regulatory Counsel, Office of Compliance and Enforcement, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

René A. Arrazola, M.P.H., Epidemiologist, Epidemiology Branch, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

David L. Ashley, Ph.D., Director, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Cathy L. Backinger, Ph.D., M.P.H., Deputy Director for Research, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Tracey E. Barnett, Ph.D., Associate Professor, Department of Epidemiology, College of Public Health and Health Professions and College of Medicine, University of Florida, Gainesville, Florida.

Neal L. Benowitz, M.D., Professor of Medicine, Bioengineering, and Therapeutic Sciences, Chief, Division of Clinical Pharmacology, University of California, San Francisco, California.

Jay M. Bernhardt, Ph.D., M.P.H., Interim Dean and Professor, Moody College of Communication; Founding Director, Center for Health Communication, The University of Texas, Austin, Texas.

Nazleen Bharmal, M.D., Ph.D., M.P.P., Director of Science and Policy, Office of the Surgeon General, U.S. Department of Health and Human Services, Washington, D.C.

Allan M. Brandt, Ph.D., Amalie Moses Kass Professor of the History of Medicine, Department of Global Health and Social Medicine, Harvard University Medical School, Boston, Massachusetts.

April Brubach, M.A., Director, Division of Public Health Education, Office of Health Communication and Education, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Priscilla Callahan-Lyon, M.D., Medical Branch Chief, Division of Individual Health Science, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Frank J. Chaloupka, Ph.D., Director, Health Policy Center, Institute for Health Research and Policy; Distinguished Professor, Department of Economics, University of Illinois at Chicago, Chicago, Illinois.

Ii-Lun Chen, M.D., Director, Division of Individual Health Science, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Beverly Chernaik, J.D., Director, Office of Regulations, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Joanna E. Cohen, Ph.D., Director, Institute for Global Tobacco Control; Bloomberg Professor of Disease Prevention, Department of Health, Behavior, and Society, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland.

Catherine G. Corey, M.S.P.H., Epidemiologist, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Kathleen Crosby, Director, Office of Health Communication and Education, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Cristine D. Delnevo, Ph.D., M.P.H., Professor and Director, Center for Tobacco Studies, Rutgers School of Public Health, New Brunswick, New Jersey.

Lauren M. Dutra, Sc.D., M.A., Postdoctoral Fellow, Center for Tobacco Control Research and Education, University of California, San Francisco, California.

Lucinda J. England, M.D., M.S.P.H., Medical Officer, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Michael P. Eriksen, Sc.D., Sc.M., Dean and Regents' Professor, Division of Health Management and Policy, School of Public Health, Georgia State University, Atlanta, Georgia.

Michael C. Fiore, M.D., M.P.H., M.B.A., University of Wisconsin Hilldale Professor of Medicine; Director, Center for Tobacco Research and Intervention, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin.

Neal D. Freedman, Ph.D., M.P.H., Senior Investigator, Metabolic Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Elizabeth M. Ginexi, Ph.D., Program Director, Tobacco Control Research Branch, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Gary A. Giovino, Ph.D., M.S., Professor and Chair, Department of Community Health and Health Behavior, School of Public Health and Health Professions, University at Buffalo, The State University of New York, Buffalo, New York.

Stanton A. Glantz, Ph.D., Professor of Medicine and American Legacy Foundation Distinguished Professor in Tobacco Control; Director, Center for Tobacco Control Research and Education, University of California, San Francisco, California.

Maciej L. Goniewicz, Ph.D., Pharm.D., Assistant Professor of Oncology, Department of Health Behavior, Roswell Park Cancer Institute, Buffalo, New York.

Rachel A. Grana, Ph.D., M.P.H., Program Director, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Bonnie Halpern-Felsher, Ph.D., FSAHM, Director of Research, Professor, Division of Adolescent Medicine, Stanford University, Palo Alto, California.

Dorothy K. Hatsukami, Ph.D., Forster Family Professor in Cancer Prevention, Masonic Cancer Center, University of Minnesota, Minneapolis, Minnesota.

Corinne Husten, M.D., M.P.H., Senior Medical Advisor, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Frances Jensen, M.D., F.A.C.P., Professor and Chair, Neurology Department, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania.

Ronald L. Johnson, Ph.D., Program Director, DNA and Chromosome Aberrations Branch, Division of Cancer Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Sarah E. Johnson, Ph.D., Social Scientist, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Annette R. Kaufman, Ph.D., M.P.H., Health Scientist and Program Director, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Ryan David Kennedy, Ph.D., Assistant Professor, Institute for Global Tobacco Control, Department of Health, Behavior, and Society, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland.

Jonathan D. Klein, M.D., M.P.H., F.A.A.P., Associate Executive Director; Director, Julius B. Richmond Center, American Academy of Pediatrics, Elk Grove Village, Illinois.

Suchitra Krishnan-Sarin, Ph.D., Professor, Department of Psychiatry, School of Medicine, Yale University, New Haven, Connecticut.

Lauren K. Lempert, J.D., M.P.H., Associate Specialist, Center for Tobacco Control Research and Education, University of California, San Francisco, California.

Maggie Mahoney, J.D., Executive Director, Tobacco Control Legal Consortium at the Public Health Law Center, St. Paul, Minnesota.

Tim McAfee, M.D., Medical Officer, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Daniel McGoldrick, M.A., Vice President, Global Health Advocacy Incubator, Campaign for Tobacco-Free Kids, Washington, D.C.

Cindy Miner, Ph.D., Associate Director for Scientific Communication, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Matthew L. Myers, J.D., President, Campaign for Tobacco-Free Kids, Washington, D.C.

Linda J. Neff, Ph.D., Senior Epidemiologist, Epidemiology Branch, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Richard J. O'Connor, Ph.D., Member and Professor of Oncology, Department of Health Behavior, Division of Cancer Prevention and Population Sciences, Roswell Park Cancer Institute, Buffalo, New York.

Mark Parascandola, Ph.D., M.P.H., Epidemiologist, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Terry F. Pechacek, Ph.D., Professor and Interim Division Director of Health Management and Policy, School of Public Health, Georgia State University, Atlanta, Georgia.

Alexander Persoskie, Ph.D., Social Scientist, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

John P. Pierce, Ph.D., Professor Emeritus, Department of Family Medicine and Public Health and the Moores Cancer Center, University of California, San Diego, La Jolla, California.

David W. Racine, M.S., Senior Program Management Officer, Office of Compliance and Enforcement, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Chad J. Reissig, Ph.D., Addiction Branch Chief, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Joelle Robinson, M.P.H., Social Scientist, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Jonathan M. Samet, M.D., M.S., Distinguished Professor and Flora L. Thornton Chair, Department of Preventive Medicine, Keck School of Medicine; Director, Institute for Global Health, University of Southern California, Los Angeles, California.

Peter G. Shields, M.D., Deputy Director, Comprehensive Cancer Center, James Cancer Hospital; Professor, College of Medicine, The Ohio State University, Columbus, Ohio.

Ann Simoneau, J.D., M.B.A., Director, Office of Compliance and Enforcement, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Theodore A. Slotkin, Ph.D., Professor, Department of Pharmacology and Cancer Biology, Duke University Medical Center, Durham, North Carolina.

Anne Sowell, Ph.D., Health Scientist, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Erin L. Sutfin, Ph.D., Associate Professor and Vice Chair, Department of Social Sciences and Health Policy, Division of Public Health Sciences, Wake Forest School of Medicine, Wake Forest University, Winston-Salem, North Carolina.

Robert E. Vollinger, Jr., M.S.P.H., (Dr.P.H. Candidate), Program Director and Public Health Advisor, Tobacco Control Research Branch, Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Kenneth E. Warner, Ph.D., Avedis Donabedian Distinguished University Professor of Public Health, Department of Health Management and Policy, University of Michigan School of Public Health, Ann Arbor, Michigan.

Geoffrey Ferris Wayne, M.A., Research Consultant, Sebastopol, California.

Deborah M. Winn, Ph.D., Deputy Director, Division of Cancer Control and Population Sciences, National Cancer Institute, National Institutes of Health, Rockville, Maryland.

Mitchell Zeller, J.D., Director, Center for Tobacco Products, U.S. Food and Drug Administration, Silver Spring, Maryland.

Other contributors were

Katherine J. Asman, M.S.P.H., Statistician, Biostatistics and Epidemiology Division, RTI International, Atlanta, Georgia.

Adam J. Burke, M.A., Research Associate Lead, The Monitoring the Future Study, University of Michigan, Ann Arbor, Michigan.

Dayana Chanson, M.P.H., Research Associate to Jonathan M. Samet, M.D., M.S., Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California.

Tara Christine Chu, M.P.H., Research Associate to Jonathan M. Samet, M.D., M.S., Department of Preventive Medicine, Keck School of Medicine, University of Southern California, Los Angeles, California.

Stephanie L. Clendennen, M.P.H., Predoctoral Fellow, Tobacco Center of Regulatory Science on Youth and Young Adults, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

Sarah J. Cross, Graduate Student Researcher, Department of Anatomy and Neurobiology, University of California, Irvine, California.

Nicholas J. Felicione, Graduate Research Assistant, Department of Psychology, West Virginia University, Morgantown, West Virginia.

Kyle R. Gregory, J.D., M.S.H.A., Postdoctoral Research Associate, Tobacco Center of Regulatory Science, School of Public Health, Georgia State University, Atlanta, Georgia.

Emily T. Hébert, M.P.H., Doctoral Student, Michael & Susan Dell Center for Healthy Living, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

Erin O'Connor Landau, M.S., Data Analyst, DB Consulting Group (Contractor), Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Pamela Lemos, M.S., Public Health Analyst, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Gerald V. [Simon] McNabb, Lead Public Health Analyst, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Washington, D.C.

Ronald L. Johnson, Ph.D., Program Director, DNA and Chromosome Aberrations Branch, Division of Cancer Biology, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

Hoda S. Magid, M.H.S., Center for Tobacco Control Research and Education, University of California, San Francisco, California.

Dale Mantey, M.P.A., Predoctoral Fellow, Tobacco Center of Regulatory Science on Youth and Young Adults, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

Mandie Mills, Photographer, Office of the Associate Director for Communication, Centers for Disease Control and Prevention, Atlanta, Georgia.

Richard Miech, Ph.D., Professor, Institute for Social Research, University of Michigan, Ann Arbor, Michigan.

Luz M. Moncayo, Executive Assistant to Jonathan M. Samet, M.D., M.S., Department of Preventive Medicine, Keck School of Medicine, Institute for Global Health, University of Southern California, Los Angeles, California.

Maureen O'Brien, J.D., Staff Attorney, Tobacco Control Legal Consortium at the Public Health Law Center, St. Paul, Minnesota.

Patrick M. O'Malley, Ph.D., Research Professor, Survey Research Center, Institute for Social Research, University of Michigan, Ann Arbor, Michigan.

Gabriela V. Portillo, Masters Student, Michael & Susan Dell Center for Healthy Living, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health, Austin, Texas.

Anna Teplinskaya, M.D., M.P.H., Public Health Analyst, Epidemiology Branch, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Tenecia Smith, M.P.H., Data Analyst, DB Consulting Group (Contractor), Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Kathryn E. Szynal, Editorial Assistant, McNeal Professional Services (Contractor), Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Teresa Wang, Ph.D., M.S., Epidemic Intelligence Service Officer, Lieutenant, U.S. Public Health Service, Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia.

Jennifer Whitmill, M.P.H., Data Analyst, DB Consulting Group (Contractor), Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

E-Cigarette Use Among Youth and Young Adults

Chapter 1
Introduction, Conclusions, and Historical Background Relative to E-Cigarettes

Introduction

Although conventional cigarette smoking has declined markedly over the past several decades among youth and young adults in the United States (U.S. Department of Health and Human Services [USDHHS] 2012), there have been substantial increases in the use of emerging tobacco products among these populations in recent years (Centers for Disease Control and Prevention [CDC] 2015c). Among these increases has been a dramatic rise in electronic cigarette (e-cigarette) use among youth and young adults. It is crucial that the progress made in reducing cigarette smoking among youth and young adults not be compromised by the initiation and use of e-cigarettes. This Surgeon General's report focuses on the history, epidemiology, and health effects of e-cigarette use among youth and young adults; the companies involved with marketing and promoting these products; and existing and proposed public health policies regarding the use of these products by youth and young adults.

E-cigarettes include a diverse group of devices that allow users to inhale an aerosol, which typically contains nicotine, flavorings, and other additives. E-cigarettes vary widely in design and appearance, but generally operate in a similar manner and are composed of similar components (Figure 1.1). A key challenge for surveillance of the products and understanding their patterns of use is the diverse and nonstandard nomenclature for the devices (Alexander et al. 2016). These devices are referred to, by the companies themselves, and by consumers, as "e-cigarettes," "e-cigs," "cigalikes," "e-hookahs," "mods," "vape pens," "vapes," and "tank systems." In this report, the term "e-cigarette" is used to represent all of the various products in this rapidly diversifying product category. The terms may differ by geographic region or simply by the prevailing preferences among young users. For example, some refer to all cigarette-shaped products as "e-cigarettes" or as "cigalikes," and some may refer to the pen-style e-cigarettes as "hookah pens" or "vape pens" (Richtel 2014; Lempert et al. 2016).

Figure 1.1 Diversity of e-cigarette products

Source: Photo by Mandie Mills, CDC.

This report focuses on research conducted among youth and young adults because of the implications of e-cigarette use in this population, particularly the potential for future public health problems. Understanding e-cigarette use among young persons is critical because previous research suggests that about 9 in 10 adult smokers first try conventional cigarettes during adolescence (USDHHS 2012). Similarly, youth e-cigarette experimentation and use could also extend into adulthood; however, e-cigarette use in this population has not been examined in previous reports of the Surgeon General. The first Surgeon General's report on the health consequences of smoking was published in 1964; of the subsequent reports, those published in 1994 and 2012 focused solely on youth and young adults (USDHHS 1994, 2012). More recently, the 2012 report documented the evidence regarding tobacco use among youth and young adults, concluding that declines in cigarette smoking had slowed and that decreases in the use of smokeless tobacco had stalled. That report also found that the tobacco industry's advertising and promotional activities are causal to the onset of smoking in youth and young adults and the continuation of such use as adults (USDHHS 2012). However, the 2012 report was prepared before e-cigarettes were as widely promoted and used in the United States as they are now. Therefore, this 2016 report documents the scientific literature on these new products and their marketing, within the context of youth and young adults. This report also looks to the future by examining the potential impact of e-cigarette use among youth and young adults, while also summarizing the research on current use, health consequences, and marketing as it applies to youth and young adults.

Evidence for this report was gathered from studies that included one or more of three age groups. We defined these age groups to be young adolescents (11–13 years of age), adolescents (14–17 years of age), and young adults (18–24 years of age). Some studies refer to the younger groups more generally as *youth*. Despite important issues related to e-cigarette use in adult populations, clinical and otherwise (e.g., their potential for use in conventional smoking cessation), that literature will generally not be included in this report unless it also discusses youth and young adults (Farsalinos and Polosa 2014; Franck et al. 2014; Grana et al. 2014).

Given the recency of the research that pertains to e-cigarettes, compared with the decades of research on cigarette smoking, the "precautionary principle" is used to guide actions to address e-cigarette use among youth and young adults. This principle supports intervention to avoid possible health risks when the potential risks remain uncertain and have been as yet partially undefined (Bialous and Sarma 2014; Saitta et al. 2014; Hagopian et al. 2015). Still, the report underscores and draws its conclusions from the known health risks of e-cigarette use in this age group.

Organization of the Report

This chapter presents a brief introduction to this report and includes its major conclusions followed by the conclusions of the chapters, the historical background of e-cigarettes, descriptions of the products, a review of the marketing and promotional activities of e-cigarette companies, and the current status of regulations from the U.S. Food and Drug Administration (FDA). Chapter 2 ("Patterns of E-Cigarette Use Among U.S. Youth and Young Adults") describes the epidemiology of e-cigarette use, including current use (i.e., past 30 day); ever use; co-occurrence of using e-cigarettes with other tobacco products, like cigarettes; and psychosocial factors associated with using e-cigarettes, relying on data from the most recent nationally representative studies available at the time this report was prepared. Chapter 3 ("Health Effects of E-Cigarette Use Among U.S. Youth and Young Adults") documents the evidence related to the health effects of e-cigarette use, including those that are associated with direct aerosol inhalation by users, the indirect health effects of e-cigarette use, other non-aerosol health effects of e-cigarette use, and secondhand exposure to constituents of the aerosol. Chapter 4 ("Activities of the E-Cigarette Companies") describes e-cigarette companies' influences on e-cigarette use and considers manufacturing and price; the impact of price on sales and use; the rapid changes in the industry, particularly the e-cigarette companies; and the marketing and promotion of e-cigarettes. Chapter 5 ("E-Cigarette Policy and Practice Implications") discusses the implications for policy and practice at the national, state, and local levels. The report ends with a Call to Action to stakeholders—including policymakers, public health practitioners and clinicians, researchers, and the public—to work to prevent harms from e-cigarette use and secondhand aerosol exposure among youth and young adults.

Preparation of this Report

This Surgeon General's report was prepared by the Office on Smoking and Health, National Center for Chronic Disease Prevention and Health Promotion, CDC, which is part of USDHHS. The initial drafts of the chapters were written by 27 experts who were selected for their knowledge of the topics addressed. These contributions are summarized in five chapters that were evaluated by approximately 30 peer reviewers. After peer review, the entire manuscript was sent to more than 20 scientists and other experts, who examined it for its scientific integrity. After each review cycle, the drafts were revised by the report's scientific editors on the basis of reviewers' comments. Subsequently, the report was reviewed by various institutes and agencies within USDHHS.

Scientific Basis of the Report

The statements and conclusions throughout this report are documented by the citation of studies published in the scientific literature. Publication lags have prevented an up-to-the-minute inclusion of all recently published articles and data. This overall report primarily cites peer-reviewed journal articles, including reviews that integrate findings from numerous studies and books that were published through December 2015. However, selected studies from 2016 have been added during the review process that provide further support for the conclusions in this report. When a cited study has been accepted for publication, but the publication has not yet occurred because of the delay between acceptance and final publication, the study is referred to as "in press." This report also refers, on occasion, to unpublished research, such as presentations at a professional meeting, personal communications from a researcher, or information available in various media. These references are employed when acknowledged by the editors and reviewers as being from reliable sources, which add to the emerging literature on a topic.

Major Conclusions

1. E-cigarettes are a rapidly emerging and diversified product class. These devices typically deliver nicotine, flavorings, and other additives to users via an inhaled aerosol. These devices are referred to by a variety of names, including "e-cigs," "e-hookahs," "mods," "vape pens," "vapes," and "tank systems."

2. E-cigarette use among youth and young adults has become a public health concern. In 2014, current use of e-cigarettes by young adults 18–24 years of age surpassed that of adults 25 years of age and older.

3. E-cigarettes are now the most commonly used tobacco product among youth, surpassing conventional cigarettes in 2014. E-cigarette use is strongly associated with the use of other tobacco products among youth and young adults, including combustible tobacco products.

4. The use of products containing nicotine poses dangers to youth, pregnant women, and fetuses. The use of products containing nicotine in any form among youth, including in e-cigarettes, is unsafe.

5. E-cigarette aerosol is not harmless. It can contain harmful and potentially harmful constituents, including nicotine. Nicotine exposure during adolescence can cause addiction and can harm the developing adolescent brain.

6. E-cigarettes are marketed by promoting flavors and using a wide variety of media channels and approaches that have been used in the past for marketing conventional tobacco products to youth and young adults.

7. Action can be taken at the national, state, local, tribal, and territorial levels to address e-cigarette use among youth and young adults. Actions could include incorporating e-cigarettes into smokefree policies, preventing access to e-cigarettes by youth, price and tax policies, retail licensure, regulation of e-cigarette marketing likely to attract youth, and educational initiatives targeting youth and young adults.

Chapter Conclusions

Chapter 1. Introduction, Conclusions, and Historical Background Relative to E-Cigarettes

1. E-cigarettes are devices that typically deliver nicotine, flavorings, and other additives to users via an inhaled aerosol. These devices are referred to by a variety of names, including “e-cigs,” “e-hookahs,” “mods,” “vape pens,” “vapes,” and “tank systems.”

2. E-cigarettes represent an evolution in a long history of tobacco products in the United States, including conventional cigarettes.

3. In May 2016, the Food and Drug Administration issued the deeming rule, exercising its regulatory authority over e-cigarettes as a tobacco product.

Chapter 2. Patterns of E-Cigarette Use Among U.S. Youth and Young Adults

1. Among middle and high school students, both ever and past-30-day e-cigarette use have more than tripled since 2011. Among young adults 18–24 years of age, ever e-cigarette use more than doubled from 2013 to 2014 following a period of relative stability from 2011 to 2013.

2. The most recent data available show that the prevalence of past-30-day use of e-cigarettes is similar among high school students (16% in 2015, 13.4% in 2014) and young adults 18–24 years of age (13.6% in 2013–2014) compared to middle school students (5.3% in 2015, 3.9% in 2014) and adults 25 years of age and older (5.7% in 2013–2014).

3. Exclusive, past-30-day use of e-cigarettes among 8th-, 10th-, and 12th-grade students (6.8%, 10.4%, and 10.4%, respectively) exceeded exclusive, past-30-day use of conventional cigarettes in 2015 (1.4%, 2.2%, and 5.3%, respectively). In contrast—in 2013–2014 among young adults 18–24 years of age—exclusive, past-30-day use of conventional cigarettes (9.6%) exceeded exclusive, past-30-day use of e-cigarettes (6.1%). For both age groups, dual use of these products is common.

4. E-cigarette use is strongly associated with the use of other tobacco products among youth and young adults, particularly the use of combustible tobacco products. For example, in 2015, 58.8% of high school students who were current users of combustible tobacco products were also current users of e-cigarettes.

5. Among youth—older students, Hispanics, and Whites are more likely to use e-cigarettes than younger students and Blacks. Among young adults—males, Hispanics, Whites, and those with lower levels of education are more likely to use e-cigarettes than females, Blacks, and those with higher levels of education.

6. The most commonly cited reasons for using e-cigarettes among both youth and young adults are curiosity, flavoring/taste, and low perceived harm compared to other tobacco products. The use of e-cigarettes as an aid to quit conventional cigarettes is not reported as a primary reason for use among youth and young adults.

7. Flavored e-cigarette use among young adult current users (18–24 years of age) exceeds that of older adult current users (25 years of age and older). Moreover, among youth who have ever tried an e-cigarette, a majority used a flavored product the first time they tried an e-cigarette.

8. E-cigarette products can be used as a delivery system for cannabinoids and potentially for other illicit drugs. More specific surveillance measures are needed to assess the use of drugs other than nicotine in e-cigarettes.

Chapter 3. Health Effects of E-Cigarette Use Among U.S. Youth and Young Adults

1. Nicotine exposure during adolescence can cause addiction and can harm the developing adolescent brain.

2. Nicotine can cross the placenta and has known effects on fetal and postnatal development. Therefore, nicotine delivered by e-cigarettes during pregnancy can result in multiple adverse consequences, including sudden infant death syndrome, and could result in altered corpus callosum, deficits in auditory processing, and obesity.

3. E-cigarettes can expose users to several chemicals, including nicotine, carbonyl compounds, and volatile organic compounds, known to have adverse health effects. The health effects and potentially harmful doses of heated and aerosolized constituents of e-cigarette liquids, including solvents, flavorants, and toxicants, are not completely understood.

4. E-cigarette aerosol is not harmless "water vapor," although it generally contains fewer toxicants than combustible tobacco products.

5. Ingestion of e-cigarette liquids containing nicotine can cause acute toxicity and possibly death if the contents of refill cartridges or bottles containing nicotine are consumed.

Chapter 4. Activities of the E-Cigarette Companies

1. The e-cigarette market has grown and changed rapidly, with notable increases in total sales of e-cigarette products, types of products, consolidation of companies, marketing expenses, and sales channels.

2. Prices of e-cigarette products are inversely related to sales volume: as prices have declined, sales have sharply increased.

3. E-cigarette products are marketed in a wide variety of channels that have broad reach among youth and young adults, including television, point-of-sale, magazines, promotional activities, radio, and the Internet.

4. Themes in e-cigarette marketing, including sexual content and customer satisfaction, are parallel to themes and techniques that have been found to be appealing to youth and young adults in conventional cigarette advertising and promotion.

Chapter 5. E-Cigarette Policy and Practice Implications

1. The dynamic nature of the e-cigarette landscape calls for expansion and enhancement of tobacco-related surveillance to include (a) tracking patterns of use in priority populations; (b) monitoring the characteristics of the retail market; (c) examining policies at the national, state, local, tribal, and territorial levels; (d) examining the channels and messaging for marketing e-cigarettes in order to more fully understand the impact future regulations could have; and (e) searching for sentinel health events in youth and young adult e-cigarette users, while longer-term health consequences are tracked.

2. Strategic, comprehensive research is critical to identify and characterize the potential health risks from e-cigarette use, particularly among youth and young adults.

3. The adoption of public health strategies that are precautionary to protect youth and young adults from adverse effects related to e-cigarettes is justified.

4. A broad program of behavioral, communications, and educational research is crucial to assess how youth perceive e-cigarettes and associated marketing messages, and to determine what kinds of tobacco control communication strategies and channels are most effective.

5. Health professionals represent an important channel for education about e-cigarettes, particularly for youth and young adults.

6. Diverse actions, modeled after evidence-based tobacco control strategies, can be taken at the state, local, tribal, and territorial levels to address e-cigarette use among youth and young adults, including incorporating e-cigarettes into smoke-free policies; preventing the access of youth to e-cigarettes; price and tax policies; retail licensure; regulation of e-cigarette marketing that is likely to attract youth and young adults, to the extent feasible under the law; and educational initiatives targeting youth and young adults. Among others, research focused on policy, economics, and the e-cigarette industry will aid in the development and implementation of evidence-based strategies and best practices.

Historical Background

Understanding the role of e-cigarettes requires understanding the long history of tobacco use in the United States, including the role of nicotine delivery, the multiple examples of "reduced-harm" products and associated health claims, and the impact of using tobacco products on the public's health. Since the late nineteenth century, when the "modern" cigarette came into use, scientists and public health officials have linked cigarette smoking to a remarkable number of adverse effects, and it is now recognized as the primary cause of premature death in the United States (USDHHS 2014). Correspondingly, for a century, manufacturers, scientists, entrepreneurs, and public health leaders have promoted or recommended product changes that might remove some of the harmful elements in cigarette smoke. E-cigarettes are among the latest products.

E-cigarettes are designed for users to inhale nicotine, flavorings, and other additives through an aerosol. The claims and marketing strategies employed by the e-cigarette companies, and the efforts made by others to develop scientific and regulatory tools to deal with these new products, both contribute to the current discourse on e-cigarettes. Many lessons for assessing the potential (and future) consequences of these products can be learned from examining the relevant experiences of the past century, especially the introduction of novel products (including e-cigarettes as well as other tobacco and nicotine products) and the claims of reduced exposure to toxins made by the industry and elsewhere.

Early Efforts to Modify Cigarettes

In the 1880s and 1890s, entrepreneurs promoted novel products that allegedly blocked nicotine and other constituents of conventional cigarettes believed to be poisonous. Dr. Scott's Electric Cigarettes, advertised in *Harper's Weekly,* claimed not only to light without matches but also to contain a cotton filter that "strains and eliminates the injurious qualities from the smoke," including nicotine (*Harper's Weekly* 1887). Nicotine delivery was essential to the development of the modern cigarette in the twentieth century; early on, this substance was thought to be addicting and thus vital to retaining customers. In 1913, the Camel brand was a new kind of cigarette that introduced high-nicotine content by using burley tobacco, which was generally too harsh to inhale into the lungs, but was made more inhalable through the addition of casings (e.g., sugars, licorice) (Tindall 1992; Proctor 2011). In 1916, American Tobacco introduced its Lucky Strike blended cigarette, and in 1918 Liggett & Myers (L&M) reformulated its Chesterfield brand to make it more palatable to users. As the market grew, advertisements for major brands routinely included health-related statements and testimonials from physicians. During the 1930s and 1940s, prominent advertising campaigns included claims like "Not a cough in a carload" (Old Gold) (Federal Trade Commission [FTC] 1964, p. LBA-5); "We removed from the tobacco harmful corrosive ACRIDS (pungent irritants) present in cigarettes manufactured in the old-fashioned way" (Lucky Strike) (FTC 1964, p. LBA-2); and "Smoking Camels stimulates the natural flow of digestive fluids … increases alkalinity" (Camel) (FTC 1964, p. LBA-1a). Thus, early modifications to the cigarette were made so that it was more palatable, had a higher nicotine delivery and uptake, and could be marketed as "safe" (FTC 1964; Calfee 1985).

Filters, Tar Reduction, and Light and Low-Tar Cigarettes

The landmark 1964 Surgeon General's report on smoking and health concluded that cigarette smoking contributed substantially to mortality from certain specific diseases, including lung cancer (U.S. Department of Health, Education, and Welfare 1964). Although the 1964 report considered the topic, it found the evidence insufficient to assess the potential health benefits of cigarette filters. Cigarettes with filters became the norm by the 1960s, and marketing them with an overt message about harm reduction became the standard (National Cancer Institute [NCI] 1996). However, the Surgeon General convened another group of experts on June 1, 1966, to review the evidence on the role played by the tar and nicotine content in health. The group concluded that "[t]he preponderance of scientific evidence strongly suggests that the lower the 'tar' and nicotine content of cigarette smoke, the less harmful are the effects" (Horn 1966, p. 16,168). Subsequent studies have repeatedly failed to demonstrate health benefits of smoking light and low-tar cigarettes versus full-flavor cigarettes (Herning et al. 1981; Russell et al. 1982; Benowitz et al. 1983, NCI 2001).

Over the years, the tobacco industry used multiple methods to reduce the machine-tested yields of tar and nicotine in cigarettes as a way to claim "healthier" cigarettes. Beginning in the 1970s, tobacco companies advertised the tar and nicotine levels for their cigarettes, which encouraged smokers to believe, without substantiation, they could reduce their risk of exposure to these constituents (Cummings et al. 2002; Pollay and Dewhirst 2002). In 1996, the FTC issued a statement that it would allow cigarette companies to include statements about tar and nicotine content in their advertising as long as they used a standardized machine-testing method (Peeler 1996).

The Role of Nicotine and Nicotine Delivery

Although the public health community understood early on that nicotine was the primary psychoactive ingredient in cigarette smoke, before the 1980s, little was known about the importance of nicotine in the addiction process beyond what the cigarette manufacturers had learned from their own research. Some scientists warned that due to nicotine addiction, a reduction in nicotine yields, along with decreases in tar, could lead smokers to change their smoking behavior, such as by smoking a greater number of cigarettes to maintain their nicotine intake or changing their behavior in more subtle ways, such as varying the depth of inhalation or smoking more of the cigarette (Jarvis et al. 2001; National Cancer Institute 2001; Thun and Burns 2001). Not until the 1970s and 1980s, as researchers studying other forms of drug abuse began to apply their research methods to cigarette smoking, did it become apparent that nicotine was similar in its addictive capability to other drugs of abuse, such as heroin and cocaine (USDHHS 1981, 1988). As described in the 1988 Surgeon General's report and in subsequent research, symptoms associated with nicotine addiction include craving, withdrawal, and unconscious behaviors to ensure consistent intake of nicotine (USDHHS 1988; al'Absi et al. 2002; Hughes 2007).

Although the tobacco industry has long understood the importance of nicotine to maintain long-term cigarette smokers through addiction, public health officials did not fully appreciate this in a broad sense until the 1988 Surgeon General's report, *The Health Consequences of Smoking: Nicotine Addiction* (USDHHS 1988).

FDA and Nicotine Regulation

In 1988 (and again in 1994), the Coalition on Smoking OR Health and other public-interest organizations petitioned FDA to classify low-tar and nicotine products as drugs and to classify Premier, the short-lived "smokeless cigarette product" from R.J. Reynolds, as an alternative nicotine-delivery system (Stratton et al. 2001). The Coalition on Smoking OR Health cited indirect claims made through advertising and marketing as evidence of R. J. Reynolds's intent to have the product used for the mitigation or prevention of disease (Slade and Ballin 1993). Meanwhile, FDA launched an investigation into the practices of the tobacco industry, including the manipulation of nicotine delivery. FDA asserted its jurisdiction over cigarettes and smokeless tobacco and issued certain rules governing access to and promotion of these products (*Federal Register* 1996). On March 21, 2000, the U.S. Supreme Court ruled 5-4 that Congress had not yet given FDA the necessary statutory authority to issue any rules pertaining to tobacco products (Gottleib 2000; *FDA v. Brown & Williamson Tobacco Corp.* 2000). The subsequent debate over control of nicotine products, including their potential impact on youth, ultimately led to the passage of the 2009 *Family Smoking Prevention and Tobacco Control Act,* which gave FDA authority to regulate tobacco products. Thus, discussions about the introduction of novel nicotine-containing tobacco products in the market during the 1980s and 1990s helped shape the current regulation of tobacco and nicotine products.

New products introduced in the 1990s or later included modified tobacco cigarettes (e.g., Advance, Omni); cigarette-like products, also called cigalikes (e.g., Eclipse, Accord); and smokeless tobacco products (e.g., Ariva, Exalt, Revel, snus). Advance, made by Brown and Williamson, was test-marketed with the slogan "All of the taste … Less of the toxins." Vector launched a national advertising campaign for its Omni cigarette with the slogan "Reduced carcinogens. Premium taste." In addition to the question of whether the claims were supported by sufficient evidence, scientists and tobacco control leaders raised concerns about the potential for adverse consequences associated with novel nicotine and tobacco products marketed for harm reduction, such as a reduction in cessation rates or increased experimentation by children (Warner and Martin 2003; Joseph et al. 2004; Caraballo et al. 2006). Studies have shown that smokers are interested in trying novel "reduced-exposure" products and perceive them to have lower health risks, even when advertising messages do not make explicit health claims (Hamilton et al. 2004; O'Connor et al. 2005; Caraballo et al. 2006; Choi et al. 2012; Pearson et al. 2012).

At FDA's request, the Institute of Medicine (IOM [now the National Academy of Medicine]) convened a committee of experts to formulate scientific methods and standards by which potentially reduced-exposure products (PREPs), whether the purported reduction was pharmaceutical or tobacco related, could be assessed. The committee concluded that "[f]or many diseases attributable to tobacco use, reducing risk of disease by reducing exposure to tobacco toxicants is feasible" (Stratton et al. 2001, p. 232). However, it also cautioned that "PREPs have not yet been evaluated comprehensively enough (including for a sufficient time) to provide a scientific basis for concluding that they are associated with a reduced risk of disease compared to conventional tobacco use" (Stratton et al. 2001, p. 232). The committee added that "the major concern for public health is that tobacco users who might otherwise quit will use PREPs instead, or others may initiate smoking, feeling that PREPs are safe. That will lead to less harm reduction for a population (as well as less risk reduction for that individual) than would occur without the PREP, and possibly to an adverse effect on the population" (Stratton et al. 2001, p. 235). Subsequently, in 2006, Judge Kessler cited these findings in her decision which demanded the removal of light and low-tar labeling due to the misleading nature of these claims (*United States v. Philip Morris* 2006).

The E-Cigarette

Invention of the E-Cigarette

An early approximation of the current e-cigarette appeared in a U.S. patent application submitted in 1963 by Herbert A. Gilbert and was patented in August 1965 (U.S. Patent No. 3,200,819) (Gilbert 1965). The application was for a "smokeless nontobacco cigarette," with the aim of providing "a safe and harmless means for and method of smoking" by replacing burning tobacco and paper with heated, moist, flavored air. A battery-powered heating element would heat the flavor elements without combustion (Gilbert 1965). The Favor cigarette, introduced in 1986, was another early noncombustible product promoted as an alternative nicotine-containing tobacco product (United Press International 1986; Ling and Glantz 2005).

The first device in the recent innovation in e-cigarettes was developed in 2003 by the Chinese pharmacist Hon Lik, a former deputy director of the Institute of Chinese Medicine in Liaoning Province. Lik's patent application described a kind of electronic atomizing cigarette (Hon 2013). With support from Chinese investors, in 2004 the product was introduced on the Chinese market under the company name Ruyan (Sanford and Goebel 2014). The product gained some attention among Chinese smokers early on as a potential cessation device or an alternative cigarette product.

The e-cigarette was part of the U.S. market by the mid-2000s, and by 2010 additional brands started to appear in the nation's marketplace, including Ruyan and Janty (Regan et al. 2013). Ruyan gained a U.S. patent for its product with the application stating that the product is "an electronic atomization cigarette that functions as substitutes (sic) for quitting smoking and cigarette substitutes." (U.S. Patent No. 8,490,628 B2, 2013). In August 2013, Imperial Tobacco Group purchased the intellectual property behind the Ruyan e-cigarette for $75 million. As of 2014 an estimated 90% of the world's production of e-cigarette technology and products came from mainland China, mainly Guangdong Province and Zhejiang Province (Barboza 2014).

Sales of e-cigarettes in the United States have risen rapidly since 2007. Widespread advertising via television commercials and through print advertisements for popular brands, often featuring celebrities, has contributed to a large increase in e-cigarette use by both adults and youth since 2010 (Felberbaum 2013; King et al. 2013; Regan et al. 2013). Additionally, marketing through social media, as well as other forms of Internet marketing, has been employed to market these devices (Huang et al. 2014; Kim et al. 2014).

In 2013, an estimated 13.1 million middle school and high school students were aware of e-cigarettes (Wang et al. 2014). According to data from the National Youth Tobacco Survey, in 2011 the prevalence of current e-cigarette use (defined as use during at least 1 day in the past 30 days) among high school students was 1.5%; prevalence increased dramatically, however, to 16% by 2015, surpassing the rate of conventional-cigarette use among high school students (CDC 2016b; see Chapter 2). This equates to 2.4 million high school students and 620,000 middle school students having used an e-cigarette at least one time in the past 30 days in 2015 (CDC 2016b).

These trends have led to substantial concern and discussion within public health communities, including state and national public health agencies, professional organizations, and school administrators and teachers. A primary concern is the potential for nicotine addiction among nonsmokers, especially youth and young adults, and that this exposure to nicotine among youth and young adults is harmful. The diversity and novelty of e-cigarette products on the market and ongoing product innovations make assessments of the biological effects of current e-cigarettes under actual conditions of use—such as their long-term harmfulness—difficult to measure. Unanswered questions remain about the risk profile of these devices, their potential use by young people as a first step to other nicotine products, and their total impact on public health. There are diverging opinions about the potential public health impact of these new products. Some public health scientists have highlighted the potential for alternative nicotine products to serve as a substitute for conventional cigarettes and thus a harm reduction tool (Henningfield et al. 2003; Abrams 2014). Others have cautioned that the use of alternative nicotine products might become a bridge that may lead to greater tobacco product use—including dual- or multiple-product use—or initiate nicotine addiction among nonsmokers, especially youth (Cobb et al. 2010; Wagener et al. 2012; Benowitz and Goniewicz 2013; Britton 2013; Chapman 2013; Etter 2013; USDHHS 2014). Current evidence is insufficient to reject either of these hypotheses.

E-Cigarette Products

Components and Devices

E-cigarette devices are composed of a battery, a reservoir for holding a solution that typically contains nicotine, a heating element or an atomizer, and a mouthpiece through which the user puffs (Figure 1.2). The device heats a liquid solution (often called e-liquid or e-juice) into an aerosol that is inhaled by the user. E-liquid typically uses propylene glycol and/or glycerin as a solvent for the nicotine and flavoring chemicals

Flavors and E-Cigarettes

The e-liquids in e-cigarettes are most often flavored; a study estimated that 7,700 unique flavors exist (Zhu et al. 2014) and that most of them are fruit or candy flavors (Figure 1.3). A content analysis of the products available via online retail websites documented that tobacco, mint, coffee, and fruit flavors were most common, followed by candy (e.g., bubble gum), unique flavors (e.g., Belgian waffle), and alcoholic drink flavors (e.g., strawberry daiquiri) (Grana and Ling 2014). Some retail stores are also manufacturers that create custom flavors, which increases the variety of flavors available.

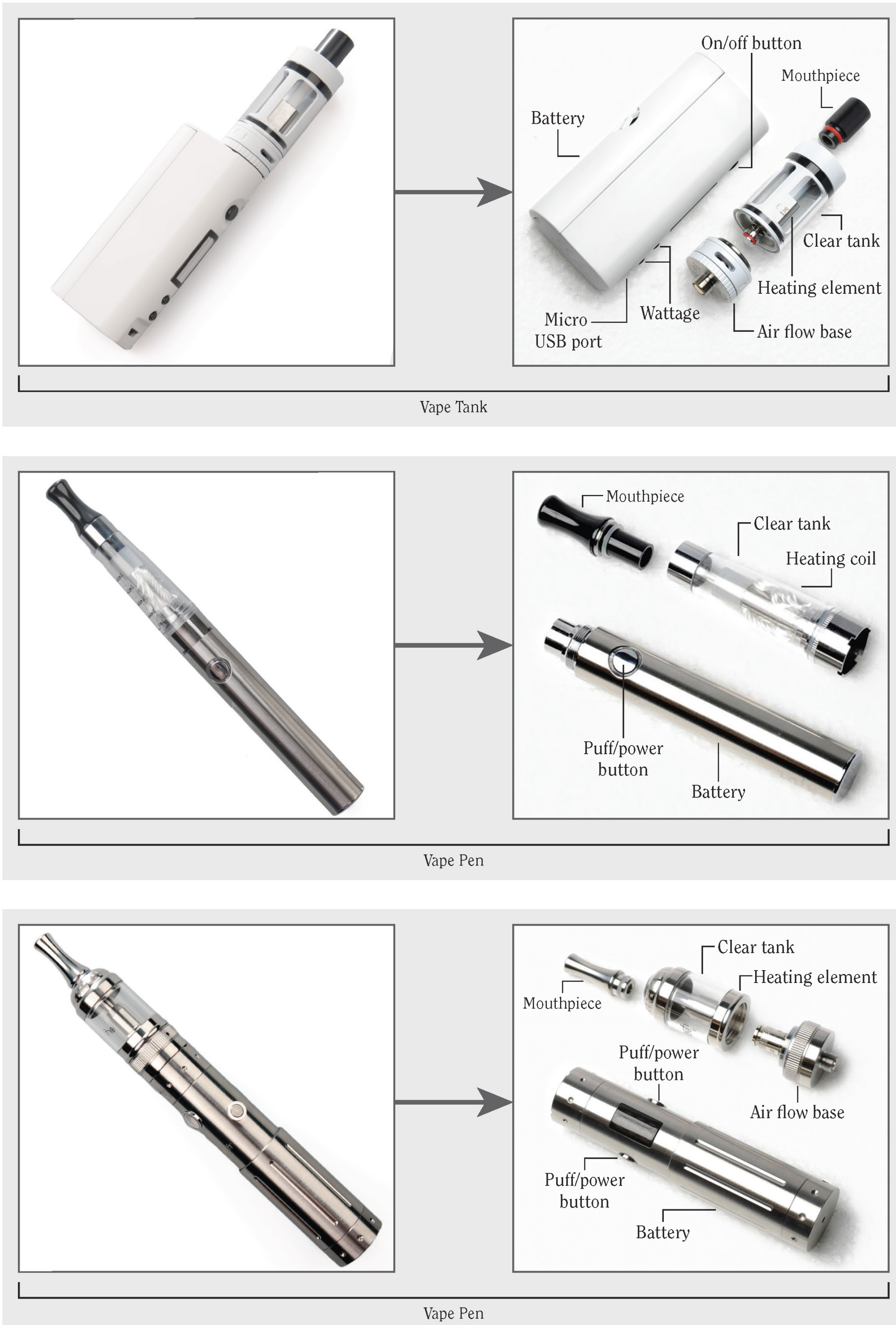
The widespread availability and popularity of flavored e-cigarettes is a key concern regarding the potential public health implications of the products. The concern, among youth, is that the availability of e-cigarettes with sweet flavors will facilitate nicotine addiction and simulated smoking behavior—which will lead to the use of conventional tobacco products (Kong et al. 2015; Krishnan-Sarin et al. 2015). Flavors have been used for decades to attract youth to tobacco products and to mask the flavor and harshness of tobacco (USDHHS 2012). Industry documents show that tobacco companies marketed flavored little cigars and cigarillos to youth and to African Americans to facilitate their uptake of cigarettes (Kostygina et al. 2014). Companies also intended flavored smokeless tobacco products to facilitate "graduation" to unflavored products that more easily deliver more nicotine to the user (USDHHS 2012). Various studies have shown that youth are more likely than adults to choose flavored cigarettes and cigars (CDC 2015b). Concern over these findings led Congress to include a ban on characterizing flavors for cigarettes, other than tobacco or menthol, in the Tobacco Control Act. A similar concern exists about e-cigarettes, and this concern is supported by studies indicating that youth and young adults who have ever used e-cigarettes begin their use with sweet flavors rather than tobacco flavors (Kong et al. 2015; Krishnan-Sarin et al. 2015). Notably, 81.5% of current youth e-cigarette users said they used e-cigarettes "because they come in flavors I like" (Ambrose et al. 2015).

E-Cigarette Devices

First-generation e-cigarettes were often similar in size and shape to conventional cigarettes, with a design that also simulated a traditional cigarette in terms of the colors used (e.g., a white body with tan mouthpiece). These devices were often called cigalikes, but there were other products designed to simulate a cigar or pipe. Other cigalikes were slightly longer or narrower than a cigarette; they may combine white with tan or may be black or colored brightly. These newer models use a cartridge design for the part of the device that holds the e-liquid, which is either prefilled with the liquid or empty and ready to be filled. The user then squeezes drops of the e-liquid onto a wick (or bit of cotton or polyfil) connected to the heating element and atomizer (Figure 1.4). As e-cigarettes have become more popular, their designs have become more diverse, as have the types of venues where they are sold (Noel et al. 2011; Zhu et al. 2014).

Second-generation devices include products that are shaped like pens, are comparatively larger and cylindrical, and are often referred to as "tank systems" in a nod to the transparent reservoir that holds larger amounts of e-liquid than previous cartridge-containing models. Third- and fourth-generation devices represent a diverse set of products and, aesthetically, constitute the greatest departure from the traditional cigarette shape, as many are square or rectangular and feature customizable and rebuildable atomizers and batteries. In addition, since the beginning of the availability of e-cigarettes and their component parts, users have been modifying the devices or building their own devices, which are often referred to as "mods." The differences in design and engineering of the products are key factors in the size, distribution, and amount of aerosol particles and the variability in levels of chemicals and nicotine present in the e-liquid/aerosol and delivered to the user (Brown and Cheng 2014).

Figure 1.2 Parts of an e-cigarette device



Source: Photo by Mandie Mills, CDC.

Figure 1.3 Examples of e-liquid flavors

Source: Photo by Mandie Mills, CDC.

Figure 1.4 E-liquids being poured into an e-cigarette device

Source: Photo by Mandie Mills, CDC.

E-Cigarette Product Components and Risks

One of the primary features of the more recent generation of devices is that they contain larger batteries and are capable of heating the liquid to a higher temperature, potentially releasing more nicotine, forming additional toxicants, and creating larger clouds of particulate matter (Bhatnagar et al. 2014; Kosmider et al. 2014). For instance, one study demonstrated that, at high temperatures (150°C), exceedingly high levels of formaldehyde—a carcinogen (found to be 10 times higher than at ambient temperatures)—are present that are formed through the heating of the e-liquid solvents (propylene glycol and glycerin), although the level of tolerance of actual users to the taste of the aerosol heated to this temperature is debated (Kosmider et al. 2014; CDC 2015a; Flavor and Extract Manufacturers Association of the United States 2015; Pankow et al. 2015). There is also concern regarding the safety of inhaling e-cigarette flavorings. Although some manufacturers have claimed their flavorants are generally recognized as safe for food additives (i.e., to be used in preparing foods for eating), little is known about the long-term health effects of inhaling these substances into the lungs (CDC 2015a).

Many devices can be readily customized by their users, which is also leading to the concern that these devices are often being used to deliver drugs other than nicotine (Brown and Cheng 2014). Most commonly reported in the news media, on blogs, and by user anecdote is the use of certain types of e-cigarette-related products for delivering different forms of marijuana (Morean et al. 2015; Schauer et al. 2016). The tank systems, for example, have been used with liquid tetrahydrocannabinol (THC) or hash oil. Some personal vaporizer devices can be used with marijuana plant material or a concentrated resin form of marijuana called “wax.” One study describes the use, in Europe, of e-cigarette devices to smoke marijuana (Etter 2015).

The various e-cigarette products, viewed as a group, lack standardization in terms of design, capacity for safely holding e-liquid, packaging of the e-liquid, and features designed to minimize hazards with use (Yang et al. 2014). All of these design features may have implications for the health impact of e-cigarette use. Notably, from 2010 to 2014, calls to poison control centers in the United States about exposures related to e-cigarettes increased dramatically. According to the American Association of Poison Control Centers (2015), 271 cases were reported in 2011, but 3,783 calls were reported in 2014. Among all calls, 51% involved exposure among children younger than 5 years of age (CDC 2014). Most poisonings appear to have been caused by exposure to nicotine-containing liquid (CDC 2014). The lack of a requirement for child-resistant packaging for e-liquid containers may have contributed to these poisonings. Since these data were released, one death in the United States has been confirmed in a child who drank e-liquid containing nicotine (Mohney 2014). Additionally, serious adverse reactions, including at least two deaths, have been reported to FDA in cases that could be attributed to the use of e-cigarettes (FDA 2013). This increase in poisonings prompted the *Child Nicotine Poisoning Prevention Act of 2015* (2016), which was enacted in January 2016. This law requires any container of liquid nicotine that is sold, manufactured, distributed, or imported into the United States to be placed in packaging that is difficult to open by children under 5 years of age.

Secondary risks are also of concern regarding e-cigarettes, including passive exposure to nicotine and other chemicals, and adverse events due to device malfunction. Nicotine is a neuroteratogen, and its use by pregnant women exposes a developing fetus to risks that are well documented in the 50th-anniversary Surgeon General’s report on smoking (USDHHS 2014) and include impaired brain development (England et al. 2015) and other serious consequences. Finally, another consequence of the lack of device regulation is the occurrence of battery failures and subsequent explosions. Explosions have typically occurred during charging, resulting in house and car fires, and sometimes causing injuries to those involved. From 2009 to late 2014, 25 incidents of explosions and fires involving e-cigarettes occurred in the United States (Chen 2013; U.S. Fire Administration 2014; FDA 2013).

E-Cigarette Companies

E-cigarette companies include manufacturers, wholesalers, importers, retailers, distributors, and some other groups that overlap with these entities (Barboza 2014; Whelan 2015). Currently, most of the products are manufactured in Shenzhen, Guangdong Province, China (Cobb et al. 2010; Grana et al. 2014; Zhu et al. 2014). One study placed the number of brands at 466 in January 2014 and found a net increase of 10.5 brands per month (Zhu et al. 2014). All the major tobacco companies (e.g., Reynolds American, Altria; Table 1.1) and many smaller, independent companies are now in the business. When e-cigarettes first entered the U.S. market, they were sold primarily by independent companies via the Internet and in shopping malls at kiosks where those interested could sample the products. A unique feature of the e-cigarette industry, compared to other tobacco and nicotine products, is the recruitment of visitors to their websites as “affiliates” or distributors to help market the products and, in turn, receive commissions on sales (Grana and Ling 2014; Cobb et al. 2015). For example, some companies offer a way for users to earn a commission by advertising the products (e.g., a banner ad is placed on one’s website, and when someone clicks on the link and subsequently purchases a product, the website owner gets a percentage commission). Some companies also offer rewards programs for recruiting new customers or for brand loyalty, with website users earning points for free or reduced-price products (Richardson et al. 2015).

E-cigarettes are now in widespread national distribution through convenience stores, tobacco stores, pharmacies, “big box” retail chains such as Costco, online retailers, and shops devoted to e-cigarette products (often called “vape shops”) (Giovenco et al. 2015; Public Health Law Center 2015). The “vape shops” offer a place to buy customizable devices and e-liquid solutions in many flavors and sometimes include a café or other elements that promote socializing, essentially making such places like a lounge. With the rapid increase in distribution and marketing in the industry, sales have increased rapidly and were projected to reach $2.5 billion in 2014 and $3.5 billion in 2015, including projections for retail and online channels, as well as “vape shops” (Wells Fargo Securities 2015).

Table 1.1 Multinational tobacco companies with e-cigarette brands

Company	E-cigarette brand
Altria (NuMark)	MarkTen, Green Smoke
Philip Morris International	Heat-not-burn, IQOS brand (Vape Ranks 2014) E-cigs, Nicolites by Nicocigs (Philip Morris International 2014)
Reynolds (Reynolds Vapor Company)	VUSE
Lorillard (Lorillard Vapor Company)	blu (until 2015)
Imperial Tobacco (Fontem Ventures)	Puritane (formerly Ruyan) blu (acquired in 2015)
British American Tobacco	Vype
Swisher	E-swisher
Japan Tobacco International (JTI)	E-Lites, offered in the United Kingdom by Zandera Ltd., which was acquired by Japan Tobacco Inc. in 2014 (Japan Tobacco Inc. 2014) Ploom (tobacco pods in heat-not-burn) and Ploom PAX (used for vaporizing marijuana) (Japan Tobacco Inc. 2015)

The advertising and marketing of e-cigarette products has engendered skepticism among public health professionals and legislators, who have noted many similarities to the advertising claims and promotional tactics used for decades by the tobacco industry to sell conventional tobacco products (Campaign for Tobacco-Free Kids 2013; CDC 2016a). Indeed, several of the e-cigarette marketing themes have been reprised from the most memorable cigarette advertising, including those focused on freedom, rebellion, and glamor (Grana and Ling 2014). E-cigarette products are marketed with a variety of unsubstantiated health and cessation messages, with some websites featuring videos of endorsements by physicians (another reprisal of old tobacco industry advertising) (Grana and Ling 2014; Zhu et al. 2014). Unlike conventional cigarettes, for which advertising has been prohibited from radio and television since 1971, e-cigarette products are advertised on both radio and television, with many ads featuring celebrities. E-cigarettes also are promoted through sports and music festival sponsorships, in contrast to conventional cigarettes and smokeless tobacco products, which have been prohibited from such sponsorships since the Master Settlement Agreement in 1998. E-cigarettes also appear as product placements in television shows and movies (Grana et al. 2011; Grana and Ling 2014).

Another key avenue for e-cigarette promotion is social media, such as Twitter, Facebook, YouTube, and Instagram. As is true in the tobacco industry, the e-cigarette industry organizes users through advocacy groups (Noel et al. 2011; Harris et al. 2014; Saitta et al. 2014; Caponnetto et al. 2015). The extensive marketing and advocacy through various channels broadens exposure to e-cigarette marketing messages and products; such activity may encourage nonsmokers, particularly youth and young adults, to perceive e-cigarette use as socially normative. The plethora of unregulated advertising is of particular concern, as exposure to advertising for tobacco products among youth is associated with cigarette smoking in a dose-response fashion (USDHHS 2012).

Federal Regulation of E-Cigarettes

A "Two-Pronged" Approach to Comprehensive Tobacco Control

Since the passage of the Tobacco Control Act in 2009, FDA has had the authority to regulate the manufacturing, distribution, and marketing of tobacco products sold in the United States. FDA had immediate jurisdiction over cigarettes, roll-your-own cigarette tobacco, and smokeless tobacco. In May 2016, FDA asserted jurisdiction over products that meet the statutory definition of a tobacco product, including e-cigarettes, except accessories of these products (*Federal Register* 2016). That regulation is currently under litigation.

The IOM's 2007 report, *Ending the Tobacco Problem: A Blueprint for the Nation,* established a "two-pronged" strategy for comprehensive tobacco control: (1) full implementation of proven, traditional tobacco control measures such as clean indoor air laws, taxation, and countermarketing campaigns; and (2) "strong federal regulation of tobacco products and their marketing and distribution" (Bonnie et al. 2007, p. 1).

Included in FDA's broad authority are the restriction of marketing and sales to youth, requiring disclosure of ingredients and harmful and potentially harmful constituents, setting product standards (e.g., requiring the reduction or elimination of ingredients or constituents), requiring premarket approval of new tobacco products and review of modified-risk tobacco products, and requiring health warnings. The standard for FDA to use many of its regulatory authorities is whether such an action is appropriate for the protection of public health (*Federal Food, Drug, and Cosmetic Act*, § 907(a)(3)(A)). The public health standard in the Tobacco Control Act also requires FDA to consider the health impact of certain regulatory actions at both the individual and population levels, including their impact on nonusers, and on initiation and cessation (*Federal Food, Drug, and Cosmetic Act*, § 907(a)(3)(B)).

Importantly, the Tobacco Control Act preserves the authority of state, local, tribal, and territorial governments to enact any policy "in addition to, or more stringent than" requirements established under the Tobacco Control Act "relating to or prohibiting the sale, distribution, possession, exposure to, access to, advertising and promotion of, or use of tobacco products by individuals of any age" (*Federal Food, Drug, and Cosmetic Act*, § 916(a)(1)). This preservation of state and local authority ensures the continuation of more local-level, comprehensive tobacco control. However, the statute expressly preempts states and localities from establishing or continuing requirements that are different from or in addition to FDA requirements regarding standards for tobacco products, premarket review, adulteration, misbranding, labeling, registration, good manufacturing practices, or modified-risk tobacco products (*Federal Food, Drug, and Cosmetic Act*, § 916(a)(2)(A)). But this express preemption provision does not apply to state and local authority to impose requirements relating to the "sale, distribution, possession, information reporting to the State, exposure to, access to, the advertising and promotion of, or use of, tobacco products by individuals of any age . . ." (*Federal Food, Drug, and Cosmetic Act*, § 916(a)(2)(b)). The interaction of these complex provisions related to federal preemption of state law has been the subject of challenges by the tobacco industry to state and local laws. Thus far, courts have upheld certain local ordinances restricting the sale of flavored tobacco products (*National Association of Tobacco Outlets, Inc. v. City of Providence* 2013; *U.S. Smokeless Tobacco Manufacturing Co. v. City of New York* 2013).

Legal Basis for Regulating E-Cigarettes as Tobacco Products

In the United States, e-cigarettes can be regulated either as products marketed for therapeutic purposes or as tobacco products. Since the advent of e-cigarettes in the United States around 2007, manufacturers have had the option to apply to FDA's Center for Drug Evaluation and Research (CDER) or Center for Devices and Radiological Health (CDRH) for approval to market e-cigarettes for therapeutic purposes; as of August 2016, no e-cigarette manufacturers have received approval through this avenue.

In 2008 and early 2009, FDA detained multiple shipments of e-cigarettes from overseas manufacturers and denied them entry into the United States on the grounds that e-cigarettes were unapproved drug-device combination products (FDA 2011). Sottera, Inc., which now does business as NJOY, challenged that determination (*Smoking Everywhere, Inc. and Sottera, Inc., d/b/a NJOY v. U.S. Food and Drug Administration, et al.* 2010; Bloomberg Business 2015). Between the filing of the lawsuit and a decision on the motion for preliminary injunction, Congress passed the Tobacco Control Act and the President signed it into law. The Tobacco Control Act defines the term "tobacco product," in part, as any product, including component parts or accessories, "made or derived from tobacco" that is not a "drug," "device," or "combination product" as defined by the *Federal Food, Drug, and Cosmetic Act* (21 U.S.C. 321(rr)) (*Family Smoking Prevention and Tobacco Control Act* 2009, § 101(a)). The District Court subsequently granted a preliminary injunction relying on the Supreme Court's decision in Brown and Williamson (1996) and the recently enacted Tobacco Control Act. FDA appealed the decision and the U.S. Court of Appeals for the D.C. Circuit held that e-cigarettes and, therefore, other products "made or derived from tobacco" are not drug/device combinations unless they are marketed for therapeutic purposes, but can be regulated by FDA as tobacco products under the Tobacco Control Act (*Sottera, Inc. v. Food & Drug Administration* 2010).

On September 25, 2015, FDA proposed regulations to describe the circumstances in which a product made or derived from tobacco that is intended for human consumption will be subject to regulation as a drug, device, or a combination product. The comment period for this proposed regulation closed on November 24, 2015.

Most e-cigarettes marketed and sold in the United States today contain nicotine made or derived from tobacco. Although some e-cigarettes claim that they contain nicotine not derived from tobacco, or that they contain no nicotine at all (Lempert et al. 2016), there may be reason to doubt some of these claims. Currently, synthetic nicotine and nicotine derived from genetically modified, nontobacco plants are cost-prohibitive for e-cigarette manufacturers, although technological advances could eventually increase the cost-effectiveness of using nicotine that was not derived from tobacco (Lempert et al. 2016). The health effects of passive exposure to e-cigarettes with no nicotine, as well as their actual use and the extent of exposure to these products, have just begun to be studied (Hall et al. 2014; Marini et al. 2014; Schweitzer et al. 2015) and some states and localities are taking steps to regulate e-cigarettes that do not contain nicotine or tobacco (Lempert et al. 2016).

Deeming Rule

The Tobacco Control Act added a new chapter to the *Federal Food, Drug, and Cosmetic Act*, which provides FDA with authority over tobacco products. The new chapter applied immediately to all cigarettes, cigarette tobacco, roll-your-own tobacco, and smokeless tobacco; and the law included "any other tobacco products that the Secretary of Health and Human Services by regulation deems to be subject to this chapter" (*Federal Food, Drug, and Cosmetic Act*, §901 (b)). Therefore, to regulate e-cigarettes as tobacco products, FDA was required to undertake a rulemaking process to extend its regulatory authority to include e-cigarettes.

Consequently, in May 2016, through its Center for Tobacco Products (CTP), FDA issued a rule—often referred to as the "deeming rule"—to extend its authority over all products meeting the definition of a tobacco product, except accessories of the newly deemed products. This rule extended FDA's tobacco product authorities to include e-cigarettes and their components and parts (e.g., nicotine cartridges), but also to such products as cigars, pipe tobacco, nicotine gels, waterpipe/hookah tobacco, and dissolvables not already regulated as smokeless tobacco products (*Federal Register* 2016). This regulation is currently under litigation. The deeming rule subjects e-cigarettes to Tobacco Control Act provisions, including:

- Prohibitions on adulterated and misbranded products;
- Required disclosure of existing health information, including lists of ingredients and documents on health effects;
- Required registration of manufacturers;
- Required disclosure of a list of all tobacco products, including information related to labeling and advertising;
- Premarket review of new tobacco products (i.e., those not on the market on February 15, 2007);
- Restrictions on products marketed with claims about modified risk.

In addition to the aforementioned Tobacco Control Act provisions applicable to all deemed tobacco products, the Tobacco Control Act grants FDA authority to undertake a broad range of other actions on specific classes of products. In its deeming rule, FDA included the following additional actions for tobacco products, including e-cigarettes:

- Minimum age restrictions to prevent sales to minors;
- Requirements to include a nicotine warning; and
- Prohibitions on vending machine sales, unless in a facility that never admits youth.

Future Regulatory Options

E-cigarette manufacturers have the option to apply to FDA to authorize the marketing of their products or to be able to manufacture and sell tobacco products marketed with modified-risk claims, in addition to the existing option to apply to FDA's CDER or CDRH for approval to market their products for therapeutic purposes. FDA also has authority to undertake a number of actions if the Secretary of USDHHS finds such actions to be appropriate for the protection of public health, including:

- Product standards, including restrictions on flavors;
- Restrictions on promotion, marketing, and advertising, and prohibitions on brand-name sponsorship of events;
- Minimum package sizes;
- Prohibitions on self-service displays;

- Child-resistant packaging and the inclusion of health warnings; and
- Regulation of nicotine levels in products.

Despite this broad authority, FDA is prohibited from certain regulatory actions, even if those actions may be appropriate for the protection of public health. Specifically, FDA generally cannot restrict tobacco use in public places, levy taxes on tobacco products, prohibit sales by a specific category of retail outlet (e.g., pharmacies), completely eliminate nicotine in tobacco products, require prescriptions for tobacco products unless it is marketed for therapeutic purposes, or establish a federal minimum age of sale for tobacco products above 18 years of age. Thus, even if FDA fully exercises all of its existing authority over e-cigarettes, regulation will still need to be complemented at the state and local levels, including efforts previously shown to be effective for conventional tobacco products, such as comprehensive smokefree laws at the state and local levels, pricing strategies, raising the minimum age of sales to minors to 21, and high-impact countermarketing campaigns. In the current context of rising rates of use by youth, localities and states can also implement policies and programs that minimize the individual- and population-level harms of e-cigarettes (see Chapter 5).

Summary

This chapter presents the major conclusions of this Surgeon General's report and the conclusions of each chapter. E-cigarettes are presented within their historical context, with an overview of the components of these devices and the types of products. In 2016, FDA announced its final rule to regulate e-cigarettes under the *Family Smoking Prevention and Tobacco Control Act*. The chapter outlines options for the regulation of e-cigarettes, particularly as they relate to youth and young adults, based on successful smoking policies. The need to protect youth and young adults from initiating or continuing the use of nicotine-containing products forms a strong basis for the need to regulate e-cigarettes at the local, state, and national levels in the future.

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Chapter 2
Patterns of E-Cigarette Use Among U.S. Youth and Young Adults

Introduction

This chapter documents patterns and trends in awareness of electronic cigarettes (e-cigarettes), their use, and perceptions about these devices among youth and young adults in the United States. Both the awareness of e-cigarettes and levels of their use have increased rapidly throughout the U.S. population. Understanding young people's patterns of e-cigarette use is essential to determining the scope of potential benefits or harms that these products may have from a public health perspective. This chapter summarizes the patterns of use of e-cigarettes, identifies subgroups at higher risk for using them, highlights the ways in which e-cigarettes are used with other tobacco products, and identifies correlates of e-cigarette use, including knowledge, attitudes, beliefs, and sociodemographic characteristics. In most cases, the term "e-cigarette(s)" is used, but when needed to accord with usage in the cited literature, the acronym "ENDS" (electronic nicotine delivery systems) is employed.

Sources of Data

Data summarized in this chapter come from nationally representative datasets that were federally funded and peer-reviewed literature of subnational and international surveillance studies of e-cigarette use that were mostly cross-sectional in design. Appendix 2.1. and Table A2.1-1 in that appendix[1] describe all the years of data available for these data sources, but only selected years are used for this report. For youth, this report relies on data from the National Youth Tobacco Survey (NYTS) and the Monitoring the Future Study (MTF), as measures of e-cigarette use were available for at least two or more time points. For this reason, the report also relies on data from the National Adult Tobacco Survey (NATS) for young adults. More recently, the Youth Risk Behavior Surveillance System and other surveys from the National Center for Health Statistics have added measures of e-cigarette use to their surveys, but only one data point was available at the time this report was prepared. Only five longitudinal studies were available on this topic at the time this report was prepared (Leventhal et al. 2015; Primack et al. 2015; Barrington-Trimis et al. 2016; Unger et al. 2016; Wills et al. 2016). Because e-cigarettes only became prevalent in the tobacco product marketplace in recent years, minimal data are available on their use before 2011. Given the paucity of surveillance information on e-cigarettes and the low prevalence of their use in the early years of their availability in the United States, peer-reviewed studies with smaller subnational samples are used in this chapter to complement national surveillance data. Surveillance of e-cigarette use presents a unique set of challenges, given the emerging and dynamic market specific to these products (see Chapter 4 for more on the latter topic). Appendix 2.1 and Tables A2.2-1 and A2.2-2 in Appendix 2.2 summarize the key terms and measures used in this chapter.

Other Literature

This chapter also summarizes findings from peer-reviewed literature on e-cigarettes that were identified through a systematic review of studies of these products from the United States and abroad. A literature search was conducted in April 2015 (Glasser et al. 2015) using the National Library of Medicine's PubMed database and the following keywords: "e-cigarette*" OR "electronic cigarette" OR "electronic cigarettes" OR "electronic nicotine delivery" OR "vape" OR "vaping." Articles were excluded from this review for any of five reasons: (1) the article was not available in English; (2) the article was not relevant to e-cigarettes; (3) the study included nonhuman subjects; (4) the study did not include original data; or (5) the study did not include findings specific to adolescents or young adults. More details about this review's methodology are available in Glasser and colleagues' (2015) report. The search was subsequently updated in November 2015, January 2016, and March 2016 during continued development of the report. For consistency, the same search strategy and databases were employed at all times. Studies on patterns of e-cigarette use behaviors for both youth and young adults are reviewed in the text and tables that follow. All other studies not explicitly described in the text are summarized in Appendix 2.3 and Tables A2.3-1 through A2.3-3.

[1]All appendixes and appendix tables that are cross-referenced in this chapter are available only online at http://www.surgeongeneral.gov/library/reports/

Key Findings

Youth

Current Prevalence

Ever Use

According to the 2015 National Youth Tobacco Survey (NYTS), an estimated 27.1% of U.S. adolescents, representing approximately 7,260,500 persons, had ever tried e-cigarettes (Centers for Disease Control and Prevention [CDC], unpublished data [NYTS 2015]). This included 13.5% of middle school students and 37.7% of high school students (Tables 2.1a and 2.1b). Among middle school students, use was comparable between boys and girls, but it was higher among Hispanics compared with other racial/ethnic groups (Table 2.1a). For high school students, use was also comparable between boys and girls, but higher among both White and Hispanic youth compared with Black youth (Table 2.1b). According to data from the 2015 Youth Risk Behavior Survey (YRBS), a larger percentage of high school students (44.9%) had ever used e-cigarettes (Kann et al. 2016), while the Monitoring the Future (MTF) survey does not collect data on ever use of e-cigarettes (Johnston et al. 2016).

Past-30-Day Use

According to the 2015 NYTS, an estimated 620,000 middle school students and 2,390,000 high school students had used e-cigarettes at least once in the past 30 days (CDC 2016). This was an increase from the 2014 NYTS, which reported 450,000 middle school students and 2,010,000 high school students had used e-cigarettes in the past 30 days (CDC 2015c). Levels of past-30-day use were 5.3% for middle school students and 16% for high school students in 2015 (Tables 2.2a and 2.2b), compared with 3.9% for middle school students and 13.4% for high school students in 2014. Sociodemographic differences in past-30-day use for middle and high school students had the same patterns as those for ever use (Tables 2.2a and 2.2b). In 2015, according to the YRBS, 24.1% of high school students had used e-cigarettes at least once in the past 30 days (Kann et al. 2016). The 2015 MTF shows past-30-day prevalence of e-cigarette use among adolescents was 9.5% among 8th graders, 14% among 10th graders, and 16% among 12th graders (Johnston et al. 2016). Notably, data from NYTS, YRBS, and MTF show that in 2014 exclusive past-30-day use of e-cigarettes exceeded exclusive past-30-day use of conventional cigarettes for the first time since these types of data were collected (University of Michigan 2014; CDC 2015c).

Frequency of Use

Among middle school students, according to the 2015 NYTS, 5.3% were current users of e-cigarettes, and 0.6% used e-cigarettes frequently (defined as using an e-cigarette 20 or more days in the past 30 days preceding the survey) (Table 2.1a). Among high school students, these estimates were 15.5% and 2.5%, respectively (Table 2.1b). Due to smaller sample sizes, confidence intervals were too wide to determine sociodemographic differences in these measures. These estimates are consistent with a report by CDC (2015b).

A recent analysis of 2014 MTF data, specific to high school seniors, showed the frequency of e-cigarette use (defined as the number of days in the past 30 days a student used an e-cigarette) increases with ever cigarette smoking (Warner et al. 2016). Among high school seniors who used at least 1 e-cigarette in the past 30 days, the frequency of e-cigarette use was almost twice as high (10.2 days) among those who regularly smoke conventional cigarettes, compared to those who had never smoked a conventional cigarette (5.8 days). However, the frequency of e-cigarette use did not vary substantially among current cigarette smokers. Among high school seniors who used at least 1 e-cigarette in the past 30 days, the frequency of e-cigarette use averaged 8–10 days for "heavy cigarette smokers" (those who smoked more than a half pack of cigarettes per day), "light cigarette smokers" (those who smoked 1–5 cigarettes per day), and "very light cigarette smokers" (those who smoked fewer than 1 cigarette per day) (Warner et al. 2016).

Susceptibility to Use

Among those who had never used an e-cigarette, 32.1% of middle school students and 38.4% of high school students were susceptible to using e-cigarettes in the future. That is, these students did not have a firm resolve not to use e-cigarettes in the future. This is according to the 2015 NYTS (Tables 2.1a and 2.1b). No differences in susceptibility to use e-cigarettes were observed by gender or race/ethnicity for either middle school or high school students.

Trends in Prevalence

Ever Use

Overall, according to the NYTS, ever use of e-cigarettes among students in grades 6–12 increased from 3.3% in 2011, to 6.8% in 2012, to 8.1% in 2013, to 19.8% in 2014, and then to 27% in 2015 (Figure 2.1). As

Table 2.1a Percentage of middle school students who have used e-cigarettes, by gender and race/ethnicity; National Youth Tobacco Survey (NYTS) 2015

	Ever use[a]		Current use[b]		Frequent use[c]: Among current users		Frequent use[c]: Among all students		Susceptibility to use[d]: Among never users		Susceptibility to use[d]: Among all students	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	13.5 (11.8–15.5)	0.9	5.3 (4.6–6.2)	0.4	11.7 (8.6–15.8)	1.8	0.6 (0.4–0.9)	0.1	32.1 (29.7–34.7)	1.3	41.4 (38.3–44.5)	1.5
Gender												
Female	12.2 (10.5–14.1)	0.9	4.8 (4.0–5.6)	0.4	11.0 (6.9–17.0)	2.5	0.5 (0.3–0.8)	0.1	33.1 (30.2–36.2)	1.5	41.4 (38.0–44.8)	1.7
Male	14.9 (12.9–17.2)	1.1	5.9 (4.7–7.2)	0.6	11.8 (8.3–16.5)	2.0	0.7 (0.5–1.0)	0.1	31.3 (28.2–34.6)	1.6	41.6 (37.9–45.4)	1.9
Race/ethnicity												
White	12.2 (10.1–14.5)	1.1	4.4 (3.6–5.5)	0.5	10.8 (6.5–17.5)	2.7	0.5 (0.3–0.8)	0.1	29.7 (26.1–33.6)	1.9	38.0 (33.7–42.5)	2.2
Black or African American	11.7 (9.5–14.3)	1.2	4.1 (3.1–5.3)	0.6	14.0 (5.9–29.6)	5.7	—	—	34.7 (30.7–39.0)	2.1	42.5 (39.0–46.2)	1.8
Hispanic or Latino	18.6 (15.9–21.5)	1.4	8.3 (6.8–10.0)	0.8	12.1 (7.5–18.9)	2.8	1.0 (0.6–1.6)	0.2	38.0 (35.2–40.8)	1.4	49.8 (46.9–52.7)	1.5
Other[e]	11.9 (8.2–17.1)	2.2	4.6 (2.7–7.7)	1.2	—	—	—	—	30.4 (24.7–36.8)	3.1	39.5 (33.2–46.2)	3.3

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015).

Notes: **CI** = confidence interval; **SE** = standard error. An em dash (—) indicates that data are statistically unstable because of a relative standard error >40%.

[a]Includes those who reported using an e-cigarette, even once or twice.

[b]Includes those who reported using e-cigarettes on 1 or more days in the past 30 days.

[c]Includes those who responded "≥20 days" to the following question: *"During the past 30 days, on how many days did you use electronic cigarettes or e-cigarettes?"* See CDC (2015b).

[d]Includes those who failed to respond "definitely not" to any of the following questions: (a) *"Do you think that you will try an electronic cigarette or e-cigarette soon?"*; (b) *"If one of your best friends were to offer you an electronic cigarette or e-cigarette, would you use it?"*; or (c) *"Have you ever been curious about using an electronic cigarette or e-cigarette, even once or twice?"*

[e]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, and non-Hispanic American Indian/Alaska Native.

Table 2.1b Percentage of high school students who have used e-cigarettes, by gender and race/ethnicity; National Youth Tobacco Survey (NYTS) 2015

	Ever use[a]		Current use[b]		Frequent use[c]: Among current users		Frequent use[c]: Among all students		Susceptibility to use[d]: Among never users		Susceptibility to use[d]: Among all students	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	37.7 (35.3–40.2)	1.2	16 .0 (14.1–18.0)	1.0	15.5 (12.9–18.4)	1.4	2.5 (1.9–3.2)	0.3	38.4 (36.5–40.4)	1.0	61.1 (59.0–63.2)	1.0
Gender												
Female	34.6 (31.9–37.3)	1.4	12.8 (11.0–15.0)	1.0	10.1 (7.2–14.0)	1.7	1.3 (0.9–1.8)	0.2	39.8 (37.4–42.2)	1.2	60.3 (58.1–62.5)	1.1
Male	40.7 (37.7–43.7)	1.5	19.0 (16.5–21.7)	1.3	19.1 (15.6–23.1)	1.9	3.6 (2.7–4.8)	0.5	36.9 (34.3–39.5)	1.3	61.8 (59.2–64.4)	1.3
Race/ethnicity												
White	38.0 (35.1–41.0)	1.5	17.2 (14.7–19.9)	1.3	16.8 (13.4–20.8)	1.9	2.9 (2.1–3.9)	0.4	36.3 (33.4–39.4)	1.5	60.1 (57.4–62.7)	1.3
Black or African American	28.5 (25.5–31.8)	1.6	8.9 (7.4–10.8)	0.8	8.5 (3.9–17.4)	3.2	0.8 (0.3–1.7)	0.3	37.2 (32.2–42.5)	2.6	54.5 (51.0–57.9)	1.7
Hispanic or Latino	43.0 (38.9–47.2)	2.1	16.4 (14.1–19.0)	1.2	12.8 (9.3–17.3)	2.0	2.1 (1.4–3.1)	0.4	44.6 (41.2–48.0)	1.7	67.8 (64.3–71.1)	1.7
Other[e]	37.4 (24.8–52.1)	7.0	18.9 (10.3–32.2)	5.5	18.2 (11.2–28.2)	4.3	3.4 (2.1–5.7)	0.9	41.2 (35.4–47.3)	3.0	62.6 (54.0–70.5)	4.2

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015).
Note: **CI** = confidence interval; **SE** = standard error.
[a]Includes those who reported using an e-cigarette, even once or twice.
[b]Includes those who reported using e-cigarettes on 1 or more days in the past 30 days.
[c]Includes those who responded "≥20 days" to the following question: *"During the past 30 days, on how many days did you use electronic cigarettes or e-cigarettes?"* See CDC (2015b).
[d]Includes those who failed to respond "definitely not" to any of the following questions: (a) *"Do you think that you will try an electronic cigarette or e-cigarette soon?"*; (b) *"If one of your best friends were to offer you an electronic cigarette or e-cigarette, would you use it?"*; or (c) *"Have you ever been curious about using an electronic cigarette or e-cigarette, even once or twice?"*
[e]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, and non-Hispanic American Indian/Alaska Native.

Table 2.2a Percentage of middle school students who used e-cigarettes in the past 30 days[a], by gender and race/ethnicity; National Youth Tobacco Survey (NYTS) 2011–2015

	2011		2012		2013		2014		2015	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	0.6 (0.4–0.9)	0.1	1.1 (0.9–1.5)	0.1	1.1 (0.8–1.5)	0.2	3.9 (3.0–5.0)	0.5	5.3 (4.6–6.2)	0.4
Gender										
Female	0.4 (0.2–0.7)	0.1	0.8 (0.5–1.1)	0.1	0.9 (0.6–1.4)	0.2	3.3 (2.5–4.3)	0.5	4.8 (4.0–5.6)	0.4
Male	0.7 (0.4–1.3)	0.2	1.5 (1.1–2.1)	0.3	1.4 (0.9–1.9)	0.2	4.5 (3.4–5.9)	0.6	5.9 (4.7–7.2)	0.6
Race/ethnicity										
White	0.6 (0.3–1.0)	0.2	0.9 (0.6–1.3)	0.2	0.9 (0.6–1.4)	0.2	3.1 (2.2–4.2)	0.5	4.4 (3.6–5.5)	0.5
Black or African American	—	—	1.1 (0.6–2.2)	0.4	1.4 (0.7–2.5)	0.4	3.8 (2.5–5.6)	0.7	4.1 (3.1–5.3)	0.6
Hispanic or Latino	0.6 (0.4–1.1)	0.2	2.0 (1.4–2.9)	0.4	1.8 (1.1–2.7)	0.4	6.2 (4.8–7.9)	0.8	8.3 (6.8–10.0)	0.8
Other[b]	—	—	—	—	—	—	3.2 (1.6–6.3)	1.1	4.6 (2.7–7.7)	1.2

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Notes: **CI** = confidence interval; **SE** = standard error. An em dash (—) indicates that data are statistically unstable because of a relative standard error >40%. Wording of questions used to measure e-cigarette use varied from 2011 to 2015.

[a]Includes those who reported using e-cigarettes on 1 or more of the past 30 days. This is also considered "current use" in this survey.

[b]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, and non-Hispanic American Indian/Alaska Native.

Table 2.2b Percentage of high school students who used e-cigarettes in the past 30 days[a], by gender and race/ethnicity; National Youth Tobacco Survey (NYTS) 2011–2015

	2011		2012		2013		2014		2015	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	1.5 (1.2–2.0)	0.2	2.8 (2.3–3.5)	0.3	4.5 (3.8–5.3)	0.4	13.4 (11.2–16.1)	1.2	16.0 (14.1–18.0)	1.0
Gender										
Female	0.7 (0.5–1.0)	0.1	1.9 (1.5–2.4)	0.2	3.5 (2.8–4.3)	0.4	11.9 (9.7–14.5)	1.2	12.8 (11.0–15.0)	1.0
Male	2.3 (1.7–3.2)	0.4	3.7 (2.9–4.8)	0.5	5.5 (4.5–6.8)	0.6	15.0 (12.4–18.2)	1.4	19.0 (16.5–21.7)	1.3
Race/ethnicity										
White	1.8 (1.3–2.4)	0.3	3.4 (2.7–4.2)	0.4	4.8 (3.8–6.1)	0.6	15.3 (12.4–18.8)	1.6	17.2 (14.7–19.9)	1.3
Black or African American	—	—	1.1 (0.7–1.9)	0.3	2.7 (1.9–3.9)	0.5	5.6 (3.7–8.5)	1.2	8.9 (7.4–10.8)	0.8
Hispanic or Latino	1.3 (0.8–2.1)	0.3	2.7 (1.9–3.8)	0.5	5.3 (4.2–6.6)	0.6	15.3 (11.8–19.5)	1.9	16.4 (14.1–19.0)	1.2
Other[b]	—	—	—	—	4.0 (2.3–6.9)	1.1	9.4 (6.8–12.9)	1.5	18.9 (10.3–32.2)	5.5

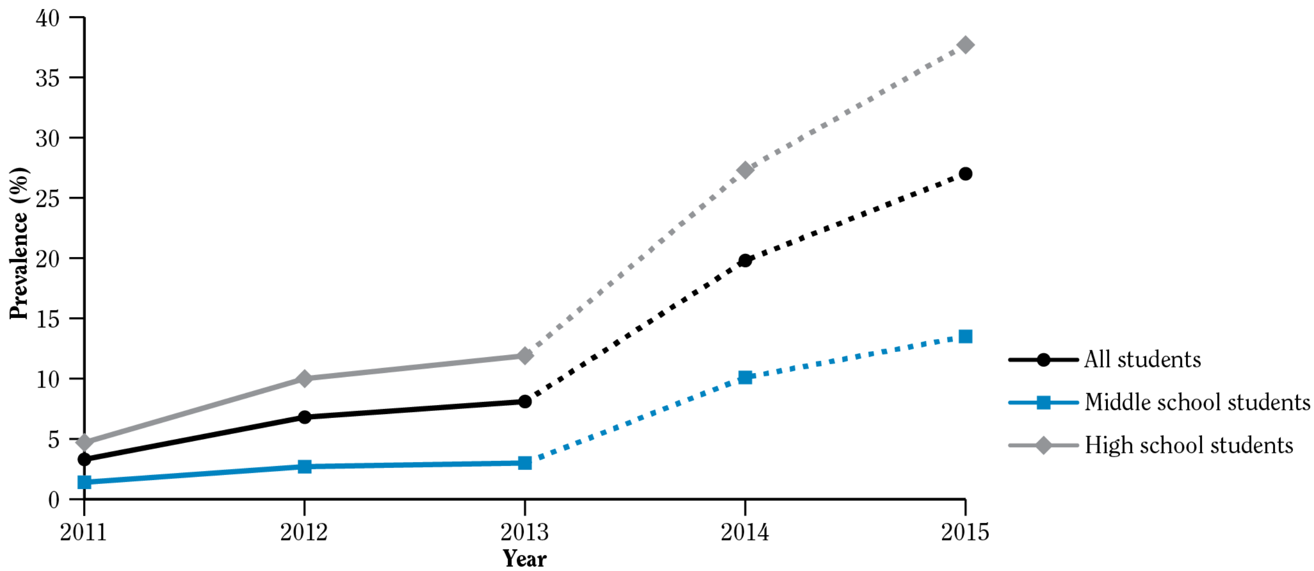
Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Notes: **CI** = confidence interval; **SE** = standard error. An em dash (—) indicates that data are statistically unstable because of a relative standard error >40%. Wording of questions used to measure e-cigarette use varied from 2011 to 2015.

[a] Includes those who reported using e-cigarettes on 1 or more of the past 30 days. This is also considered “current use” in this survey.

[b] Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, and non-Hispanic American Indian/Alaska Native.

Figure 2.1 Trends in ever e-cigarette use[a] among U.S. middle and high school students; National Youth Tobacco Survey (NYTS) 2011–2015



Source: Centers for Disease Control and Prevention 2013a, 2014b; unpublished data (data: NYTS 2015).
Note: In 2014, modifications were made to the e-cigarette measure to enhance its accuracy, which may limit the comparability of this estimate to those collected in previous years. The dotted lines from 2013 to 2015 represent these differences.
[a]Includes those who responded "1 or more" to the following question: *During the last 30 days, on how many days did you use electronic cigarettes or e-cigarettes?*

discussed in Appendix 2.2 (see NYTS Measures—Special Issues), measures of e-cigarette use were changed for the 2014 NYTS, as signaled by the dotted line in the figure. Research conducted using the New Jersey Youth Tobacco Survey suggests that the NYTS measures used in 2011–2013 may potentially underestimate use, compared with the 2014 measure (Delnevo et al. 2016). For the 2011–2015 period, use of e-cigarettes was higher in each year among high school students than among middle school students (Tables 2.3a and 2.3b).

Middle school students. Trends in ever use of e-cigarettes among U.S. middle school students are presented in Table 2.3a and Figure 2.1, using data from the 2011–2015 NYTS. The prevalence of ever use increased from 1.4% in 2011 to 2.7% in 2012, to 3.0% in 2013, to 10.1% in 2014, and then to 13.5% in 2015. The jump in prevalence between 2013 and 2014 may be an artifact of a change in how the use item was asked (see Appendix 2.2. Key Measures of Use). Nonetheless, prevalence of use would be expected to be minimal prior to 2011, suggesting that a considerable increase in use was still observed during this relatively short 4-year period. In 2015, among middle school students, an estimated 1,595,481 had ever tried e-cigarettes (CDC, unpublished data [NYTS 2015]). From 2011 to 2013, the prevalence of ever use did not differ significantly by gender or race/ethnicity. There remained no significant difference in ever use by gender in the 2014 or 2015 NYTS, but by 2014 and still in 2015, a greater percentage of Hispanic middle school students (18.6%) had tried e-cigarettes than White (12.2%) or Black (11.7%) students or students of other races/ethnicities (11.9%) (Table 2.3a).

High school students. Trends in ever use of e-cigarettes among U.S. high school students are presented in Tables 2.3b and Figure 2.1, using data from the 2011–2015 NYTS. The prevalence of ever use increased from 4.7% in 2011 to 10% in 2012, to 11.9% in 2013, to 27.3% in 2014, and then to 37.7% in 2015. In that year, an estimated 5,624,876 high school students had ever used e-cigarettes (CDC, unpublished data [NYTS 2015]). In 2011–2013, male high school students had a higher rate of ever use each year compared with female students, but in 2014 the genders did not differ significantly in their rates. From 2011 to 2015, White and Hispanic high school students were more likely each year to be ever users than were Black students: In 2015, these figures were 38% and 43%, respectively, for White and Hispanic students compared with 28.5% for Black students.

Table 2.3a Percentage of middle school students who have ever used e-cigarettes[a], by gender and race/ethnicity; National Youth Tobacco Survey (NYTS) 2011–2015

	2011		2012		2013		2014		2015	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	1.4 (1.0–2.0)	0.2	2.7 (2.2–3.2)	0.2	3.0 (2.5–3.5)	0.2	10.1 (8.5–11.9)	0.8	13.5 (11.8–15.5)	0.9
Gender										
Female	1.2 (0.8–1.6)	0.2	2.4 (1.9–3.0)	0.3	2.8 (2.3–3.5)	0.3	9.9 (7.8–12.6)	1.2	12.2 (10.5–14.1)	0.9
Male	1.7 (1.1–2.7)	0.4	3.0 (2.4–3.6)	0.3	3.1 (2.5–3.9)	0.3	10.3 (8.6–12.3)	0.9	14.9 (12.9–17.2)	1.1
Race/ethnicity										
White	1.5 (0.9–2.3)	0.3	2.6 (2.1–3.3)	0.3	3.0 (2.4–3.7)	0.3	8.9 (7.2–11.1)	1.0	12.2 (10.1–14.5)	1.1
Black or African American	1.2 (0.7–2.0)	0.3	2.3 (1.3–4.2)	0.7	2.7 (1.9–3.7)	0.5	9.7 (7.9–11.9)	1.0	11.7 (9.5–14.3)	1.2
Hispanic or Latino	1.6 (1.1–2.3)	0.3	3.3 (2.3–4.6)	0.6	3.9 (2.9–5.2)	0.6	14.6 (12.2–17.4)	1.3	18.6 (15.9–21.5)	1.4
Other[b]	—	—	1.0 (0.5–2.2)	0.4	—	—	6.5 (3.9–10.9)	1.7	11.9 (8.2–17.1)	2.2

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Notes: **CI** = confidence interval; **SE** = standard error. An em dash (—) indicates that data are statistically unstable because of a relative standard error >40%. Wording of questions used to measure e-cigarette use varied from 2011 to 2015.

[a]Includes those who reported ever trying e-cigarettes.

[b]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, and non-Hispanic American Indian/Alaska Native.

Table 2.3b Percentage of high school students who have ever used e-cigarettes[a], by gender and race/ethnicity; National Youth Tobacco Survey (NYTS) 2011–2015

	2011		2012		2013		2014		2015	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	4.7 (3.8–5.7)	0.5	10.0 (8.6–11.6)	0.7	11.9 (10.5–13.5)	0.8	27.3 (24.4–30.5)	1.5	37.7 (35.3–40.2)	1.2
Gender										
Female	3.5 (2.7–4.4)	0.4	8.0 (6.7–9.5)	0.7	9.9 (8.3–11.7)	0.8	24.5 (21.4–27.9)	1.6	34.6 (31.9–37.3)	1.4
Male	5.9 (4.7–7.3)	0.7	12.0 (10.2–14.1)	1.0	13.8 (12.1–15.8)	0.9	30.1 (27.2–33.3)	1.5	40.7 (37.7–43.7)	1.5
Race/ethnicity										
White	5.8 (4.6–7.4)	0.7	12.3 (10.5–14.4)	1.0	14.7 (12.8–16.9)	1.0	29.7 (26.2–33.4)	1.8	38.0 (35.1–41.0)	1.5
Black or African American	1.5 (0.9–2.4)	0.4	4.0 (3.1–5.1)	0.5	4.9 (3.6–6.6)	0.7	17.6 (14.1–21.8)	1.9	28.5 (25.5–31.8)	1.6
Hispanic or Latino	3.7 (2.5–5.5)	0.7	8.5 (6.6–10.8)	1.0	10.4 (8.6–12.5)	1.0	29.9 (25.4–34.9)	2.4	43.0 (38.9–47.2)	2.1
Other[b]	2.8 (1.7–4.6)	0.7	6.0 (3.3–10.8)	1.8	8.3 (5.3–12.8)	1.8	18.7 (14–24.5)	2.6	37.4 (24.8–52.1)	7.0

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Notes: **CI** = confidence interval; **SE** = standard error. Wording of questions used to measure e-cigarette use varied from 2011 to 2015.

[a]Includes those who reported ever trying e-cigarettes.

[b]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, and non-Hispanic American Indian/Alaska Native.

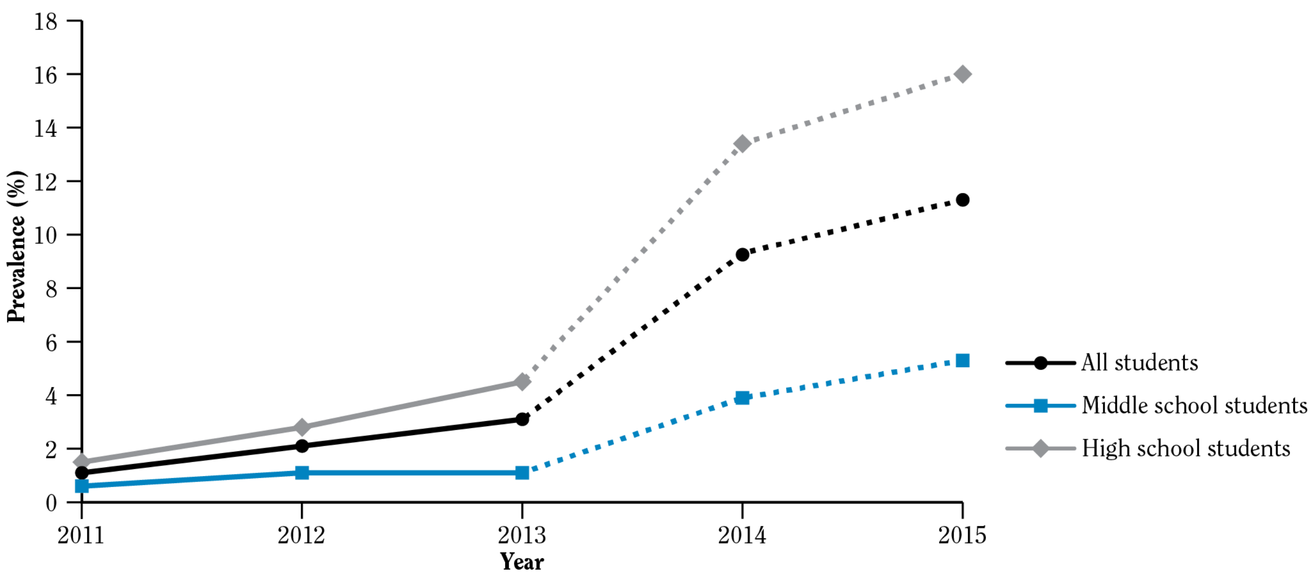
Past-30-Day Use

According to the NYTS, past-30-day use of e-cigarettes among students in grades 6–12 in the United States increased from 1.1% in 2011 to 2.1% in 2012, to 3.1% in 2013, to 9.3% in 2014, and then 11.3% in 2015 (CDC 2013b; Ambrose et al. 2014; Lippert 2015; CDC, unpublished data) (Figure 2.2). In 2015, approximately 3,038,000 middle and high school students were past-30-day users of e-cigarettes (CDC, unpublished data [NYTS 2015]). Across all years, past-30-day use of e-cigarettes was higher among high school students than middle school students (Figure 2.2; Tables 2.2a and 2.2b). In the MTF, estimates were stable from 2014 to 2015; among 8th, 10th, and 12th graders, past-30-day use went from 8.7% to 9.5%, 16.2% to 14%, and 17.1% to 16.2%, respectively (University of Michigan, Institute for Social Research, unpublished data). Differences in trends in past-30-day use between the NYTS and MTF may be due to differences in age groups (e.g., the NYTS includes all grades in middle school and all grades in high schools) and the way in which these measures were asked on the instruments (see Table A2.2-1 in Appendix 2.2).

Middle school students. Trends in past-30-day use of e-cigarettes among middle school students in the United States are presented in Table 2.2a and Figure 2.2, again using data from the 2011–2015 NYTS. The prevalence of such use in this population increased from 0.6% in 2011 to 1.1% in 2012 and 2013, to 3.9% in 2014, and then to 5.3% in 2015 (Table 2.2a) (CDC 2016). Between 2011 and 2015, there were no significant differences in prevalence by gender; unstable estimates (see notes to the table) precluded an examination of differences in past-30-day e-cigarette use by race/ethnicity for 2011–2013. In 2014, the prevalence of past-30-day use was higher among Hispanics (6.2%) than Whites (3.1%), a trend that was also seen in 2015 with 8.3% of Hispanics and 4.4% of Whites reporting past-30-day use. From 2011 to 2015, increases were seen among females (0.4% to 4.8%), males (0.7% to 5.9%), Whites (0.6% to 4.4%), Hispanics (0.6% to 8.3%), and Blacks (1.1% in 2012 to 4.1%) (Table 2.2a) (CDC 2013b; CDC 2015c; CDC 2016).

High school students. Trends in past-30-day use of e-cigarettes among high school students are also presented in Table 2.2b and Figure 2.2, again using data from the 2011–2015 NYTS. The prevalence of such use in this population increased from 1.5% in 2011 to 2.8% in 2012,

Figure 2.2 Trends in past-30-day e-cigarette use[a] among U.S. middle and high school students; National Youth Tobacco Survey (NYTS) 2011–2015



Source: Centers for Disease Control and Prevention 2013a, 2014b; unpublished data (data: NYTS 2015).

Note: In 2014, modifications were made to the e-cigarette measure to enhance its accuracy, which may limit the comparability of this estimate to those collected in previous years. The dotted lines from 2013 to 2015 represent these differences.

[a]Includes those who responded "1 or more" for the following question: *"During the last 30 days, on how many days did you use electronic cigarettes or e-cigarettes?"*

to 4.5% in 2013, to 13.4% in 2014, and then to 16% in 2015. From 2011 to 2013 and in 2015, males were significantly more likely each year to be past-30-day users than were females, but this difference was not significant in 2014 (Table 2.2b). From 2012 to 2015, Black high school students were less likely each year to be past-30-day users than were White or Hispanic high school students (Table 2.2b). During 2011–2015, large increases in past-30-day use were seen among females (0.7% to 12.8%), males (2.3% to 19%), Whites (1.8% to 17.2%), and Hispanics (1.3% to 16.4%) (Table 2.2b) (CDC 2013b, 2015c, 2016).

Young Adults

Current Prevalence

According to the 2013–2014 National Adult Tobacco Survey (NATS), among young U.S. adults aged 18–24 years, the prevalence of ever use and current use of e-cigarettes was 35.8% and 13.6%, respectively (Table 2.4a). These percentages were significantly higher than for the same measures among adults aged 25 years or over (16.4% and 5.7%, respectively) (Table 2.4b). Among young adults, ever and current use were both higher among males than females and for Whites than in other racial/ethnic groups (Table 2.4a). By educational attainment, among young adults, both ever and current use were lowest among those with a college degree (Table 2.4a). Among all young adults, 2% reported using e-cigarettes "every day"; while among current users in this age group, 15% reported this frequency (Table 2.4a). Use of e-cigarettes "every day" among older adults (≥25 years of age) was 1.3% overall and 22% among current users (Table 2.4b). Among young adults, sociodemographic differences in frequent use followed the same pattern as those for ever and current use (Table 2.4a).

Trends in Prevalence

According to the Styles (also known as HealthStyles or Summer Styles) survey, the prevalence of ever use of e-cigarettes among young adults aged 18–24 years was 6.9% in 2011, 4.1% in 2012, 7.8% in 2013, and 14.3% in 2014, a year that saw the addition of other products to this measure, including e-hookahs and e-pipes or e-cigars (Figure 2.3). Although the prevalence of ever use of e-cigarettes among young adults remained consistent from 2010 to 2013, it doubled from 2013 to 2014, presumably reflecting in part the addition of new products to the definition of e-cigarettes. In 2010, young adults (18–24 years) were more likely than older adults (25–44 and 45–64 years of age) to be ever users of e-cigarettes (King et al. 2015). In 2014, ever use of e-cigarettes or similar products was statistically equivalent between young adults (18–24 years old) at 14.3%, adults 25–44 years old at 15%, and adults 45–64 years old at 11.9% ($p > 0.05$) (CDC, unpublished data [Styles 2014]).

E-Cigarette Use and Use of Other Tobacco Products

Evidence from both national and regional studies suggests that e-cigarette use is strongly associated with other tobacco use, especially the use of combustible products (including conventional cigarettes, cigar products, and hookahs). However, many youth and young adults use e-cigarettes exclusively, too. Estimates from cross-sectional surveys such as the NYTS, MTF, and NATS are presented below for youth and young adults, followed by longitudinal studies that examine whether e-cigarette use precedes the use of other tobacco products (Leventhal et al. 2015; Primack et al. 2015; Barrington-Trimis et al. 2016; Unger et al. 2016; Wills et al. 2016).

Cross-Sectional Studies

Youth

Current prevalence. Using data from the 2015 MTF survey, Figure 2.4 and Table 2.5 show past-30-day use of e-cigarettes and conventional cigarettes, including both exclusive and combined use of these products, among 8th-, 10th-, and 12th-grade students. In the 2015 MTF survey, 10.4% of 12th graders used e-cigarettes only, 5.3% used conventional cigarettes only, and 5.8% used both e-cigarettes and conventional cigarettes at least once in the past 30 days (Table 2.5) (MTF 2015a,b). For all grade levels, exclusive use of e-cigarettes was more prevalent (6.8%, 10.4%, and 10.4% of 8th, 10th, and 12th graders, respectively) than exclusive use of conventional cigarettes alone (1.4%, 2.2%, 5.3%, respectively). In the 8th and 10th grades, the combined or dual use of e-cigarettes and conventional cigarettes was also more prevalent than the use of conventional cigarettes alone (2.4% vs. 1.4%, and 3.5% vs. 2.2% for 8th and 10th graders, respectively); while in the 12th grade, the prevalence in the two categories was nearly identical (5.8% vs. 5.3%). As grade level increases, the ratio of any e-cigarette use to any conventional cigarette use decreases. Among 12th graders, dual use of these products was higher among boys than girls and among Whites than Blacks. In all grade levels, dual use was much higher among students who planned to attend fewer than 4 years of college compared to those who planned to attend 4 years of college. No other sociodemographic

Table 2.4a Percentage of young adults (18–24 years of age) who have used e-cigarettes, by gender, race/ethnicity, and education; National Adult Tobacco Survey (NATS) 2013–2014

	Ever use[a]		Current use[b]		Frequent use[c]: Among current users		Frequent use[c]: Among all young adults	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	35.8 (34.1–37.6)	0.9	13.6 (12.5–14.8)	0.6	15.0 (12.1–18.5)	1.6	2.0 (1.6–2.6)	0.2
Gender								
Female	28.4 (26.1–30.8)	1.2	9.8 (8.3–11.5)	0.8	10.0 (6.5–15.1)	2.2	1.0 (0.6–1.5)	0.2
Male	42.9 (40.4–45.3)	1.2	17.1 (15.4–19.0)	0.9	17.8 (13.9–22.5)	2.2	3.0 (2.3–4.0)	0.4
Race/ethnicity								
White	39.7 (37.4–41.9)	1.2	16.1 (14.5–17.8)	0.9	15.3 (11.7–19.7)	2.0	2.5 (1.9–3.2)	0.4
Black or African American	23.1 (19.0–27.8)	2.3	5.4 (3.7–7.9)	1.1	—	—	—	—
Hispanic or Latino	36.6 (32.6–40.7)	2.1	13.4 (10.9–16.4)	1.4	12.0 (6.8–20.2)	3.3	1.6 (0.9–2.8)	0.5
Other[d]	30.8 (25.8–36.3)	2.7	10.8 (8.1–14.2)	1.6	21.5 (11.6–36.4)	6.3	2.3 (1.2–4.4)	0.8
Education								
< High school	44.8 (38.9–50.9)	3.1	15.2 (11.5–19.7)	2.1	9.8 (4.8–18.8)	3.4	1.5 (0.7–3.0)	0.5
High school	39.4 (36.7–42.2)	1.4	14.9 (13.1–17.0)	1.0	17.6 (13.0–23.4)	2.6	2.6 (1.9–3.6)	0.4
Some college[e]	34.3 (31.6–37.0)	1.4	14.7 (12.8–16.8)	1.0	14.8 (10.2–21.0)	2.7	2.2 (1.5–3.2)	0.4
College degree[f]	16.9 (14.2–20.0)	1.5	4.5 (3.1–6.4)	0.8	—	—	—	—

Source: Centers for Disease Control and Prevention, unpublished data (data: NATS 2013–2014).

Notes: **CI** = confidence interval; **SE** = standard error. An em dash (—) indicates that data are statistically unstable because of a relative standard error >40%.

[a]Includes those who reported they had heard of e-cigarettes and tried e-cigarettes.

[b]Includes those who reported they had heard of, tried, and used e-cigarettes every day, some days, or rarely at the time of the interview.

[c]Includes those who reported they had heard of e-cigarettes, tried e-cigarettes, and reported using e-cigarettes every day at the time of the interview.

[d]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, non-Hispanic American Indian/Alaska Native, and multiracial.

[e]Includes some college, no degree; associate's degree, academic program; associate's degree, unspecified; certificate; diploma; or associate's degree.

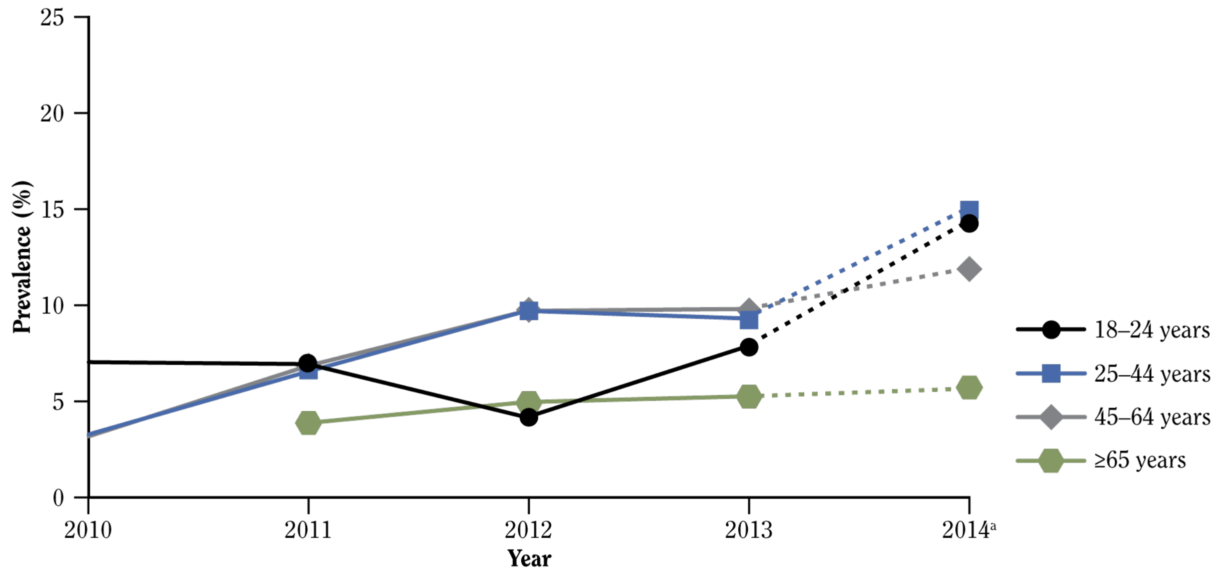
[f]Includes bachelor's degree, master's/professional school degree, or doctoral degree.

Table 2.4b Percentage of adults (≥25 years of age) who have used e-cigarettes, by gender, race/ethnicity, and education; National Adult Tobacco Survey (NATS) 2013–2014

	Ever use[a]		Current use[b]		Frequent use[c]: Among current users		Frequent use[c]: Among all adults	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	16.4 (15.9–16.8)	0.2	5.7 (5.5–6.0)	0.1	22.0 (20.1–24.0)	1.0	1.3 (1.1–1.4)	0.1
Gender								
Female	14.7 (14.2–15.3)	0.3	5.0 (4.7–5.4)	0.2	20.6 (18.1–23.3)	1.3	1.0 (0.9–1.2)	0.1
Male	18.3 (17.6–18.9)	0.3	6.6 (6.1–7.0)	0.2	23.0 (20.2–25.9)	1.5	1.5 (1.3–1.7)	0.1
Race/ethnicity								
White	16.2 (15.8–16.7)	0.2	6.0 (5.7–6.4)	0.2	23.9 (21.7–26.3)	1.2	1.4 (1.3–1.6)	0.1
Black or African American	15.1 (13.9–16.5)	0.7	3.8 (3.2–4.5)	0.3	15.2 (10.2–22.2)	3.0	0.6 (0.4–0.9)	0.1
Hispanic or Latino	15.6 (14.3–17.0)	0.7	4.9 (4.1–5.8)	0.4	15.8 (10.4–23.4)	3.3	0.8 (0.5–1.2)	0.2
Other[d]	21.0 (19.2–22.9)	0.9	8.0 (6.7–9.4)	0.7	19.4 (14.0–26.2)	3.1	1.5 (1.1–2.1)	0.3
Education								
<High school	18.2 (16.8–19.7)	0.8	5.2 (4.4–6.1)	0.4	20.8 (15.2–27.7)	3.2	1.1 (0.8–1.5)	0.2
High school	20.6 (19.7–21.6)	0.5	7.6 (7.0–8.3)	0.3	19.2 (16.1–22.7)	1.7	1.5 (1.2–1.8)	0.1
Some college[e]	19.7 (18.9–20.5)	0.4	7.4 (6.8–7.9)	0.3	24.5 (21.4–27.8)	1.6	1.8 (1.6–2.1)	0.1
College degree[f]	8.7 (8.2–9.1)	0.2	2.8 (2.5–3.1)	0.1	22.0 (18.1–26.4)	2.1	0.6 (0.5–0.8)	0.1

Source: Centers for Disease Control and Prevention, unpublished data (data: NATS 2013–2014).
Note: **CI** = confidence interval; **SE** = standard error.
[a]Includes those who reported they had heard of and tried e-cigarettes.
[b]Includes those who reported they had heard, tried, and used e-cigarettes every day, some days, or rarely at the time of the interview.
[c]Includes those who reported they had heard of, tried, and reported using e-cigarettes every day at the time of the interview.
[d]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, non-Hispanic American Indian/Alaska Native, and multiracial.
[e]Includes some college, no degree; associate's degree, academic program; associate's degree, unspecified; certificate; diploma; or associate's degree.
[f]Includes bachelor's degree, master's/professional school degree, or doctoral degree.

Figure 2.3 Trends in ever e-cigarette use[a] among U.S. adults by age group; Styles 2010–2014

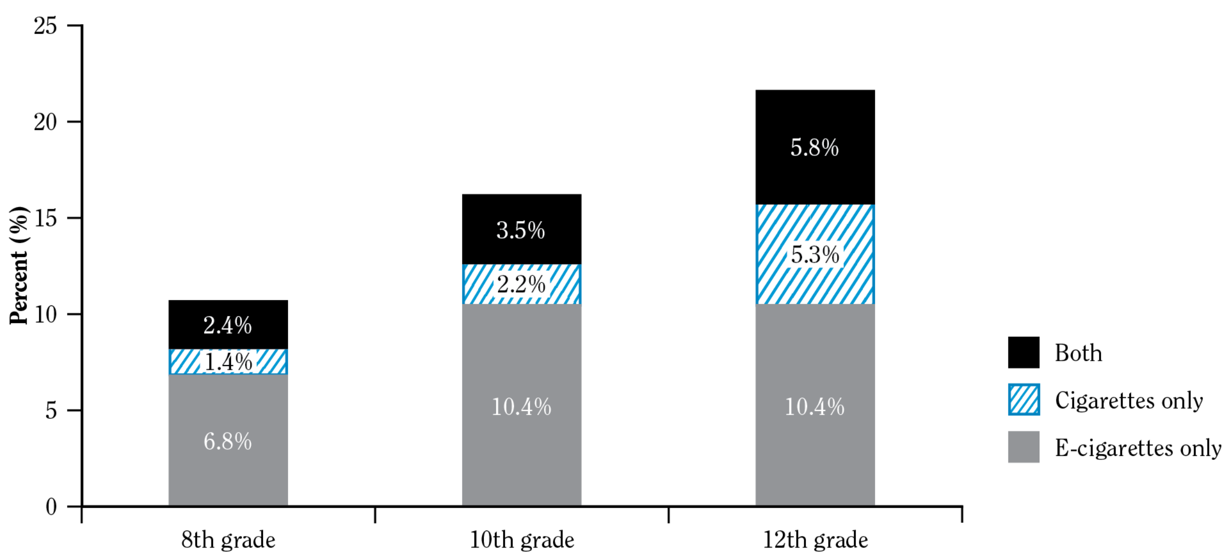


Source: King et al. (2015) (data: HealthStyles 2010–2013); Centers for Disease Control and Prevention, unpublished data (data: HealthStyles 2014).

Note: In 2014, modifications were made to the e-cigarette measure to enhance its accuracy, which may limit the comparability of this estimate to those collected in previous years. The dotted lines from 2013 to 2014 represent these differences.

[a]Includes those who responded "electronic cigarettes or e-cigarettes" to the following question, *"Have you ever tried any of the following products, even just one time? Electronic cigarettes or e-cigarettes, such as Ruyan or NJOY?"*

Figure 2.4 Percentage of students in grades 8, 10, and 12 who used e-cigarettes and cigarettes in the past 30 days; Monitoring the Future (MTF) 2015



Source: University of Michigan, Institute for Social Research, unpublished data (data: MTF 2015).

Note: Questions on e-cigarette use were asked on four of six questionnaire forms. Data presented here are based on those four forms only.

Table 2.5 Percentage of students in grades 8, 10, and 12 who used e-cigarettes, cigarettes, or both products in the past 30 days, by sociodemographic characteristics; Monitoring the Future (MTF) 2015

	8th grade				10th grade				12th grade			
	Neither: % (95% CI)	E-cigarettes only: % (95% CI)	Cigarettes only: % (95% CI)	Both: % (95% CI)	Neither: % (95% CI)	E-cigarettes only: % (95% CI)	Cigarettes only: % (95% CI)	Both: % (95% CI)	Neither: % (95% CI)	E-cigarettes only: % (95% CI)	Cigarettes only: % (95% CI)	Both: % (95% CI)
Overall	89.4 (88.4–90.5)	6.8 (5.8–7.8)	1.4 (0.9–1.8)	2.4 (1.9–2.9)	83.9 (81.9–85.9)	10.4 (9.0–11.8)	2.2 (1.7–2.7)	3.5 (2.8–4.3)	78.5 (76.7–80.3)	10.4 (9.1–11.8)	5.3 (4.6–6.0)	5.8 (5.0–6.6)
Gender												
Female	90.2 (88.7–91.7)	6.2 (4.9–7.5)	1.4 (0.7–2.0)	2.2 (1.6–2.9)	85.6 (83.6–87.6)	8.6 (7.2–10.1)	2.4 (1.6–3.1)	3.4 (2.5–4.3)	84.4 (82.8–86.0)	7.1 (6.2–8.0)	4.7 (3.6–5.7)	3.8 (3.1–4.6)
Male	88.9 (87.3–90.4)	7.2 (6.0–8.5)	1.4 (0.7–2.0)	2.5 (1.7–3.3)	82.2 (79.6–84.7)	12.2 (10.2–14.2)	2.0 (1.3–2.7)	3.6 (2.6–4.7)	72.9 (70.2–75.6)	14.1 (11.8–16.3)	5.6 (4.6–6.6)	7.5 (6.1–8.9)
Race/ethnicity												
White	90.1 (88.6–91.6)	6.2 (4.9–7.4)	1.2 (0.6–1.8)	2.6 (1.7–3.4)	82.1 (79.5–84.7)	11.2 (9.2–13.2)	2.3 (1.6–2.9)	4.4 (3.4–5.4)	75.2 (72.7–77.7)	12.0 (10.4–13.6)	5.8 (4.7–6.9)	7.1 (5.9–8.3)
African American	91.2 (88.2–94.1)	5.3 (2.7–7.8)	2.1 (0.6–3.7)	1.5 (0.0–2.9)	89.9 (85.7–94.1)	6.6 (3.6–9.5)	1.8 (0.4–3.1)	1.7 (0.4–3.1)	87.7 (85.1–90.3)	5.2 (3.8–6.6)	5.1 (3.3–6.8)	2.0 (1.1–3.0)
Hispanic	88.7 (85.8–91.5)	8.2 (6.1–10.4)	0.9 (0.2–1.6)	2.2 (1.2–3.2)	84.6 (81.5–87.6)	10.5 (7.6–13.4)	2.4 (0.9–4.0)	2.5 (0.8–4.2)	80.9 (78.0–83.7)	10.3 (8.0–12.5)	4.4 (3.2–5.5)	4.5 (3.1–6.0)
College plans												
None or <4 years	76.8 (71.0–82.5)	10.1 (6.1–14.0)	4.9 (1.7–8.1)	8.3 (4.8–11.8)	66.3 (61.1–71.5)	15.4 (11.3–19.4)	7.0 (3.8–10.2)	11.3 (7.6–15.1)	65.1 (61.2–68.9)	13.0 (9.7–16.3)	10.2 (8.2–12.3)	11.7 (9.5–13.9)
Complete 4 years	90.5 (89.4–91.5)	6.5 (5.5–7.4)	1.1 (0.7–1.5)	2.0 (1.5–2.5)	85.7 (83.6–87.7)	9.8 (8.3–11.4)	1.7 (1.3–2.2)	2.8 (2.1–3.5)	81.6 (79.9–83.2)	9.9 (8.6–11.1)	4.1 (3.4–4.8)	4.5 (3.8–5.2)

Table 2.5 Continued

	8th grade				10th grade				12th grade			
	Neither: % (95% CI)	**E-cigarettes only: % (95% CI)**	**Cigarettes only: % (95% CI)**	**Both: % (95% CI)**	**Neither: % (95% CI)**	**E-cigarettes only: % (95% CI)**	**Cigarettes only: % (95% CI)**	**Both: % (95% CI)**	**Neither: % (95% CI)**	**E-cigarettes only: % (95% CI)**	**Cigarettes only: % (95% CI)**	**Both: % (95% CI)**
Parental education[a]												
1–2 (Low)	88.1 (83.9–92.2)	5.9 (3.3–8.4)	1.8 (0.3–3.2)	4.3 (2.1–6.6)	77.2 (72.0–82.4)	12.6 (9.0–16.2)	4.8 (1.5–8.0)	5.4 (3.1–7.8)	77.3 (73.4–81.2)	10.1 (7.3–13.0)	7.9 (5.4–10.4)	4.7 (3.1–6.3)
2.5–3	86.2 (83.3–89.1)	9.4 (6.7–12.1)	1.8 (0.6–3.1)	2.6 (1.2–3.9)	81.7 (78.3–85.2)	10.6 (8.1–13.0)	2.5 (1.3–3.7)	5.2 (3.2–7.1)	75.2 (72.4–78.1)	11.1 (9.0–13.3)	7.2 (5.5–8.8)	6.5 (5.0–7.9)
3.5–4	89.6 (87.5–91.8)	7.3 (5.5–9.2)	1.3 (0.3–2.3)	0.8 (1.7–2.7)	83.5 (80.3–86.7)	10.0 (7.7–12.3)	2.8 (1.7–3.9)	3.7 (2.5–5.0)	78.7 (75.9–81.5)	9.9 (7.9–11.8)	4.6 (3.6–5.6)	6.8 (5.3–8.4)
4.5–5	91.0 (89.1–92.8)	6.2 (4.5–7.9)	1.3 (0.4–2.1)	1.5 (0.6–2.5)	86.1 (83.5–88.8)	9.7 (7.5–11.8)	1.4 (0.7–2.0)	2.9 (1.7–4.1)	78.6 (75.7–81.5)	11.2 (9.1–13.2)	4.4 (3.3–5.5)	5.8 (4.4–7.2)
5.5–6 (High)	91.9 (89.4–94.5)	5.2 (3.3–7.0)	1.0 (0.0–2.1)	1.9 (0.4–3.4)	87.6 (83.6–91.6)	9.2 (6.3–12.2)	1.0 (0.2–1.8)	2.2 (0.7–3.7)	82.7 (79.7–85.7)	10.4 (8.1–12.7)	3.2 (2.1–4.3)	3.7 (2.2–5.2)

Source: University of Michigan, Institute for Social Research, unpublished data (data: MTF 2015).

Notes: Questions on e-cigarette use were asked on four of six questionnaire forms. Data presented here are based on those four forms only.

[a]Parental education is an average score of mother's education and father's education.

differences were observed among dual users (Table 2.5). For 10th and 12th graders, exclusive use of e-cigarettes was higher among boys than girls.

Tables 2.6a and 2.6b present data from the 2015 NYTS for middle and high school students. These data represent the percentages of tobacco users who were either lifetime or past-30-day users of e-cigarettes, by tobacco-use category (e.g., cigarettes only, other combustibles only). In these data, a correlation among the increasing levels of tobacco use, increasing complexity of poly-tobacco use, and e-cigarette use is apparent, with ever use and past-30-day use of e-cigarettes emerging as least prevalent among never tobacco users and most prevalent among the highest category of poly-tobacco users (conventional cigarettes plus other combustibles and noncombustibles) for both age groups. As an example, past-30-day e-cigarette use was rare (2.8%) among middle school students who did not use other tobacco products in that time period. However, using the standard of past-30-day-use for each category, the level of such use grew from 44.9% among those who had used cigarettes only; to 61.3% among those who had used cigarettes and other combustibles only; to 74.6% among those who had used cigarettes, other combustibles, and other noncombustibles only (Table 2.6a). These data are consistent with results from the 2013–2014 PATH study (n = 13,651 youth, 12–17 years old), which showed that 52.6% of past-30-day tobacco users also used e-cigarettes (Kasza et al. 2016).

According to the 2015 NYTS, among high school students, past-30-day use of e-cigarettes was also rare (3.4%) among never users of other tobacco products (Table 2.6b). In contrast, 18.4% of ever smokers of cigarettes only; 36.3% of ever smokers of cigarettes and other combustible products only; and 55% of ever users of cigarettes, other combustibles, and other noncombustible products only had used e-cigarettes in the past 30 days. Although the survey found that just 7.3% of high school students were past-30-day exclusive users of e-cigarettes, many types of tobacco product users in the past 30 days were found to have used e-cigarettes in that period: 41.1% of cigarette-only smokers; 58.8% of cigarette smokers and smokers of other combustible tobacco products only; and 77% of cigarette, other combustible, and noncombustible product users only. Similarly, 27.4% of high school students who had not used tobacco products in the past 30 days had ever tried e-cigarettes, as had 80.8% of past-30-day cigarette-only smokers and 95.5% of those who had used cigarettes, other combustible, and other noncombustible tobacco products only (Table 2.6b).

Figure 2.5 presents data from the 2015 NYTS on the prevalence of past-30-day use of various tobacco products among middle and high school students. Although the overall level of tobacco use was lower in middle school, the patterns of poly-tobacco use were similar between the two groups, albeit with a larger proportion of poly-tobacco use in high school. An estimated 6.6% of high school students and 1.8% of middle school students were dual users of combustible tobacco products and e-cigarettes in 2015. Combined use of combustible tobacco, noncombustible tobacco, and e-cigarettes in the past 30 days was rare, with this pattern found for just 0.7% of middle school and 2.6% of high school students in 2015 (Figure 2.5). Longitudinal data are needed to follow individuals over time, ideally for several years, to more precisely examine both the trajectories into and out of cigarette and e-cigarette use and to determine if dual use is a steady state or a pathway-to-persistent-use-of-combustible-tobacco state (Cobb et al. 2015). The small number of such studies that currently exist are discussed below.

Trends in prevalence. Tables 2.7a and 2.7b and Figures 2.6 and 2.7 present patterns of ever e-cigarette and poly-tobacco use over time, using the NYTS data from 2011 to 2015. Among both middle school and high school students, the exclusive use of combustible products declined over time, while both the exclusive use of e-cigarettes and the dual use of e-cigarettes with combustible products increased, especially from 2013 to 2015.

Middle school students. In 2011, an estimated 21% of middle school students had ever used some form of tobacco in their lifetimes, compared to just 1.4% of middle school students who had ever used e-cigarettes (Table 2.7a). By 2015, 13.5% of middle school students had ever tried a tobacco product, while 3.5% had tried e-cigarettes. In that year, 4.5% of middle school students were ever users of e-cigarettes only; 6.2% were ever users of e-cigarettes and combustible products only; and 2.2% were ever users of combustible products, noncombustible products, and e-cigarettes. This means that 70% of middle school students who had ever used e-cigarettes had also experimented with a combustible tobacco product, although which came first is unknown. In 2015, for past-30-day use, exclusive e-cigarette use was 2.6% and exclusive combustible tobacco use was 1.2%. Also in 2015, the prevalence of past-30-day dual use of e-cigarettes and any other combustible or noncombustible product was similar to those estimates, at 2.7% (1.8% for e-cigarettes plus combustibles only, 0.2% for noncombustibles and e-cigarettes only, and 0.7% for e-cigarettes plus combustibles and noncombustibles only). In 2015, ever use of cigarettes in combination with combustibles (6.2%) was equal to or higher than ever use of e-cigarettes only (4.5%) or combustibles only (4.4%) (Table 2.7a).

High school students. In 2011, an estimated 47.2% of high school students had ever used other tobacco products in their lifetimes, compared to 4.7% who had ever used e-cigarettes (Table 2.7b). By 2015, 50.4% of high

Table 2.6a Lifetime and past-30-day e-cigarette use among U.S. middle school students, by other tobacco product use; National Youth Tobacco Survey (NYTS) 2015

		Lifetime e-cigarette use[a]		Past-30-day e-cigarette use[b]	
	N[c]	% (95% CI)	SE	% (95% CI)	SE
Ever other tobacco use[d] (n = 1,757)	8,162				
Never	6,942	5.3 (4.5–6.2)	0.4	1.6 (1.3–2.0)	0.2
Cigarettes only	343	54.3 (46.7–61.7)	3.8	20.8 (15.7–27.0)	2.8
Other combustibles only	261	59.0 (51.5–66.1)	3.7	24.8 (19.0–31.7)	3.2
Noncombustibles only	89	30.7 (23.2–39.3)	4.1	—	—
Cigarettes + other combustibles only	300	70.6 (62.9–77.3)	3.6	35.0 (27.5–43.3)	4.0
Cigarettes + noncombustibles only	67	69.5 (54.5–81.3)	6.9	21.7 (12.7–34.6)	5.5
Other combustibles + noncombustibles only	27	80.3 (56.1–92.9)	9.2	39.4 (20.3–62.3)	11.2
Cigarettes + other combustibles + noncombustibles only	133	84.1 (73.3–91.1)	4.4	45.0 (34.7–55.7)	5.3
Past-30-day other tobacco use[e] (n = 417)	8,145				
No	7,728	10.5 (9.1–12.0)	0.7	2.8 (2.3–3.4)	0.3
Cigarettes only	70	80.6 (68.3–89.0)	5.2	44.9 (32.0–58.6)	6.8
Other combustibles only	153	82.8 (74.0–89.1)	3.8	69.2 (59.1–77.8)	4.7
Noncombustibles only	50	49.0 (34.9–63.3)	7.3	23.1 (12.7–38.2)	6.4
Cigarettes + other combustibles only	63	77.3 (58.8–89.0)	7.6	61.3 (43.9–76.2)	8.4
Cigarettes + noncombustibles only	18	87.2 (65.2–96.1)	7.2	67.8 (40.0–87.0)	12.6
Other combustibles + noncombustibles only	20	87.5 (63.2–96.6)	7.7	64.8 (42.2–82.3)	10.6
Cigarettes + other combustibles + noncombustibles only	43	85.8 (67.5–94.6)	6.5	74.6 (43.4–91.8)	12.7

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015).

Notes: **CI** = confidence interval; **SE** = standard error. *Cigarettes Only* includes those who reported trying cigarettes but not any other tobacco product. *Other combustibles* includes cigars, pipes, and hookah or bidis. *Noncombustibles* includes smokeless tobacco, dissolvables, or snus. *Other Combustibles Only* includes those who reported trying other combustibles but not cigarettes nor noncombustibles. *Noncombustibles Only* includes those who reported trying noncombustibles but not cigarettes nor other combustibles. *Cigarettes and Other Combustibles Only* includes those who reported trying cigarettes and other combustibles but not noncombustibles. *Cigarettes and Noncombustibles Only* includes those who reported trying cigarettes and noncombustibles but not other combustibles. *Other Combustibles and Noncombustibles Only* includes those who reported trying other combustibles and noncombustibles but not cigarettes. *Cigarettes, Other Combustibles, and Noncombustibles* includes those who reported trying a product from each group.

[a]Includes those who responded "yes" to the following question, *"Have you ever used an electronic cigarette or e-cigarette, even once or twice?"*

[b]Includes those who responded "1 or more days" to the following question, *"During the past 30 days, on how many days did you use electronic cigarettes or e-cigarettes?"*

[c]Includes all respondents categorized into each group. It does not exclude those missing for e-cigarette status.

[d]Includes those who reported trying at least one of the following products (e-*cigarettes not included in the definitions*): *Cigarettes Only; Other Combustibles Only; Noncombustibles Only; Cigarettes and Other Combustibles Only; Cigarettes and Noncombustibles Only; Other Combustibles and Noncombustibles Only;* and *Cigarettes, Other Combustibles, and Noncombustibles*.

[e]Includes those who reported using at least one of the following products on 1 of the past 30 days *(e-cigarettes were not included in the definitions): Cigarettes Only; Other Combustibles Only; Noncombustibles Only; Cigarettes and Other Combustibles Only; Cigarettes and Noncombustibles Only; Other Combustibles and Noncombustibles Only;* and *Cigarettes, Other Combustibles, and Noncombustibles.*

Table 2.6b Lifetime and past-30-day e-cigarette use among U.S. high school students, by other tobacco product use; National Youth Tobacco Survey (NYTS) 2015

		Lifetime e-cigarette use[a]		Past-30-day e-cigarette use[b]	
	N[c]	% (95% CI)	SE	% (95% CI)	SE
Ever other tobacco use[d] (n = 5,094)	9,422				
Never	5,326	13.1 (11.7–14.8)	0.8	3.4 (2.5–4.4)	0.5
Cigarettes only	675	54.7 (48.5–60.6)	3.0	18.4 (13.7–24.4)	2.7
Other combustibles only	947	60.0 (54.4–65.3)	2.7	21.7 (18.0–25.9)	2.0
Noncombustibles only	137	39.8 (30.8–49.6)	4.7	20.2 (12.5–31.0)	4.6
Cigarettes + other combustibles only	1,307	79.6 (74.7–83.8)	2.3	36.3 (31.5–41.3)	2.5
Cigarettes + noncombustibles only	131	61.5 (48.7–72.9)	6.2	25.5 (18.5–34.0)	3.9
Other combustibles + noncombustibles only	171	69.5 (57.1–79.6)	5.7	35.3 (26.1–45.8)	5.0
Cigarettes + other combustibles + noncombustibles only	728	89.2 (82.6–93.5)	2.7	55.0 (47.5–62.4)	3.8
Past-30-day other tobacco use[e] (n = 2,389)	9,416				
No	7,542	27.4 (25.2–29.7)	1.1	7.3 (6.1–8.8)	0.7
Cigarettes only	288	80.8 (74.2–86.0)	2.9	41.1 (32.2–50.6)	4.7
Other combustibles only	701	77.2 (71.2–82.3)	2.8	50.4 (45.0–55.8)	2.7
Noncombustibles only	192	69.6 (54.6–81.4)	6.8	31.2 (23.0–40.9)	4.5
Cigarettes + other combustibles only	353	87.1 (77.5–93.0)	3.8	58.8 (49.1–67.8)	4.7
Cigarettes + noncombustibles only	62	76.9 (59.8–88.2)	7.2	50.8 (27.9–73.5)	12.3
Other combustibles + noncombustibles only	108	88.7 (78.8–94.3)	3.8	74.1 (61.3–83.9)	5.7
Cigarettes + other combustibles + noncombustibles only	170	95.9 (87.2–98.8)	2.4	77.0 (66.6–84.8)	4.6

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015).

Notes: **CI** = confidence interval; **SE** = standard error. *Cigarettes Only* includes those who reported trying cigarettes but not any other tobacco product. *Other combustibles* includes cigars, pipes, and hookah or bidis. *Noncombustibles* includes smokeless tobacco, dissolvables, or snus. *Other Combustibles Only* includes those who reported trying other combustibles but not cigarettes nor noncombustibles. *Noncombustibles Only* includes those who reported trying noncombustibles but not cigarettes nor other combustibles. *Cigarettes and Other Combustibles Only* includes those who reported trying cigarettes and other combustibles but not noncombustibles. *Cigarettes and Noncombustibles Only* includes those who reported trying cigarettes and noncombustibles but not other combustibles. *Other Combustibles and Noncombustibles Only* includes those who reported trying other combustibles and noncombustibles but not cigarettes. *Cigarettes, Other Combustibles, and Noncombustibles* includes those who reported trying a product from each group.

[a]Includes those who responded "yes" to the following question, *"Have you ever used an electronic cigarette or e-cigarette, even once or twice?"*

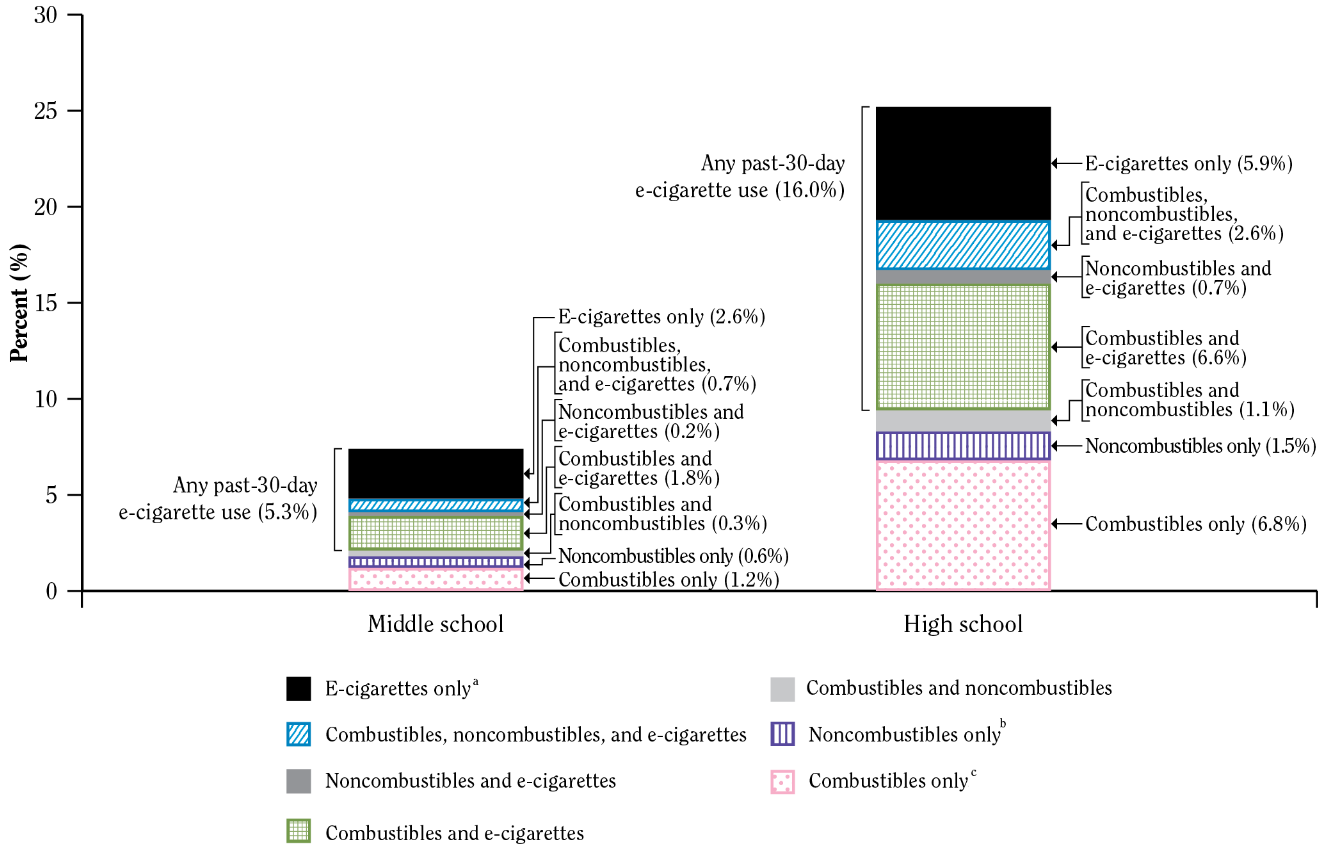
[b]Includes those who responded "1 or more days" to the following question, *"During the past 30 days, on how many days did you use electronic cigarettes or e-cigarettes?"*

[c]Includes all respondents categorized into each group. It does not exclude those missing for e-cigarette status.

[d]Includes those who reported trying at least one of the following products (e-*cigarettes not included in the definition*s): *Cigarettes Only; Other Combustibles Only; Noncombustibles Only; Cigarettes and Other Combustibles Only; Cigarettes and Noncombustibles Only; Other Combustibles and Noncombustibles Only;* and *Cigarettes, Other Combustibles, and Noncombustibles*.

[e]Includes those who reported using at least one of the following products on 1 of the past 30 days *(e-cigarettes were not included in the definitions): Cigarettes Only; Other Combustibles Only; Noncombustibles Only; Cigarettes and Other Combustibles Only; Cigarettes and Noncombustibles Only; Other Combustibles and Noncombustibles Only;* and *Cigarettes, Other Combustibles, and Noncombustibles.*

Figure 2.5 Past-30-day use of various tobacco products among U.S. middle and high school students; National Youth Tobacco Survey (NYTS) 2015



Source: Centers for Disease Control and Prevention 2015b; unpublished data (data: NYTS 2015).

[a]Includes exclusive use of e-cigarettes. It does not include use of any other product.

[b]Includes exclusive use of smokeless tobacco, snus, and/or dissolvable tobacco. It does not include use of combustible products or e-cigarettes.

[c]Includes the use of cigarettes, cigars, pipes, bidis, kreteks, and/or hookahs. It includes participants who reported use of combustible and noncombustible products but not e-cigarettes.

Table 2.7a Percentage of middle school students who have ever used tobacco, by type of product; National Youth Tobacco Survey (NYTS) 2011–2015

	2011		2012		2013		2014		2015	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Any lifetime[a] tobacco use	21.0 (19.2–22.9)	0.9	17.9 (15.9–20.0)	1.0	17.6 (15.6–19.9)	1.1	19.1 (16.7–21.8)	1.3	19.4 (17.0–22.0)	1.2
Any lifetime e-cigarette use[b]	1.4 (1.0–2.0)	0.2	2.7 (2.2–3.2)	0.2	3.0 (2.5–3.5)	0.2	10.1 (8.5–11.9)	0.8	13.5 (11.8–15.5)	0.9
Ever tobacco use[c]										
E-cigarettes only	0.3 (0.2–0.6)	0.1	0.4 (0.3–0.5)	0.1	0.5 (0.3–0.9)	0.1	2.9 (2.3–3.5)	0.3	4.5 (3.9–5.2)	0.3
Combustibles and e-cigarettes only	0.4 (0.3–0.6)	0.1	1.1 (0.9–1.4)	0.1	1.5 (1.1–1.9)	0.2	4.5 (3.9–5.3)	0.4	6.2 (5.4–7.2)	0.5
Noncombustibles and e-cigarettes only	ND	ND	—	—	—	—	0.3 (0.1–0.6)	0.1	0.4 (0.2–0.7)	0.1
Combustibles, noncombustibles, and e-cigarettes	0.5 (0.3–0.9)	0.1	1.1 (0.8–1.4)	0.1	0.8 (0.6–1.2)	0.1	2.2 (1.45–3.2)	0.4	2.2 (1.7–2.9)	0.3
Combustibles only	13.9 (12.5–15.4)	0.7	10.7 (9.5–12.1)	0.7	11.6 (10.1–13.3)	0.8	6.9 (5.6–8.4)	0.7	4.4 (3.7–5.2)	0.4
Noncombustibles only	1.5 (1.1–1.9)	0.2	1.2 (0.9–1.6)	0.2	0.8 (0.6–1.1)	0.1	0.8 (0.5–1.2)	0.2	1.0 (0.7–1.4)	0.2
Combustibles and noncombustibles only	4.3 (3.5–5.1)	0.4	3.4 (2.8–4.0)	0.3	2.4 (1.8–3.2)	0.3	1.5 (1.1–2.1)	0.2	0.7 (0.4–1.1)	0.2
Any past-30-day tobacco use[d]	7.5 (6.4–8.8)	0.6	6.7 (5.8–7.7)	0.5	6.5 (5.43–7.8)	0.6	7.7 (6.7–8.9)	0.6	7.4 (6.3–8.7)	0.6
Any past-30-day e-cigarette use[e]	0.6 (0.4–0.9)	0.1	1.1 (0.9–1.5)	0.1	1.1 (0.8–1.5)	0.2	3.9 (3.0–5.0)	0.5	5.3 (4.6–6.2)	0.4
Past-30-day tobacco use										
E-cigarettes only[f]	0.2 (0.1–0.4)	0.1	0.3 (0.2–0.4)	0.1	0.4 (0.2–0.8)	0.1	1.9 (1.4–2.5)	0.3	2.6 (2.2–3.2)	0.3
Combustibles and e-cigarettes only	0.1 (0.1–0.3)	0.0	0.5 (0.3–0.7)	0.1	0.4 (0.3–0.6)	0.1	1.3 (1.0–1.7)	0.2	1.8 (1.4–2.2)	0.2
Noncombustibles and e-cigarettes only	—	—	—	—	—	—	0.1 (0.1–0.2)	0.0	0.2 (0.1–0.3)	0.0
Combustibles, noncombustibles, and e-cigarettes	0.2 (0.1–0.3)	0.1	0.4 (0.2–0.5)	0.1	0.2 (0.1–0.4)	0.1	0.6 (0.4–0.8)	0.1	0.7 (0.4–1.1)	0.1
Combustibles only	4.5 (3.7–5.5)	0.4	3.7 (3.2–4.3)	0.3	4.0 (3.3–4.9)	0.4	2.7 (2.1–3.3)	0.3	1.2 (0.9–1.6)	0.2
Noncombustibles only	0.9 (0.6–1.3)	0.2	0.7 (0.5–1.0)	0.1	0.6 (0.3–0.9)	0.2	0.7 (0.4–1.2)	0.2	0.6 (0.3–1.2)	0.2
Combustibles and noncombustibles only	1.6 (1.3–2.0)	0.2	1.2 (0.9–1.5)	0.2	0.8 (0.5–1.1)	0.1	0.5 (0.4–0.8)	0.1	0.3 (0.1–0.6)	0.1

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Notes: **CI** = confidence interval; **ND** = no data for this cell; **SE** = standard error. An em dash (—) indicates that data are statistically unstable because of a relative standard error >40%. Wording of questions used to measure e-cigarette use varied from 2011 to 2015. Cigarettes were not included in this analysis. *Combustibles* includes cigars, pipes, hookahs, or bidis. *Noncombustibles* includes smokeless tobacco, dissolvables, or snus. *Combustibles and E-Cigarettes Only* includes those who reported trying e-cigarettes and combustibles but not noncombustibles. *Noncombustibles and E-Cigarettes Only* includes those who reported trying e-cigarettes and noncombustibles but not combustibles.

Table 2.7a Continued

Combustibles, Noncombustibles, and E-Cigarettes includes those who reported trying e-cigarettes, noncombustibles, and combustibles. *Combustibles Only* includes those who reported trying combustibles but not noncombustibles or e-cigarettes. *Noncombustibles Only* includes those who reported trying noncombustibles but not combustibles or e-cigarettes. *Combustibles and Noncombustibles Only* includes those who reported trying noncombustibles and combustibles but not e-cigarettes.

[a]Includes those who reported having tried at least one tobacco product in their lives (e-cigarettes, combustibles, and noncombustibles).

[b]Includes those who reported having tried e-cigarettes in their lives.

[c]Includes those who reported having tried at least one tobacco product in their lives.

[d]Includes those who reported using at least one other tobacco product on at least 1 of the past 30 days.

[e]Includes those who reported using e-cigarettes on at least 1 of the past 30 days.

[f]Includes those who reported using e-cigarettes only on at least 1 of the past 30 days.

Table 2.7b Percentage of high school students who have ever used tobacco, by type of product; National Youth Tobacco Survey (NYTS) 2011–2015

	2011		2012		2013		2014		2015	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Any lifetime[a] tobacco use	47.2 (44.0–50.4)	1.6	45.7 (43.0–48.5)	1.4	46.0 (43.3–48.7)	1.4	47.1 (44.5–49.8)	1.3	50.4 (47.9–52.9)	1.3
Any lifetime e-cigarette use[b]	4.7 (3.8–5.7)	0.5	10.0 (8.6–11.6)	0.7	11.9 (10.5–13.5)	0.8	27.3 (24.4–30.5)	1.5	37.7 (35.3–40.2)	1.2
Ever tobacco use[c]										
E-cigarettes only	0.1 (0.1–0.2)	0.0	0.2 (0.2–0.4)	0.0	0.3 (0.2–0.6)	0.1	3.7 (2.9–4.8)	0.5	7.4 (6.6–8.4)	0.5
Combustibles and e-cigarettes only	1.6 (1.3–2.0)	0.2	4.2 (3.5–5.0)	0.4	6.0 (5.2–6.9)	0.4	14.5 (13.2–16.0)	0.7	20.0 (18.6–21.6)	0.8
Noncombustibles and e-cigarettes only	—	—	—	—	—	—	0.3 (0.1–0.4)	0.1	0.6 (0.4–0.8)	0.1
Combustibles, noncombustibles, and e-cigarettes	2.8 (2.2–3.6)	0.4	5.2 (4.3–6.2)	0.5	5.2 (4.2–6.3)	0.5	8.3 (7.0–9.7)	0.7	9.1 (7.6–10.9)	0.8
Combustibles only	29.1 (27.3–30.9)	0.9	25.1 (23.1–27.1)	1.0	25.2 (22.7–27.8)	1.3	15.8 (14.3–17.5)	0.8	10.2 (8.8–11.8)	0.8
Noncombustibles only	1.8 (1.3–2.4)	0.3	1.3 (1.0–1.8)	0.2	1.5 (1.1–1.9)	0.2	1.2 (0.9–1.7)	0.2	0.9 (0.7–1.2)	0.1
Combustibles and noncombustibles only	11.8 (9.8–13.9)	1.1	9.7 (8.6–10.9)	0.6	7.8 (6.6–9.3)	0.7	3.3 (2.6–4.2)	0.4	2.2 (1.6–3.0)	0.4
Any past-30-day tobacco use[d]	24.0 (22.0–26.5)	1.2	23 (21.5–25.2)	0.9	22.9 (21.1–24.9)	0.9	24.6 (22.6–26.7)	1.0	25.3 (23.1–27.6)	1.1
Any past-30-day e-cigarette use[e]	1.5 (1.2–2.0)	0.2	2.8 (2.3–3.5)	0.3	4.5 (3.8–5.3)	0.4	13.4 (11.2–16.1)	1.2	16.0 (14.1–18.0)	1.0
Past-30-day tobacco use										
E-cigarettes only[f]	0.1 (0.1–0.2)	0.0	0.3 (0.2–0.4)	0.1	0.7 (0.5–0.9)	0.1	4.4 (3.4–5.7)	0.6	5.9 (4.9–7.0)	0.5
Combustibles and e-cigarettes only	0.7 (0.5–0.9)	0.1	1.4 (1.1–1.8)	0.2	2.6 (2.1–3.2)	0.3	5.8 (4.9–6.8)	0.5	6.6 (5.7–7.7)	0.5
Noncombustibles and e-cigarettes only	ND	ND	—	—	—	—	0.6 (0.4–0.8)	0.1	0.7 (0.5–0.9)	0.1
Combustibles, noncombustibles, and e-cigarettes	0.6 (0.4–0.9)	0.1	1.1 (0.8–1.4)	0.1	1.1 (0.8–1.4)	0.1	2.5 (2.0–3.2)	0.3	2.6 (2.1–3.3)	0.3
Combustibles only	15.6 (14.5–16.8)	0.6	14.4 (13.2–15.6)	0.6	13.5 (12.4–14.8)	0.6	8.1 (7.2–9.2)	0.5	6.8 (5.9–7.8)	0.5
Noncombustibles only	2.3 (1.7–3.0)	0.3	1.9 (1.4–2.4)	0.2	1.6 (1.2–2.2)	0.3	1.5 (1.1–2.0)	0.2	1.5 (1.0–2.2)	0.3
Combustibles and noncombustibles only	4.9 (4.0–6.1)	0.5	4.3 (3.7–5.2)	0.4	3.4 (2.7–4.3)	0.4	1.6 (1.2–2.2)	0.2	1.1 (0.7–1.8)	0.2

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Table 2.7b Continued

Notes: **CI** = confidence interval; **ND** = no data for this cell; **SE** = standard error. An em dash (—) indicates that data are statistically unstable because of a relative standard error >40%. Wording of questions used to measure e-cigarette use varied from 2011 to 2015. Cigarettes were not included in this analysis. *Combustibles* includes cigars, pipes, hookahs, or bidis. *Noncombustibles* includes smokeless tobacco, dissolvables, or snus. *Combustibles and E-Cigarettes Only* includes those who reported trying e-cigarettes and combustibles but not noncombustibles. *Noncombustibles and E-Cigarettes Only* includes those who reported trying e-cigarettes and noncombustibles but not combustibles. *Combustibles, Noncombustibles, and E-Cigarettes* includes those who reported trying e-cigarettes, noncombustibles, and combustibles. *Combustibles Only* includes those who reported trying combustibles but not noncombustibles or e-cigarettes. *Noncombustibles Only* includes those who reported trying noncombustibles but not combustibles or e-cigarettes. *Combustibles and Noncombustibles Only* includes those who reported trying noncombustibles and combustibles but not e-cigarettes.

[a]Includes those who reported having tried at least one tobacco product in their lives (e-cigarettes, combustibles, and noncombustibles).

[b]Includes those who reported having tried e-cigarettes in their lives.

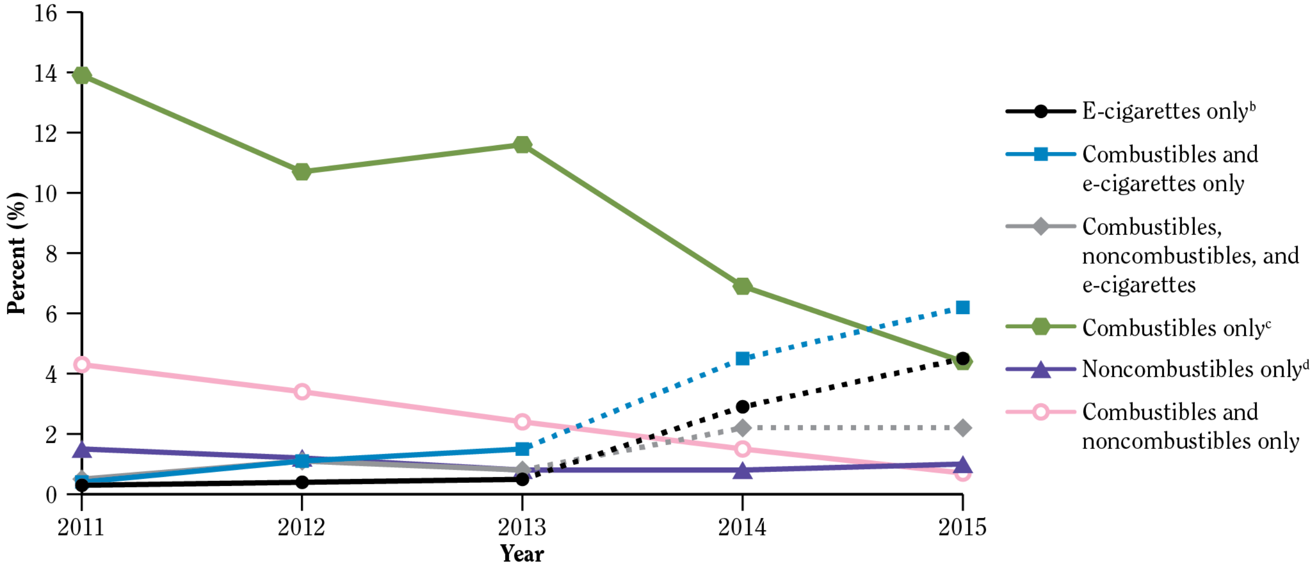
[c]Includes those who reported having tried at least one tobacco product in their lives.

[d]Includes those who reported using at least one other tobacco product on at least 1 of the past 30 days.

[e]Includes those who reported using e-cigarettes on at least 1 of the past 30 days.

[f]Includes those who reported using e-cigarettes only on at least 1 of the past 30 days.

Figure 2.6 Percentage of U.S. middle school students who have ever used tobacco[a], by type of product; National Youth Tobacco Survey (NYTS) 2011–2015



Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Notes: For more information see Table 2.10a. In 2014, modifications were made to the e-cigarette measure to enhance its accuracy, which may limit the comparability of this estimate to those collected in previous years. The dotted lines from 2013 to 2015 represent these differences.

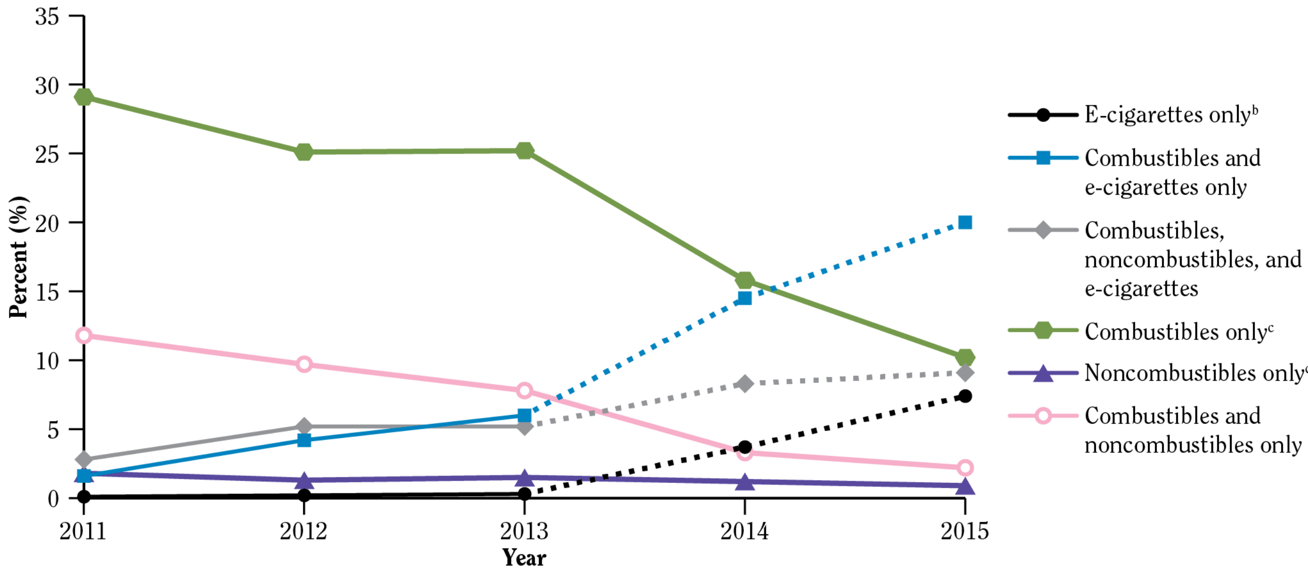
[a]Includes those who reported having tried at least one other tobacco product in their lives.

[b]Includes exclusive use of only e-cigarettes. It does not include use of any other product. Ever e-cigarette use includes those who responded "electronic cigarettes or e-cigarettes, such as Ruyan or NJOY" to the following question: *"Which of the following tobacco products have you ever tried, even just one time?"*

[c]Includes exclusive use of only cigarettes, cigars, pipes, bidis, kreteks, and/or hookahs. It does not include use of noncombustible products or e-cigarettes. They were defined using the following questions: Conventional cigarettes: "*Have you ever tried cigarette smoking, even one or two puffs?*" and *"During the past 30 days, on how many days did you smoke cigarettes?";* cigars: *"Have you ever tried smoking cigars, cigarillos, or little cigars, such as Black and Milds, Swisher Sweets, Dutch Masters, White Owl, or Phillies Blunts, even one or two puffs?"* and *"During the past 30 days, on how many days did you smoke cigars, cigarillos, or little cigars?";* pipes: *"Have you ever tried smoking tobacco in a pipe, even one or two puffs?"* and *"During the past 30 days, on how many days did you smoke tobacco in a pipe?";* and hookahs, kreteks, and bidis: *"Which of the following tobacco products have you ever tried, even just one time? (CHOOSE ALL THAT APPLY)"* and *"During the past 30 days, which of the following products have you used on at least 1 day? (CHOOSE ALL THAT APPLY)."*

[d]Includes exclusive use of only smokeless tobacco, snus, and/or dissolvable tobacco. It does not include use of combustible products or e-cigarettes. They were defined using the following questions: Smokeless tobacco: *"Have you ever used chewing tobacco, snuff, or dip, such as Red Man, Levi Garrett, Beechnut, Skoal, Skoal Bandits, or Copenhagen, even just a small amount?"* and *"During the past 30 days, on how many days did you use chewing tobacco, snuff, or dip?";* and dissolvables and snus: *"Which of the following tobacco products have you ever tried, even just one time? (CHOOSE ALL THAT APPLY)"* and *"During the past 30 days, which of the following products have you used on at least 1 day? (CHOOSE ALL THAT APPLY)."*

Figure 2.7 Percentage of U.S. high school students who have ever used tobacco[a], by type of product; National Youth Tobacco Survey (NYTS) 2011–2015



Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2011–2015).

Notes: For more information see Table 2.10b. In 2014, modifications were made to the e-cigarette measure to enhance its accuracy, which may limit the comparability of this estimate to those collected in previous years. The dotted lines from 2013 to 2015 represent these differences.

[a]Includes those who reported having tried at least one other tobacco product in their lives.

[b]Includes exclusive use of only e-cigarettes. It does not include use of any other product. Ever e-cigarette use includes those who selected "electronic cigarettes or e-cigarettes, such as Ruyan or NJOY" for the following question: *"Which of the following tobacco products have you ever tried, even just one time?"*

[c]Includes exclusive use of only cigarettes, cigars, pipes, bidis, kreteks, and/or hookahs. It does not include use of noncombustible products or e-cigarettes. They were defined using the following questions: Conventional cigarettes: *"Have you ever tried cigarette smoking, even one or two puffs?"* and *"During the past 30 days, on how many days did you smoke cigarettes?"*; cigars: *"Have you ever tried smoking cigars, cigarillos, or little cigars, such as Black and Milds, Swisher Sweets, Dutch Masters, White Owl, or Phillies Blunts, even one or two puffs?"* and *"During the past 30 days, on how many days did you smoke cigars, cigarillos, or little cigars?"*; pipes: *"Have you ever tried smoking tobacco in a pipe, even one or two puffs?"* and *"During the past 30 days, on how many days did you smoke tobacco in a pipe?"*; and hookahs, kreteks, and bidis: *"Which of the following tobacco products have you ever tried, even just one time? (CHOOSE ALL THAT APPLY)"* and *"During the past 30 days, which of the following products have you used on at least 1 day? (CHOOSE ALL THAT APPLY)."*

[d]Includes exclusive use of only smokeless tobacco, snus, and/or dissolvable tobacco. It does not include use of combustible products or e-cigarettes. They were defined using the following questions: Smokeless tobacco: *"Have you ever used chewing tobacco, snuff, or dip, such as Red Man, Levi Garrett, Beechnut, Skoal, Skoal Bandits, or Copenhagen, even just a small amount?"* and *"During the past 30 days, on how many days did you use chewing tobacco, snuff, or dip?"*; and dissolvables and snus: *"Which of the following tobacco products have you ever tried, even just one time? (CHOOSE ALL THAT APPLY)"* and *"During the past 30 days, which of the following products have you used on at least 1 day? (CHOOSE ALL THAT APPLY)."*

school students had ever tried a tobacco product, and 37.7% had ever used an e-cigarette. In 2015, 7.4% of high school students had ever used e-cigarettes exclusively; 20% were ever dual users of e-cigarettes and combustible products; 0.6% were ever dual users of noncombustible products and e-cigarettes only; and 9.1% were ever poly users of combustibles, noncombustibles, and e-cigarettes. However, the order of the use (i.e., which product came first) remains unknown. In 2015, 5.9% of high school students were exclusive past-30-day users of e-cigarettes; 6.6% were past-30-day dual users of e-cigarettes and combustible tobacco products; 0.7% were past-30-day dual users of e-cigarettes and noncombustible tobacco products only; and 2.6% were past-30-day poly users of e-cigarettes, combustible, and noncombustible tobacco products. Exclusive use of combustible products (6.8%) remained as prevalent as past-30-day dual use of e-cigarettes and combustible products (6.6%) among high school students (Table 2.7b).

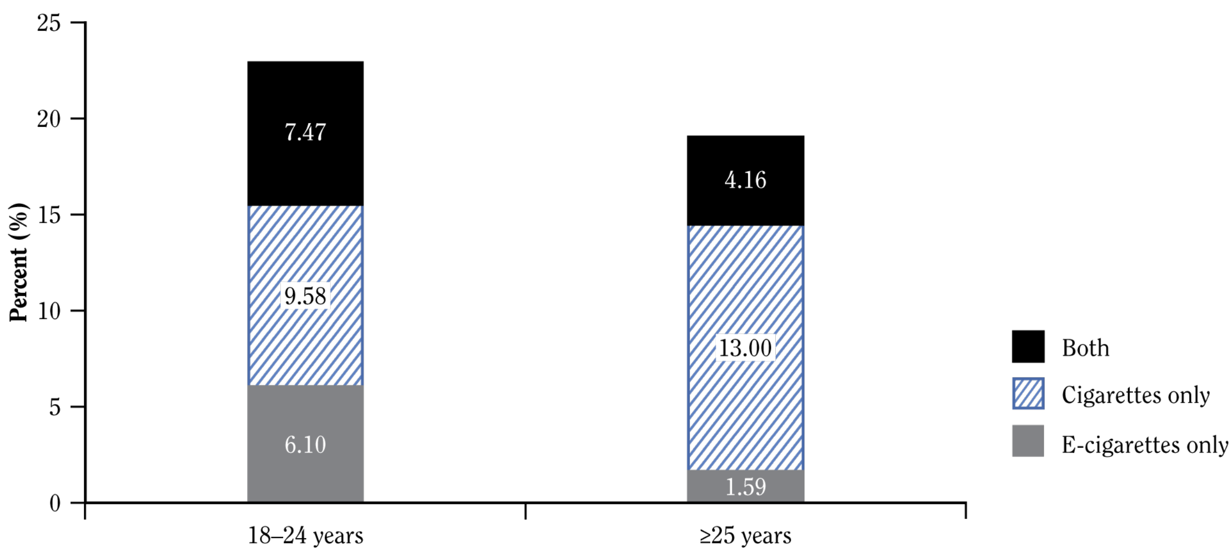
Young Adults[2]

Current prevalence. Using data from the 2013–2014 NATS, current exclusive and combined use of e-cigarettes and cigarettes are presented in Figure 2.8 and Table 2.8a for young adults (18–24 years old), and in Figure 2.8 and Table 2.8b for adults 25 years of age and older. For both age groups, exclusive use of regular cigarettes was the most prevalent pattern of behavior (9.6%, young adults; 13%, adults), followed by dual use of cigarettes and e-cigarettes (7.5%, young adults; 4.2%, adults), and exclusive use of e-cigarettes (6.1%, young adults; 1.6%, adults). Among young adults, combined use of the two products and exclusive use of e-cigarettes were both higher among males than females; combined use was higher among Whites than in Hispanics or Blacks; and both combined use of the two products and exclusive use of e-cigarettes were lowest among those with a college degree.

Longitudinal Studies

Understanding the role that e-cigarettes play in the initiation of tobacco product use, especially conventional cigarettes and other combustible tobacco products, such as cigars and hookahs, is extremely important for informing public health policy, planning, and practice. It is unclear what impact e-cigarette use will have on the overall toll of tobacco use on public health (Cobb et al. 2015). Some researchers and policymakers are concerned about the order in which the initiation of tobacco products takes place, positing that the use of e-cigarettes

Figure 2.8 Percentage of young adults who currently use e-cigarettes[a] and conventional cigarettes; National Adult Tobacco Survey (NATS) 2013–2014



Source: Centers for Disease Control and Prevention, unpublished data (data: NATS 2013–2014).
[a]Current e-cigarette use was defined as those who reported they had heard of e-cigarettes and had tried e-cigarettes, and reported using e-cigarettes every day, some days, or rarely at the time of the interview.

[2]As opposed to the situation in youth, cigarettes are the most commonly used tobacco product among young adults. Therefore, this chapter does not assess co-use of e-cigarettes and other tobacco products among young adults.

Table 2.8a Percentage of young adults (18–24 years of age) who currently use e-cigarettes[a], cigarettes[b], or both[c] products, by gender, race/ethnicity, and education: National Adult Tobacco Survey (NATS) 2013–2014

	Neither[d]		E-cigarettes only[e]		Cigarettes only[f]		Both[c]	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	76.8 (75.3–78.3)	0.8	6.1 (5.3–7.0)	0.4	9.6 (8.6–10.7)	0.5	7.5 (6.6–8.4)	0.5
Gender								
Female	81.8 (79.7–83.7)	1.0	4.0 (3.1–5.2)	0.5	8.4 (7.1–9.9)	0.7	5.8 (4.7–7.2)	0.6
Male	72.3 (70.1–74.4)	1.1	8.1 (6.9–9.4)	0.6	10.6 (9.2–12.2)	0.8	9.0 (7.7–10.4)	0.7
Race/ethnicity								
White	72.8 (70.7–74.8)	1.1	6.3 (5.3–7.5)	0.6	11.2 (9.8–12.8)	0.8	9.7 (8.4–11.2)	0.7
Black or African American	84.8 (80.8–88.2)	1.9	2.9 (1.7–4.9)	0.8	9.8 (7.0–13.5)	1.6	2.5 (1.4–4.4)	0.7
Hispanic or Latino	80.5 (77.0–83.6)	1.7	7.5 (5.7–9.7)	1.0	6.1 (4.3–8.5)	1.1	5.9 (4.2–8.3)	1.1
Other[g]	79.8 (75.5–83.5)	2.1	5.7 (3.8–8.6)	1.2	9.4 (6.9–12.5)	1.4	5.1 (3.4–7.6)	1.0
Education								
<High school	67.4 (61.7–72.6)	2.8	5.8 (3.7–9.1)	1.3	17.3 (13.4–22.1)	2.2	9.4 (6.6–13.3)	1.7
High school	74.4 (71.9–76.7)	1.2	6.5 (5.3–7.8)	0.6	10.7 (9.2–12.5)	0.8	8.5 (7.0–10.1)	0.8
Some college[h]	78.2 (75.8–80.4)	1.2	7.3 (5.9–9.0)	0.8	7.2 (5.9–8.7)	0.7	7.3 (6.1–8.8)	0.7
College degree[i]	92.5 (90.2–94.4)	1.1	2.3 (1.4–3.9)	0.6	3.1 (2.0–4.7)	0.7	2.1 (1.2–3.5)	0.6

Source: Centers for Disease Control and Prevention, unpublished data (data: NATS 2013–2014).
Note: **CI** = confidence interval; **SE** = standard error.
[a]Includes those who reported they had heard of, tried, and used e-cigarettes every day, some days, or rarely at the time of the interview.
[b]Includes those who smoked at least 100 cigarettes and reported using cigarettes every day or some days at the time of the interview.
[c]Includes those who reported currently using both e-cigarettes and conventional cigarettes.
[d]Includes those who reported currently using neither conventional cigarettes nor e-cigarettes.
[e]Includes those who reported currently using e-cigarettes but not conventional cigarettes.
[f]Includes those who reported currently using conventional cigarettes but not electronic e-cigarettes.
[g]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, non-Hispanic American Indian/Alaska Native, and multiracial.
[h]Includes some college, no degree; associate's degree, academic program; associate's degree, unspecified; certificate; diploma; or associate's degree.
[i]Includes bachelor's degree, master's/professional school degree, or doctoral degree.

Table 2.8b Percentage of adults (≥25 years of age) who currently use e-cigarettes[a], cigarettes[b], or both[c] products, by gender, race/ethnicity, and education: National Adult Tobacco Survey (NATS) 2013–2014

	Neither[d]		E-cigarettes only[e]		Cigarettes only[f]		Both[c]	
Characteristic	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**	**% (95% CI)**	**SE**
Overall	81.3 (80.8–81.7)	0.2	1.6 (1.5–1.7)	0.1	13.0 (12.6–13.4)	0.2	4.2 (3.9–4.4)	0.1
Gender								
Female	83.4 (82.8–84.0)	0.3	1.3 (1.1–1.4)	0.1	11.5 (11.0–12.0)	0.3	3.8 (3.5–4.1)	0.2
Male	78.8 (78.1–79.5)	0.4	2.0 (1.7–2.2)	0.1	14.6 (14.0–15.3)	0.3	4.6 (4.2–5.0)	0.2
Race/ethnicity								
White	82.1 (81.6–82.6)	0.3	1.6 (1.5–1.8)	0.1	11.9 (11.5–12.3)	0.2	4.4 (4.1–4.7)	0.1
Black or African American	76.2 (74.6–77.7)	0.8	0.9 (0.7–1.3)	0.2	20.0 (18.6–21.5)	0.7	2.9 (2.4–3.5)	0.3
Hispanic or Latino	83.2 (81.6–84.6)	0.8	1.5 (1.1–2.0)	0.2	12.0 (10.7–13.3)	0.7	3.4 (2.7–4.2)	0.4
Other[g]	77.5 (75.6–79.4)	1.0	2.5 (1.9–3.3)	0.4	14.5 (13.0–16.1)	0.8	5.5 (4.4–6.7)	0.6
Education								
<High school	71.3 (69.5–73.1)	0.9	1.0 (0.7–1.4)	0.2	23.5 (21.8–25.2)	0.9	4.2 (3.5–5.1)	0.4
High school	75.4 (74.4–76.4)	0.5	1.8 (1.5–2.2)	0.2	16.9 (16.1–17.8)	0.4	5.9 (5.3–6.5)	0.3
Some college[h]	79.2 (78.4–80.0)	0.4	2.0 (1.8–2.3)	0.1	13.4 (12.7–14.1)	0.3	5.3 (4.9–5.8)	0.2
College degree[i]	92.5 (92.1–93.0)	0.2	1.2 (1.0–1.4)	0.1	4.7 (4.3–5.0)	0.2	1.6 (1.4–1.8)	0.1

Source: Centers for Disease Control and Prevention, unpublished data (data: NATS 2013–2014).

Note: **CI** = confidence interval; **SE** = standard error.

[a]Includes those who reported they had heard of, tried, and used e-cigarettes every day, some days, or rarely at the time of the interview.

[b]Includes those who smoked at least 100 cigarettes and reported using cigarettes every day or some days at the time of the interview.

[c]Includes those who reported currently using both e-cigarettes and conventional cigarettes.

[d]Includes those who reported currently using neither conventional cigarettes nor e-cigarettes.

[e]Includes those who reported currently using e-cigarettes but not conventional cigarettes.

[f]Includes those who reported currently using conventional cigarettes but not e-cigarettes.

[g]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, non-Hispanic American Indian/Alaska Native, and multiracial.

[h]Includes some college, no degree; associate's degree: academic program; associate's degree, unspecified; certificate; diploma; or associate's degree.

[i]Includes bachelor's degree, master's/professional school degree, or doctoral degree.

could increase the likelihood that adolescents and young adults who have never used any tobacco products, but initiate e-cigarettes, will become lifetime users of conventional cigarettes or other tobacco products in sufficiently large numbers, resulting in a net harm to public health (USDHHS 2012). Other researchers suggest that the order of product initiation for tobacco products is unimportant and that experimentation with a variety of substances may be a marker of a common vulnerability to tobacco, alcohol, marijuana, and other substance-use behaviors (Vanyukov et al. 2012). Regardless, both of these perspectives on the effect of e-cigarette use on youth and young adults require longitudinal data to understand how current behaviors may affect health outcomes.

Five longitudinal studies to date suggest that e-cigarette use among youth (Leventhal et al. 2015; Barrington-Trimis et al. 2016; Wills et al. 2016) and youth and young adults (Primack et al. 2015; Unger et al. 2016) might lead to initiation of the use of combustible tobacco products in the future. The first study to appear was by Leventhal and colleagues (2015). In this study, a cohort of 9th graders in Los Angeles, California, was followed up at both 6 and 12 months, into 10th grade. Those who at baseline had never used combustible tobacco, but were ever users of an e-cigarette, were more likely to use combustible tobacco products at both follow-up points (odds ratio [OR] = 4.27, 95% confidence interval [CI], 3.19–5.71). Product-specific analyses showed that e-cigarette use in 9th grade was associated with the use of cigars (OR = 4.85, 95% CI, 3.38–6.96), hookahs (OR = 3.25, 95% CI, 2.29–4.62), and cigarettes (OR = 2.65, 95% CI, 1.73–4.05) in 10th grade. It was also associated with the number of different combustible products used in 10th grade (OR = 4.26, 95% CI, 3.16–5.74) (all ORs presented here were averaged across the two time points). In these analyses, Leventhal and colleagues (2015) adjusted for demographic characteristics (age, gender, race/ethnicity, highest parental education), social factors (peer smoking, parental smoking), and intrapersonal factors (depression, impulsivity, delinquent behaviors) linked with cigarette smoking in previous research.

Primack and colleagues (2015), in a national cohort study, followed youth and young adults, 16–26 years of age, for 1 year. At baseline, only 16 participants (2.3%) had ever used e-cigarettes. In adjusted models that included only those who did not use conventional cigarettes at baseline and adjusted for gender, age, race/ethnicity, maternal educational level, sensation seeking, parental cigarette smoking, and peer cigarette smoking, baseline e-cigarette use was independently associated with progression to cigarette smoking (OR = 8.3, 95% CI, 1.2–58.6) and susceptibility to cigarette smoking (OR = 8.5, 95% CI, 1.3–57.2). Susceptibility was defined as a lack of a firm commitment not to smoke using established measures of this construct (Evans et al. 1995; Pierce et al. 1996).

Wills and colleagues (2016) followed a cohort of 2,338 students in grades 9 and 10 in Hawaii for 1 year. At baseline, 31% of the sample had ever used an e-cigarette, and 15% had ever used a conventional cigarette. One year later, these increased to 38% and 21%, respectively. Of those who had not used either of these products at baseline, 10% initiated exclusive e-cigarette use 1 year later; 2% initiated exclusive conventional cigarette use; and 4% initiated use of both products. Students who had never smoked a conventional cigarette at baseline but had used an e-cigarette at baseline were three times more likely to smoke conventional cigarettes 1 year later (adjusted OR = 2.87, $p < 0.001$). By comparison, among those who smoked conventional cigarettes at baseline, use of e-cigarettes at that same point in time was not related to any reduction in the use of conventional cigarettes 1 year later ($p > 0.05$). Moreover, students were more likely to transition from never use to dual use of both products 1 year later if they were older, Caucasian or Native Hawaiian (compared with Asian-American), more rebellious, and perceived e-cigarettes as healthier (adjusted OR = 2.05, 2.15, 3.10, 3.32, 2.59, respectively, all $p < 0.001$).

Barrington-Trimis and colleagues (2016) followed a cohort of 11th and 12th grade students in California for more than 1 year (median 15.6 months). In this cohort, at baseline, 146 were ever e-cigarette users and 152 were never e-cigarette users; none had ever smoked a cigarette. Among never e-cigarette users at baseline, 16 participants (10.5%) reported using cigarettes at follow-up; among ever e-cigarette users at baseline, 59 participants (40.4%) reported the same (OR = 6.17; 95% CI, 3.30–11.60). After adjusting for cigar, pipe, or hookah use at baseline, the relationship attenuated only somewhat (OR = 5.48; 95% CI, 2.69–11.20). When stratified by susceptibility to cigarette smoking at baseline (defined, like Primack and colleagues [2015], as the lack of a firm commitment not to smoke using established measures of this construct [Evans et al. 1995; Pierce et al. 1996]), the relationship was actually stronger among those who were not susceptible (OR = 9.69; 95% CI, 4.02–23.40) compared to those who were susceptible (OR = 2.12; 95% CI, 0.79–5.74). The latter relationship was not statistically significant. In additional analyses that were restricted to those who reported no use of any combustible tobacco product at baseline, e-cigarette users were more likely to initiate use of any combustible tobacco product at follow-up (OR = 4.98; 95% CI, 2.37–10.4), including the use of cigarettes (OR = 4.29; 95% CI; 1.84–10.0), hookahs (OR = 2.86; 95% CI, 1.21–6.78), cigars (OR = 4.39; 95% CI, 1.72–11.2), and pipes (OR = 8.21; 95% CI, 1.20–56.2). The models used by Barrington-Trimis and colleagues (2016) adjusted for a variety of demographic characteristics (grade, gender, race/ethnicity, highest parental education) and social factors (peer and parental smoking). Additionally, gender, race/ethnicity (Hispanic White, non-Hispanic White, other), grade (11th or 12th), and ever use of hookahs were tested as potential effect modifiers of these associations, but no evidence was found for the same.

Unger and colleagues (2016) followed a cohort of 1,332 Hispanic young adults in California who provided survey data in 2014 and 2015. At baseline, these participants were an average of 22.7 years old. E-cigarette use at baseline was significantly associated with cigarette smoking (OR = 3.32; 95% CI, 1.55–7.10, among non-cigarette smokers at baseline) and marijuana use (OR = 1.97; 95% CI, 1.01–3.86, among non-marijuana users at baseline) at follow-up. Among those who did not smoke cigarettes at baseline (n = 1,056), 42 reported past month e-cigarette use in 2014; 26% of those who smoked e-cigarettes at baseline became cigarette smokers in 2015, compared to 7% of those who did not smoke e-cigarettes. Further, among those who did not smoke marijuana at baseline (n = 1,028), 68 reported past month e-cigarette use in 2014; 24% of those who smoked e-cigarettes at baseline became marijuana smokers in 2015, compared to 12% of those who did not smoke e-cigarettes. Moreover, in this study, e-cigarette use at baseline was *not* associated with cessation of cigarette smoking (OR = 1.31; 95% CI, 0.73– 2.36) or marijuana use (OR = 1.05; 95% CI. 0.54–2.01) at follow-up. Among those who did smoke cigarettes at baseline (n = 276), 76% reported past month e-cigarette use in 2014; and 63% of those who smoked e-cigarettes at baseline were still smoking cigarettes at follow-up, compared to 58% of those who did not smoke e-cigarettes. Covariates in these regression models included age, gender, past month use of alcohol, and past month use of other tobacco products (hookah, cigars, little cigars, smokeless tobacco).

Despite the several strengths of these studies, including their longitudinal nature, they had weaknesses as well. Rigotti (2015) notes, for example, that the study by Leventhal and colleagues (2015) could not distinguish between those who merely began experimenting with a combustible product and those who became regular smokers at follow-up. The same could be said for the studies by Barrington-Trimis and colleagues (2016), Primack and colleagues (2015), and Wills and colleagues (2016). Similarly, the single exposure measure of the independent variable (i.e., any e-cigarette use) in these studies did not allow the authors to assess whether there was a dose–response relationship between the extent of prior e-cigarette use and subsequent use of combustible tobacco products. In addition, the studies by Primack and colleagues (2015) and Wills and colleagues (2016) did not assess prior use at baseline of other tobacco products, marijuana, or alcohol. Though it is not highlighted prominently in their article, Leventhal and colleagues (2015) showed a bidirectional relationship between e-cigarette use and other combustible tobacco product use in their study: Use of other combustible tobacco products at baseline was significantly associated with the onset of e-cigarette use in two follow-ups. This hypothesis was not tested by Barrington-Trimis and colleagues (2016), Wills and colleagues (2016), or Primack and colleagues (2015). However, at the 1-year follow-up, Wills and colleagues (2016) did consider other demographics, personality, and psychosocial predictors of exclusive e-cigarette use and dual use of conventional cigarettes and e-cigarettes.

Concerns about the samples for the two studies can be raised as well. The samples in the studies by Barrington-Trimis and colleagues (2016) and Leventhal and colleagues (2015) were limited to youth in California; the study by Primack and colleagues (2015) suffered from a small sample size, with only 16 e-cigarette users at baseline (Leventhal et al. 2015; Primack et al. 2015); and the study by Wills and colleagues (2016) was limited to 9th- and 10th-grade students in Hawaii. Additional studies are still needed in the future to further elucidate any causal relationship in either direction between the use of e-cigarettes and other types of tobacco products, such as combustibles.

E-Cigarette Use and Other Substance Use

Few studies have investigated the co-occurrence of e-cigarette use and other risk behaviors in adolescents and young adults. The available evidence suggests that e-cigarette use is associated not only with the use of other tobacco products, but also with alcohol and other substance use, such as marijuana. This is consistent with the common liability model for substance use and other risky behaviors (Vanyukov et al. 2012). Because nearly all currently available studies on this topic focus on regional, international, and at-risk samples, the conclusions from most studies cannot be generalized to the U.S. population as a whole, however.

In the only nationally representative study examining the associations between e-cigarettes, alcohol, and other drug use in young adults 18–24 years of age, the odds of alcohol use were nine times as high and the odds of everyday/some-day marijuana use were three-and-a-half times as high among past-30-day e-cigarette users as they were for those who had not used these products in that period (Cohn et al. 2015). Elsewhere, in a nonprobability sample of college students 17–25 years of age, 66% of current e-cigarette users and 67% of current dual users were heavy drinkers, defined as consuming at least once, five or more drinks (men) or four or more drinks (women) in a single sitting during the course of 1 month (Littlefield et al. 2015). In another study, this one of college students in New York, past-30-day use of e-cigarettes was positively associated with current binge drinking and tobacco product use, and it was less common among those 20–23 years of age (versus those 18 years of age), females, non-Hispanic non-Whites (compared with non-Hispanic Whites), and those reporting better-than-average school performance (Saddleson et al. 2015).

Data from a longitudinal cohort study of children with alcoholic parents found that adolescents (both middle and late adolescence) who used cigarettes, marijuana, or alcohol were significantly more likely to have ever used e-cigarettes. Among those who had used marijuana, e-cigarette use was associated with greater use of marijuana during the previous 30 days (Lessard et al. 2014). In a cross-sectional pilot study of seventh-grade students in Southern California, ever use of e-cigarettes was 11%, compared to 6.8% for cigarettes, 38.1% for alcohol, and 39% for cigarettes or alcohol. In this study, 80% of ever users of e-cigarettes had used alcohol, and 42.2% had used conventional cigarettes (Pentz et al. 2015).

In a 2013 sample of students (n = 2,002) in two states in the southeastern United States, 53.4% of e-cigarette users also used marijuana (Berg et al. 2015). Elsewhere, in a sample of young adults (18–23 years of age) at colleges and universities that was taken in 2013 in upstate New York (n = 1,437), 54.2% of past-30-day marijuana users, 23.9% of past-30-day alcohol users, and 40.3% of past-30-day binge drinkers had ever used e-cigarettes (Saddleson et al. 2015). In Switzerland, among a sample of eighth graders, nearly 60% of regular e-cigarette users “had been drunk” at least once in the past 30 days (defined as an affirmative response to the question, “have you been drunk in the previous 30 days”), and 44.8% had used marijuana at least once during that period (Suris et al. 2015).

There are several limitations to these observational studies. For example, when considering the associations derived from these observational studies, the order of initiation of the products of interest cannot be inferred. In addition, some biases cannot be ruled out because of the nature of the samples, and patterns of associations may reflect an underlying common liability to use substances and take part in other risky behaviors. Some studies adjusted for risk taking, sensation seeking, and impulsivity, while others did not.

E-Cigarettes and Marijuana

Because of their design, e-cigarettes may facilitate drug use among youth and young adults, as these products can be used as a delivery system for cannabinoids and other illicit drugs (Giroud et al. 2015; Morean et al. 2015; Schauer et al. 2016). The aerosolization of cannabis is a relatively new technology used to deliver inhaled tetrahydrocannabinol (THC) and other cannabinoids while reducing the toxic byproducts of smoked cannabis, which are primarily caused by combustion (Abrams et al. 2007).

Laboratory studies of prototype aerosolizers have demonstrated that they can provide a relatively effective mode of delivering THC, with plasma THC concentrations similar to those obtained from smoking a standard marijuana cigarette (Abrams et al. 2007; Giroud et al. 2015). In addition, thermal metered-dose cannabis inhalers have been developed for medical applications; their technology is similar to that of e-cigarettes (Eisenberg et al. 2014). While the first generation of cannabis aerosolizers was developed to aerosolize dry cannabis, the widespread availability of e-cigarettes and rapid advances in their technology have led to the development of liquid/oil forms of cannabis/THC that can be used with e-cigarettes in a fashion similar to that employed when they are filled with nicotine (Giroud et al. 2015). Articles explaining how to acquire and use THC-containing liquid using e-cigarette technology are accessible on the Internet and are strongly suggestive of relatively widespread awareness and use (Gray 2013).

The actual prevalence of users of marijuana aerosolizers and their experiences remain unclear and understudied (Van Dam and Earleywine 2010; Malouff et al. 2014). In one of the few published studies on this issue specific to youth, Morean and colleagues (2015) found that, among high school students in Connecticut, vaporizing cannabis was common among ever e-cigarette users (18%), ever cannabis users (18.4%), and ever dual users (26.5%). This finding suggests a need for more specific surveillance measures that take into account the use of drugs other than nicotine in e-cigarettes.

Use of Flavored E-Cigarettes

The liquid that is vaporized in an e-cigarette is available to consumers in a wide variety of flavors, including tobacco, mint/menthol, and fruit flavors. Although characterizing “flavors” are prohibited in cigarettes (with the exception of menthol and tobacco) by the *Family Smoking Prevention and Tobacco Control Act of 2009,* this practice is not currently prohibited in other tobacco products, like e-cigarettes. Retail sales data suggest that the consumption of flavored e-cigarettes and tobacco products, such as flavored cigars, has increased in recent years (Delnevo et al. 2015; Giovenco et al. 2015), and recent studies show that youth and young adults may find these flavored products more appealing than their unflavored counterparts (Table 2.9) (Ambrose et al. 2015; Krishnan-Sarin et al. 2015; McDonald and Ling 2015).

Data on the use of flavored e-cigarettes among youth and young adults is presented in Table 2.9. In the 2015 NYTS, participants were asked about any current use of e-cigarettes that were "flavored to taste like menthol (mint), alcohol (wine, cognac), candy, fruit, chocolate, or other sweets" (CDC 2015a, 1066). Among middle and high school students who were past-30-day users of e-cigarettes, 1.26 million, or 44.6%, had used a flavored e-cigarette in that timeframe (CDC, unpublished data [NYTS 2015]); this included 42.6% of middle school students and 45.1% of high school students (Table 2.9) (CDC 2015a). The use of flavored e-cigarettes did not differ by gender and was lowest among Blacks (Table 2.9) (CDC 2015a). The use of flavored e-cigarettes was highest among young adults, according to the 2013–2014 NATS (Table 2.9): among those who reported using e-cigarettes every day or some days, 91.6% of young adults (18–24 years old) reported using an e-cigarette flavored to taste like menthol, mint, clover, spice, candy, fruit, chocolate, or other sweets. On the other hand, 66.6% of adults (≥25 years of age) who reported using e-cigarettes every day or some days had used flavored e-cigarettes. No gender differences were noted for young adults, but Blacks, as with middle and high school students, reported the lowest rate of using flavored e-cigarette products.

Data from the 2013–2014 wave of the PATH study revealed that a majority of adolescents who used e-cigarettes use flavors. Of those who had ever tried e-cigarettes, 81% used flavors the first time they tried an e-cigarette; of past-30-day users, 85.3% regularly used flavored e-cigarettes (Ambrose et al. 2015). Ambrose and colleagues (2015) also reported that 81.5% of respondents aged 12–17 reported that they used e-cigarettes because "they come in flavors I like." Elsewhere, among 8th, 10th, and 12th graders in the 2015 MTF study, about 40% said that the primary reason they used e-cigarettes was "because they tasted good." In contrast, about 10% said they used e-cigarettes to quit smoking conventional cigarettes (University of Michigan 2015). In the 2015 MTF study, about two-thirds of 8th-, 10th-, and 12th-grade students said that they used "just flavouring" in their vaporizer when they "last used" a vaporizer, while only 20% reported that they used nicotine (Miech et al. 2016). While the findings specific to nicotine are unexpected, it is important to note that these data are self-reported. It is questionable whether youth know what nicotine is, let alone whether it is contained in the e-cigarette products that they are using. Moreover, even if youth were accurately reporting nicotine strength according to the label on the package, a study by Buettner-Schmidt and colleagues (2016) found that more than half of the labels on assessed e-cigarette products did not accurately reflect actual nicotine content in the product. Therefore, further research on nicotine content using objective measures (e.g., retail sales data) is warranted. Both the PATH and MTF studies, however, reinforce that flavorings may play an important role in the initiation of e-cigarette use.

Other regional studies have reinforced the popularity of flavored e-cigarette use among youth. Table 2.10 summarizes these data on the use of flavored e-cigarettes among youth and young adults. Krishnan-Sarin and colleagues (2015), for example, found that sweet-flavored e-cigarettes were popular among middle and high school students. In another study, which examined nonsmoking middle and high school students and college-aged adults in New Haven County, Connecticut, Kong and colleagues (2015) found that "appealing flavors" was the second most common reason cited for experimenting with e-cigarettes, and in a qualitative study of young adults living in New York City, flavors were identified as an attractive aspect of e-cigarettes (McDonald and Ling 2015). In a study examining nonsmoking teens and adult smokers, the e-cigarette flavors tested appealed more to adults than to teens; nonsmoking teens demonstrated equally low levels of interest in tobacco, fruit, and candy flavors (Shiffman et al. 2015). It should be noted, however, that this study was funded by NJOY, an e-cigarette company and, therefore, may have suffered from commercial bias. Additional concerns about this study concerning selection bias, validity of the survey measures, and reliability of the findings have been raised (Glantz 2015).

Consumer Perceptions of E-Cigarettes

Perceived Harm of E-Cigarettes

In the general population of U.S. adults, e-cigarettes have been perceived to be generally less harmful (Pearson et al. 2012; Czoli et al. 2014; Gallus et al. 2014; Richardson et al. 2014; Berg et al. 2015; Pokhrel et al. 2015) and less addictive (Dockrell et al. 2013; Li et al. 2013; Brown et al. 2014; Farsalinos et al. 2015; Harrell et al. 2015; Hendricks et al. 2015; Kadimpati et al. 2015; Wackowski and Delnevo 2015) than conventional cigarettes. The perceived harm of e-cigarettes relative to conventional cigarettes was lowest among those who were current smokers, followed by former smokers and then nonsmokers (Pearson et al.

Table 2.9 Percentage of youth (middle and high school students), young adults (18–24 years of age), and adults (≥25 years of age) using tobacco products who reported using flavored e-cigarette products, by gender and race/ethnicity; National Youth Tobacco Survey (NYTS)[a] and National Adult Tobacco Survey (NATS)[b]

Characteristic	NYTS 2015[a] (youth): Middle school students		NYTS 2015[a] (youth): High school students		NATS 2013–2014[b] (young adults): 18–24 years of age		NATS 2013–2014[b] (adults): ≥25 years of age	
	% (95% CI)	SE	% (95% CI)	SE	% (95% CI)	SE	% (95% CI)	SE
Overall	42.6 (36.1–49.3)	3.3	45.1 (40.4–49.9)	2.4	91.6 (87.0–94.6)	1.9	66.6 (63.4–69.5)	1.6
Gender								
Female	45.5 (36.2–55.2)	4.8	46.8 (40.5–53.2)	3.2	90.1 (78.6–95.7)	4.1	68.2 (63.7–72.3)	2.2
Male	40.2 (32.2–48.7)	4.2	44.0 (39.3–48.8)	2.4	92.2 (87.0–95.4)	2.1	65.2 (60.7–69.4)	2.2
Race/ethnicity								
White	52.5 (42.0–62.8)	5.3	51.4 (45.7–57.0)	2.9	90.9 (84.7–94.7)	2.5	61.2 (57.5–64.8)	1.9
Black or African American	32.9 (18.5–51.6)	8.6	20.4 (12.8–31.0)	4.5	100 (100–100)[c]	0.0[c]	92.0 (82.1–96.6)	3.5
Hispanic or Latino	28.5 (20.5–38.1)	4.4	38.8 (32.7–45.3)	3.2	89.8 (75.3–96.2)[c]	5.0[c]	85.9 (76.6–91.9)	3.8
Other[d]	57.3 (39.4–73.5)	8.9	34.1 (24.8–44.9)	5.1	94.4 (82.1–98.4)[c]	3.5[c]	67.4 (57.0–76.3)	5.0

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015; NATS 2013–2014).

Note: **CI** = confidence interval; **SE** = standard error.

[a]Flavored e-cigarette product use in NYTS was determined by the response to the question, "*Which of the following tobacco products that you used in the past 30 days were flavored to taste like menthol (mint), alcohol (wine, cognac), candy, fruit, chocolate, or other sweets?*" Participants could select from a list of options to designate the flavored tobacco product(s) they used. (Among those who reported any use of e-cigarettes in the preceding 30 days.) Those who selected e-cigarettes were coded as "yes" for flavored e-cigarettes. Those who did not select e-cigarettes were categorized as "no" for flavored e-cigarettes. Excludes 82 current e-cigarette users whose answers were missing for all flavored tobacco response options.

[b]Flavored e-cigarette product use in NATS was determined by the response to the question, "*Were any of the electronic cigarettes that you used in the past 30 days flavored to taste like menthol, mint, clover, spice, candy, fruit, chocolate, or other sweets*?" (Among those who reported using e-cigarettes every day or some days.) Those who selected "yes" were categorized as "yes" for flavored e-cigarettes. Those who selected "no" were categorized as "no" for flavored e-cigarettes. Excludes five every-day or some-day users who reported not using any noncigarette tobacco product in the past 30 days.

[c]Sample size <50. No estimates had a relative SE >.40.

[d]Includes non-Hispanic Asian, non-Hispanic Native Hawaiian/Other Pacific Islander, and non-Hispanic American Indian/Alaska Native. For young adults and adults, this group also includes multiracial.

Table 2.10 Summary of studies on e-cigarette flavors among youth and young adults

Study	Design/population	Measures	Outcomes/findings
Ambrose et al. (2015)	• Cross-sectional • Wave 1 of PATH study • Household-based, nationally representative survey of 13,651 youth 12–17 years of age	• For each product ever used, youth were asked if it was flavored to taste like menthol, mint, clove, spice, candy, fruit, chocolate, alcohol (such as wine or cognac), or other sweets	• 81% of e-cigarette ever users used a flavored product at first use • 85.3% of past-30-day e-cigarette users used a flavored product • 81.5% of past-30-day users cited “because they come in flavors I like” as a reason for using e-cigarettes
Berg et al. (2015)	• Cross-sectional • Recruitment through Facebook targeting of tobacco and marijuana users and nonusers • 2014 • 1,567 participants, 18–34 years of age, living in the United States	• E-cigarette use (ever tried, number of days in past 30 days) • Flavors used or of interest	• Most commonly used flavor was fruit flavors (67%), which was most commonly reported by never cigarette smokers. • Current smokers were most likely to report using tobacco flavors, but least likely to report using caramel, vanilla, chocolate, cream, or candy flavors.
CDC (2015a)	• Cross-sectional • 2014 NYTS data • Three-stage cluster sampling procedure • Nationally representative sample of 22,007 U.S. middle and high school students	• Participants were asked about any current use of tobacco products that were “flavored to taste like menthol (mint), alcohol (wine, cognac), candy, fruit, chocolate, or other sweets” • Participants could select from a list of options	• Among current e-cigarette users, 63.3% used a flavored product
Kong et al. (2015)	• Cross-sectional • 18 focus groups, schoolwide survey • Recruitment by flyers and active recruitment sessions • Years sample drawn: 2012–2013 • New Haven County, Connecticut • Youth: Middle and high school students; focus group n = 127 (youth); survey n = 4,780 • Young adults: New Haven County, Connecticut, college students; focus group n = 127 (young adults); survey n = 625	• Why did you try an e-cigarette?	• 43.8% of e-cigarette ever users experimented with e-cigarettes for the availability of appealing flavors • School-level differences: $\chi^2(2, N = 1{,}157) = 18.63$, $p \leq 0.001$ • Compared with college students, high school students were more likely to experiment with e-cigarettes because of flavors (47% vs. 32.8%): $\chi^2(1, N = 1{,}116) = 13.61$, $p \leq 0.001$

Table 2.10 Continued

Study	Design/population	Measures	Outcomes/findings
Krishnan-Sarin et al. (2015)	• Cross-sectional • School-based survey • Recruitment by selected district reference groups • Year sample drawn: 2013 • Youth: Connecticut middle (n = 1,166) and high school (n = 3,614) students • Young adults: n/a	• Which of the following flavors of e-cigarettes have you tried?	• Most e-cigarette ever users preferred sweet flavors: – Sweet flavors: 56.8% – Menthol: 8.7% – Combos: 7.7% – Tobacco: 3% – Other: 2.8% • Menthol and tobacco flavors used mostly by e-cigarette users who were also cigarette smokers. – Menthol preference: ○ 3.5% (never smokers) ○ 5.5% (ever smokers) ○ 18.6 (current smokers) – Tobacco preference: ○ 0.5% (never smokers) ○ 2.4% (ever smokers) ○ 7.1% (current smokers)
McDonald and Ling (2015)	• Focus groups and semistructured interviews • Recruitment from bars through screener surveys • Years sample drawn: 2012–2013 • Youth: n/a • Young adults: 87 young adults, 18–27 years of age, in the boroughs of Manhattan, Brooklyn, and Queens in New York City	• Attraction to flavors	• Flavors were an attractive e-cigarette characteristic
Shiffman et al. (2015)	• Cross-sectional • Participants drawn from online research panel • Year sample drawn: 2014 • Youth: Nonsmoking teenagers, 13–17 years of age • Young adults: n/a	• Interest in e-cigarettes paired with various flavor descriptors	• Nonsmoking teens' interest in e-cigarettes was very low (mean = 0.41 ± 0.14 [SE] on 0–10 scale). • Teen interest did not vary by flavor ($p = .75$)

Table 2.10 Continued

Study	Design/population	Measures	Outcomes/findings
Ford et al. (2016)	• Cross-sectional in-home survey • Wave 7 of the Youth Tobacco Policy Survey (YTPS) • Random location quota sampling • 1,205 youth, 11–16 years of age, in the United Kingdom	• Awareness of e-cigarettes • E-cigarette use • E-cigarette flavor awareness • Perceptions of harm	• 12% had tried e-cigarettes • 2% were regular users (confined to adolescents who had also smoked tobacco) • 82% were aware of at least one promotional channel (82%) • 69% were aware that e-cigarettes came in different flavours • Brand awareness was low • E-cigarettes were perceived as harmful (mean = 3.54, SD = 1.19)
Vasiljevic et al. (2016)	• Randomized controlled trial • Participants exposed to advertisements of candy-like flavored e-cigarettes, non-flavoured cigarettes, or control • Youth: 598 English children, 11–16 years of age	• Appeal of using e-cigarettes • Appeal of e-cigarette ads • Interest in buying and trying e-cigarettes following ad exposure	• Exposure to e-cigarette ads did not seem to increase the appeal of tobacco smoking in children. • Exposure to flavoured e-cigarette ads (compared with non-flavoured ads) increased the appeal and interest in buying and trying e-cigarettes in children.

Note: **NYTS** = National Youth Tobacco Survey; **PATH** = Population Assessment of Tobacco and Health Study; **SD** = standard deviation; **SE** = standard error.

2012; Richardson et al. 2014). In a nationally representative sample of U.S. adults, young adults 18–34 years of age were more likely than their older counterparts to perceive e-cigarettes as being less harmful than conventional cigarettes (Tan and Bigman 2014).

Common theories of health behavior, such as the Theory of Reasoned Action and the Health Belief Model, posit that perceptions of harm influence tobacco-use behavior, with lower perceived harm encouraging higher levels of experimentation and current tobacco use (Primack et al. 2008). Monitoring both absolute perceived harm and perceived harm relative to conventional cigarettes could be an indicator of later product adoption. Table 2.11 presents studies of the perceived harm of e-cigarettes among adolescents and young adults that are included in this chapter.

Youth

Table 2.12a presents NYTS data from middle school and high school students on the perceived harm of using e-cigarettes on some days but not every day. In 2015, 61.9% of these students, overall, believed that e-cigarettes caused "little or some harm" under such conditions; 14.5%, "no harm"; and 23.6%, "a lot of harm." However, when these data are stratified by students' history of e-cigarette use, important differences become clear. Notably, 34.2% of past-30-day e-cigarette users believed e-cigarettes cause "no harm," compared with 22.4% of ever e-cigarette users and only 9.5% of never e-cigarette users. Conversely, 29.4% of never e-cigarette users believed that e-cigarettes cause "a lot of harm," compared with 8.3% of ever e-cigarette users and 6.8% of past-30-day e-cigarette users. These important differences by e-cigarette use status, which suggest perceptions of no harm related to e-cigarette use, were consistent for both middle school students and high school students (Tables 2.12b and 2.12c).

Three studies that used data from the 2012 NYTS examined the correlates of U.S. adolescents' opinions about the perceived harm of e-cigarettes relative to the harm of conventional cigarettes. Non-Hispanic Whites, students who lived with a smoker (Cardenas et al. 2015) or had a family member who used tobacco (Amrock et al. 2015), and past-30-day users of tobacco products other than cigarettes were more likely to believe that e-cigarettes were safer than conventional cigarettes (Amrock et al. 2015). Conversely, girls and students 17 years of age or older were more likely to believe that e-cigarettes were more harmful than regular cigarettes (Amrock et al. 2015). The perceived harm of e-cigarettes decreased with increasing levels of cigarette smoking, such that in 2012, 25% of adolescent never smokers, 41.3% of adolescent ever smokers, and 54.2% of adolescent past-30-day smokers believed that e-cigarettes were less harmful than cigarettes (Ambrose et al. 2014). Prior use of e-cigarettes was also associated with perceived harm of that product. Among students who had ever tried e-cigarettes in 2012, 71.8% believed that they were less harmful than cigarettes, 12.1% equally harmful, and 5% more harmful. These estimates were similar to those for students who had used e-cigarettes in the past 30 days (Amrock et al. 2015). In addition, susceptibility to cigarette smoking among never smokers was associated with perceptions of low harm for e-cigarettes (Ambrose et al. 2014).

Although not all studies reviewed in this section included "don't know" as a response option for questions on the harms of e-cigarettes, those that did, found that a large number of students were unsure of the relative harmfulness of e-cigarettes compared to conventional cigarettes (Ambrose et al. 2014; Amrock et al. 2015). In fact, among U.S. adolescents responding to the 2012 NYTS, "don't know" was the most common response (41.1–53.3%) across all the demographic subgroups examined (gender, age, and race/ethnicity) (Amrock et al. 2015). In this sample, more never smokers (57.4%) than ever smokers (37.5%) or past-30-day smokers (24%) had not heard of or did not know enough about e-cigarettes to make a judgment of harm (Ambrose et al. 2014). Future studies will benefit from examining the effect of harm perception on the use of e-cigarettes and other tobacco-use behaviors among adolescents.

Young Adults

Table 2.12d presents data from the 2013–2014 NATS on beliefs about harm from e-cigarettes among young adults (18–24 years old). Just over half (53.8%) of young adults believed that e-cigarettes were "moderately harmful," 26.8% believed they were "very harmful," and 19.4% believed they caused "no harm." Levels of belief in moderate harm were quite similar by type of e-cigarette use: 52.8% of never users, 56.8% of ever (but not current) users, and 53.6% of current users. Ever and current users were more likely than never users to report that e-cigarettes were "not at all harmful," while never users were more likely than the other two groups to report that e-cigarettes were "very harmful."

Published studies on perceived harm of e-cigarettes from regional samples, primarily of college and university students, are presented in Table 2.11. A large survey (n = 4,444) of college students in North Carolina conducted in 2009 found that, as with adolescents, perceived harm of e-cigarettes, compared with conventional cigarettes, was lower among college students who had ever used e-cigarettes (45%) than among those who had never used

Table 2.11 Summary of studies on perceptions of e-cigarette harm among youth and young adults

Study	Design/population	Measures	Outcomes/findings	Comments
Choi et al. (2012)	• Focus groups • Recruitment by (1) online advertisements, (2) flyers on one 4-year and two 2-year college campuses, (3) announcements in student life newsletter at a 2-year college, and (4) recruitment booth on a 2-year college campus • Year sample drawn: 2010 • Youth: n/a • Young adults: Individuals in Minneapolis-St. Paul, MN, enrolled in or who had graduated from 4-year colleges, or those who were enrolled in or had graduated from 2-year colleges, or those who had not enrolled in postsecondary education; N = 66	• Perceived harmfulness relative to cigarettes	• No consensus among participants • Lack of information on (1) ingredients, (2) health impact, and (3) mechanism used to vaporize nicotine • Some noted e-cigarettes to be as harmful as cigarettes ("all one product, in different forms")	• Generalizability • Limited sample size
Adkison et al. (2013)	• Parallel prospective cohort • Telephone interview and web-based surveys • Probability sampling methods (random-digit dialing) • Years sample drawn: 2010–2011 (Wave 8), 2008–2009 (Wave 7, where available) • Youth: n/a • Young adults: current smokers, ≥18 years of age; N = 5,939 (Canada: n = 1,581; United States: n = 1,520; United Kingdom: n = 1,325; Australia: n = 1,513)	• Are electronic cigarettes more harmful than, less harmful than, or equally harmful as regular cigarettes to one's health?	• Not explicitly reported for young adults	• Inclusion of only current and former cigarette smokers • Limited set of questions

Table 2.11 Continued

Study	Design/population	Measures	Outcomes/findings	Comments
Faletau et al. (2013)	• Qualitative exploratory • Structured focus groups and individual interviews • Recruited from two low socioeconomic primary schools in East and South Auckland, New Zealand • Year sample drawn: 2011 • Youth: Maori, Tongan, Samoan, Cook Island, and Niuean children, 6–10 years of age; N = 20 • Young adults: n/a	• Viewed tobacco cigarette and electronic cigarette videos	• Still allows smokers to smoke, despite its function as a cessation aid	• Generalizability • Unknown if saturation was reached in children between focus groups and individual interviews
Sutfin et al. (2013)	• Cross-sectional • Web-based survey (part of a randomized group trial) • Stratified random sample • Year sample drawn: 2009 • Youth: n/a • Young adults: undergraduate students attending eight universities in North Carolina; N = 4,857 (completers of e-cigarette question, n = 4,444).	• Compared with a regular cigarette, how harmful do you think e-cigarettes are? – Less harmful – As harmful – More harmful – Do not know	• Among the overall sample: – 17% indicated "as harmful" – 23% indicated "less harmful" – 2% indicated "more harmful" – 50% indicated "do not know" • Among ever e-cigarette users: – 17% indicated "as harmful" – 45% indicated "less harmful" – 3% indicated "more harmful" – 23% indicated "do not know" • Among never e-cigarette users: – 16% indicated "as harmful" – 22% indicated "less harmful" – 2% indicated "more harmful" – 51% indicated "do not know" • Ever e-cigarette use significantly associated with harm perceptions ($p < 0.001$)	• Low response rate • Generalizability • Inability to differentiate former smokers from experimenters • Cross-sectional analysis

Table 2.11 Continued

Study	Design/population	Measures	Outcomes/findings	Comments
Ambrose et al. (2014)	• NYTS • Cross-sectional • School-based survey • Three-stage cluster sampling • Year sample drawn: 2012 • Youth: U.S. middle and high school students (grades 6–12); N = 24,658 • Young adults: n/a	• Do you believe that electronic cigarettes or e-cigarettes, such as Ruyan or NJOY, are less harmful, equally harmful, or more harmful than regular cigarettes?	• 30.6% (CI, 29.3–31.9%) of respondents believed e-cigarettes are less harmful than cigarettes: never smokers: 25% (CI, 23.9–26.2%); ever smokers: 41.3% (CI, 39.1–43.6%); current smokers: 54.2% (CI, 51.0–57.4%) • Female and Hispanics were less likely to perceive e-cigarettes as less harmful than cigarettes compared with males and Whites, across all smoking statuses • Current smokers that had ever used e-cigarettes were more than twice as likely to perceive e-cigarettes as less harmful, compared with smokers who had never used e-cigarettes (AOR = 2.48; CI, 1.87–3.29) • Never smokers who had ever used e-cigarettes were almost six times as likely to perceive e-cigarettes as less harmful, compared with never smokers who had never used e-cigarettes (AOR = 5.88; CI, 3.07–11.25)	• Perceived graduated risk • Self-reported items • Social desirability bias • Generalizability

Table 2.11 Continued

Study	Design/population	Measures	Outcomes/findings	Comments
Czoli et al. (2014)	• Cross-sectional • Survey • Recruitment through online panel of commercial market research company • Year sample drawn: 2012 • Youth: Canadian youth recruited from online panel, 16–30 years of age; n = 1,188 • Young adults: Canadian young adults recruited from same online panel (see above)	• Is this product harmful to your health? • Have you ever experienced any side-effects or adverse outcome(s) while using e-cigarettes?	• Mean score for agreement with e-cigarettes as harmful to your health (higher score indicates greater agreement): – Among cigarette nonsmokers: 5.5 (e-cigarette nonuser) vs. 4.4 (e-cigarette ever user) – Among former smokers: 5.2 (e-cigarette nonuser) vs. 3.6 (e-cigarette ever user) – Among current smokers: 2.6 (e-cigarette nonuser) vs. 3.5 (e-cigarette ever user)	• Cross-sectional analysis • Generalizability
Gallus et al. (2014)	• Cross-sectional • In-person survey • Representative multistage sampling • Year sample drawn: 2013 • Youth: n/a • Young adults: Italians ≥15 years of age; N = 3,000	• Indicate your opinion (true/false) concerning e-cigarettes on the following: – (1) Are not harmful for health – (2) Are less harmful than traditional cigarettes because they do not contain nicotine – (3) Are less harmful because there is no tobacco combustion – (4) Are less harmful because they contain only nicotine – (5) Are more harmful than traditional cigarettes – (6) Are an efficient tool to quit smoking – (7) Allow smoking even where it is forbidden	• Findings not explicitly reported for young adults	• Unstable estimates due to small sample of e-cigarette users • Unvalidated survey

Table 2.11 Continued

Study	Design/population	Measures	Outcomes/findings	Comments
Tan and Bigman (2014)	• Cross-sectional • Health Information National Trends Survey 4 Cycle 2 • Collected between October 2012 and January 2013 • U.S. adults ≥18 years of age • N = 3,630, 29.8% 18–34 years of age	• Compared to smoking cigarettes, would you say that electronic cigarettes are: – Much less harmful – Less harmful – Just as harmful – More harmful – Much more harmful – I've never heard of electronic cigarettes	• Compared with younger respondents (18–34 years of age), older respondents had 38%–72% lower odds of believing that e-cigarettes are less harmful than regular cigarettes	—
Tucker et al. (2014)	• Cross-sectional • Paper-based survey • Probability-based sampling • Year sample drawn: not reported • Youth: n/a • Young adults: homeless young adults, 17–25 years of age; N = 292 (subset of lifetime e-cigarette users, n = 83)	• Rate whether they perceive e-cigarettes to be less harmful, more harmful, or just as harmful as smoking cigarettes	• 44.9% viewed e-cigarettes as less harmful than conventional cigarettes • 26.6% viewed e-cigarettes as just as harmful as conventional cigarettes • 3.7% viewed e-cigarettes as more harmful than conventional cigarettes • 24.8% did not know the relative harm	• Did not collect information on youth's attitudes about alternate tobacco products besides e-cigarettes • Did not collect information on the conditions under which they used various products
Amrock et al. (2015)	• NYTS • Cross-sectional • School-based survey • Three-stage cluster sampling • Year sample drawn: 2012 • Youth: U.S. middle and high school students (grades 6–12); N = 24,658 • Young adults: n/a	• Do you believe that electronic cigarettes or e-cigarettes, such as Ruyan or NJOY, are less harmful, equally harmful, or more harmful than regular cigarettes?	• 34.2% (CI, 32.8–35.6%) of adolescents considered e-cigarettes to be less harmful than cigarettes • Females were less likely than males to perceive e-cigarettes as less harmful than cigarettes • Lifetime e-cigarette users were more likely than never users to report e-cigarettes as less harmful than cigarettes (71.8% vs. 31%) • Past-30-day e-cigarette users were more likely than nonrecent users to report e-cigarettes as less harmful than cigarettes (73.8% vs. 33.1%)	• Missingness • Perceived graduated risk • Self-reported items • Social desirability bias • Generalizability

Table 2.11 Continued

Study	Design/population	Measures	Outcomes/findings	Comments
Berg et al. (2015)	• Cross-sectional • Online-based survey • Recruitment by random selection • Year sample drawn: 2013 • Youth: n/a • Young adults: U.S. university students; n = 2,002	• How harmful to your health do you think electronic cigarettes are? • How addictive do you think electronic cigarettes are? • How socially acceptable among your peers do you think electronic cigarettes are?	• Respondents considered e-cigarettes among the least harmful (4.26 ±1.95), addictive (4.29 ± 2.08), and socially acceptable (4.12 ± 2.03) of the products considered • Electronic cigarettes were among the most positively perceived products (11.56 ± 4.22) • Predictors of more favorable perceptions included: – Being male (p = 0.03) – Parental tobacco smoking (p = 0.02) – More friends who smoke cigarettes (p <0.001) – More friends who use hookah (p <0.001) – More friends who use electronic cigarettes (p = 0.04) • Recent cigarette smoking (p <0.001).	• Generalizability • Responder bias • Cross-sectional analysis
Camenga et al. (2015)	• Focus groups • Purposive sampling • Years sample drawn: 2012–2013 • Youth: middle and high school students in Connecticut; n = 68 • Young adults: college students in Connecticut; n = 59	• Discuss the comparison between e-cigarettes and cigarettes.	• Compared with nonsmokers, college and high school smokers were more likely to believe the use of e-cigarettes could lead to a persistent “craving” that would prevent successful smoking cessation • Compared with nonsmokers, college and high school smokers were more likely to believe that e-cigarette use would maintain nicotine addiction	• Transferability • Generalizability • Limited definition of e-cigarettes

Table 2.11 Continued

Study	Design/population	Measures	Outcomes/findings	Comments
Cardenas et al. (2015)	• Cross-sectional • School-based survey • Three-stage cluster sampling • Year sample drawn: 2012 • Youth: U.S. middle and high school students; full sample size not reported; subsample of children who never tried smoking cigarettes, n = 14,861 • Young adults: n/a	• Do you believe that electronic cigarettes or e-cigarettes, such as Ruyan or NJOY, are less harmful, equally harmful, or more harmful than regular cigarettes?	• Participants who lived with a smoker were more likely to report e-cigarettes are less harmful than regular cigarettes (16.2% vs. 24.8%) • E-cigarette users were more likely to believe e-cigarettes are less harmful than regular cigarettes (70.9% vs. 27.5%)	• No limitations reported
Chaffee et al. (2015)	• Cross-sectional • Year sample drawn: 2014 • Youth: male high school students from San Francisco; n = 104	• Participants were asked to estimate the probability (0–100%) that specific health or social outcomes would happen to them as a result of e-cigarette use (e.g., heart attack, lung cancer, get into trouble, upset family, etc.)	• Ever use of electronic cigarettes was associated with lower perceived probabilities that unfavorable outcomes would happen	—
Lotrean (2015)	• Cross-sectional • 2013 • Students 19–24 years of age from Cluj-Napoca, Romania; n = 480	• Belief that e-cigarettes are less dangerous than cigarettes: agree, partially agree, disagree, partially disagree, don't know	• 55.9% of the total sample agreed or partially agreed that e-cigarettes are less dangerous, 35.8% did not know, and 8.3% disagreed or partially disagreed • More smokers than nonsmokers or ex-smokers agreed or partially agreed that e-cigarettes are less dangerous (62.3% vs. 58.7% and 33.3%, respectively)	• Very small sample • Measures not clearly defined

Table 2.11 Continued

Study	Design/population	Measures	Outcomes/findings	Comments
McDonald and Ling (2015)	• Focus groups and semistructured interviews • Recruitment from bars through screener surveys • Years sample drawn: 2012–2013 • Youth: n/a • Young adults: young adults in the boroughs of Manhattan, Brooklyn, and Queens in New York City, 18–27 years of age; N = 87	• Perceived risks	• Little knowledge of the devices • Belief that e-cigarettes contain harmless “water vapor” rather than smoke • Belief that “water vapor” is less harmful or even “good” for users	• No limitations reported
Roditis and Halpern-Felsher (2015)	• Focus groups • Recruitment from after-school programs in urban Northern California • 2–6 participants in each group • 24 adolescents: 9 female, 15 male	• Perceived risks and benefits associated with conventional cigarettes versus e-cigarettes	• Little knowledge of risks of e-cigarette use • Belief that e-cigarettes have no nicotine	—
Cooper et al. (2016)	• Cross-sectional • Drawn from 2014 Texas Youth Tobacco Survey, a school-based survey • Youth: students in grades 6–12 from 27 counties in Texas; N = 13,602	• “How dangerous do you think it is for a person your age to use electronic cigarettes?”	• Those in the e-cigarette-only group viewed conventional cigarettes as more harmful than did those in the dual user group • No differences in how harmful those in the e-cigarette-only group and the dual user group rated e-cigarettes • Those in the cigarette-only group rated e-cigarettes as more harmful than did those in the dual user group	—

Note: Studies in this table are sorted by year of publication and then alphabetically. **AOR** = adjusted odds ratio; **CI** = confidence interval; **NYTS** = National Youth Tobacco Survey.

Table 2.12a Percentage of middle school and high school students who reported that using e-cigarettes on some days but not every day caused no harm, little/some harm, or a lot of harm[a], by e-cigarette smoking status; National Youth Tobacco Survey (NYTS) 2015

	No harm		Little/some harm		A lot of harm	
Characteristic	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**
Overall	2,511	14.5 (13.4–15.8)	10,471	61.9 (60.3–63.5)	4,070	23.6 (22.2–25.0)
E-cigarette use						
Never[b]	1,200	9.5 (8.4–10.8)	7,528	61.0 (59.4–62.6)	3,653	29.4 (28.0–30.9)
Ever, but not past 30 days[c]	601	22.4 (20.3–24.6)	1,748	69.3 (66.4–72.1)	249	8.3 (7.0–9.9)
Past 30 days[d]	641	34.2 (31.2–37.3)	1,089	59.0 (55.9–62.0)	126	6.8 (5.4–8.7)

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015).
Notes: **CI** = confidence interval. There were 325 youth excluded due to missing responses for e-cigarette use.
[a]Includes responses to the question, "*How much do you think people harm themselves when they use e-cigarettes some days but not every day?*" Responses for "little harm" and "some harm" were combined.
[b]Includes those who reported never trying e-cigarettes.
[c]Includes those who reported trying e-cigarettes but not using e-cigarettes on 1 or more days in the past 30 days.
[d]Includes those who reported using e-cigarettes on 1 or more days in the past 30 days.

Table 2.12b Percentage of middle school students who reported that using e-cigarettes on some days but not every day caused no harm, little/some harm, or a lot of harm[a], by e-cigarette smoking status; National Youth Tobacco Survey (NYTS) 2015

	No harm		Little/some harm		A lot of harm	
Characteristic	**n**	**% (95% CI)**	**n**	**% (95% CI)**	**n**	**% (95% CI)**
Overall	1,089	13.5 (11.9–15.4)	4,579	57.6 (56.1–59.2)	2,260	28.8 (27.1–30.6)
E-cigarette use						
Never[b]	658	9.9 (8.3–11.6)	3,927	58.0 (56.5–59.4)	2,141	32.2 (30.5–33.9)
Ever, but not past 30 days[c]	211	31.9 (27.7–36.3)	383	60.6 (55.7–65.4)	60	7.5 (5.4–10.4)
Past 30 days[d]	193	41.5 (35.6–47.6)	220	50.0 (44.3–55.7)	38	8.5 (6.0–12.0)

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015).
Notes: **CI** = confidence interval. There were 132 middle students excluded due to missing responses for e-cigarette use.
[a]Includes responses to the question, *"How much do you think people harm themselves when they use e-cigarettes some days but not every day?"* Responses for "little harm" and "some harm" were combined.
[b]Includes those who reported never trying e-cigarettes.
[c]Includes those who reported trying e-cigarettes but not using e-cigarettes on 1 or more days in the past 30 days.
[d]Includes those who reported using e-cigarettes, on 1 or more days in the past 30 days.

Table 2.12c Percentage of high school students who reported that using e-cigarettes on some days but not every day caused no harm, little/some harm, or a lot of harm[a], by e-cigarette smoking status; National Youth Tobacco Survey (NYTS) 2015

	No harm		Little/some harm		A lot of harm	
Characteristic	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Overall	1,422	15.3 (14.0–16.7)	5,892	65.3 (63.2–67.3)	1,810	19.4 (18.0–20.9)
E-cigarette use						
Never[b]	542	9.2 (7.8–10.9)	3,601	64.3 (62.0–66.7)	1,512	26.4 (24.6–28.3)
Ever, but not past 30 days[c]	390	19.5 (17.5–21.8)	1,365	71.9 (68.6–74.9)	189	8.6 (6.9–10.6)
Past 30 days[d]	448	32.3 (28.8–35.9)	869	61.3 (57.8–64.8)	88	6.4 (4.8–8.4)

Source: Centers for Disease Control and Prevention, unpublished data (data: NYTS 2015).

Notes: **CI** = confidence interval. There were 166 high school students excluded due to missing responses for e-cigarette use.

[a]Includes responses to the question, *"How much do you think people harm themselves when they use e-cigarettes some days but not every day?"* Responses for "little harm" and "some harm" were combined.

[b]Includes those who reported never trying e-cigarettes.

[c]Includes those who reported trying e-cigarettes but not using electronic cigarettes on 1 or more days in the past 30 days.

[d]Includes those who reported using e-cigarettes, on 1 or more days in the past 30 days.

Table 2.12d Percentage of young adults (18–24 years of age) who reported that e-cigarettes were not at all harmful, moderately harmful, or very harmful[a], by e-cigarette smoking status; National Adult Tobacco Study (NATS) 2013–2014

	Not at all harmful		Moderately harmful		Very harmful	
Characteristic	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)
Overall	796	19.4 (17.9–20.9)	2,260	53.8 (51.9–55.7)	1,053	26.8 (25.1–28.6)
E-cigarette use						
Never[b]	359	14.3 (12.7–16.2)	1,423	52.8 (50.4–55.2)	814	32.9 (30.6–35.2)
Ever, but not current[c]	210	22.9 (19.7–26.4)	520	56.8 (52.7–60.8)	186	20.3 (17.2–23.8)
Current[d]	227	36.4 (31.8–41.2)	317	53.6 (48.6–58.5)	53	10.0 (7.2–13.9)

Source: Centers for Disease Control and Prevention, unpublished data (data: NATS 2013–2014).

Notes: **CI** = confidence interval. There were three young adults who were excluded because of missing responses for both ECIGEVER and ECIGNOW.

[a]Includes responses to the question, "*How harmful do you think using e-cigarettes are to a person's health*?"

[b]Includes those who reported having never tried e-cigarettes or having never heard of them.

[c]Includes those who reported having heard of e-cigarettes and tried e-cigarettes but reported using them "not at all" at the time of the interview.

[d]Includes those who reported having heard of e-cigarettes, tried e-cigarettes, and using e-cigarettes some days, every day, or rarely at the time of the interview.

e-cigarettes (22%) (Sutfin et al. 2013). Just over half of the participants in this study who had never tried e-cigarettes, however, said that they did not know enough to judge the relative harm of e-cigarettes compared to conventional cigarettes. In this study and another study, lack of knowledge about the perceived harm of e-cigarettes relative to conventional cigarettes was associated with lower odds of using e-cigarettes (Sutfin et al. 2013; Choi and Forster 2014b). In the study by Choi and Forster (2014b), lower perceived harm of e-cigarettes and the belief at baseline that e-cigarettes can help people quit smoking were both associated at follow-up with a higher likelihood of having tried e-cigarettes.

Reasons for Use and Discontinuation

Reasons for Use

Table 2.13 summarizes studies of reasons for using and discontinuing e-cigarettes. The most commonly cited reasons for use by adolescent and young adult e-cigarette users included curiosity (Schmidt et al. 2014; Biener and Hargraves 2015; Biener et al. 2015; Kong et al. 2015; McDonald and Ling 2015; Suris et al. 2015; Sutfin et al. 2015), flavorings/taste (Ambrose et al. 2015; University of Michigan 2015), use as a less harmful/less toxic alternative to conventional cigarettes (Peters et al. 2013; Tucker et al. 2014; Ambrose et al. 2015; Kong et al. 2015; McDonald and Ling 2015; Sutfin et al. 2015), and avoidance of indoor smoking restrictions or disturbing people with secondhand smoke from conventional cigarettes (Tucker et al. 2014; Ambrose et al. 2015; Kong et al. 2015; McDonald and Ling 2015; Suris et al. 2015; Sutfin et al. 2015). Other reasons youth and young adults reported trying or using e-cigarettes included affordability and lower cost than conventional cigarettes (Tucker et al. 2014; Ambrose et al. 2015); accessibility and convenience (Choi et al. 2012; Kong et al. 2015); social approval and/or offer from a family member or friend (Peters et al. 2013; Kong et al. 2015; Suris et al. 2015; Sutfin et al. 2015); perception that e-cigarettes are “cool,” “modern,” or “high-tech” (Choi et al. 2012; Kong et al. 2015); avoidance of smelling cigarette smoke (Peters et al. 2013; Tucker et al. 2014; Ambrose et al. 2015; Kong et al. 2015; Sutfin et al. 2015); ease of keeping hidden from parents/teachers (Peters et al. 2013; Kong et al. 2015); and weight control (Tucker et al. 2014). Young adults also perceived that e-cigarettes were more socially acceptable than smoking conventional cigarettes in public (Trumbo and Harper 2013).

Some youth and young adults also reported using e-cigarettes as an aid to reducing and/or quitting their use of conventional cigarettes (Li et al. 2013; Schmidt et al. 2014; Tucker et al. 2014; Suris et al. 2015; Sutfin et al. 2015; Bold et al. 2016). Data from the 2012 NYTS, however, suggest that while e-cigarette use among U.S. youth may be associated with intentions to smoke conventional cigarettes, it is not associated with intentions to quit conventional cigarette smoking (Park et al. 2016). This is further reinforced by a study of young adults from Switzerland, which found that after 15 months of follow-up, e-cigarette use was not associated with either cessation or reduction in the use of conventional cigarettes (Gmel et al. 2016). There is some evidence to suggest that curiosity was a stronger driver of an e-cigarette trial among young adults than smoking cessation, and that smoking cessation was a stronger driver of such a trial among older adults (Schmidt et al. 2014). Other evidence suggests that reasons for use were driven by tobacco-use status, with regular adolescent e-cigarette users much more likely than adolescents who had used e-cigarettes just once to give the reason for use as smoking cessation, smoking reduction, or avoidance of smoke-free air regulations (Suris et al. 2015). Nationwide, according to the 2015 MTF (University of Michigan 2015), “because they tasted good” was cited as a reason to use e-cigarettes among 40% of 8th-, 10th-, and 12th-grade users, versus just 10% who reported they used them in an attempt to quit smoking conventional cigarettes. In a New Zealand study, interest in using e-cigarettes to quit using conventional cigarettes was higher among young adults than older adults (Li et al. 2013). Finally, another study, this one conducted among high school, middle school, and college students in Connecticut in 2012–2013, found that although the students were aware that e-cigarettes could be used to aid in smoking cessation, they thought that few smokers had successfully used e-cigarettes to quit smoking (Camenga et al. 2015). However, in an article published by this group (Bold et al. 2016), trying e-cigarettes to quit smoking was the most robust predictor of continued e-cigarette use 6 months later, using a multivariable model that included all reasons simultaneously, though this reason was only endorsed at baseline by 5.9% of youth. Low cost was the most robust predictor of more frequent use 6 months later, though only 10% of students endorsed this reason at baseline (Bold et al. 2016). Therefore, the reasons to experiment with e-cigarettes are likely different from the reasons to continue using them, over time.

No randomized controlled trials specific to the efficacy of using e-cigarettes for quitting conventional cigarette smoking for young adults have been conducted to date. Although use of e-cigarettes as a potential cessation device for conventional cigarette smoking among adults is important to examine (e.g., McRobbie et al. 2014; McNeill et al. 2015), none of this evidence is included here, as it does not directly discuss youth and young adults. Three observational studies specific to this issue, however, have been conducted among young adults to date. Data from

Table 2.13 Summary of studies on reasons for use and discontinuation of e-cigarettes among youth and young adults

Study	Design/population	Measures	Outcomes/findings
Adkison et al. (2013)	• Parallel prospective cohort • Telephone interview and web-based surveys • Probability sampling methods (random-digit dialing) • Years sample drawn: 2010–2011 (Wave 8), 2008–2009 (Wave 7; where available) • Youth: n/a • Young adults: current smokers, ≥18 years of age; N = 5,939 (Canada, n = 1,581; U.S., n = 1,520; United Kingdom, n = 1,325; Australia, n = 1,513)	• Four questions were asked regarding reasons for use (yes/no): 1. Electronic cigarettes may not be as bad as cigarettes for your health 2. Easier to cut down on the number of cigarettes you smoke 3. Can smoke in places where smoking conventional cigarettes is prohibited 4. Might help you quit	• Not explicitly reported for young adults
Choi et al. (2012)	• Focus groups • Recruitment by (1) online advertisements, (2) flyers on one 4-year and two 2-year college campuses, (3) announcements in student life newsletter at a 2-year college, and (4) recruitment booth on a 2-year college campus • Year sample drawn: 2010 • Youth: n/a • Young adults: Individuals in Minneapolis-St. Paul, MN, enrolled in or who had graduated from 4-year colleges, or those who were enrolled in or had graduated from 2-year colleges, or those who had not enrolled in postsecondary education; N = 66	• Potential as quit aids	• Ineffective as quit aids because: – Contain nicotine – Potential to be addicted to e-cigarettes – Eliminate social interaction aspect • Potential to help quit smoking because: – Potential for gradual reduction in nicotine

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Choi and Forster (2013)	• Population-based prospective cohort study • Interview • Cluster random sampling • Years sample drawn: 2010–2011 • Youth: n/a • Young adults: U.S. midwestern adults, 20–28 years of age; n = 2,624 (sample from Minnesota)	• Indicate your level of agreement: 1. E-cigarettes can help people quit smoking 2. E-cigarettes are less harmful than cigarettes 3. E-cigarettes are less addictive than cigarettes	• 44.5% agreed e-cigarettes can help quit smoking; associated with the following characteristics: – Not being non-Hispanic White (AOR = 0.60; CI, 0.44–0.84) – Enrolled/graduated from 2-year college (AOR = 1.47; CI, 1.09–1.98) – Current smoker (AOR = 1.35; CI, 1.05–1.73) – At least one close friend who smokes (AOR = 1.27; CI, 1.03–1.57) • 52.9% agreed e-cigarettes are less harmful than cigarettes; associated with the following characteristics: – Not being non-Hispanic White (AOR = 0.73; CI, 0.53–0.99) – Male (AOR = 1.39; CI, 1.15–1.67) – Current smoker (AOR = 1.42; CI, 1.11–1.83) • 26.4% agreed e-cigarettes are less addictive than cigarettes; associated with the following characteristics: – Current smoker (AOR = 1.51; CI, 1.15–1.99) – Former smoker (AOR = 1.64; CI, 1.19–2.25) – At least one close friend who smokes (AOR = 1.28; CI, 1.00–1.63)
Faletau et al. (2013)	• Qualitative exploratory • Structured focus groups and individual interviews • Recruited from two low socioeconomic primary schools in East and South Auckland, New Zealand • Year sample drawn: 2011 • Youth: Maori, Tongan, Samoan, Cook Island, and Niuean children, 6–10 years of age; N = 20 • Young adults: n/a	• Viewed tobacco cigarette and electronic cigarette videos	• Stops people from smoking • People won't die • Protects those around e-cigarette users from sickness

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Li et al. (2013)	• Cross-sectional • Telephone-based survey • Random-digit-dial sampling • Years sample drawn: 2011–2012 • Youth: n/a • Young adults: current smokers and recent quitters, ≥18 years of age, in New Zealand; N = 840	• Indicate your level of agreement: 1. E-cigarettes are safer to use than tobacco cigarettes (n = 317) 2. E-cigarettes can help people quit smoking tobacco (n = 313)	• OR = 1.81 (.78–4.18) among participants 18–24 years of age for perceived safety of e-cigarettes compared with participants ≥45 years of age • OR = 0.50 (0.21–1.17) among participants 18–24 years of age for perceived efficacy of e-cigarettes compared with participants ≥45 years of age
Pepper et al. (2013)	• Cross-sectional • Web-based survey • Recruited through parents who were members of an online panel assembled by random-digit dialing and address-based sampling. • Year sample drawn: 2011 • Youth: U.S. males, 11–17 years of age; N = 228 • Young adults: n/a	• If one of your best friends were to offer you an e-cigarette, would you try it? • If one of your best friends were to offer you a flavored e-cigarette (chocolate, mint, apple, etc.), would you try it?	• Overall, 18% were willing to try an e-cigarette if offered by a best friend: – 13% willing to try a plain e-cigarette – 5% willing to try flavored e-cigarettes or both kinds • Willingness to try e-cigarettes by age: – 11–13: 11% – 14–16: 15% – 17–19: 29% • OR = 3.26 (CI, 1.27–8.35) among those 17–19 years of age for willingness to try an e-cigarette, compared with those 11–13 years of age • Willingness to try e-cigarettes by smoking status: – Nonsmoker: 13% – Smoker: 74% • OR = 18.67 (6.22–55.98) among smokers for willingness to try an e-cigarette, compared with nonsmokers
Peters et al. (2013)	• Focus groups • Recruitment through large, diverse high school in southwestern United States • Year sample drawn: 2012 • Youth: U.S. teenage boys; N = 47 • Young adults: n/a	• Why do youth use electronic cigarettes? • What do your friends think about electronic cigarettes? • Why are electronic cigarettes so popular?	• Reported reasons for use among youth: – Expeditious consumption and concealment: 40% – High school approval: 26% – Healthier than cigarettes: 19% – Odorless: 15% • Reported perceptions of friends: – High school approval: 49% – Healthier than cigarettes: 36% – Safe high: 15% • Reported reasons for popularity: – Accessibility: 43% – Healthier than cigarettes: 30% – Aesthetics: 23% • Don't know: 4%

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Trumbo and Harper (2013)	• Cross-sectional • Web-based survey • Recruitment by offer of extra credit to students in a 100-level course • Year sample drawn: 2011 • Youth: n/a • Young adults: freshmen and sophomores in a 100-level mass media in society course; n = 244	• Indicate your level of agreement with relative advantage: 1. I think e-cigarettes are safer in terms of “secondhand” smoke compared to tobacco cigarettes 2. I think e-cigarettes are not as harmful to users as tobacco cigarettes • Indicate your level of agreement with compatibility: 1. I think e-cigarette users can easily make use of existing smoking areas 2. I believe using e-cigarettes would fit in well with the lifestyle of most smokers • Indicate your level of agreement with complexity: 1. I believe it will not be difficult for smokers to learn how to use e-cigarettes 2. Overall, e-cigarettes are no more complicated to use than ordinary tobacco cigarettes • Indicate your level of agreement with “trialability”: 1. I think it will be easy for people to purchase e-cigarettes 2. Smokers could easily give e-cigarettes a try to see if they like them better than tobacco	• Mean score (SD) of innovation items: 36.0 (4.7)
Zhu et al. (2013)	• Population • Online-based surveys • National probability sample • Year sample drawn: 2012 • Youth: n/a • Young adults: U.S. adults, >18 years of age; N = 10,041	• Why did you use e-cigarettes (yes/no)? 1. Safer than cigarettes 2. Cheaper than cigarettes 3. Easy to use when I can’t smoke 4. To try to quit smoking cigarettes 5. Just because	• Not explicitly reported for young adults

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Choi and Forster (2014b)	• Population-based prospective cohort study • Survey • Cluster random sampling • Years sample drawn: 2011–2012 • Youth: n/a • Young adults: participants in Minnesota Adolescent Community Cohort; n = 1,379	• Indicate your level of agreement with the following: 1. Using e-cigarettes can help people quit smoking 2. Using e-cigarettes is less harmful to health of the user than smoking cigarettes 3. E-cigarettes are less addictive than cigarettes	• 10% agreed that e-cigarettes can help people quit smoking; associated with e-cigarette experimentation at follow-up (AOR = 1.98; CI, 1.29–3.04) • 10.1% agreed that e-cigarettes are less harmful than cigarettes; associated with e-cigarette experimentation at follow-up (AOR = 2.34; CI, 1.49–3.69) • 9.3% agreed that e-cigarettes are less addictive than cigarettes
Czoli et al. (2014)	• Cross-sectional • Survey • Recruitment through online panel of commercial market research company • Year sample drawn: 2012 • Youth: Canadian youth recruited from online panel, 16–30 years of age; n = 1,188 • Young adults: Canadian young adults recruited from same online panel	• Indicate your agreement with the following reasons for trying e-cigarettes: 1. In places where you can't smoke cigarettes 2. For times when you don't want to smoke around others 3. To help you cut back on the amount you smoke 4. To help you while you are trying to quit smoking 5. As a long-term replacement for cigarettes 6. As a cheaper alternative to cigarettes	• Reasons for trying e-cigarettes among current cigarette smokers: – To help cut back on the amount they smoked (77.7%) – As a long-term replacement for cigarettes (77.8%) – For the times when they don't want to smoke around others (78.8%) – To help them while they are trying to quit smoking (80.4%) – As a cheaper alternative to cigarettes (80.7%) – In places where they can't smoke cigarettes (80.9%)
Li et al. (2014)	• Cross-sectional • Telephone-based survey • Recruitment by telephone-based omnibus survey and quitline client database • Year sample drawn: 2013 • Youth: n/a • Young adults: current smokers and recent quitters, ≥18 years of age, in New Zealand; N = 267	• Indicate your level of agreement: 1. Electronic cigarettes are for people who want to stop smoking completely 2. Electronic cigarettes are for people who want to cut down on their smoking 3. Electronic cigarettes are for people who want to still smoke in restricted public places such as inside a cafe, restaurant, or pub	• OR = 1.99 (CI, 0.99–3.97) among those 18–34 years of age for agreeing that "electronic cigarettes are for people who want to stop smoking completely," compared with individuals ≥35 years of age • OR = 0.72 (CI, 0.24–2.21) among those 18–34 years of age for agreeing that "electronic cigarettes are for people who want to cut down on their smoking," compared with individuals ≥35 years of age • OR = 0.93 (0.47–1.85) among those 18–34 years of age for agreeing that "electronic cigarettes are for people who want to still smoke in restricted public places such as inside a cafe, restaurant or pub," compared with individuals ≥35 years of age

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Schmidt et al. (2014)	• Cross-sectional • Telephone-based survey • Random-digit-dial sampling • Year sample drawn: 2013 • Youth: n/a • Young adults: noninstitutionalized adults in Montana; n = 5,000	• Select all of the reasons you initiated use of e-cigarettes: 1. To quit smoking cigarettes 2. To reduce cigarette consumption 3. To try something new (curiosity) 4. To not disturb other people with smoke 5. To smoke in a place where cigarette smoking is prohibited 6. To save money 7. E-cigarettes might be less harmful than cigarettes 8. E-cigarettes taste better 9. Other	• Among those 18–34 years of age, approximately 50% reported trying e-cigarettes to quit or reduce cigarette use • Among those 18–34 years of age, approximately 70% reported trying e-cigarettes to try something new (curiosity)
Tucker et al. (2014)	• Cross-sectional • Paper-based survey • Probability-based sampling • Year sample drawn: not reported • Youth: n/a • Young adults: homeless young adults, 17–25 years of age; N = 292 (subset of lifetime e-cigarette users, n = 83)	• 18-item measure of reasons for using e-cigarettes, rating each reason on a 4-point scale (1 = not at all true, 4 = very true)	• Most common reasons for use included: – Not having to go outside to smoke cigarettes (38%) – To deal with situations or places where they cannot smoke (36%) – To avoid bothering other people with tobacco smoke (31%) • Less common to report using e-cigarettes was to quit smoking (17–18%)
Ambrose et al. (2015)	• Cross-sectional • Wave 1 of PATH study • Household-based, nationally representative survey • Youth: 12–17 years of age; n = 13,651 • Young adults: n/a	• Past 30-day e-cigarette users were asked to report reasons for product use, including “it comes in flavors I like”	• 81.5% of past-30-day users cited “because they come in flavors I like” as a reason for using e-cigarettes • Other common reasons for use were “they might be less harmful to me than cigarettes” (79.1%); “they might be less harmful to people around me than cigarettes” (78.1%); and “I can smoke/use them at times when or in places where smoking cigarettes isn’t allowed” (58.9%)
Biener et al. (2015)	• Cross-sectional • Population-based mail survey • Dual-frame sample • Youth: n/a • Young adults: 18–25 years of age; n = 4,740	• Reasons for trying: curiosity, use by friends, health risks relative to cigarettes, absence of smell, for use where smoking is prohibited, and to quit or cut down on smoking • Reasons for stopping e-cigarette use: health concerns, negative reactions to taste and feeling sick, inferiority to other forms of tobacco, expense, lack of availability, and social disapproval	• Most common reason cited was curiosity, with never smokers more likely to cite this (77.3%) than former or current cigarette smokers (59% and 61%)

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Camenga et al. (2015)	• Focus groups • Purposive sampling • Years sample drawn: 2012–2013 • Youth: middle and high school students in Connecticut; n = 68 • Young adults: college students in Connecticut; n = 59	• Discuss your motivations to use e-cigarettes	• Maintain smoking actions while allowing individuals to use a "healthier" nicotine product • Maintain tactile sensations to help with conditioned-smoking cues • College students believed e-cigarettes to be healthier than cigarettes
Kong et al. (2015)	• Cross-sectional • Focus groups, schoolwide survey • Recruitment by flyers and active recruitment sessions • Years sample drawn: 2012–2013 • Youth: New Haven County, Connecticut, middle and high school students; focus group n = 127 (youth and young adults); survey n = 4,780 • Young adults: New Haven County, Connecticut, college students; focus group n = 127 (youth and young adults); survey n = 625	• Focus group: – Why do you think people your age would use e-cigarettes? • Survey: – Why did you try an e-cigarette? – If you tried an e-cigarette but stopped using it, why did you stop?	• Focus group responses: – Reasons for use: ○ Influence of family and friends ○ To be "cool" ○ Curiosity ○ Readily available ○ Flavors – Comparison to cigarettes: ○ Healthier ○ Less harsh ○ Cheaper ○ Smells better ○ More convenient ○ Can hide it ○ Use it indoors – Reasons for discontinuation: ○ Losing interest ○ Negative physical effects (e.g., light-headed) ○ Bad taste ○ High cost ○ Less satisfying than cigarettes • Survey responses: – Reasons for experimentation (among lifetime e-cigarette users): ○ Curiosity (54.4%) ○ Friends' influence (31.6%) – Reasons for discontinuation: ○ Uncool (16.3%) ○ Health risks (12.1%)

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Li et al. (2015)	• Cross-sectional • 2014 • Nationwide, in-home survey in New Zealand • Multistage, stratified, clustered, and random probability sampling method (oversampling of Maori and Pacific peoples) • Participants ≥15 years of age; n = 2,594: – Youth: 15–17 years of age, 3.8% of sample – Young adults: 18–24 years of age, 13.4% of sample	• Why did you try using an electronic cigarette? (Multiple responses allowed—wanted to quit smoking cigarettes completely/wanted to replace smoking cigarettes some of the time/wanted to smoke in places where cigarette smoking is not allowed/cheaper than tobacco cigarettes/safer than tobacco cigarettes/curiosity/recommendation/other)	• 57.1% of ever users cited curiosity as a reason for first trying, followed by 31.3% of ever users who cited wanting to quit smoking completely • Current e-cigarette users were more likely than noncurrent users to report wanting to quit smoking completely as a reason for using e-cigarettes
McDonald and Ling (2015)	• Focus groups and semistructured interviews • Recruitment from bars through screener surveys • Years sample drawn: 2012–2013 • Youth: n/a • Young adults: young adults in the boroughs of Manhattan, Brooklyn, and Queens in New York City, 18–27 years of age; N = 87	• Bodily sensations • Use in response to clean air laws	• Vapor described as “harsh” or “burning” • Discontinued use because believed it would cause one to smoke more • Discontinued use due to fear of nicotine hangover • Use to smoke in places where conventional smoking is not allowed
Pokhrel et al. (2015)	• Cross-sectional • Web-based survey • Recruitment by flyers across three college campuses • Year sample drawn: 2013 • Youth: n/a • Young adults: U.S. students from a 4-year university and two 2-year community colleges in Oahu, Hawaii; n = 307	• Fourteen items, scored on a scale of 1 (do not agree) to 7 (agree), address three main beliefs. E-cigarettes: – Are less harmful than cigarettes – Improve the health of current smokers – May be used to quit smoking	• Participants generally scored harm-reduction items higher • Among health benefit items, “e-cigarettes improve breathing and reduce coughing” received the highest average score: mean (SD) = 3.9 (1.6) • Among smoking-cessation items, “e-cigarettes are a good compromise for people trying to quit smoking” received the highest average score: mean (SD) = 4.6 (1.8) • Across all items, “e-cigarettes cut down on the harmful effects of secondhand smoke” was scored the highest: mean (SD) = 5.3 (1.7) • 69% of participants agreed with the above item

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Suris (2015)	• Cross-sectional • Data drawn from spring 2014 wave of *ado @ internet.ch*, a longitudinal study on Internet use • Representative sample of students in French-speaking part of Switzerland • Sample of 621 students included never e-cigarette users (n = 353), experimenters (n = 120), and users (n = 148); mean age = 16.2 years	• Reason for having used e-cigarettes? – Curiosity – To smoke where it is forbidden – To reduce smoking – To do like my friends – To quit smoking – Other	• Experimenters were significantly more likely to have used e-cigarettes for curiosity while users were more likely to use them where it is forbidden to smoke ($p<.01$)
Sutfin (2015)	• Longitudinal cohort study • Data from the Smokeless Tobacco Use in College Students Study • College students from North Carolina and Virginia • Reasons for e-cigarette use were evaluated at Wave 6 of the study, n = 271	• Why did you try e-cigarettes? (check all that apply): – "I was curious about the product" – "It might be better for my health than smoking cigarettes" – "My friends use e-cigarettes" – "I can use it in places where cigarette smoking is not allowed" – "To help me quit smoking" – "To cut down on smoking" – "It doesn't smell bad"	• The majority (91.6%) reported curiosity as a reason for trying e-cigarettes • More than 70% tried e-cigarettes because their friends used them • About 70% tried e-cigarettes because they believed them to be better for their health than cigarettes • Fifty percent cited, "It doesn't smell bad," and "I can use it where cigarette smoking is not allowed" • About 31% said that they used e-cigarettes to cut down on smoking • Twenty percent said that they tried e-cigarettes to help them quit smoking
University of Michigan (2015)	• Cross-sectional • Data from the Monitoring the Future Study • School-based, self-administered, paper-and-pencil questionnaire with cross-sectional and longitudinal components • Students from 8th, 10th, and 12th grades • Weighted sample of students responding to the "reasons for use of electronic vaporizer" question: 603 (8th grade), 846 (10th grade), and 1,449 (12th grade)	• "What have been the most important reasons for your using an electronic vaporizer, such as an e-cigarette?" – To help me quit regular cigarettes – Because regular cigarette use is not permitted – To experiment to see what it's like – To relax or relieve tension – To feel good or get high – Because it looks cool – To have a good time with my friends – Because of boredom—nothing else to do – Because it tastes good – Because I am "hooked"—I have to have it	• More than half of all students in 8th, 10th, and 12th grades reported that curiosity to see what they were like was a primary reason for use • Forty percent said that they used e-cigarettes because they tasted good • About 10% said they used them in an attempt to quit smoking regular cigarettes

Table 2.13 Continued

Study	Design/population	Measures	Outcomes/findings
Berg (2016)	• Cross-sectional • Recruitment through Facebook targeting of tobacco and marijuana users and nonusers • 2014 • Youth: n/a • Young adults: 18–34 years of age, living in the United States; N = 1,567	• Reasons for use: For what reasons do you/ might you use e-cigarettes? • Reasons for discontinued use: Why have you not used recently?	• Reasons for use among current e-cigarette users: – "They might be less harmful than cigarettes" (77%) – "They do not smell" (77%) – "They help people quit smoking" (66%) – "They cost less than other forms of tobacco" (62%) • Reasons for use among nonusers: – "They might be less harmful than cigarettes" (41%) – "They don't smell" (34%) • Reasons for discontinuation: – "Using other tobacco products instead" (43%) – "They are too expensive" (35%) – "I just don't think about it" (31%)
Bold (2016)	• Longitudinal • Youth: New Haven County, Connecticut, middle and high school students • 2013–2014 • 340 e-cigarette users at baseline	• Reasons for first trying e-cigarettes: – Curiosity – It is cool – Good flavors – Does not smell bad – Can hide it from adults – Low cost – My friends use it – My parents/family use it – Can use it anywhere – To quit smoking regular cigarettes – It is healthier than regular cigarettes	• In multivariable model, including all reasons simultaneously, trying e-cigarettes to quit smoking was the most robust predictor of current (i.e., past 30 days) e-cigarette use 6 months later; however, this reason was endorsed by very few youth (5.9%) • In multivariable model, including all reasons simultaneously, trying e-cigarettes because of low cost was the most robust predictor of more frequent e-cigarette use (i.e., more days/month) 6 months later; this reason was endorsed by few youth (10%)

Note: Studies in this table are sorted by year of publication and then alphabetically. **AOR** = adjusted odds ratio; **OR** = odds ratio; **PATH** = Population Assessment of Tobacco and Health Study; **SD** = standard deviation.

a population-based cohort study of U.S. young adults in the Midwest suggest that e-cigarettes are not effective as a technique for quitting the use of conventional cigarettes. In that study, 11% of cigarette smokers who had used e-cigarettes in the past 30 days at baseline quit smoking at the 1-year follow-up, compared with 17% of cigarette smokers who had never used e-cigarettes (OR = 0.93, p = 0.93) (Choi and Forster 2014a). Another cohort study of Swiss young adult men concluded that there were no beneficial effects of vaping for conventional cigarette smoking cessation or smoking reduction (Gmel et al. 2016). In this study, e-cigarette users reported lower cigarette smoking cessation rates at follow-up among those who were occasional cigarette smokers at baseline (OR = 0.43; 95% CI, 0.19–0.96). No differences between e-cigarette users and nonusers were noted among those who were daily cigarette smokers at baseline (OR = 0.42; 95% CI, 0.15–1.18). No differential changes between e-cigarette users and nonusers in the number of conventional cigarettes smoked per week were noted at follow-up, either (Gmel et al. 2016). In a study by Unger and colleagues (2016), which focused on Hispanic young adults in California, e-cigarette use at baseline (2014) was *not* associated with cessation of cigarette smoking (OR = 1.31; 95% CI, 0.73–2.36) or marijuana use (OR = 1.05; 95% CI, 0.54–2.01) at follow-up (2015), though e-cigarette use at baseline did increase the likelihood of transitioning from nonuser to user of cigarettes (OR = 3.32; 95% CI, 1.55–7.10) and marijuana (OR = 1.97; 95% CI, 1.01–3.86) (Unger et al. 2016). Additional research is required to determine any potential efficacy of e-cigarette use for conventional cigarette smoking cessation in young adults.

Reason for Discontinuation

In the small number of published studies on reasons for discontinuation of e-cigarette use in young users, adolescent and young adult smokers have cited lack of satisfaction and e-cigarettes' poor taste and cost (Kong et al. 2015) as reasons for discontinuing. Additional reasons have included negative physical effects (e.g., feeling lightheaded) (Kong et al. 2015) and loss of interest. In one study of young adults aged 18–35, former and never smokers of conventional cigarettes also cited the idea that e-cigarettes were "bad for their health" as a reason for discontinuation (Biener and Hargraves 2015; Biener et al. 2015).

Evidence Summary

The most recent estimates available show that 13.5% of middle school students (2015), 37.7% of high school students (2015), and 35.8% of young adults (2013–2014) had ever used an e-cigarette (Tables 2.1a, 2.1b, and 2.4a). The most recent data also show that past-30-day use of e-cigarettes is higher among high school students (16% in 2015) and young adults (13.6% in 2013–2014) than among middle school students (5.3% in 2015) and adults (25 years of age and older) (5.7% in 2013–2014) (Tables 2.1b, 2.4a, and 2.4b). Among youth and young adults, rates of ever and past-30-day use of e-cigarettes have increased greatly since the earliest e-cigarette surveillance efforts began in 2011. The increases among adults 25 years of age and older, by comparison, have been less steep. Among middle school and high school students, both ever use and past-30-day use of e-cigarettes more than tripled from 2011 to 2015 (NYTS 2011–2015; Figures 2.1 and 2.2) (CDC 2013a; Ambrose et al. 2014; Lippert 2015), and among young adults (18–24 years of age), the prevalence of ever use more than doubled from 2013 to 2014 (Styles 2013–2014; Figure 2.3).

Among youth, past-30-day exclusive use of e-cigarettes among 8th, 10th, and 12 graders (6.8%, 10.4%, and 10.4%, respectively) was more common than exclusive use of conventional cigarettes (1.4%, 2.2%, and 5.3% in those grades) or dual use of e-cigarettes and conventional cigarettes (2.4%, 3.5%, and 5.8% in those grades) (Table 2.5; Figure 2.4). However, among young adults 18–24 years of age, the patterns were different. In that group, exclusive use of conventional cigarettes surpassed exclusive use of e-cigarettes and use of both types of products (Figure 2.8). For example, in 2013–2014, 9.6% of young adults smoked conventional cigarettes exclusively, 6.1% were current users of e-cigarettes, and 7.5% currently used both. The use of e-cigarettes and other tobacco products, such as combustibles, appeared to co-vary among youth and young adults (Figures 2.6, 2.7, and 2.8). Although five longitudinal studies suggest that e-cigarette use is related to the onset of other tobacco product and marijuana use among youth and young adults (Leventhal et al. 2015; Primack et al. 2015; Barrington-Trimis et al. 2016; Unger et al. 2016; Wills et al. 2016), some studies had limitations in their ability to distinguish experimental smokers from regular smokers at follow-up (Leventhal et al. 2015; Primack et al. 2015; Barrington-Trimis et al. 2016; Wills et al. 2016). Therefore, more studies are needed to elucidate the nature of any true causal relationship between e-cigarette use and combustible tobacco products. Investigation of whether e-cigarette use is related to other types of substance abuse (e.g., marijuana, alcohol) might help distinguish the extent to which e-cigarette use may precede or follow other forms of substance use in the context of the common liability/vulnerability model (Vanyukov et al. 2012).

Although use of other tobacco products has been the strongest correlate of ever and past-30-day e-cigarette use among youth and young adults, sociodemographic characteristics have also been associated with the use of these products. Across both ever use and past-30-day use measures, e-cigarette use has been more common among high school than middle school students, a pattern similar to trends seen in other categories of tobacco products (CDC 2015c). Among middle school students in 2014 and 2015 (CDC 2016), ever e-cigarette use was highest for Hispanics (Table 2.1a); among high school students, ever use was highest among Hispanics and Whites (Table 2.1b). No differences between boys and girls were observed among middle school students in 2015 (Tables 2.1a, 2.1b). However, in 2015 male high school students were significantly more likely to report past-30-day use than their female counterparts (Table 2.2b) (CDC 2016). For young adults, ever and past-30-day use of e-cigarettes were significantly higher among males than females (Table 2.4a). Current e-cigarette use was significantly lower among Blacks than in other racial/ethnic groups (Table 2.4a). Ever and past-30-day e-cigarette use was also significantly lower among those with a college education. Continued research is warranted to monitor patterns of e-cigarette use across population groups by gender, age, race/ethnicity, and education, as well as by sociodemographic characteristics for which disparities in tobacco use have been noted. Availability of data on e-cigarette use among youth and young adults is currently limited, including geography (e.g., subnational data at the state or local levels), sexual orientation and gender identity (e.g., lesbian, gay, bisexual, transgender), and socioeconomic status (e.g., household income, poverty status) (CDC 2014a; Johnson et al. 2016).

Research on youth and young adults' e-cigarette-related knowledge, attitudes, and beliefs is still developing and remains relatively sparse. Perceived harm is the most developed area of research. Most youth and young adults believe e-cigarettes are "less harmful" than conventional cigarettes (Table 2.11). However, up to 50% of respondents in some of these studies felt they did not know enough about the potential dangers associated with e-cigarettes to answer questions about perceived harm (Ambrose et al. 2014; Amrock et al. 2015). Although relative harm compared with cigarettes is important to assess, equally important is determining young people's perception of the absolute harm from e-cigarettes. National data show that only 23.6% of middle and high school students combined believed that e-cigarettes cause "a lot of harm" (Table 2.12a), and only 26.8% of young adults believed e-cigarettes are "very harmful" (Table 2.12d). However, significant differences emerge in these perceptions of harm when examined by whether or not youth and young adults use e-cigarettes. Among both middle and high school students and young adults, perceptions of "no harm" were much more prevalent among those with prior experience with e-cigarettes (Tables 2.12b–2.12d). Current e-cigarette users were two to three times more likely to report that e-cigarettes convey "no harm" compared to never e-cigarette users, for both age groups (Tables 2.12a and 2.12d).

The most commonly cited reasons that youth and young adults reported using e-cigarettes included curiosity (Schmidt et al. 2014; Biener and Hargraves 2015; Biener et al. 2015; Kong et al. 2015; McDonald and Ling 2015; Suris et al. 2015; Sutfin et al. 2015), flavorings/taste (Ambrose et al. 2015; University of Michigan 2015), use as a less harmful/less toxic alternative to conventional cigarettes (Peters et al. 2013; Tucker et al. 2014; Ambrose et al. 2015; Kong et al. 2015; McDonald and Ling 2015; Sutfin et al. 2015), and avoidance of indoor smoking restrictions or disturbing people with secondhand smoke from conventional cigarettes (Tucker et al. 2014; Ambrose et al. 2015; Kong et al. 2015; McDonald and Ling 2015; Suris et al. 2015; Sutfin et al. 2015). Using e-cigarettes as an aid to conventional cigarette smoking reduction/cessation (Li et al. 2013; Schmidt et al. 2014; Tucker et al. 2014) was not a primary motivator among youth and young adults. Youth and young adult smokers cited lack of satisfaction, poor taste, and cost (Kong et al. 2015) as reasons for discontinuing e-cigarette use. Additional research is needed to examine how reasons for use, including the appeal of flavored e-cigarettes, are causally related to the onset and progression of e-cigarette use among youth and young adults. Data from the first wave of the PATH study suggest that flavors may play an important role in the initiation of e-cigarette use among youth (Ambrose et al. 2015), while data from the 2014 NYTS (Corey et al. 2015) and 2013–2014 NATS (Table 2.9) underscore that use of flavored e-cigarettes remains prevalent among youth and young adults who currently use e-cigarettes.

Conclusions

1. Among middle and high school students, both ever and past-30-day e-cigarette use have more than tripled since 2011. Among young adults 18–24 years of age, ever e-cigarette use more than doubled from 2013 to 2014 following a period of relative stability from 2011 to 2013.

2. The most recent data available show that the prevalence of past-30-day use of e-cigarettes is similar among high school students (16% in 2015, 13.4% in 2014) and young adults 18–24 years of age (13.6% in 2013–2014) compared to middle school students (5.3% in 2015, 3.9% in 2014) and adults 25 years of age and older (5.7% in 2013–2014).

3. Exclusive, past-30-day use of e-cigarettes among 8th-, 10th-, and 12th-grade students (6.8%, 10.4%, and 10.4%, respectively) exceeded exclusive, past-30-day use of conventional cigarettes in 2015 (1.4%, 2.2%, and 5.3%, respectively). In contrast—in 2013–2014 among young adults 18–24 years of age—exclusive, past-30-day use of conventional cigarettes (9.6%) exceeded exclusive, past-30-day use of e-cigarettes (6.1%). For both age groups, dual use of these products is common.

4. E-cigarette use is strongly associated with the use of other tobacco products among youth and young adults, particularly the use of combustible tobacco products. For example, in 2015, 58.8% of high school students who were current users of combustible tobacco products were also current users of e-cigarettes.

5. Among youth—older students, Hispanics, and Whites are more likely to use e-cigarettes than younger students and Blacks. Among young adults—males, Hispanics, Whites, and those with lower levels of education are more likely to use e-cigarettes than females, Blacks, and those with higher levels of education.

6. The most commonly cited reasons for using e-cigarettes among both youth and young adults are curiosity, flavoring/taste, and low perceived harm compared to other tobacco products. The use of e-cigarettes as an aid to quit conventional cigarettes is not reported as a primary reason for use among youth and young adults.

7. Flavored e-cigarette use among young adult current users (18–24 years of age) exceeds that of older adult current users (25 years of age and older). Moreover, among youth who have ever tried an e-cigarette, a majority used a flavored product the first time they tried an e-cigarette.

8. E-cigarette products can be used as a delivery system for cannabinoids and potentially for other illicit drugs. More specific surveillance measures are needed to assess the use of drugs other than nicotine in e-cigarettes.

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Chapter 3
Health Effects of E-Cigarette Use Among U.S. Youth and Young Adults

Introduction

This chapter focuses on the short-term and potential long-term health effects related to the incidence and continued use of electronic cigarettes (e-cigarettes) by youth and young adults. The sharp increase in the prevalence of e-cigarette use among youth and young adults, especially from 2011 to 2015 (Centers for Disease Control and Prevention [CDC] 2015, 2016), highlights the compelling need to learn more about this evolving class of products. This chapter highlights the scientific literature that addresses potential adverse health effects caused by direct exposure to aerosolized nicotine, flavorants, chemicals, and other particulates of e-cigarettes; secondhand exposure to e-cigarette aerosol; and exposure to the surface-deposited aerosol contaminants. Literature regarding harmful consequences of close contact with malfunctioning e-cigarette devices and ingestion of the nicotine-containing liquids (e-liquids) are also explored. This chapter examines available data on e-cigarettes and youth, reviews established human and animal data on harmful developmental effects of nicotine (prenatal and adolescent), and reviews data on e-cigarettes among adults when data on youth are not available. Of note, given the relatively recent emergence of e-cigarettes, data are not yet available that address the long-term health effects of use or exposure over several years compared with nonuse or exposure to air free from secondhand tobacco smoke and aerosol from e-cigarettes; thus, the discussion is limited in that regard.

Conclusions from Previous Surgeon General's Reports

This chapter comprehensively reviews a new and emerging body of scientific evidence related to the use of e-cigarettes by youth and young adults. The enormous knowledge base on tobacco smoking and human health is also relevant to this discussion. That literature, which has been accumulating for more than 50 years, provides incontrovertible evidence that smoking is a cause of disease in almost every organ of the body (U.S. Department of Health and Human Services [USDHHS] 2004, 2014). Laboratory research has characterized the components of tobacco smoke and probed the mechanisms by which these constituents cause addiction and injury to cells, tissues, organs, and the developing fetus.

The evidence on the harmful consequences of nicotine exposure in conventional cigarettes, including addiction, and other adverse effects, is particularly relevant to e-cigarettes. Nicotine doses from e-cigarettes vary tremendously depending on characteristics of the user (experience with smoking conventional cigarettes or e-cigarettes), technical aspects of the e-cigarette, and levels of nicotine in the e-liquid. Although studies of nicotine doses in youth and young adults are lacking, studies of adults have found delivery of nicotine from e-cigarettes in doses ranging from negligible to as large as (Lopez et al. 2016; Vansickel and Eissenberg 2013; Spindle et al. 2015; St. Helen et al. 2016) or larger than (Ramôa et al. 2016) conventional cigarettes. Similarly, passive exposure to secondhand nicotine from e-cigarettes is just as large (Flouris et al. 2013) or lower than (Czogala et al. 2014) conventional cigarettes.

The findings of scientific research on smoking and involuntary exposure to tobacco smoke have been reviewed thoroughly in the 32 reports on smoking and health produced by the Surgeon General to date (there is one report on smokeless tobacco) (Table 3.1). The landmark first report was published in 1964 (U.S. Department of Health, Education, and Welfare [USDHEW] 1964), and the 50th-anniversary report, released in January 2014, comprehensively covered multiple aspects of cigarette smoking and health and lengthened the list of diseases caused by smoking and involuntary exposure to tobacco smoke (USDHHS 2014). Other Surgeon General's reports that are particularly relevant to the present report include reports on the health consequences of smoking and involuntary exposure to tobacco smoke (USDHHS 2004, 2006), on the mechanisms by which smoking causes disease (USDHHS 2010), and on the health consequences of smoking on youth and young adults (USDHHS 1994, 2012). The Surgeon General's reports on smoking and health have provided powerful conclusions on the dangers of nicotine. The 1988 report, released by Surgeon General C. Everett Koop, was the first to characterize smoking as addictive, and it identified nicotine as "…the drug in tobacco that causes addiction" (Appendix 3.1)[1] (USDHHS 1988, p. 9).

[1]All appendixes and appendix tables that are cross-referenced in this chapter are available only online at http://www.surgeongeneral.gov/library/reports/

Table 3.1 Relevant conclusions from previous Surgeon General's reports on smoking and health

Report	Year	Conclusions
The Health Consequences of Smoking: Nicotine Addiction (USDHHS 1988, p. 9)	1988	**Major Conclusions** 1. Cigarettes and other forms of tobacco are addicting. 2. Nicotine is the drug in tobacco that causes addiction. 3. The pharmacologic and behavioral processes that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.
How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease (USDHHS 2010, p. 183)	2010	**Chapter 4. Nicotine Addiction: Past and Present** 1. Nicotine is the key chemical compound that causes and sustains the powerful addicting effects of commercial tobacco products. 2. The powerful addicting effects of commercial tobacco products are mediated by diverse actions of nicotine at multiple types of nicotinic receptors in the brain. 3. Evidence is suggestive that there may be psychosocial, biologic, and genetic determinants associated with different trajectories observed among population subgroups as they move from experimentation to heavy smoking. 4. Inherited genetic variation in genes such as *CYP2A6* contributes to the differing patterns of smoking behavior and smoking cessation. 5. Evidence is consistent that individual differences in smoking histories and severity of withdrawal symptoms are related to successful recovery from nicotine addiction.
Preventing Tobacco Use Among Youth and Young Adults (USDHHS 2012, pp. 8, 460)	2012	**Major Conclusions** 1. Cigarette smoking by youth and young adults has immediate adverse health consequences, including addiction, and accelerates the development of chronic diseases across the full life course. 2. Prevention efforts must focus on both adolescents and young adults because among adults who become daily smokers, nearly all first use of cigarettes occurs by 18 years of age (88%), with 99% of first use by 26 years of age. 3. Advertising and promotional activities by tobacco companies have been shown to cause the onset and continuation of smoking among adolescents and young adults. 4. After years of steady progress, declines in the use of tobacco by youth and young adults have slowed for cigarette smoking and stalled for smokeless tobacco use. 5. Coordinated, multicomponent interventions that combine mass media campaigns, price increases including those that result from tax increases, school-based policies and programs, and statewide or community-wide changes in smokefree policies and norms are effective in reducing the initiation, prevalence, and intensity of smoking among youth and young adults. **Chapter 4. Social, Environmental, Cognitive, and Genetic Influences on the Use of Tobacco Among Youth** 1. Given their developmental stage, adolescents and young adults are uniquely susceptible to social and environmental influences to use tobacco. 2. Socioeconomic factors and educational attainment influence the development of youth smoking behavior. The adolescents most likely to begin to use tobacco and progress to regular use are those who have lower academic achievement. 3. The evidence is sufficient to conclude that there is a causal relationship between peer group social influences and the initiation and maintenance of smoking behaviors during adolescence. 4. Affective processes play an important role in youth smoking behavior, with a strong association between youth smoking and negative affect. 5. The evidence is suggestive that tobacco use is a heritable trait, more so for regular use than for onset. The expression of genetic risk for smoking among young people may be moderated by small-group and larger social-environmental factors.

Table 3.1 Continued

Report	Year	Conclusions
The Health Consequences of Smoking—50 Years of Progress (USDHHS 2014, p. 126)	2014	**Chapter 5: Nicotine** 1. The evidence is sufficient to infer that at high-enough doses nicotine has acute toxicity. 2. The evidence is sufficient to infer that nicotine activates multiple biological pathways through which smoking increases risk for disease. 3. The evidence is sufficient to infer that nicotine exposure during fetal development, a critical window for brain development, has lasting adverse consequences for brain development. 4. The evidence is sufficient to infer that nicotine adversely affects maternal and fetal health during pregnancy, contributing to multiple adverse outcomes such as preterm delivery and stillbirth. 5. The evidence is suggestive that nicotine exposure during adolescence, a critical window for brain development, may have lasting adverse consequences for brain development. 6. The evidence is inadequate to infer the presence or absence of a causal relationship between exposure to nicotine and risk for cancer.

Note: **USDHHS** = U.S. Department of Health and Human Services.

Subsequent reports expanded on the conclusions in the 1988 report related to nicotine—reaffirming that nicotine causes addiction, describing nicotine's effects on key brain receptors (USDHHS 2010), and emphasizing that youth are more sensitive to nicotine than adults and can become dependent to nicotine much faster than adults (USDHHS 2012). This is of particular concern in the context of e-cigarettes because blood nicotine levels in e-cigarette users have been reported as being comparable to or higher than levels in smokers of conventional cigarettes (Lopez et al. 2016; Spindle et al. 2015), and serum cotinine (a nicotine metabolite) levels have been reported as being equal to that found in conventional cigarette users (Etter 2016; Marsot and Simon 2016). Because of their sensitivity to nicotine and subsequent addiction, about 3 out of 14 young smokers end up smoking into adulthood, even if they intend to quit after a few years; among youth who continue to smoke as adults, one-half will die prematurely from smoking (Peto et al. 1994; CDC 1996; Hahn et al. 2002; Doll et al. 2004). Surgeon General's reports have also emphasized the critical role of environmental determinants of tobacco use, including the causal roles of the tobacco industry's advertising and promotional activities and of the peer social environment (USDHHS 2012).

The 2014 Surgeon General's report included a chapter that addressed the numerous adverse consequences of nicotine other than addiction (USDHHS 2014). The review documented the broad biological activity of nicotine, which can activate multiple biological pathways, and the adverse effects of nicotine exposure during pregnancy on fetal development and during adolescence on brain development. Of concern with regard to current trends in e-cigarette use among youth and young adults, the evidence suggests that exposure to nicotine during this period of life may have lasting deleterious consequences for brain development, including detrimental effects on cognition (USDHHS 2014).

Finally, the aerosol from e-cigarettes may include other components that have been addressed in previous Surgeon General's reports, such as tobacco-specific nitrosamines (TSNAs), acrolein, and formaldehyde (USDHEW 1979; USDHHS 2010). Aerosols generated with vaporizers contain up to 31 compounds, including nicotine, nicotyrine, formaldehyde, acetaldehyde glycidol, acrolein, acetol, and diacetyl (Sleiman et al. 2016). Glycidol is a probable carcinogen not previously identified in the vapor, and acrolein is a powerful irritant (Sleiman et al. 2016). Although these constituents have been identified in e-cigarette aerosol, current evidence is unclear on whether typical user dosages achieve levels as high as conventional cigarettes, or at harmful or potentially harmful levels. More information will be available in the coming years as e-cigarette manufacturers begin reporting harmful or potential harmful constituents in compliance with the Tobacco Control Act.

Health Effects of E-Cigarette Use

The potential adverse health effects for youth who inhale e-cigarette aerosol include those on the body from acute administration of nicotine, flavorants, chemicals, other particulates, and additional effects, such as (1) nicotine addiction; (2) developmental effects on the brain from nicotine exposure, which may have implications for cognition, attention, and mood; (3) e-cigarette influence initiating or supporting the use of conventional cigarettes and dual use of conventional cigarettes and e-cigarettes; (4) e-cigarette influence on subsequent illicit drug use; (5) e-cigarette effects on psychosocial health, particularly among youth with one or more comorbid mental health disorders; and (6) battery explosion and accidental overdose of nicotine.

Effects of Aerosol Inhalation by the E-Cigarette User

Determining the potential health effects of inhaling e-cigarette aerosol is challenging due to the number of possible combinations of customizable options (Seidenberg et al. 2016), including battery power, nicotine concentration, e-liquids (Goniewicz et al. 2015; Buettner-Schmidt et al. 2016), and use behaviors and puff topography (Dawkins et al. 2016; Lopez et al. 2016). The amount of nicotine, flavorants, and other e-liquid constituents in e-cigarettes available for consumers to purchase varies widely, and the aerosolized constituents delivered vary by the type and voltage of the e-cigarette device being used (Cobb et al. 2015). Studies of commercial products have shown that e-liquids can contain as little as 0 milligrams/milliliter (mg/mL) to as much as 36.6 mg/mL of nicotine (Goniewicz et al. 2015); can be mislabeled (Peace et al. 2016); can vary by propylene glycol (PG)/vegetable glycerin (VG) ratio; and can contain one or more of several thousand available flavorants (Zhu et al. 2014b). Some liquids intended for use in e-cigarettes contain adulterants not named on ingredient lists (Varlet et al. 2015), and under at least some user conditions, the aerosolization process, which involves heating, produces additional toxicants that may present health risks (Talih et al. 2015). The sections that follow comprehensively cover the effects of inhaling aerosolized nicotine and then consider what is known about solvents (i.e., PG and VG, flavorants, and other chemicals) added to e-cigarettes, adulterants in e-liquids formed in the nicotine extraction process (e.g., *N*-nitrosonornicotine), and toxicants formed during the heating and aerosolization process (e.g., acrolein and formaldehyde) (Sleiman et al. 2016).

Dose and Effects of Inhaling Aerosolized Nicotine

Nicotine addiction via e-cigarette use is a primary public health concern due to the exponential growth in e-cigarette use among youth. The potential for widespread nicotine addiction among youth is high, as are the harmful consequences of nicotine on fetal development and the developing adolescent brain (USDHHS 2014). Nicotine, a psychomotor stimulant drug, is the primary psychoactive and addictive constituent in the smoke of conventional cigarettes and an important determinant in maintaining smoking dependence (e.g., USDHHS 2014). E-liquids typically contain nicotine, although in more widely variable concentrations than those found in conventional cigarettes (Trehy et al. 2011; Cameron et al. 2014; Cheng 2014; Goniewicz et al. 2015; Marsot and Simon 2016). The concentration of liquid nicotine is only one factor that influences the amount of aerosolized nicotine available for inhalation (Lopez et al. 2016); other factors include the power of the device being used (e.g., battery voltage, heater resistance) and user behavior (e.g., puff duration, interpuff interval) (Shihadeh and Eissenberg 2015; Talih et al. 2016; Etter 2016). The interplay of these factors may help to explain the variability in plasma nicotine concentration when adults use e-cigarettes under controlled conditions which can be higher (Ramôa et al. 2016), lower (Bullen et al. 2010; Vansickel et al. 2010, 2012; Farsalinos et al. 2014b; Nides et al. 2014; Oncken et al. 2015; Yan and D'Ruiz 2015), or similar to those obtained by smoking conventional cigarettes (Vansickel and Eissenberg 2013; Spindle et al. 2015; St. Helen et al. 2016; see Figure 3.1). Generalization across studies is difficult due to variations in devices, e-liquids, and e-cigarette use behavior within the study sample. As demonstrated in Figure 3.1, in studies where a variety of products were used under similar laboratory conditions (i.e., blood sampling before and immediately after a 10-puff episode), there was wide variability in nicotine delivery between devices, with "cigalike" products (cigarette-like products) delivering less nicotine than "tank" products (Farsalinos et al. 2014b; Yan and D'Ruiz 2015), and low-resistance, dual-coil "cartomizer" products having the capacity to deliver less or more nicotine than a conventional cigarette, depending on the concentration of liquid nicotine (Ramôa et al. 2016).

When the device type and liquid dose were held constant in a controlled session in one study, plasma nicotine concentrations (in this case in nanograms [ng]/mL) varied considerably across participants (0.8 to 8.5 ng/mL) (Nides et al. 2014). This variation was likely attributable to the manner in which the users puffed when using e-cigarettes, or that person's "puff topography," which includes the number of puffs, the intake volume and duration, the interpuff interval, and the flow rate (Zacny and Stitzer 1988; Blank et al. 2009).

Available data suggest that puff durations among adult cigarette smokers who are new e-cigarette users are comparable to those observed with conventional cigarettes (at least about 2 seconds [sec]) (Farsalinos et al. 2013b; Hua et al. 2013; Norton et al. 2014). However, puff durations during e-cigarette use among experienced e-cigarette users may be twice as long (~4 sec) (Farsalinos et al. 2013b; Hua et al. 2013; Spindle et al. 2015) as puff duration during conventional cigarette use. Puff duration is directly related to the nicotine content of the e-cigarette aerosol (i.e., the yield or dose) (Talih et al. 2016), suggesting that smokers of conventional cigarettes who switch to e-cigarettes may increase the duration of their puffs when using the new product in an attempt to extract more nicotine. Research also suggests that cigarette smokers may learn to alter other aspects of their puffing behavior when using an e-cigarette (Spindle et al. 2015). Relative to smokers of conventional cigarettes (Kleykamp et al. 2008), experienced e-cigarette users were found to have puff volumes that were significantly higher (101.4 mL vs. 51.3 mL) and puff flow rates that were significantly lower (24.2 mL/sec vs. 37.9 mL/sec) (Spindle et al. 2015). In a different study, adult cigarette smokers who had never used e-cigarettes but switched to e-cigarettes showed significantly increased puff durations and decreased puff flow rates within 1 week (Lee et al. 2015). Elsewhere, adult cigarette smokers given an e-cigarette appeared to show an enhanced ability to extract nicotine from their device after 4 weeks of use (Hajek et al. 2015). Thus, the health effects of aerosolized nicotine in e-cigarette users may depend on a variety of factors, including the e-liquid used, the user's behavior, and the user's experience with the product.

Aerosolized Nicotine and Cardiovascular Function

Smoking is a major cause of death from cardiovascular disease (USDHHS 2014), and exposure to nicotine has been identified as a potential initiating factor in the atherogenic process (Lee et al. 2011; Santanam et al. 2012; Benowitz and Burbank 2016). Acute administration of nicotine causes a variety of well-characterized, dose- and route-dependent effects in adults, including cardiovascular effects, such as increases in heart rate and blood pressure (BP) and greater cardiac output, leading to an increase in myocardial oxygen demand (Rosenberg et al. 1980; USDHHS 2014). Reports from cell biology and animal studies have established biologic plausibility between nicotine alone and negative cardiovascular effects (Hanna 2006; Santanam et al. 2012). These studies have shown that nicotine induces the production of various inflammatory mediators involved with atherosclerotic pathogenesis (Lau and Baldus 2006), and that at the cellular level, nicotine induces C-reactive protein (CRP) expression in macrophages that contribute pro-inflammatory and pro-atherosclerotic effects (Mao et al. 2012).

Long-term studies on the safety of nicotine-only exposure (e.g., as with using e-cigarettes rather than smoking conventional cigarettes) among youth have not been conducted, and little is known about the cardiovascular effects of e-cigarette use among adults. However, when e-cigarettes are accompanied by a measurable increase in plasma nicotine concentration, it increases heart rate (Vansickel et al. 2012; Vansickel and Eissenberg 2013; Nides et al. 2014; Yan and D'Ruiz 2015), and diastolic BP rises.

Given the paucity of long-term data on the impact of e-cigarette smoking in relation to cardiovascular disease, other nicotine products offer a useful analogy. A meta-analysis reported that replacing the consumption of conventional cigarettes with nicotine replacement therapy (NRT) reduces cardiovascular risk among former smokers without significant adverse consequences (compared with current smokers) (Greenland et al. 1998; Moore et al. 2009). However, most NRT use is temporary (<26 months), and the adverse consequences of longer term NRT therapy are unknown.

Elsewhere, investigators examined the relationship between the use of Swedish-type moist snuff (or "snus"), which contains high levels of nicotine and low levels of TSNAs, and the incidence of acute myocardial infarction among men with a mean age of 35 years who had never smoked cigarettes. The researchers, who pooled data from eight prospective cohort studies, found no support for any association between the use of snus and the development of acute myocardial infarction (Hansson et al. 2012), regardless of timing, intensity, duration, or period of use among the men who were followed for 4–29 years.

In summary, despite overwhelming epidemiologic evidence linking the use of conventional cigarettes with cardiovascular disease, the precise components of cigarette smoke responsible for this relationship and the mechanisms by which they exert their effects have not yet been fully explained (Hanna 2006). For e-cigarettes, biological data support a potential association with cardiovascular disease, and short-term use of these products is accompanied by a measurable increase in plasma nicotine concentrations in adults as well as increases in heart rate and blood pressure. Much more research is needed, but the limited data available suggest the typical cardiovascular effects exerted by nicotine are also exerted by e-cigarettes (Benowitz and Burbank 2016; Bhatnagar 2016).

Aerosolized Nicotine and Dependence

Although a great deal is known about self-administration of nicotine and the development of nicotine dependence among adults (USDHHS 2014) and youth (Colby et al. 2000; USDHHS 2012; O'Loughlin et al. 2014; Yuan et al. 2015), more research is needed on nicotine dependence in youth and young adults as a result of using e-cigarettes. Nicotine dependence, also referred to as nicotine addiction (USDHHS 2010) or tobacco use disorder (American Psychiatric Association [APA] 2013), is defined as a neurobiological adaptation to repeated drug exposure that is manifested behaviorally by highly controlled or compulsive use; psychoactive effects such as tolerance, physical dependence, and pleasant effect; and nicotine-reinforced behavior, including an inability to quit despite harmful effects, a desire to quit, and repeated cessation attempts (USDHHS 1988; APA 2013). In tobacco-dependent users of conventional cigarettes, a predictable consequence of short-term abstinence (e.g., for more than a few hours) is the onset of withdrawal symptoms indicated by self-reported behavioral, cognitive, and physiological symptoms and by clinical signs (USDHHS 2010). Subjective withdrawal symptoms are manifested by affective disturbance, including irritability and anger, anxiety, and depressed mood. The behavioral symptoms include restlessness, sleep disturbance, and increased appetite. Cognitive disturbances usually center on difficulty in concentrating (USDHHS 2010).

Early studies of conventional cigarette smokers using e-cigarettes reported poor nicotine delivery with little to no increase in blood nicotine levels after puffing (Eissenberg 2010; Vansickel et al. 2010). Later studies reported that the effect on serum cotinine levels among new e-cigarette users can be similar to that generated by conventional cigarettes (Flouris et al. 2013; Lopez et al. 2016). Studies examining this discrepancy found that e-cigarette users require longer puffs to deliver equivalent nicotine doses (Lee et al. 2015), and within a week, inexperienced e-cigarette users adjust their puffing patterns after switching (Hua et al. 2013b; Lee et al. 2015; Talih et al. 2015).

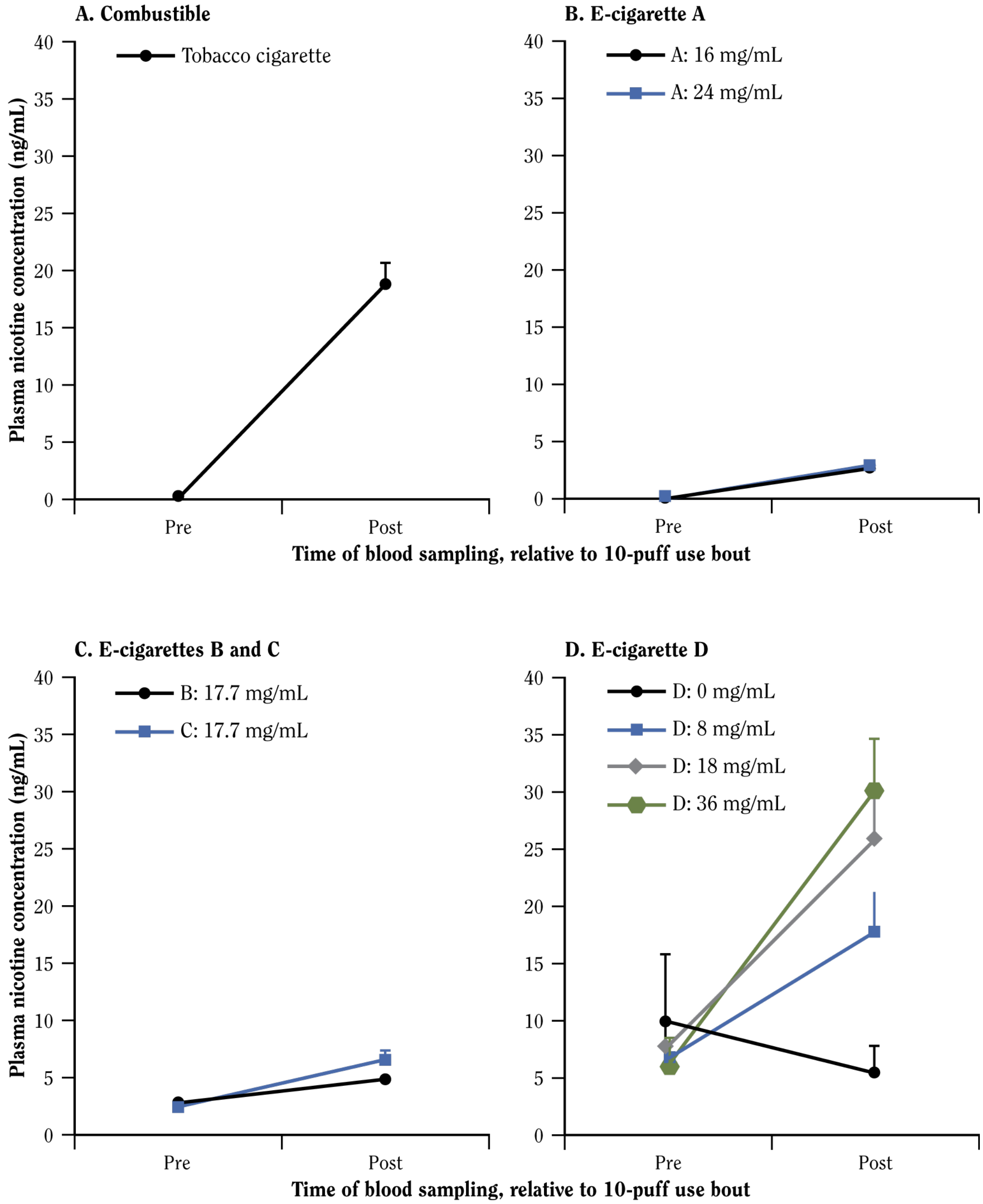
In more experienced e-cigarette users, blood nicotine levels appear to be influenced by puffing patterns, such as puff length. Volume and frequency and plasma nicotine levels ranging from 2.50 to 13.4 ng/mL have been observed after 10 puffs of an e-cigarette (Dawkins and Corcoran 2014). Dawkins and colleagues (2016) used 24 mg/mL nicotine strength liquid and observed high blood nicotine levels that were achieved very quickly, matching and even exceeding those reported in conventional cigarette smokers. St. Helen and colleagues (2016) conducted a similar study and reported that e-cigarettes can deliver levels of nicotine that are comparable to or higher than conventional cigarettes. Finally, Etter (2016) reported cotinine levels among experienced e-cigarette users similar to levels usually observed in conventional cigarette smokers. Figure 3.1 and Table A3.1-1 in Appendix 3.1 summarize studies on aerosolized nicotine from e-cigarettes and dependence using dependency criteria.

The ability of e-cigarettes to deliver comparable or higher amounts of nicotine compared to conventional cigarettes raises concerns about e-cigarette use generating nicotine dependence among young people (Dawkins et al. 2016; Etter 2016; St. Helen et al. 2016). The reported blood levels of nicotine, or cotinine, in e-cigarette users is likely to cause physiological changes in nicotinic acetylcholine receptors in the brain that would sustain nicotine addiction (Kandel and Kandel 2014; Yuan et al. 2015). This is particularly concerning for adolescents and young adults, given that early exposure to nicotine increases the severity of future nicotine dependence (St. Helen et al. 2016; USDHHS 2014).

Symptoms of nicotine dependence can occur soon after the initiation of conventional smoking, and even before established use, among adolescents and young adults (DiFranza et al. 2002; O'Loughlin et al. 2003; Dierker et al. 2007; Ramôa et al. 2016). Furthermore, some adolescents have reported nicotine dependence symptoms while using tobacco as little as 1–3 days per month (Rose et al. 2010). Using the National Comorbidity Survey-Adolescent dataset, Dierker and colleagues (2012) reported that nicotine dependence in adolescents was likely to occur within 1 year of the initiation of weekly or daily smoking, regardless of sociodemographic variables. Importantly, when smoking onset began at a younger age, the transition to weekly and daily smoking was more rapid, indicating a youthful neurobiological sensitivity to nicotine (Dierker et al. 2012). Zhan and colleagues (2012) found that symptoms of nicotine dependence could be detected among teenagers before they had smoked even 100 cigarettes.

Because few validated measures exist for assessing dependence on e-cigarette use, some researchers have adapted those originally developed to measure dependence in smokers of conventional cigarettes. Among adults, scores on these measures have been consistently lower in e-cigarette users than in smokers of conventional cigarettes (Farsalinos et al. 2013a; Etter and Eissenberg 2015; Foulds et al. 2015). Still, scores for e-cigarette dependence among former cigarette smokers were positively associated with the nicotine concentration of the e-cigarette liquid and the type of device used (Etter 2015; Etter and Eissenberg 2015; Foulds et al. 2015). Research in this area is challenging to interpret because measurement of youth e-cigarette dependence has not been standardized

Figure 3.1 Plasma nicotine concentration from different human laboratory studies and four different products with blood sampled before and immediately after a 10-puff bout with the products



Source: Vansickel et al. (2010); Farsalinos et al. (2014b); Yan and D'Ruiz (2015); and Ramôa et al. (2016).
Notes: Data for conventional cigarettes are from 32 tobacco cigarette smokers using their usual brand of cigarette (Vansickel et al. 2010). E-cigarette A is a cigalike called "blu" loaded with two different concentrations of liquid nicotine (16 or 24 mg/mL, both containing 20% propylene glycol and 50% vegetable glycerin). Data are from 23 smokers of tobacco cigarettes with 7 days of experience with the e-cigarette product (Yan and D'Ruiz 2015). E-cigarette B is a cigalike called "V2cigs", and E-cigarette C is a "tank" product called "EVIC" with an "Evod" heating element; both were loaded with an 18 mg/mL liquid containing 34% propylene glycol and 66% vegetable glycerin. Data are from 23 experienced users of e-cigarettes (Farsalinos et al. 2014b). E-cigarette D uses a 3.3-volt "Ego" battery fitted with a 1.5-Ohm dual coil cartomizer ("Smoktech") and filled with ~1 mL of a 70% propylene glycol, 30% vegetable glycerin liquid that varied by liquid nicotine concentration (0, 8, 18, or 36 mg/mL). Data are from 16 experienced users of e-cigarettes (Ramôa et al. 2016).

and there is a wide variation in device/e-liquid combinations, which allow for adjustable nicotine delivery among study participants. Regardless, among 766 adults, who were daily users of e-cigarettes (with nicotine) and who were either former cigarette smokers (83%) or current cigarette smokers (17%), 30.7% indicated that they would likely be unable to stop using e-cigarettes, 28.2% that they would find it "very difficult" or "impossible" to stop using e-cigarettes, and 27.5% that they were unable to stop e-cigarette use (Etter and Eissenberg 2015). However, it is important to note that e-cigarettes were less addictive than conventional cigarettes in this sample (Etter and Eissenberg 2015).

In summary, the addictive liability of e-cigarettes has the potential to be at least equivalent to that of conventional cigarettes, given nicotine dose levels produced by these products, particularly among experienced users operating new-generation devices (Ramôa et al. 2016). More generally, the delivery of nicotine in sufficient doses and blood concentration would be expected to produce and maintain dependence in e-cigarette users. Further work would be useful to determine the natural course and history of e-cigarette use among smokers of conventional cigarettes, former smokers, and never smokers and to more accurately determine the nicotine addiction liability of e-cigarette use. Unfortunately, these issues have not been explored in adolescents, although the prevalence of e-cigarette use has increased considerably in that population since 2011 (see Chapter 2).

Effects of Nicotine in Youth Users

Nicotine is the prime psychoactive substance in conventional cigarettes (Yuan et al. 2015), and given that the developing adolescent brain is immature and vulnerable to neurobiological insults (Bernheim et al. 2013; Lydon et al. 2014), it is important to understand how nicotine delivered by e-cigarette use affects adolescent brain development and how responses to nicotine in adolescents differ from those seen in adults. Substantial evidence suggests that nicotine can negatively influence both adolescent and prenatal brain development (USDHHS 2014). For example, Weiss and colleagues (2008) reported a strong mechanistic link among early nicotine exposure (younger than 16 years of age), common genes related to the severity of nicotine addiction (CHRNA5-A3-B4 haplotypes), and adult nicotine addiction in three independent populations of European origins. Although much of the literature on nicotine addiction arises from studies of nicotine exposure among adults, and with combustible tobacco products (see Table A3.1-2 in Appendix 3.1), there is a growing body of biological mechanistic literature from animal studies that model the effects of nicotine in doses equivalent to those for humans (see Table A3.1-3 in Appendix 3.1). These animal and human studies, taken together with studies of rising e-cigarette prevalence in youth (see Chapter 2), point to an age-dependent susceptibility to nicotine as a neurobiological insult.

Limited direct human experimental data exist on the effects of nicotine exposure from e-cigarettes on the developing adolescent brain, but experimental laboratory data have been found to be relevant in animal models to contextualize effects in humans (Stevens and Vaccarino 2015). Even if the full complexity of human brain development and behavioral function during adolescence cannot be completely modeled in other species, the similarities across adolescents of different species support the use of animal models of adolescence when examining neural and environmental contributors to adolescent-characteristic functioning (Spear 2010).

Animal studies provide an effective method to examine the persistent effects of prenatal, child, and adolescent nicotine exposure, in addition to human epidemiologic data. When considering an epidemiologic causal argument of exposure (risk factor) to health outcome (disease), one should note that animal models lend biological plausibility when experimentation with humans is not possible (or ethical) (Rothman et al. 2008). Furthermore, animal studies offer significant advantages compared to human studies—with the ability to control for many confounding factors, to limit nicotine exposure to differing levels of physical and neural development—and are pivotal for understanding the neural substrates associated with adolescence. The validity of any causal argument when examining animal models requires careful consideration, and yet in combination with epidemiologic data—such as prevalence, incidence, and strength of association between exposure and outcome—a causal argument can be constructed with literature from animal models representing biologic plausibility. Using a variety of study designs and research paradigms including humans and animals, research in this area provides evidence for neuroteratogenic and neurotoxic effects on the developing adolescent brain (Lydon et al. 2014; England et al. 2015).

The brain undergoes significant neurobiological development during adolescence and young adulthood, which are critical periods of sensitivity to neurobiological insults (such as nicotine) and experience-induced plasticity (Spear 2000; Dahl 2004; Gulley and Juraska 2013). Although maturation occurs in different regions of the brain at different rates, a similar progression occurs in all areas characterized by a rapid formation of synaptic connections in early childhood, followed by a loss of redundant or unnecessary synapses (called pruning) and the formation of myelin. Myelination is the process by which a fatty layer, called myelin, accumulates around nerve cells (neurons). Because of myelin, nerve cells can transmit information faster, allowing for more complex brain processes. Pruning allows for more focused concentration, and myelination allows for faster electrical and neural signaling; both allow for more efficient cognitive processing. During adolescence and into young adulthood, myelination occurs rapidly in the frontal lobe, a place in the brain that controls executive functioning, reasoning, decision-making skills, self-discipline, and impulse control. Plasticity refers to the current understanding that the brain continues to change throughout life, not only because of normal, maturational neural growth and development but also because of changes in environmental neurobiological exposures (such as nicotine), injuries, behaviors, thinking, and emotions (Mills and Tamnes 2014).

Across species, and in humans, adolescence is a key period of increased plasticity and rapid growth of brain circuits that regulate social, emotional, and motivational processes and decision making (Spear 2000, 2011; Nelson et al. 2005; Ernst and Fudge 2009; Counotte et al. 2011). The prefrontal cortex, which is involved in higher level regulatory control of complex behaviors (such as planning, impulse control, and working memory), continues normal structural and functional development into young adulthood, to about 25 years of age (Giedd and Rapoport 2010; Somerville and Casey 2010). Because of the immaturity and rapid growth of the prefrontal cortex, adolescents and young adults normally exhibit moody, risk-taking, and unpredictable impulsive behaviors. The combination of delayed maturation of frontal cognitive control and increased reactivity of subcortical reward-related and emotion-processing systems may lead to increased risk-taking behavior and a greater susceptibility to initiating substance use and the development of dependence (Steinberg 2008; Ernst and Fudge 2009; Counotte et al. 2011; Spear 2011). Thus, myelination is vitally important to the healthy functioning of the central nervous system, and any exposure that significantly interferes with the myelination process can cause mild-to-severe cognitive and learning problems (Brady et al. 2012).

Brain development in juvenile rodents has been reported to display patterns that resemble those of human beings, suggesting that the rodent model might be relevant to studying the neurobiological underpinnings of brain maturation in teenagers (Spear 2000). Studies across species have revealed unique characteristics of adolescent nonhuman brain structure, mechanisms, and function that provide biological plausibility to the hypothesis that human adolescents are particularly vulnerable to nicotine uptake (O'Loughlin et al. 2015; Yuan et al. 2015). There is evidence for rapid growth of gray matter, followed by activity-dependent synaptic pruning (the process of synapse elimination that occurs between early childhood and the onset of puberty) and increasing myelination throughout the brain (Casey et al. 2005; Lenroot and Giedd 2006; Giedd and Rapoport 2010; Counotte et al. 2011).

Nicotine has more significant and durable damaging effects on adolescent brains compared to adult brains, the former suffering more harmful effects. Preclinical animal studies have shown that in rodent models, nicotinic acetylcholine receptor (nAChR) signaling is still actively changing during adolescence, with higher expression and functional activity of nAChRs in the forebrain of adolescent rodents compared to their adult counterparts (Britton et al. 2007; Kota et al. 2007; Doura et al. 2008). Furthermore, in rodent models, nicotine actually enhances neuronal activity in several reward-related regions and does so more robustly in adolescents than in adults (Schochet et al. 2005; Shram et al. 2007; Dao et al. 2011). This increased sensitivity to nicotine in the reward pathways of adolescent rats is associated with enhanced behavioral responses, such as strengthening the stimulus-response reward for administration of nicotine. In conditioned place-preference tests—where reward is measured by the amount of time animals spend in an environment where they receive nicotine compared to an environment where nicotine is not administered—adolescent rodents have shown an increased sensitivity to the rewarding effects of nicotine at very low doses (0.03 mg/kg) (Vastola et al. 2002; Belluzzi et al. 2004; Brielmaier et al. 2007; Kota et al. 2007; Natarajan et al. 2011) and exhibited a unique vulnerability to oral self-administration during the early-adolescent period (Adriani et al. 2002). Adolescent rodents also have shown higher levels of nicotine self-administration than adults (Levin et al. 2003; Chen et al. 2007; Natividad et al. 2013), decreased sensitivity to the aversive effects of nicotine (Adriani et al. 2002; Shram et al. 2006; Torres et al. 2008), and less prominent withdrawal symptoms following chronic nicotine exposure (O'Dell et al. 2006). This characteristic in rodent models of increased positive and decreased negative short-term effects of nicotine during adolescence (versus adulthood) highlights the possibility that human adolescents might be particularly vulnerable to developing dependency to and continuing to use e-cigarettes. These biological mechanisms are of great public health importance as exposure to nicotine grows among nonsmoking youth through the increasing prevalence of e-cigarette use.

Beyond their unique vulnerability to nicotine use, and thus smoking uptake, human adolescents may be particularly vulnerable to the detrimental consequences of nicotine exposure, including an increase in drug-seeking behaviors (Kandel and Kandel 2014), deficits in attention and cognition, and mood disorders (Yuan et al. 2015). In animal models, chronic nicotine exposure during adolescence has been shown to produce long-lasting, unique effects that are not observed in mature adult animals. Moreover, animal models have provided substantial evidence that the limbic system—which controls cognition, emotion, and drug-reward—is actively maturing during adolescence and during this age is vulnerable to long-term modification by nicotine.

Reward-Seeking Behaviors. A very strong argument can be made about the association between adolescent exposure to nicotine by smoking conventional cigarettes and the subsequent onset of using other dependence-producing substances. Strong, temporal, and dose-dependent associations have been reported (Isensee et al. 2003; John et al. 2004b; Bronisch et al. 2008; Kandel and Kandel 2015), and a plausible biological mechanism (via rodent and human modeling) suggests that long-term changes in the neural reward system take place as a result of adolescent smoking (Lewinsohn et al. 1999; Huang et al. 2013; Kandel and Kandel 2014). Adolescent smokers of conventional cigarettes have disproportionately high rates of comorbid substance abuse (Kandel et al. 1992; Lai et al. 2000; Hanna et al. 2001), and longitudinal studies have suggested that early adolescent smoking may be a starting point or "gateway" for substance abuse later in life (Kandel et al. 1992; Lewinsohn et al. 1999; Wagner and Anthony 2002; Brook et al. 2007), with this effect more likely for persons with attention deficit hyperactivity disorder (ADHD) (Biederman et al. 2006; Wilens et al. 2008). Although factors such as genetic comorbidity, innate propensity for risk taking, and social influences may underlie these findings (Lindsay and Rainey 1997; Smith et al. 2015), both human neuroimaging and animal studies suggest a neurobiological mechanism also plays a role. In addition, behavioral studies in adolescent and young adult smokers have revealed an increased propensity for risk taking, both generally and in the presence of peers, and neuroimaging studies have shown altered frontal neural activation during a risk-taking task as compared with nonsmokers (Lejuez et al. 2005; Cavalca et al. 2013; Galvan et al. 2013). Rubinstein and colleagues (2011b) used neuroimaging to show decreased brain response to a natural reinforcer (pleasurable food cues) in adolescent light smokers (1–5 cigarettes per day), with their results highlighting the possibility of neural alterations consistent with nicotine dependence and altered brain response to reward even in adolescent low-level smokers.

Nicotine exposure in rodents at an age of physical development corresponding to human adolescence has been found to increase the reinforcing effects of other drugs of abuse, including cocaine, methamphetamine, and alcohol, without having a major impact on responding for other rewards, thus providing further evidence in support of nicotine as an initiation toward other substance use and abuse (McQuown et al. 2007; Dao et al. 2011; Dickson et al. 2014; Pipkin et al. 2014; Kandel and Kandel 2014). In several rodent studies, treatment with very low doses of nicotine for a few days during early adolescence, but not in late adolescence or adulthood, produced lasting changes in D2 and D3 dopamine receptors and in the self-administration of other abused drugs (McQuown et al. 2007; Dao et al. 2011; Mojica et al. 2014). Nicotine exposure in adolescent rats also induced rapid and long-lasting dendritic remodeling in the nucleus accumbens shell, a critical component of reward learning and addiction, via a D1 dopamine receptor-mediated mechanism (Ehlinger et al. 2016). This persistent form of nicotine-induced neuroplasticity has the potential to alter synaptic connectivity within reward-processing centers and enhance the addictive effects of drugs of abuse.

Attention and Cognition. Both cognitive improvements (Jasinska et al. 2014) and cognitive deficits (Hall et al. 2014) have been reported after nicotine exposure in healthy human adults, while smoking during adolescence impairs cognition and attention processes. Results of a genetically sensitive, longitudinal "concordant" and "discordant" twin study from the Netherlands Twin Registry indicated a larger increase in attention problems from adolescence to adulthood in twins who smoked than in their never-smoking co-twins (Treur et al. 2015). In another study, adolescent smokers were found to have chronic impairments in the accuracy of their working memory (e.g., in processing information from two sensory modalities simultaneously), which were more severe with an earlier age of onset of smoking (Jacobsen et al. 2005). Functional imaging studies have shown that 24-hour smoking abstinence in adolescent smokers causes acute impairments of verbal memory and working memory, along with chronic decrements in cognitive performance (Jacobsen et al. 2007a). In another study, adolescent users of conventional cigarettes showed decreased prefrontal cortex activation (versus never smokers) during attention tasks, and duration of smoking (in years) was directly correlated with the extent of reduction in prefrontal cortical activity (Musso et al. 2007).

Thus, longitudinal and imaging studies in humans provide support for the hypothesis that adolescent use of conventional cigarettes has both acute and long-term effects on attention and memory. Although nicotine exposure cannot be cited as the sole cause of cognitive defects (or even one of several combined effects in humans), other studies have shown that adolescent nicotine exposure in rats induces lasting synaptic changes in the prefrontal cortical regions critical for normal attention, memory, and cognition that likely underlie observed impairments in attentional and cognitive function (Bergstrom et al. 2008). Adolescent nicotine exposure in rats has induced impairments in stimulus-response-discrimination-learning processes but not in abstract rule-learning processes, which are dependent on dissociable cognitive systems, thus showing the selective effects of nicotine (Pickens et al. 2013). In addition, adolescent, but not postadolescent, treatment of rats with nicotine resulted in diminished attention span and enhanced impulsivity in adulthood (Counotte et al. 2009, 2011). The biological causes of these cognitive disturbances (reduced attention span and impulse control) were associated with reduced regulation of prefrontal cortex excitatory synapses function in metabotropic glutamate receptor 2 (mGluR2) (Counotte et al. 2011; Goriounova and Mansvelder 2012). In addition, hippocampal function, which is critical for memory, was altered in adult mice by nicotine exposure during adolescence. Contextual fear conditioning—a hippocampus-dependent task in which animals learn and remember to associate a fearful stimulus (e.g., a foot shock) with a particular context—was disrupted in adult mice that had been treated during adolescence with chronic nicotine but not following chronic treatment with nicotine in adulthood (Portugal et al. 2012). Rodent studies have implications for human adolescents, suggesting that exposure to tobacco during youth may lead to long-lasting changes in behavioral and neuronal plasticity into adulthood.

Mood Disorders. Adolescents with symptoms of mental health disorders (e.g., anxiety, aggressive and disruptive behaviors, mood disorders) are at increased risk for initiation of conventional cigarette use and long-term nicotine dependence compared with those without such disorders (Gehricke et al. 2007; Morris et al. 2011). Although this risk may reflect a common genetic predisposition, or the use of nicotine to self-medicate in the hope of improving mental health symptoms, the question arises of whether the smoking of conventional cigarettes by adolescents contributes to the development of mood disorders. A meta-analysis of existing studies showed consistent evidence that both tobacco use and dependence on tobacco products among adolescents indeed increased their risk of anxiety disorders (Moylan et al. 2012). Other studies have shown that an early onset of smoking is associated with a shorter time to first onset of an anxiety disorder (Jamal et al. 2011), and there is a positive association between adolescent smoking, particularly through a nicotine pathway, and anxiety in early adulthood (Moylan et al. 2013). Bidirectional relationships between adolescent smoking and disruptive disorders (e.g., ADHD; oppositional defiant disorder [ODD] [Griesler et al. 2011]) as well as depression (Tjora et al. 2014) also have been reported, while a longitudinal birth cohort found evidence to support a causal relationship between teen smoking and onset of depression (Boden et al. 2010). Although these findings are complex and warrant further study using comparisons of genetic polymorphisms associated with smoking or twin and sibling discordant/concordant studies (Munafo and Araya 2010; Leventhal and Zvolensky 2015), they do suggest that nicotine exposure during adolescence could contribute to long-term mental health disorders.

Findings of animal studies support the theory that adolescent nicotine exposure results in long-term alterations in emotional response, specifically enhanced anxiety and fear (Slawecki et al. 2003; Smith et al. 2006), and in persistent alterations in serotonin systems involved in mediating mood disorders by reprogramming the future response of 5-HT systems to nicotine (Slotkin and Seidler 2009). Even a single day of nicotine treatment in adolescent rats can enhance sensitivity to aversive stimuli later in life and result in a depression-like state in adulthood that is normalized by treatment with nicotine or antidepressants (Iniguez et al. 2009).

In summary, given the existing evidence from human and animal studies of the detrimental impact of nicotine exposure on adolescent brain development, the use of e-cigarettes by youth should be avoided and actively discouraged. Both preadolescence and adolescence are developmental periods associated with increased vulnerability to nicotine addiction, and exposure to nicotine during these periods may lead to long-lasting changes in behavioral and neuronal plasticity. Studies reveal that for most tobacco users, initial use begins before 18 years of age. Moreover, in some adolescents, symptoms of nicotine dependence can develop after exposure to very low levels of nicotine—less than 100 cigarettes. Cross-species studies have identified characteristics of the adolescent brain that may render it vulnerable at this age to nicotine uptake in the form of equivalent doses via nonsmoking administration mechanisms. In addition, animal models of nicotine exposure in adolescence reveal neural and behavioral alterations consistent with an increased likelihood of future nicotine use, increased activation of reward pathways and, unlike in adult animals, decreased aversive effects. Regarding e-cigarettes, data demonstrate adolescent use of these devices is associated with use of tobacco, alcohol, and other drugs (Dutra and Glantz 2014; Kristjansson et al. 2015; Wills et al. 2015a, b; Schneider and Diehl 2016). Finally, animal and human studies suggest a bidirectional relationship between the smoking of conventional cigarettes and exposure to nicotine during adolescence and factors related to disruptive disorders, such as ADHD and ODD that impair academic performance, as well as to depression. Because the adolescent brain is still developing, nicotine use during adolescence can disrupt the formation of brain circuits that control attention, learning, and susceptibility to addiction. Further research is warranted to more fully understand the effects of e-cigarette use on youth.

Nicotine Exposure from Maternal Nicotine Consumption: Prenatal and Postnatal Health Outcomes

Prenatal nicotine exposure through maternal cigarette use during pregnancy is one of the most widespread perinatal insults in the world (Levin and Slotkin 1998; Xiao et al. 2008; USDHHS 2014). Despite medical and societal sanctions and ongoing public health campaigns, the prevalence of maternal cigarette use during pregnancy in the United States was estimated to be 11–15% in 2013 (Tong et al. 2013). Smoking rates were even higher among women who were poor, young, or less educated, with rates as high as 25–30%, indicating that infants born to mothers who are poor have disproportionately higher exposure to nicotine (Dietz et al. 2011; Hamilton et al. 2012; Tong et al. 2013). Despite these adverse consequences, an estimated one-half of pregnant smokers continue to smoke into the third trimester (Osterman et al. 2013; Tong et al. 2013).

Because adults who use e-cigarettes can achieve plasma nicotine concentrations similar to those found among smokers of equivalent amounts of conventional cigarettes (Vansickel et al. 2010; Lopez et al. 2016; St. Helen et al. 2016), it is important that research continues in this area. Nicotine has been shown to cross the placenta and has been found in placental tissue as early as 7 weeks of embryonic gestation, and nicotine concentrations are higher in fetal fluids than in maternal fluids (Luck et al. 1985; Jauniaux et al. 1999). nAChRs are widely distributed in the fetal brain. As has been clearly demonstrated in animal models, acetylcholine acts on nAChRs to modulate functional connections during critical periods of development when regions are most sensitive to environmental input (Dwyer et al. 2008). When nicotine in the maternal bloodstream crosses the placental barrier, it binds to these receptors (Pentel et al. 2006; Wong et al. 2015), and in rodents this can result in long-term changes in neural structure and function. Results from animal studies show consistent associations between prenatal nicotine exposure and upregulation of nAChRs associated with disruption of fetal brain cell replication and differentiation (Slotkin 1998). Highlighting the role of nicotine in the effects of maternal smoking during pregnancy, nAChRs have been shown to be present in the human embryonic brain from 5 weeks of gestation (Hellstrom-Lindahl et al. 1998), and their normal maturation is altered in a region- and receptor subtype-dependent fashion by maternal cigarette smoking during pregnancy (Falk et al. 2005; Duncan et al. 2008). In those brainstem nuclei important for arousal, prenatal nicotine exposure decreases [^{3}H]-nicotine binding (Duncan et al. 2008) and prevents normal age-related increases in $\alpha4$ and $\alpha7$ mRNA (Falk et al. 2005).

Prenatal nicotine exposure also has been associated with dysregulation of catecholaminergic, serotonergic, and other neurotransmitter systems. In addition, animal work suggests significant adverse effects of nicotine alone at levels commensurate with exposure to secondhand smoke (10-fold below those seen in active smokers), and that the non-nicotine components of tobacco smoke can exacerbate nicotine's teratogenic effects (Slotkin et al. 2015). Offermann (2015) concluded that e-cigarettes emit many harmful chemicals into the air and that indirect exposure to nicotine exceeded exposure-level standards for noncarcinogenic health effects established by the California Environmental Protection Agency. No safe level of prenatal nicotine exposure has been established (England et al. 2015).

Airborne nicotine exposure through secondhand aerosol from e-cigarettes has been observed, as has salivary cotinine concentrations of nonsmokers in the homes of e-cigarette users (Ballbe et al. 2014; Czogala et al. 2014). Ballbe and colleagues (2014) reported the geometric means of airborne nicotine were 0.74 µg/m3 in the homes of smokers, 0.13 µg/m3 in the homes of e-cigarette users, and 0.02 µg/m3 in the homes of nonsmoking controls. While airborne nicotine exposure from combustible cigarette smoke was 5.7 (Ballbe et al. 2014) to 10 times higher (Czogala et al. 2014) than e-cigarette aerosol, one study reported only a twofold increase in salivary cotinine (0.38 ng/ml in the homes of smokers versus 0.19 ng/ml in the homes of e-cigarette users) (Ballbe et al. 2014), and another study found that exposure to cigarette smoke and exposure to e-cigarette aerosol had similar effects on the serum cotinine levels of bystanders (Flouris et al. 2013). Thus, the passive exposure to nicotine from e-cigarette smoking has been reported to be just as large (Flouris et al. 2013; Grana et al. 2013) or lower than (Czogala et al. 2014) conventional cigarettes, but exposure to nicotine from e-cigarette smoking is not negligible and is higher than in nonsmoking environments. This evidence suggests the importance of avoiding secondhand exposure of e-cigarette vapor and secondhand smoke during pregnancy (Flouris et al. 2013; Grana et al. 2013; Czogala et al. 2014).

Of the components of tobacco smoke, nicotine has been cited as the most important toxicant in terms of interfering with fetal development. Because of the health risks to the developing fetus associated with nicotine exposure during pregnancy, the U.S. Food and Drug Administration (FDA) (2015) recommends that pregnant women seek medical approval before using NRT, and the American College of Obstetricians and Gynecologists (2011) recommends consideration of NRT only if a woman fails behavioral interventions to quit smoking conventional cigarettes and has discussed the potential harms and benefits of NRT with her physician. NRT is most often used during pregnancy as a last resort to avoid exposing the fetus to the other toxic ingredients found in conventional tobacco smoke (Fiore et al. 2008). A Cochrane Database systematic review concluded that both the effectiveness and safety of NRT during pregnancy are unclear (Coleman et al. 2012). Table A3.1-4 in Appendix 3.1 presents a summary of studies in humans on the effects of tobacco exposure on fetal brain development.

Even with a firm understanding of the negative health consequences of nicotine on the developing fetus (Fiore et al. 2008; USDHHS 2014; Ekblad et al. 2015), little is known about the prevalence of e-cigarette use among pregnant women or the direct harmful effects on their fetus by other toxicants delivered by the aerosol from e-cigarettes (England et al. 2015; Suter et al. 2015). In one of the few studies identified, a survey of 316 pregnant women in a Maryland clinic found that the majority had heard of e-cigarettes, 13% had ever used them, and 0.6% were current daily users (Mark et al. 2015). These findings are of concern because the dose of nicotine delivered by e-cigarettes can be as high or higher than that delivered by conventional cigarettes. Therefore, plasma nicotine concentrations delivered while using e-cigarettes have the potential to harm the developing fetus. Furthermore, in 2013 in the United States, there were 26.5 births for every 1,000 adolescent females (15–19 years of age), or 273,105 babies born to females in this age group (Hamilton et al. 2013). Currently, the rate of e-cigarette use among pregnant adolescents is unknown, but the effects of nicotine and the potential for harm by other e-cigarette toxicants indicate that the use of e-cigarettes is a fetal risk factor among pregnant adolescent girls.

As outlined below, the specific effects of nicotine on prenatal development and postnatal outcomes include sudden infant death syndrome (SIDS) and may include altered development of the corpus callosum, deficits in auditory processing, and alterations in appetitive behavior, attention, and cognition.

SIDS. SIDS is the sudden and unexplained death of an infant younger than 1 year of age (Krous 2014). Maternal smoking and infant exposure to secondhand smoke have been causally associated with SIDS, with 20–29% of deaths from SIDS attributable to maternal smoking of conventional cigarettes during pregnancy (Dietz et al. 2010; Zhang and Wang 2013; USDHHS 2014). Prenatal exposure to cigarettes and to smokeless tobacco have been associated with increased risk for apnea events, which have been linked to increased risk for SIDS (Gunnerbeck et al. 2011; Zhang and Wang 2013; Inamdar et al. 2015).

Although the mechanistic pathways underlying SIDS remain largely unknown, nicotine has effects on pathways that could be related to SIDS and is related to known risk factors, particularly lung and respiratory development (England et al. 2015; Holbrook 2016; Spindel and McEvoy 2016). Evidence from animal models supports the hypothesis that prenatal nicotine exposure alters both fetal autonomic function and arousal, which could increase the risk of SIDS (Slotkin 1998; Task Force on Sudden Infant Death Syndrome and Moon 2011). In humans, a dose–response relationship between cotinine (the major nicotine metabolite) and altered arousal patterns has been shown in preterm infants (Richardson et al. 2009), and this relationship is suggestive of nicotine's role in arousal deficits that could be linked to SIDS. There is widespread distribution of nAChRs in the brainstem nuclei in both humans and animals that control cardiopulmonary integration and arousal in the newborn (Dwyer et al. 2008). In some animal studies, prenatal exposure to nicotine has increased mortality in newborns that were exposed to reduced oxygen (Slotkin et al. 1995; Fewell and Smith 1998). Prenatal exposure to nicotine is also associated with altered serotonin signaling in the brainstem in the rat model, leading to an exaggerated trigeminocardiac reflex and resulting in bradycardia, hypotension, and apnea (Gorini et al. 2013).

Altered Development of the Corpus Callosum. The corpus callosum, the largest white matter structure in the brain, facilitates communication between the left and right cerebral hemispheres. Several human studies have revealed alterations in the structure of the corpus callosum in offspring following their exposure to maternal cigarette use during pregnancy (Jacobsen et al. 2007b; Paus et al. 2008). In animal models, prenatal exposure to nicotine has been shown to result in widespread alterations in gene expression in the brains of adolescent offspring (Cao et al. 2011, 2013; Wei et al. 2011). In particular, the expression of a number of genes involved in myelination—the formation of white matter via the addition of protective myelin sheaths to axons—is altered in a sex-dependent manner, with upregulation in males and downregulation in females (Cao et al. 2013). Such changes in the expression profiles of myelin-related genes may influence the structure and function of white matter, and both hypermyelination and hypomyelination have been associated with cognitive deficits (Quaranta et al. 2002; Sokolov 2007).

Deficits in Auditory Processing. A number of human studies, using a variety of methods, have investigated the effects of maternal cigarette smoking during pregnancy on auditory processing from the fetal period through childhood (Jacobson and Morehouse 1984; Kristjansson et al. 1989; McCartney et al. 1994; Franco et al. 1999; Leech et al. 1999; Cowperthwaite et al. 2007). Deficits in auditory processing in fetuses are of concern because they affect later language development (Kisilevsky and Davies 2007; Kisilevsky et al. 2014). Various studies in infants have investigated the brain's physiological activity response to auditory stimuli (the cochlea translates sound into nerve impulses to be sent to the brain), neuroelectric activity of the auditory nerve, and cochlear response (Key et al. 2007; Korres et al. 2007; Kable et al. 2009; Peck et al. 2010; Katbamna et al. 2013). Key and colleagues (2007) reported prenatal exposure to cigarette use (compared with nonexposed infants) to be associated with alterations in hemispheric asymmetry and suboptimal brain activity related to speech processing in otherwise healthy newborns at least 2 days of age. Korres and associates (2007) found altered cochlear responses to auditory stimuli in newborns that were exposed to maternal cigarette smoking (n = 200) compared with those that were unexposed (n = 200), regardless of degree of cigarette exposure. Similar findings were reported by Durante and colleagues (2011) in two case-control studies.

Two additional studies investigated effects of maternal cigarette use during pregnancy on auditory brainstem responses in newborns (≤2 days old) (Peck et al. 2010) and infants (6 months old) (Kable et al. 2009). Both studies found greater neuroelectric response to sound stimuli, a phenomenon that may disrupt an infant's ability to encode auditory information, potentially leading to deficits in language development. Furthermore, both studies demonstrated dose–response relationships between altered auditory processing and maternal cotinine levels. Finally, in a study of a small sample of newborns that sought to understand the direct biological pathway, maternal smoking during pregnancy produced changes in newborn cochlear and auditory brainstem functions and changes in placental gene expression in genes that appear to modulate the motility of cochlear hair cells (Katbamna et al. 2013). Thus, all three studies indicate effects based on consumption of conventional cigarettes, and they highlight the possibility of a mediating role of maternal nicotine use in altered infant auditory processing, although further work must rule out confounding effects and effect modification by other constituents (e.g., arsenic, benzene, and cadmium).

A study using functional magnetic resonance imaging (fMRI) in older offspring exposed to tobacco in utero assessed response to auditory and visual attention tasks in adolescent smokers (Jacobsen et al. 2007a). Teens whose mothers smoked during pregnancy exhibited decreased accuracy in the tasks, with greater activation of both the temporal lobe and the occipital lobe, regions of the brain that are critical for auditory and visual processing. Additive effects of maternal cigarette use during pregnancy and of adolescent smoking on activation of the temporal and occipital lobes also emerged, indicative of reduced coordination among brain regions during auditory attention tasks.

Animal studies have shown that nAChRs play a critical developmental role in establishing synaptic connections between sensory thalamic afferents and those cortical targets that are necessary for normal sensory processing (Table A3.1-5 in Appendix 3.1). Brief nicotine exposure during this critical postnatal period of sensory cortex development disrupts glutamate transmission (Aramakis et al. 2000) and eliminates nAChR regulation of signal processing in the adult auditory cortex, inhibiting normal auditory learning (Liang et al. 2006). Animals that are prenatally exposed to nicotine also exhibit deficits in cognitive processing in response to an auditory cue, which appears to be mediated by a loss of function of the nAChR β2 subunit (Liang et al. 2006; Horst et al. 2012).

Appetitive and Consummatory Behaviors. Clinical studies and animal studies have linked prenatal exposure to nicotine to subsequent appetitive behaviors (an active searching process that is performed consciously) and consummatory behaviors (such as ingestion of food or drugs) in offspring. Associations have been demonstrated in humans between maternal cigarette use during pregnancy and risk to the child of smoking uptake/nicotine dependence, drug abuse, and obesity; parallel relationships have been shown in animal models between prenatal exposure to nicotine and similar appetitive behaviors of offspring.

Parental use of tobacco is one of many well-known risk factors for offspring initiation of tobacco, progression to heavy use, and nicotine dependence. Tobacco use by parents influences their children through social, environmental, cognitive, and genetic mechanisms (USDHHS 2012). As a subset of these influences, mothers' use of tobacco during pregnancy has been studied as an independent risk factor and has been associated with offspring susceptibility, initiation, regular use, and dependence (Kandel et al. 1994; Griesler et al. 1998; Kandel and Udry 1999; Buka et al. 2003; Lieb et al. 2003; Oncken et al. 2004; Al Mamun et al. 2006; O'Callaghan et al. 2009; Tehranifar et al. 2009; Agrawal et al. 2010; Rydell et al. 2012; Weden and Miles 2012; Stroud et al. 2014; Shenassa et al. 2015). Wakschlag and colleagues (2010, 2011) suggest that maternal smoking during pregnancy has a teratologic effect with abnormalities stemming from the in utero environment which disrupt neural (Kandel et al. 1994; Jacobsen et al. 2006) and dopamine systems that promote sensitivity to nicotine dependence (Kandel et al. 1994; Selya et al. 2013). For example, nicotinic receptors of laboratory animals exposed to nicotine in utero are upregulated, suggesting a latent vulnerability to nicotine dependence among animals exposed to nicotine in utero (Slotkin et al. 2006, 2015).

At issue with all human studies investigating maternal use of tobacco during pregnancy and offspring use of tobacco is isolating the independent effect on the fetus in relation to the other social, environmental, and cognitive factors that also predict offspring tobacco use. After controlling for maternal smoking during the offspring's childhood, several studies have reported that maternal smoking during pregnancy is associated with higher nicotine dependence in offspring (Kardia et al. 2003; Lieb et al. 2003; Selya et al. 2013; Shenassa et al. 2015), increased or earlier smoking initiation, and heavier smoking among adolescent girls and adult offspring (Kandel et al. 1994; Cornelius et al. 2005). However, the association was attenuated and nonsignificant among several studies that controlled for a variety of environmental, social, and cognitive confounders between maternal cigarette use during pregnancy and initiation of offspring smoking (but not nicotine dependence) (Cornelius et al. 2005; Roberts et al. 2005; Munafo et al. 2006; Kandel et al. 2007; D'Onofrio et al. 2012; Rydell et al. 2014; Taylor et al. 2014), leaving speculation for the independent effect. In summary, evidence from animal models offers a biologic mechanism for, and human evidence is suggestive of, an association between maternal tobacco use during pregnancy with offspring smoking and nicotine dependence, but is insufficient to infer causation. Further research and longitudinal studies that examine these outcomes while assessing the full spectrum of environmental, social, and cognitive mediating pathways are needed to disentangle these issues.

A smaller set of literature has documented associations between maternal cigarette smoking during pregnancy and use of other substances by the child (Fergusson et al. 1998; Weissman et al. 1999; Porath and Fried 2005; Nomura et al. 2011). In utero exposure to nicotine also affects behavioral responses for drug rewards in both adolescent and adult experimental animals. Prenatal exposure to nicotine increases the preference of adolescents for a saccharin solution containing nicotine compared with saccharin alone (Klein et al. 2003), and it results in self-administration of nicotine either during acquisition of the task (Chistyakov et al. 2010) or after forced abstinence (Levin et al. 2006). Prenatal exposure to nicotine also increases subsequent oral intake of alcohol (Chang et al. 2013), and intravenous self-administration of both cocaine and methamphetamine is enhanced in a dose-dependent manner in adolescent rats (Franke et al. 2008) and adult rats (Lacy et al. 2014).

In contrast, in a study that used a discordant sibling pair design to reduce confounding by genetic and environmental factors, initial associations between prenatal smoking and alcohol use disorder were attenuated and were no longer statistically significant (D'Onofrio et al. 2012). In a large longitudinal study that spanned 40 years, Shenassa and colleagues (2015) found evidence to support effects on nicotine dependence among children of mothers who smoked during pregnancy, but no effects on their progression to marijuana dependence were observed. A possible explanation for these discordant findings is suggested by a study that found significant effects from prenatal smoking of conventional cigarettes on drug use among adolescents, but showed that these effects were restricted to a genetic subpopulation of carriers of a specific α6 nAChR gene (*rs2304297*) polymorphism (Lotfipour et al. 2010). In sum, a number of studies have documented associations between cigarette use by the mother during pregnancy and smoking initiation, heavy use, and nicotine dependence among her children, although control of confounding reduces this association. In addition, the literature is sparse and inconsistent regarding a connection between maternal cigarette use during pregnancy and the use of nontobacco substances by the child.

A large body of literature has demonstrated effects of maternal cigarette use during pregnancy on weight levels and obesity in childhood. For example, three meta-analytic reviews found a 47–64% increased risk of obesity in children following exposure to maternal cigarette smoking during pregnancy (Oken et al. 2008; Ino 2010; Weng et al. 2012; Behl et al. 2013). Additional systematic reviews (Bruin et al. 2010) and other studies (Harrod et al. 2015; La Merrill et al. 2015; Mourtakos et al. 2015; Bao et al. 2016) have all concluded that prenatal exposure to nicotine likely acts as a developmental obesogen in humans. However, unmeasured residual confounding or confounding by familial factors, which have not been fully explored, could attenuate the observed associations (Gilman et al. 2008; Iliadou et al. 2010). Animal studies support the epidemiologic literature suggesting a potentially causal relationship here by defining biologic pathways (Wong et al. 2015). Fetal and neonatal exposure to nicotine in rodents has resulted in neurochemical, neurobehavioral, and metabolic changes in the children that are consistent with obesity and type 2 diabetes (Williams and Kanagasabai 1984; Newman et al. 1999; Grove et al. 2001; Chen and Kelly 2005; Gao et al. 2005; Holloway et al. 2005).

In humans, studies involving structural MRI and fMRI have shown alterations in the size and sensitivity of brain reward centers in the teenage offspring of maternal smokers. Several of these studies revealed a thinning of the orbitofrontal cortex among persons who were prenatally exposed to maternal cigarette smoking, a thinning that was associated with drug use and experimentation during adolescence (Toro et al. 2008; Lotfipour et al. 2009); decreased amygdalar volume, which is associated with increased fat intake (Haghighi et al. 2013); and altered response to reward anticipation in the ventral striatum, an area associated with risk taking and drug use (Muller et al. 2013). In addition, highlighting the role of altered nicotinic pathways in the disruption of neural circuits from prenatal tobacco exposure, changes in striatal volume, and a propensity for drug use in adolescent offspring have been linked to interactions between prenatal exposure to cigarette smoking and a polymorphism in the gene encoding the α6 nAChR (Lotfipour et al. 2010). Structural alterations in the orbital frontal cortex have also been shown to result from interactions between maternal cigarette smoking during pregnancy and polymorphisms of brain-derived neurotrophic factor, a growth factor that regulates growth and differentiation of new neurons and supports existing neurons (Lotfipour et al. 2009). Although these clinical findings are specific to conventional cigarettes, they converge with results of animal studies of the effects of prenatal nicotine on brain reward centers and thus highlight the potential pernicious effects of e-cigarettes in pregnant women.

Animal studies have shown that the dopamine system, which is critically involved in satisfaction-seeking or appetitive behaviors, is modulated by nAChRs from the fetal period to adulthood (Azam et al. 2007). Prenatal nicotine exposure alters dopamine's content, turnover, release, and receptor expression in forebrain regions, which are important for motor and cognitive functions (Navarro et al. 1988; Richardson and Tizabi 1994; Muneoka et al. 1999; Zhu et al. 2012) and for assigning motivational value to natural and drug rewards (Kohlmeier 2015; McNair and Kohlmeier 2015). Prenatal exposure to nicotine also modifies the structure of dendritic targets of dopamine innervations in the nucleus accumbens (a critical component of reward learning and addiction) (Mychasiuk et al. 2013) and alters neuronal signaling that affects dopamine function (Chang et al. 2013; Morgan et al. 2013).

Prenatal exposure to nicotine has been shown in a variety of animal studies to induce complex effects on behavioral response to natural rewards. Although adolescent offspring of nicotine-exposed mothers show an initial decrease in motivation to work for sucrose reward (Franke et al. 2008), they exhibit enhanced sensitivity to the rewarding effects as the task becomes harder (Lacy et al. 2012). Prenatal exposure to nicotine also results in enhanced intake of fatty foods, with no change in the intake of normal chow (Chang et al. 2013).

Attention and Cognition. Numerous human studies have investigated the effects of maternal cigarette use during pregnancy on disruptive behavior and attention deficits in the child. The 2014 Surgeon General's report included results of a systematic review of effects of maternal cigarette use during pregnancy on disruptive-behavior disorders—including ADHD, conduct disorder, and ODD—in offspring (USDHHS 2014). The evidence for effects of maternal cigarette use during pregnancy on disruptive-behavior disorders, and ADHD in particular, was suggestive but not sufficient to infer a causal relationship. Several systematic reviews using meta-analyses have found evidence for associations between exposure to maternal cigarette use during pregnancy and ADHD in offspring, including dose–response relationships between number of cigarettes smoked per day and ADHD symptoms (Linnet et al. 2003; Langley et al. 2005; Latimer et al. 2012; Massey et al. 2016). However, similar to effects on nicotine dependence and obesity in offspring, the possibility of unmeasured confounding remains (D'Onofrio et al. 2008; Thapar et al. 2009; Langley et al. 2012). Evidence for associations with maternal cigarette use during pregnancy is perhaps more consistent for offspring conduct disorders than it is for ADHD. In particular, although some studies that used a gene–environment interaction design or a propensity score-matching approach to exposure to control for confounding, they found no effect of maternal cigarette smoking during pregnancy on conduct disorders (D'Onofrio et al. 2008; Gilman et al. 2008; Boutwell and Beaver 2010; Lavigne et al. 2011). However, several other studies—including a meta-analytic review across three studies using "genetically sensitive"[2] research designs—have suggested a direct causal relationship between maternal smoking during pregnancy and conduct disorders in offspring (McCrory and Layte 2012; Gaysina et al. 2013; Kuja-Halkola et al. 2014; Estabrook et al. 2015; Paus and Pausova 2015).

To explore the potential role of nicotine exposure in these associations, a small number of studies have included a prospective measure of confirmed tobacco exposure, maternal cotinine levels, in addition to maternal report of smoking, to study relationships with disruptive behaviors among offspring (Wakschlag et al. 2011; O'Brien et al. 2013; Massey et al. 2016). Wakschlag and colleagues (2011) found associations between maternal cigarette smoking and aggression and noncompliance among offspring. Studies have also shown alterations in the structure and

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[2]Genetically sensitive designs typically include monozygotic and dizygotic twins and a broader inclusion of sibling pairs, mother–child pairs, and grandparent–grandchild pairs. Genetically sensitive multigroup designs allow for simultaneous testing of additive and nonadditive genetic, common, and specific environmental effects, including cultural transmission and twin-specific environmental influences.

function of the orbital frontal cortex, a region important for emotional regulation and cognition, in relation to maternal cigarette smoking during pregnancy (Toro et al. 2008; Bennett et al. 2009). Consistent with animal models of altered dopamine regulation, two studies have shown interactions of maternal cigarette smoking during pregnancy with dopamine regulation genotype (DAT1) in influencing disruptive-behavior phenotypes in offspring (Wakschlag et al. 2011; O'Brien et al. 2013). In another study, Wakschlag and colleagues (2010) demonstrated a sex-dependent interaction of maternal smoking during pregnancy with monoamine oxidase A (MAOA) genotype, which is associated with the development of antisocial behavior. In this study, maternal smoking during pregnancy further increased the risk for conduct disorder. In sum, although issues of confounding remain, much evidence from human studies is suggestive of a causal association between maternal cigarette smoking during pregnancy and disruptive behaviors among offspring. This was confirmed by the 2014 Surgeon General's report on tobacco (USDHHS 2014). Since then, newer studies, controlling for personal and genetic confounders, have reported significant associations as well as nonsignificant, attenuated associations. Biologic evidence of nicotine-induced alterations in dopamine regulation also provides a possible mechanism for the role of nicotine in these outcomes.

Animal studies have shown that cholinergic modulation of prefrontal cortex function, via nAChRs, is essential for attention and cognition (Poorthuis and Mansvelder 2013; Proulx et al. 2014). Prenatal exposure to nicotine alters the morphology and nAChR functional response of prefrontal cortical neurons (Mychasiuk et al. 2013; Bailey et al. 2014). When tested as adolescents, animals that were exposed prenatally to nicotine show some behaviors characteristic of ADHD. For example, exposed offspring were found in two studies to show less impulse control and/or slower learning acquisition on two cognitive tests that tax attentional processes (Sorenson et al. 1991; Schneider et al. 2012). In addition, some studies have found hyperactivity in exposed offspring (Pauly et al. 2004; Schneider et al. 2012; Zhu et al. 2012), which was found in another study to be transmitted via maternal lineage from one generation to the next and to be ameliorated by methylphenidate treatment across all generations, showcasing the long-term impact of prenatal nicotine exposure (Zhu et al. 2014a). This transgenerational transmission of prenatal nicotine-induced hyperactivity must reflect long-term changes to the epigenome (Leslie 2013). Finally, emerging animal studies suggest that prenatal exposure to nicotine affects the proliferation and maturation of progenitor cells to glutamatergic neurons during neurodevelopment in the medial prefrontal cortex, resulting in behavioral impairments in attentional function and behavioral flexibility in adulthood (Aoyama et al. 2016; Poon and Leibowitz 2016; Powell et al. 2016).

Summary

Because of the rising prevalence of e-cigarette use, there is potential for widespread nicotine exposure to youth and young adults, resulting in nicotine addiction and related harmful consequences associated with exposure to nicotine. During pregnancy, there is neural sensitivity to the number and volume of substances, including nicotine, transported through the placenta. From prenatal development through adolescence and early adulthood, exposure to nicotine poses a serious threat, because these are critical times for brain development and brain plasticity. Furthermore, youth and young adults are more vulnerable than adults to the long-term consequences of nicotine exposure, including susceptibility to nicotine addiction and potentially reduced impulse control, deficits in attention and cognition, and mood disorders. An additional public health concern is exposure to e-cigarettes among persons who have never used conventional tobacco products. If the prevalence of e-cigarette use continues to rise among those who do not use conventional tobacco products, the harmful consequences of exposure to nicotine will rise accordingly.

The 2014 Surgeon General's report (USDHHS 2014) states there is sufficient evidence to infer that: (a) nicotine activates multiple biological pathways through which smoking increases risk for disease; (b) nicotine exposure during fetal development, a critical window for brain development, has lasting adverse consequences for brain development; (c) nicotine adversely affects maternal and fetal health during pregnancy, contributing to multiple adverse outcomes such as preterm delivery and stillbirth; and (d) nicotine exposure during adolescence, a critical window for brain development, may have lasting adverse consequences for brain development and cognition. The literature presented in this section attempts to differentiate the risks to fetal and child health associated with nicotine in tobacco versus nicotine alone or in e-cigarettes. Evidence is sufficient to conclude tobacco use increases the risk of SIDS (USDHHS 2014), but further research is necessary with regard to nicotine alone or nicotine in e-cigarettes. The review finds evidence that tobacco is associated with structural brain changes and alterations in cognition, attention, and appetitive behaviors in human offspring. Less well known is the role that nicotine plays in mediating these associations, although animal models provide support for a role for nicotine in these outcomes. nAChRs, the chief receptor targets for nicotine, are widely expressed in the fetal brain, and their normal functioning is negatively affected by smoking and, in animals, by prenatal exposure to nicotine through experimental treatment. Furthermore, both human genetic studies and animal studies implicate a neurotoxic effect of fetal nicotine exposure. Pregnant women and women intending to become pregnant should be cautioned against using e-cigarettes to avoid unnecessary nicotine exposure to their baby.

Effects of the Inhalation of Aerosol Constituents Other than Nicotine

The scientific literature on the health effects of exposure to constituents other than nicotine in the e-cigarette aerosol is still developing. One study found that after 5 minutes of ad lib e-cigarette use, healthy adult cigarette smokers showed an increase in airway resistance, but no effect on other spirometry parameters such as forced vital capacity (FVC), forced expiratory volume in 1 second FEV1, and ratios of these values (FEV1/FVC) (Vardavas et al. 2012).

A noninvasive marker of airway inflammation is the fraction of exhaled nitric oxide (FeNO) (Taylor et al. 2006; Munakata 2012). NO is a gaseous molecule that produces vasodilation and bronchodilation (decreasing resistance in the respiratory airway and increasing airflow to the lungs). FeNO is reduced by acute and chronic cigarette smoking (resulting in poorer vasodilation and bronchodilation) and is increased among smokers following cessation (see Vleeming et al. 2002 for a review). Studies examining current adult cigarette smokers revealed a reduction in FeNO after use of an e-cigarette with and without nicotine (Vardavas et al. 2012; Marini et al. 2014; Ferrari et al. 2015). One study found that these reductions did not differ significantly between e-cigarettes containing nicotine and those without nicotine (Marini et al. 2014), suggesting non-nicotine factors mediated the effect.

However, a study of occasional smokers (<10 cigarettes per week), but non-e-cigarette users, found an increase in FeNO after use of an e-cigarette containing nicotine (Schober et al. 2014). Furthermore, this study found no statistical difference in FeNO after use of an e-cigarette not containing nicotine. This variation in findings suggests the impact of e-cigarette use on FeNO may vary based on smoking history, nicotine content of e-liquid, or other environmental or biological factors.

Limited studies have examined chronic exposure on the potential inhalation toxicity of PG and VG. Prior to e-cigarettes, consumer products containing these chemicals were almost exclusively liquids or creams, or the substance was contained in a matrix. Animal models have shown few toxicological effects resulting from nose-only exposure to VG aerosol, with the exception of minimal or mild squamous metaplasia in rats exposed to the highest concentration (0.662 mg glycerol) for 13 weeks (Anderson et al. 1950; Renne et al. 1992). Other inhalation studies testing PG in rats and monkeys did not observe treatment-related effects on respiratory physiology, clinical chemistry, hematology, gross pathology, or respiratory tract histology (Robertson et al. 1947). However, neither of these studies examined potential inhalation toxicity of PG and VG in humans using e-cigarette devices. In summary, other than nicotine, very little is known from human studies about the long-term health effects of inhaling PG and VG from e-cigarette aerosol, although adverse effects have been detected in animal models. Further investigation would improve our understanding of the effects of nicotine-related compounds, aerosolized solvents (PG and VG), aerosolized flavorants, aerosolized adulterants in e-liquids, and toxicants produced during the aerosolization process—or a combination of these chemicals.

Aerosolized Nicotine-Related Compounds

The nicotine used in e-liquids is extracted from tobacco. The extraction process may produce some potentially harmful tobacco-specific impurities, including minor alkaloids like nornicotine, anatabine, anabasine, myosmine, cotinine, nicotine-N-oxides (cis and trans isomers), β-nicotyrine, and β-nornicotyrine (Etter et al. 2013; Farsalinos et al. 2015a; Lisko et al. 2015; Oh and Shin 2015). The correlation between nicotine and the concentrations of minor alkaloids is much stronger in conventional tobacco products (Jacob et al. 1999) than in e-cigarettes (Lisko et al. 2015). While the cause of these differing concentrations of minor alkaloids is unknown, Lisko and colleagues (2015) speculated potential reasons may derive from the e-liquid extraction process (i.e., purification and manufacturing) used to obtain nicotine from tobacco, as well as poor quality control of e-liquid products.

The American E-Liquid Manufacturing Standards Association (2014), an industry group with no regulatory authority, has called for the use of U.S. Pharmacopeia (USP)-grade nicotine in its e-cigarette products. USP specifications for nicotine allow for a maximum of 0.5% (5 mg/g) of a single impurity and 1% (10 mg/g) of total impurities (U.S. Pharmacopeia n.d.). Although the health implications of nicotine-related impurities are not known, toxicology studies are needed to demonstrate the effects of high levels of these products.

Aerosolized Solvents

Although e-cigarettes produce PG aerosols at levels known to cause eye and respiratory irritation to both users and nonusers (Offermann 2015), only mild effects (e.g., upper respiratory irritation) have been described in humans exposed to PG mist for 1 minute (Wieslander et al. 2001), and little is known about long-term effects. Inhaling PG can increase the risk of developing asthma (Choi et al. 2010). Animal studies of PG and VG aerosolizing agents not produced by e-cigarettes concluded that these substances are relatively safe when inhaled by animals for up to 28 days (Werley et al. 2011) or 18 months (Robertson et al. 1947).

Particles emitted from e-cigarettes are assumed to be formed from supersaturated PG (i.e., concentration beyond the point of saturation) in e-liquids (Schripp et al. 2013). Several studies designed to characterize the aerosol generated by e-cigarettes examined the chemical composition of the particles and their concentrations as measured by their number and distribution by size (Trehy et al. 2011; Ingebrethsen et al. 2012; Schripp et al. 2013; Zhang et al. 2013; Fuoco et al. 2014; Ruprecht et al. 2014; Saffari et al. 2014 ; Mikheev et al. 2016). E-cigarettes are recognized as a new source of submicron-sized particles, leading to possible high exposure to these particles in users. Concentrations in the range of 10^9 particles $\times$ cm^{-3} were measured in the mainstream of e-cigarette aerosols (Fuoco et al. 2014). An in vitro study by Zhang and colleagues (2013) found that under the conditions of a single-puff experiment, an e-cigarette generated an aerosol having particle sizes in the range of 100–600 nm (nanometers), similar to that of conventional cigarettes. Mikheev and colleagues (2016) reported that the size distribution of e-cigarette aerosol differs from that of combustible tobacco smoke and that e-cigarettes normally exhibit a bimodal particle size distribution: nanoparticles (11–25 nm count median diameter) and submicron particles (96–175 nm count median diameter). Each mode has comparable number concentrations (10^7–10^8 particles/cm^3). Goel and colleagues (2015) detected radicals in aerosols from all e-cigarettes and e-liquids tested (2.5–10.3 x10^{13} radicals per puff at 3.3 V [voltage]), from e-liquid solvents PG and VG, and from "dry puffing" (overheating of e-liquid) (Farsalinos et al. 2015c).

Because the aerosols deriving from e-liquids are mainly made of droplets that are expected to dissolve as they reach the lung's epithelium, not only the number but also the volume (size) of particles needs to be considered. Manigrasso and colleagues (2015) found that e-cigarettes are a source of extremely high doses of particles in the human respiratory system. On average, 6.25 $\times 10^{10}$ particles were deposited in the respiratory tree after a single 2-second puff, an estimated 30% of the daily doses of particles for a nonsmoking person. After 10 puffs, the relevant mean-layer thickness of the e-liquid on the lung epithelium was comparable to the thickness of surfactant layer covering the alveolar and bronchial regions, suggesting a higher susceptibility to irritant endpoints (Manigrasso et al. 2015). These results demonstrate that e-cigarettes produce submicron-sized particles and highly oxidizing free radicals that may present a potential toxicologic risk to e-cigarette users.

Aerosolized Flavorants

Little is known about the flavorants used in e-cigarettes, and more than 7,700 unique flavors are on the market (Zhu et al. 2014b). Flavored e-cigarette products are popular with adult users, and sweet and candy-like flavors may make these products attractive to children and adolescents (Villanti et al. 2013; Farley et al. 2014; King et al. 2014). Many of the chemicals used in e-liquid flavorings are "generally recognized as safe" for ingesting (e.g., in food). However, these substances have not been tested adequately for safety when heated at various temperatures when inhaled in aerosolized form (Barrington-Trimis et al. 2014). The Flavor and Extract Manufacturers Association of the United States (2015), in an official statement, notes that ingredients in flavors are evaluated for exposure through ingestion only; thus, any results cannot be extrapolated to use through inhalation. Further, flavoring compounds often remain undeclared on e-cigarette and e-liquid packaging (Tierney et al. 2016).

CDC tested 36 e-cigarette products for 10 flavor compounds commonly used as additives in tobacco products (Lisko et al. 2015). Measurable levels of eucalyptol and pulegone were found in the menthol-flavored varieties for all manufacturers. Menthol concentrations ranged from 3,700 to 12,000 µg/g in flavored e-liquids, levels similar to those found in the filler of conventional cigarettes. Interestingly, menthol was found at low concentrations in 40% of the tobacco-flavored nonmenthol products tested. Other flavor compounds found were camphor, methyl, salicylate, pulegone, cinnamaldehyde (CAD), and eugenol (Lisko et al. 2015).

Tierney and colleagues (2016) analyzed 30 e-cigarette products on the U.S. market and found 13 products contained more than 1% flavor chemicals by weight. Among the chemicals identified were aldehydes (e.g., benzaldehyde and vanillin), which are categorized as primary irritants of the respiratory tract (Roberts et al. 2015). Tierney and colleagues (2016) also found that tobacco-flavored e-liquids were derived from confection-flavored chemicals (e.g., bubble gum and cotton candy flavoring) rather than tobacco extract.

Some chemicals in e-cigarettes, although approved for ingestion, have established adverse health effects when inhaled. In vitro studies of cytotoxicity suggest that different flavored e-cigarette products may vary in their potential to adversely affect health. Bahl and colleagues (2012) reported cytotoxic effects of the solutions used in e-cigarettes that were not attributable to the nicotine but to the concentration of chemicals employed as flavors. These effects were most pronounced on mouse neural stem cells and human embryonic stem cells compared to human pulmonary fibroblast (Bahl et al. 2012).

Similar findings were reported by Behar and colleagues (2014) who found a greater cytotoxic effect of flavored e-liquid solutions on human embryonic stem cells compared to human pulmonary fibroblast. Further, two cinnamon-related chemicals, CAD and 2-methoxycinnamaldehyde, were particularly cytotoxic at doses found in the refill liquids (Behar et al. 2014). CAD, which is derived from the essential oil of cinnamon bark, is a highly bioactive compound (Jayaprakasha and Rao 2011). It has been used as an anticancer agent (Nagle et al. 2012), an insecticide (Cheng et al. 2009), and a bactericide (Nostro et al. 2012), and it is employed commercially as an additive in many foods and fragrances (Cocchiara et al. 2005).

Farsalinos and colleagues (2014a) analyzed 159 e-liquids obtained from a variety of manufacturers and retailers in Europe and the United States for the presence of two flavorings: diacetyl (DA) and acetyl propionyl (AP). The study revealed that these substances were present in the majority of the samples tested, with a significant proportion containing both chemicals. Furthermore, Allen and colleagues (2016) detected DA above the laboratory limit of detection in 39 of 51 flavors tested. DA, also known as 2, 3-butanedione, is a member of a general class of organic compounds referred to as diketones, α-diketones, or α-dicarbonyls. It provides a characteristic buttery flavor, is naturally found in various foods, and is used as a synthetic flavoring agent in food products such as butter, caramel, cocoa, coffee, dairy products, and alcoholic beverages. Although it is generally recognized as safe when ingested, it has been associated with a decline in respiratory function in persons exposed to it through inhalation (Egilman et al. 2011; Clark and Winter 2015). Inhaling DA and artificial butter-flavored powders and aerosols can cause fixed obstructive lung disease in exposed workers (Chaisson et al. 2010). In addition, it has been implicated in the development of bronchiolitis obliterans, an irreversible respiratory disease also called “popcorn lung disease” (Harber et al. 2006). AP, also called 2, 3-pentanedione, is a α-diketone that is chemically and structurally similar to DA. Although it has become a popular replacement for DA, acute inhalation exposure to AP has been shown to cause airway epithelial damage similar to DA (Hubbs et al. 2012).

The analysis by Farsalinos and colleagues (2014a) found that 74.2% of the sample contained one or both of these chemicals, with 69.2% of the sample containing DA. Both DA and AP were found in 28.3% of the sample e-liquids. These chemicals were detected even in samples coming from manufacturers that stated these flavorings were not present in their products. However, exposure to DA and AP was 100 and 10 times lower, respectively, than exposure to these chemicals from cigarette smoking. Few studies have examined safe levels of DA and AP via tobacco product; however, 47.3% of DA- and 41.5% of AP-containing samples exposed consumers to levels higher than the safety limits outlined by the National Institute for Occupational Safety (NIOSH) for occupational exposure. This exposure threshold outlined by NIOSH is not intended to suggest exposure at or below that limit should be considered sufficiently safe (Hubbs et al. 2015).

Aerosolized Adulterants

TSNAs, potent carcinogens identified in tobacco and tobacco smoke, include N-nitrosonornicotine (NNN), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), N-nitrosoanabasine (NAB), and N-nitrosoanatabine (NAT) (Hecht 1998, 1999; USDHHS 2010, 2014). NNN and NNK are classified by the International Agency for Research on Cancer (IARC) as Group 1 human carcinogens (IARC 2004). Their presence in e-liquids is mostly attributable to the processes used in extracting nicotine from tobacco leaves or the addition of tobacco flavorings (Kim and Shin 2013; Cheng 2014). These compounds are formed from their alkaloid precursors and from nitrite or nitrate, predominantly during tobacco curing, fermentation, and aging. NNN, NAB, and NAT are formed primarily from their corresponding secondary amines (nornicotine, anatabine, and anabasine) in the early stages of tobacco curing and processing, while the majority of NNK is formed from the tertiary amine nicotine at the later stages of tobacco curing and fermentation (Hecht 1998). Nitrosation reactions of corresponding amines can occur in e-liquids, especially during inadequate storage or manufacturing processes; inadequate storage is believed to increase the levels of NNN as a consequence of the nitrosation of nornicotine converted from nicotine in liquids (Kim and Shin 2013).

Some studies have identified traces of TSNAs in e-liquids, but at levels far below those seen in combustible tobacco (Trehy et al. 2011; Farsalinos et al. 2015a). Further, Goniewicz and colleagues (2014b) found that the aerosol of some e-cigarettes contains traces of the carcinogenic nitrosamines NNN and NNK, but neither was detected in aerosol from the Nicorette inhalator (an NRT product).

Several studies have reported the presence of other hazardous compounds in e-liquids or in the aerosol produced by e-cigarettes (Exponent Inc. 2009; Hadwiger et al. 2010; Lim and Shin 2013; Uchiyama et al. 2013; Williams et al. 2013; Bekki et al. 2014; Goniewicz et al. 2014a,b; Kosmider et al. 2014; Jensen et al. 2015; Kavvalakis et al. 2015; Laugesen 2015; Oh and Shin 2015; Varlet et al. 2015; Khlystov and Samburova 2016). For example, an FDA study detected the presence of amino-tadalafil and rimonabant in e-liquids (Hadwiger et al. 2010); amino-tadalafil is a structural analogue of tadalafil, the active pharmaceutical ingredient in Cialis, a prescription drug approved in the United States for treatment of erectile dysfunction. Rimonabant (trade name Zimulti) was approved in Europe for the treatment of obesity, but its marketing authorization was withdrawn by the European Medicines Agency in 2009. FDA approval of this drug has been withheld because of unresolved issues involving rimonabant therapy and increased frequencies of psychiatric adverse events, including suicide and an ill-defined constellation of neurologic symptoms and seizures (FDA 2007). The presence of unapproved active pharmaceutical ingredients suggests that some e-cigarettes may expose users to pharmacologically active substances with undocumented and unknown effects.

Oh and Shin (2015) conducted a study to identify and quantify the presence of diethyl phthalate (DEP) and diethylhexyl phthalate (DEHP) in e-liquids. DEP is used as a solvent to bind cosmetics and fragrances and in various industrial applications, including plasticizers, detergent bases, and aerosol sprays. DEHP is used widely as a plasticizer in the manufacture of articles made of polyvinylchloride. DEP and DEHP were detected in 47.6% and 79.1% of e-liquids, respectively, with concentration ranges of 0.01–1745.20 mg/L and 0.06–81.89 mg/L (Oh and Shin 2015). Both DEP and DEHP have estrogenic and antiandrogenic activity that cause premature breast development in girls. DEHP is classified by IARC as a possible carcinogen in humans (IARC 2000). Although the amounts of the two phthalates detected in this study were lower than the safety levels, the source of these toxicants is unknown, perhaps coming from packaging materials and the production procedure.

Carbonyls are present in e-cigarettes, and levels increase with device voltage (Kosmider et al. 2014; Jensen et al. 2015). Long-term exposure to carbonyl compounds, such as formaldehyde, acetaldehyde, and acrolein, increases the risk of cancer. IARC and the U.S. Environmental Protection Agency (EPA) have classified formaldehyde as "carcinogenic to humans" (USDHHS 1999; IARC 2009). EPA has set the acceptable daily intake (ADI) of formaldehyde as 0.2 mg/kg (kilograms) body weight and has warned of the potential adverse health effects of exceeding ADI. Acetaldehyde is also toxic, an irritant, and a probable carcinogen (USDHHS 1999). Acrolein is toxic through all routes of administration and may cause respiratory and ocular irritation (Faroon et al. 2008; Bein and Leikauf 2011). Acrolein in cigarette smoke has been linked to several pulmonary diseases, including increased risk of lung cancer (Feng et al. 2006), as well as asthma and chronic obstructive pulmonary disease (Bein and Leikauf 2011). One study found an association between acrolein exposure and risk of cardiovascular disease (DeJarnett et al. 2014).

Lim and Shin (2013) detected formaldehyde and acetaldehyde in 225 replacement liquids for e-cigarettes purchased in Korea, with ranges of 0.02–10.09 mg/L (mean 2.16 mg/L) and 0.10–15.63 mg/L (mean = 4.98 mg/L). Although the amounts of formaldehyde and acetaldehyde detected in replacement liquids for e-cigarettes are relatively low compared to conventional cigarettes, they should be controlled to the lowest possible concentrations in raw materials, as they may be formed when e-liquids are heated. Furthermore, as larger capacity batteries and heating mechanisms are developed (Farsalinos et al. 2014b; Sleiman et al. 2016), users will be exposed to higher concentrations of formaldehyde, acetaldehyde, acrolein, and other carbonyls (Kosmider et al. 2014). Jensen and colleagues (2015) reported formaldehyde concentrations higher than conventional cigarettes in high-voltage e-cigarettes. Havel and colleagues (2016) reported acetaldehyde, acrolein, and formaldehyde generation increased markedly at voltages at or above 5 volts. Geiss and colleagues (2016) reported that formaldehyde exceeded safety levels at the lowest wattage (5 watts), which is the wattage applied in most second generation e-cigarettes.

Summary

Although some typical constituents of the e-cigarette aerosol have been identified, the potential short- and long-term health consequences of inhalation of the heated and aerosolized constituents of the e-liquids, including solvents, flavorants, and toxicants, still require further investigation to quantify health effects. Commercial and custom-mixed e-liquids are produced with undisclosed manufacturing procedures, packaging materials, and purity standards for their constituents, increasing the risks of potential health consequences. E-cigarettes are a source of extremely high doses of fine particles (e.g., aerosol) in the human respiratory system. Fine particles are emitted when the solvents PG and VG are aerosolized, and mild respiratory effects have been documented, but adequate assessments are lacking. An additional concern is the aerosolization and inhalation of flavor additives in e-liquids. While some of the chemicals used may be generally recognized as safe for use in foods, they have not been thoroughly tested for their potential sensitizing, toxic, or irritating characteristics when inhaled. Further, given the extent of possible variations in the ratio of flavor additives, with up to 7,700 unique e-liquid varieties available (Zhu et al. 2014b), these chemicals may be toxic in the concentrations present in manufactured or do-it-yourself e-liquids. Finally, other hazardous compounds and carcinogens have been detected in e-liquids, or in the heated aerosol produced by e-cigarettes, including formaldehyde, acetaldehyde, and acrolein.

Effects of Toxicants Produced During Aerosolization

A primary reason for investigating the health effects of heated and aerosolized e-liquids is that, under such conditions, chemical reactions may result in the formation of new compounds (Sleiman et al. 2016). In some devices, the temperature in the center of a heating coil can exceed 350°C, causing changes in the chemical components of the e-liquid. When carbonyl compounds are present in the refill liquids, heating can enhance their concentrations in the aerosol (Talih et al. 2015). Carbonyl compounds result from dehydration and fragmentation of VG and PG, which can be oxidized to formaldehyde and acetaldehyde during heating. Hutzler and colleagues (2014) applied headspace gas chromatography-mass spectrometry to enable incubation of liquids at various temperatures. At 150°C, the levels of acetaldehyde and formaldehyde were found to be up to 10-fold higher than they were at ambient temperatures for samples in which PG was a main component. The generation of carbonyl compounds seems to increase when liquids touch the heating element inside an e-cigarette, which is indicated by a color change around the wire, as has been reported in some devices (Uchiyama et al. 2013). Evidence suggests when e-liquid touches the heating element (heated nichrome wire), it is oxidized to formaldehyde, acetaldehyde, acrolein, glyoxal, and methylglyoxal in the presence of oxygen (Bekki et al. 2014; Goniewicz et al. 2014b; Kosmider et al. 2014).

Several studies have reported that short-chain aldehydes, such as formaldehyde, acetaldehyde, or acrolein, are produced during heating. Uchiyama and colleagues (2013) measured carbonyl compounds in e-cigarette aerosols generated according to the Canadian "intense regimen" (55mL puff volume, 2-second puff duration, 30 seconds between puffs, and a total of 10 puffs). Thirteen brands of e-cigarettes were assessed, and investigators detected several carbonyl compounds, such as formaldehyde, acetaldehyde, acetone, acrolein, propanol, crotonaldehyde, and butanol. They also detected two other harmful carbonyl compounds that had not been detected in the mainstream smoke from conventional cigarettes: glyoxal and methylglyoxal. Jensen and colleagues (2015) observed that formaldehyde-containing hemiacetals can be formed during the aerosolization process. These molecules are known to release formaldehyde and are used as industrial biocides, but it is not currently known how formaldehyde-releasing agents affect the respiratory tract.

The amount of carbonyl compounds in e-cigarette aerosols varies substantially, not only among different brands but also among different samples of the same products (Ohta et al. 2011; Bekki et al. 2014; Kosmider et al. 2014; Jensen et al. 2015), from 100-fold less than tobacco to nearly equivalent values. Notably, the amount of voltage the battery puts out affects the concentration of the carbonyl compounds in the emission. Some e-cigarettes allow users to increase aerosol production and nicotine delivery by raising the battery's output voltage. In addition, some users elect to directly drip e-liquid onto an exposed heater coil, reportedly for greater aerosol production and "throat hit." Talih and colleagues (2015) showed that use of such direct-drip atomizers may involve greater exposure to toxic carbonyls, including formaldehyde, because of the potentially higher temperatures reached by the coil. The adverse effects of acrolein (2-propenal), an unsaturated aldehyde, depend on dose and cell type and are influenced by experimental conditions (Bein and Leikauf 2011). In vitro studies found that acrolein inhibits DNA repair and forms acrolein-deoxyguanosine DNA adducts that are mutagenic (Wang et al. 2009, 2012; Tang et al. 2011). Despite the known DNA-damaging effects of acrolein, its mutagenicity in mammalian cells remains uncertain, and according to an evaluation by the IARC, there is inadequate evidence for carcinogenicity in humans or animals (IARC 1995). Because of its extreme toxicity, acrolein has been difficult to characterize in standard animal carcinogenicity tests. Animal experiments showed that acrolein can have a range of adverse effects, including a role in carcinogenesis (Cohen et al. 1992); excessive mucus production and macrophage and neutrophil accumulation with consequent production of proinflammatory cytokines and proteases (Moretto et al. 2012); damage to neurons and myelin disruption (Shi et al. 2011); and it may play a role in the progression of atherosclerosis and cardiovascular disease (Park and Taniguchi 2008; DeJarnett et al. 2014).

Other volatile organic compounds (VOCs) found in e-cigarette aerosol include a variety of chemicals (e.g., aliphatic and aromatic hydrocarbons), some of which may have short- or long-term adverse health effects. Benzene (classified as group 1 by IARC) and other solvents (toluene, xylenes, and styrene) could be present in e-cigarettes because of their use in the extraction of nicotine from tobacco leaves. Goniewicz and colleagues (2014b) detected both toluene and m- and p-xylene in e-cigarette aerosols. A wide variety of other VOCs in e-cigarette liquids produce aromas and flavor through heating (Tierney et al. 2016).

Heavy metals such as tin, lead, and nickel were discovered by Williams and colleagues (2013) in a brand of e-liquids and the resulting aerosols. Those researchers analyzed the contents of e-cigarette cartomizers (a polyfill wrapped heating coil capable of longer puff durations than an atomizer) and the aerosols by using light and electron microscopy, x-ray microanalysis, particle counting, and inductively coupled plasma optical emission spectrometry. The aerosol contained particles >1 µm that were composed of tin, silver, iron, nickel, aluminum, and silicate, and nanoparticles (<100 nm) of tin, chromium, and nickel. Small particles composed of various elements (tin, other metals, semimetals, and silicates) passed through the cartomizer fibers and were present in aerosols. These particles likely originated from parts of the device (i.e., atomizer/cartomizer) (Williams et al. 2013).

Concentrations of 9 of the 11 elements in e-cigarette aerosol identified by Williams and colleagues (2013) were higher than or equal to concentrations in conventional cigarette smoke. Many of the metals identified in e-cigarette aerosol, such as lead and cadmium (Farsalinos et al. 2015b), are known to cause respiratory distress and disease (Zalups and Ahmad 2003). These metals are produced by the aerosolization of e-liquids (Farsalinos et al. 2015b) and by flaws in e-cigarette heating mechanisms and poor quality control (Williams et al. 2013; Farsalinos et al. 2015b; Mikheev et al. 2016). While these initial analyses indicate potential exposures, additional measures are needed because of challenges in measuring trace levels of metals.

Summary

E-liquids produce chemical reactions that may result in the formation of new, harmful compounds. Carcinogens (e.g., formaldehyde, acetaldehyde, and acrolein) and toxic heavy metals (e.g., lead and cadmium) have been found in e-cigarette aerosols in laboratory tests conducted at temperatures within the range of most e-cigarette products. These chemicals and metals have been detected in e-liquids and e-cigarette aerosols, signifying the need for further study on the potential short- and long-term health ramifications.

A limitation to understanding the health impact of chemical reactions is the heterogeneity of e-cigarette devices (e.g., voltage), e-liquids (e.g., quality, content), and use behaviors (e.g., puff duration), as emissions may be altered by any combination of these mechanical and behavioral differences. Further, it is difficult to fully contextualize the carcinogenic emissions of e-cigarette aerosol given the diversity of products currently available, as well as those that may become available as the devices continue to evolve (Farsalinos et al. 2014b).

Effects Not Involving Inhalation of Aerosol by the E-Cigarette User

Health effects not attributable to direct inhalation of e-cigarette aerosol include explosion or fire associated with malfunctioned devices, poisoning through contact exposure or intentional or unintentional ingestion of e-liquid, and exposure to secondhand aerosol or its condensate.

Health Effects Attributable to Explosions and Fires Caused by E-Cigarettes

Most reports of explosions and fires caused by e-cigarettes have appeared in print and online media and on televised programs. From August 2009 to March 2014, a search of U.S. media by the U.S. Fire Administration (2014) found 25 reports of e-cigarette explosions or fires. These data suggest that the number of such events is small when compared with the number of e-cigarette users. Of the 25 incidents found in the search, 2 caused serious harm, and there were no deaths attributable to explosions. In most cases, the resulting fires did not spread far from the site of the explosion. However, in one case an entire bedroom was lost to fire (U.S. Fire Administration 2014). As for explosions, several have occurred during an e-cigarette's use, causing severe facial damage or injuries to bodies and hands (Brennan 2015; Corona and Marcus 2015; Duranty 2015; Fox 5 Digital Team 2015; Goff and Schwartz 2015; Jablow and Sexton 2015; Shastry and Langdorf 2016), but most occurred while the device's batteries were being charged. Overcharging lithium batteries can lead to thermal runaway, causing the e-cigarette battery or container to be propelled, often with portions catching fire (U.S. Fire Administration 2014; Bohr et al. in press).

Health Effects Caused by Ingestion of E-Cigarette Liquids

The liquids in both e-cigarettes and the containers used to refill them can cause nicotine poisoning. Consequences of nicotine intoxication in the e-liquid include nausea, vomiting, headaches, dizziness, and diarrhea at low doses; seizures; tachycardia; abdominal pain; confusion; and even death (Cervellin et al. 2013). The amount of nicotine needed to cause death in humans is uncertain and, according to a reevaluation, may be higher than previously thought (Mayer 2014). The total amount of nicotine in refill liquids varies and can be as high as 1,000 mg/10 mL in do-it-yourself bottles (Davis et al. 2015), which could be lethal if consumed (Mayer 2014).

The increase in poisonings prompted enactment of the *Child Nicotine Poisoning Prevention Act of 2015* (2016) in January 2016. This law requires any container of liquid nicotine sold, manufactured, distributed, or imported into the United States be placed in special packaging that is difficult to open by children under 5 years of age. Although labels may indicate the concentrations of nicotine, such labels can be incomplete, confusing, or inaccurate (Trtchounian and Talbot 2011; Cameron et al. 2014), and some bottles have not been labeled at all (Davis et al. 2015). Of most concern, some bottles of e-cigarette refill liquids labeled "no nicotine" have been found to contain significant amounts of that substance (e.g., 25.6 mg/mL; Trehy et al. 2011). Regardless, many e-cigarette users may not be aware of the toxic effects of nicotine and may not know that refill liquids should be kept away from toddlers and children. These liquids are often sold in colorful bottles with flavors that are attractive to children (Bahl et al. 2012). The liquids usually come in small dropper bottles that can be mistaken for bottles containing food dye or eye drops. Finally, many refill liquids are made in local "vape shops," which have only recently come under FDA regulation (*Federal Register* 2016), with no uniform training process for mixers, a lack of standards and protections, and unknown concentrations of nicotine.

The rapid growth in popularity of e-cigarettes and the ease with which refill liquids can be purchased have made e-cigarettes an increasingly common item in many households, thereby elevating the possibility of accidental nicotine poisoning. Instances of related case reports, often involving children or infants, are increasing. For example, an 18-month-old girl was treated at an emergency room for hypertension and tachycardia after drinking about 2 mL of refill liquid from a bottle on a nightstand (Shawn and Nelson 2013). Unintentional exposure to nicotine can occur through ingestion, absorption through the skin, inhalation, or dropping refill liquids into one's eyes (Cantrell 2014).

Figure 3.2 shows data from 2011 to 2016 on exposures to e-cigarettes or liquid nicotine (i.e., any contact with e-cigarettes or liquid nicotine, not necessarily resulting in any health effects) (American Association of Poison Control Centers 2016). These data show a dramatic increase in exposures through 2014 with a slight reduction of exposures in 2015. Fifty-one percent of the calls to poison control centers regarding exposures to e-cigarettes involved children 5 years of age or younger (CDC 2014). Increased e-cigarette exposures have also been reported by state and local poison centers (Banerji et al. 2014; Cantrell 2014; Guttenburg et al. 2014; Lee et al. 2014; California Department of Public Health 2015).

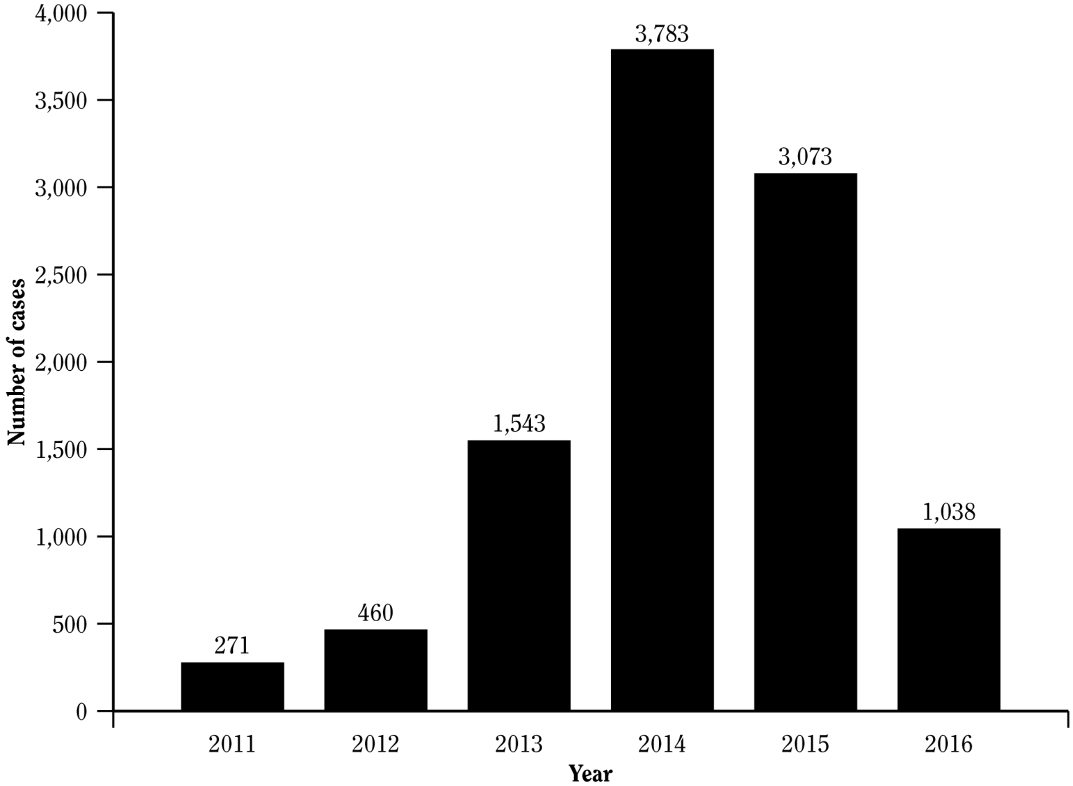
Secondhand Exposure to the Constituents of E-Cigarette Aerosol

Exposure to secondhand smoke from combustible tobacco products is a known cause of morbidity and mortality (USDHHS 2006). Secondhand smoke, a mixture of the sidestream smoke from a smoldering cigarette and the mainstream smoke exhaled by a smoker, is known to contaminate both indoor and outdoor environments. In addition, when the constituents of smoke deposit on surfaces, nonsmokers can be exposed to them via touch, ingestion, or inhalation. These deposited constituents of combustible smoke are known as "thirdhand smoke" (Matt et al. 2011; Protano and Vitali 2011). E-cigarettes represent another potential source of exposure to toxicants for nonusers, via secondhand or thirdhand exposure to aerosol.

Exposure to Nonusers

In contrast to combustible tobacco products, e-cigarettes do not produce sidestream emissions; aerosol is produced during activation of the device. Some of this aerosol is subsequently exhaled into the environment where nonusers may be exposed through inhalation, ingestion, or dermal contact. As previously described in this chapter, constituents of the emissions may include nicotine, carbonyl compounds, VOCs, polyaromatic hydrocarbons, TSNAs, heavy metals, and glycols. It is not clear how much of inhaled e-cigarette aerosol is exhaled into the environment where nonusers can be exposed. Some studies have used machines to produce e-cigarette aerosols and measured the pollutants emitted (McAuley et al. 2012; Czogala et al. 2014; Geiss et al. 2015); others have involved the use by one or more persons of an e-cigarette and measured the change in pollutants in either a room or a test chamber after use (Schripp et al. 2013; Schober et al. 2014). One study measured airborne nicotine in the homes of e-cigarette users (Ballbe et al. 2014). The concentration of e-cigarette aerosol in a given microenvironment depends primarily on the strength of the source or the number of e-cigarettes used and the emission rate of the aerosol for that device. E-cigarettes, however, are heterogeneous in their design and in the liquids used, and the specific product combination significantly affects the secondhand emissions (Kosmider et al. 2014; Geiss et al. 2015). The number of puffs and depth of inhalation may be particularly relevant to the amount exhaled by the user and may also affect e-cigarette emissions (Talih et al. 2016).

Figure 3.2 Data showing exponential increase in the number of cases of human exposure to e-cigarette products and liquid nicotine between 2011 and 2016



Source: American Association of Poison Control Centers (2016).
Note: These numbers reflect the closed human exposures to e-cigarettes and liquid nicotine reported to poison centers as of July 31, 2016. The numbers may change as cases are closed and additional information is received.

Movement of E-Cigarette Aerosol

Similar to the case with secondhand tobacco smoke, e-cigarette aerosol is an inherently dynamic mixture that changes over time in terms of constituents and concentrations. Czogala and colleagues (2014) demonstrated a significant signal from a laser photometer indicating the presence of ambient aerosol in a room after e-cigarette use. However, this aerosol disappeared in just seconds to a few minutes as it either evaporated to the gas phase or deposited on surfaces in the room. In contrast, in the same study, secondhand cigarette smoke exhibited a particulate phase that stayed suspended in the room at high concentrations for more than 30 minutes. For the VOCs in e-cigarette aerosol, such as formaldehyde, acrolein, and acetaldehyde, the source strength and ventilation rate will largely determine their concentration in indoor air. Semi-VOCs, such as nicotine and TSNAs, are also largely affected by sorption on and subsequent desorption from surfaces and dust in a room (Singer et al. 2002, 2003; Goniewicz and Lee 2015). The extent of this type of thirdhand contamination from e-cigarettes in real-world settings has not been established but would be of particular concern for children living in homes of e-cigarette users, as they spend more time indoors, are in proximity to and engage in greater activity in areas where dust collects and may be resuspended (e.g., carpets on the floor), and insert nonfood items in their mouths more frequently (EPA 2008; Matt et al. 2011).

Exposure to E-Cigarette Aerosol and Considerations of Dose

A large body of studies has measured exposure to secondhand and thirdhand smoke from conventional cigarettes using personal or area air monitoring, surface testing, and dust testing. Studies of the exposure of e-cigarette aerosol to nonusers, however, are limited. Schripp and colleagues (2013) observed small increases of fine and ultrafine particles and some VOCs, including PG, flavoring substances, and nicotine, indicating passive inhalation of e-cigarette aerosols by nonusers in the presence of e-cigarette users. Those authors demonstrated that the distribution in the sizes of the aerosol's component particles changes in the lungs and results in the exhalation of smaller particles, likely caused by the evaporation of the liquid particles in the lungs and in the environment after exhalation. Schober and colleagues (2014) found substantially higher amounts of PG, VG, particulate matter (PM), and nicotine in a 45-m^3 chamber during e-cigarette use sessions with volunteers compared to controlled sessions. They also found a 20% increase in the level of polycyclic aromatic hydrocarbons (PAHs) and a 2.4-fold increase in aluminum concentrations.

Williams and colleagues (2013) demonstrated contamination by metal and silicate particles in e-liquid and its aerosol using scanning electron microscopy. In a different study measuring machine-generated secondhand e-cigarette aerosol in an emission chamber, Geiss and colleagues (2015) found significant levels of PG, VG, and nicotine in the chamber's air. Carbonyl compounds of concern (e.g., formaldehyde, acetaldehyde, acrolein, and acetone) were below the limits of detection in this study. O'Connell and colleagues (2015), who assessed secondhand e-cigarette emissions in a small meeting room (12.8 m^2) with three e-cigarette users during a 165-minute session, found a significant increase in PG but did not see the expected increase in VG or nicotine. This study reported no increase in PAHs, trace metals, TSNAs, or acrolein, but did find an increase in total VOCs, formaldehyde, and acetaldehyde. However, the compounds were found at levels below guidelines for the quality of indoor air from the World Health Organization or European Union. Ruprecht and colleagues (2014) found significantly lower concentrations and counts for particles from an e-cigarette used in a 50-m^3 room compared with conventional cigarettes. Interestingly, they also found that nicotine-free e-cigarettes produced higher particle levels than e-cigarettes containing nicotine. Saffari and colleagues (2014) found that total particulate exposure was 10-fold lower in e-cigarettes than it was in conventional cigarettes. Emissions of heavy metals from e-cigarettes were also dramatically less, with the exception of nickel, zinc sulfide, and silver, which showed higher emission rates from e-cigarettes. PAH levels were not elevated by e-cigarette use in this study.

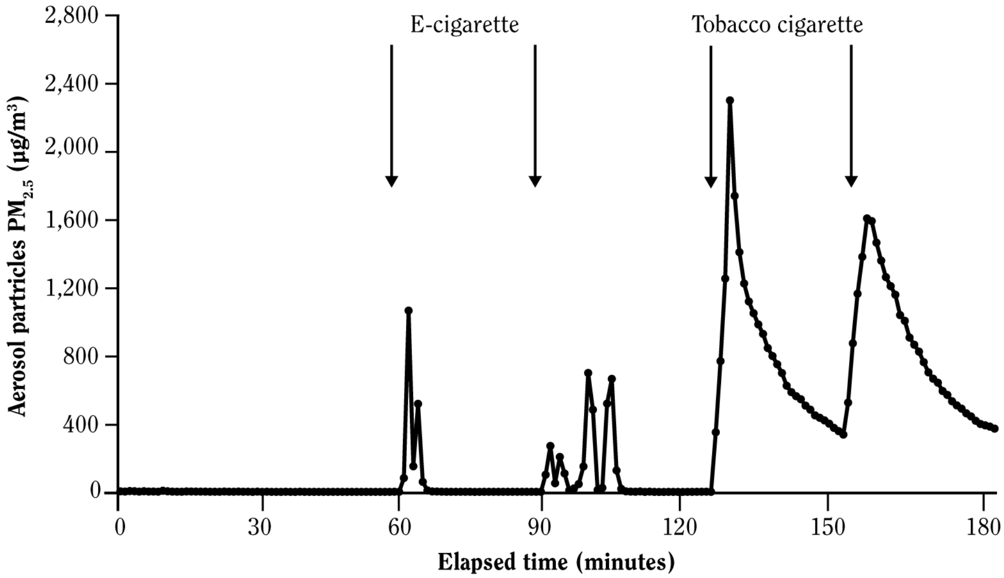
Concentrations of PM, especially $PM_{2.5}$, which is fine PM, and nicotine are the two most common markers used to measure exposure to secondhand smoke (Avila-Tang et al. 2010; Apelberg et al. 2013). Indirect measures of the mass concentration of PM from secondhand smoke using real-time particle monitors are well validated in terms of the accuracy of these measurements in relation to other constituents of secondhand smoke and to health effects (Hyland et al. 2008; Apelberg et al. 2013). These same types of particle monitors are often used in studies of e-cigarette aerosol to compare PM levels from conventional cigarettes with those from e-cigarettes, though PM findings may not directly relate to the short- and long-term health effects of each product (Czogala et al. 2014; Schober et al. 2014).

Caution is warranted when interpreting the results of PM measurements comparing e-cigarettes with conventional cigarettes. The aerosols produced are fundamentally different, with the former resulting from aerosolization of liquid and the latter resulting from combustion of organic matter. The true $PM_{2.5}$ mass concentration of e-cigarette aerosol from commonly used light-scattering instruments (Czogala et al. 2014) cannot be determined without calibrating the device to a reference standard for the aerosol in question. Even this calibration would be questionable given the highly volatile nature of e-cigarette aerosol, making it difficult to capture and accurately determine the mass. Real-time $PM_{2.5}$ measurements such as this are useful, however, to determine the presence of an aerosol and to see the *relative* changes in this aerosol over time and under various conditions, such as changing source strength. Figure 3.3 shows the significant increase in aerosol concentration from e-cigarettes after about 1 hour and the subsequent rapid decline, presumably from initial aerosolization and deposition of this aerosol. There may still be significant amounts of this e-cigarette aerosol in the environment, but the particle monitor can no longer measure it, as it is either in the aerosol phase or deposited on surfaces. For these reasons, it is important not to rely solely on PM mass concentrations for determining exposure to e-cigarette aerosol and for making comparisons with conventional cigarettes. Measurement of the individual toxicants of concern in the aerosol phase and on surfaces is warranted.

Health Effects of Secondhand Exposure to E-Cigarette Aerosols

Flouris and colleagues (2012, 2013) conducted two clinical studies of the health effects of secondhand exposure to e-cigarette aerosol. The researchers found no short-term change in markers of complete blood count after 1 hour of exposure to e-cigarette aerosol in a group of 15 nonsmokers (Flouris et al. 2012). Similarly, the same exposure caused no significant change in short-term lung function, although the results were of borderline statistical significance (Flouris et al. 2013). However, these studies demonstrated that passive exposure to e-cigarettes causes an increase in serum cotinine that is similar to that from passive exposure to cigarette smoke, suggesting the need to

Figure 3.3 Changes in aerosol particle $PM_{2.5}$ concentrations during experiment of e-cigarette use and tobacco cigarette smoking in an exposure chamber



Source: Czogala et al. (2014).
Note: **PM** = particulate matter.

examine the impact of passive aerosolized nicotine inhalation on long-term lung function. Furthermore, limited effects would likely occur in the short exposure observed through the methodologies used by Flouris and colleagues (2012, 2013), as these studies did not account for prolonged and persistent passive exposure to e-cigarette aerosols.

Several researchers have modeled the health risks of passive exposure to e-cigarettes (Colard et al. 2015) on the basis of the limited exposure data available and have come to various conclusions. Offermann (2015) concluded that, for indirect exposure, two chemicals—nicotine and PG—exceeded California EPA exposure level standards for noncarcinogenic health effects. Burstyn (2014), who compared e-cigarette aerosol exposure to workplace exposure standards, concluded that only PG and VG warrant attention in e-cigarette users while, for bystanders, none of the constituents of e-cigarette aerosol pose apparent concern. It is important to note that standards for workplace exposure are typically not appropriate to apply to the population as a whole, as they are intended for a healthy working population during a typical work day, not accounting for the risks to children, pregnant women, or those with preexisting health conditions. Further, standards for workplace exposure are very different in concentration and duration than what is to be expected from e-cigarette use.

An additional consideration for regulating e-cigarettes in indoor environments is the potential for allergic reactions in nonusers. Dermal and oral PG exposures are known causes of dermatitis and allergic sensitization (Warshaw et al. 2009; Al Jasser et al. 2011). Several e-liquids contain flavorants derived from nuts and in fact have labels cautioning persons who have nut allergies not to use these products. Research has not evaluated whether nonusers can have allergic reactions from these potential allergens in e-cigarette aerosol, but this is a risk that should be explored as 8% of U.S. children have food allergies (Gupta et al. 2011).

Evidence Summary

E-cigarette use among youth and young adults in the United States has increased considerably in recent years (see Chapter 2). There is little doubt that the use of e-cigarettes by youth and young adults represents self-administration of the drug nicotine, and this self-administration of nicotine puts youth at risk for addiction and many related harmful consequences. Animal research indicates adolescent brains are particularly sensitive to nicotine's effects, such that subsequent self-administration is more likely, and that same literature indicates that this age group is at risk for a constellation of nicotine-induced neural and behavioral alterations. Studies of the effects of maternal smoking of conventional cigarettes during pregnancy, coupled with preclinical literature examining the effects of maternal self-administration of nicotine during pregnancy, suggest that e-cigarette use by mothers during pregnancy presents a wide variety of risks to fetal, infant, and child brain development.

Users of e-cigarettes risk respiratory exposure to a variety of aerosolized chemicals, including solvents and flavorants added intentionally to e-liquids, adulterants added unintentionally, and other toxicants produced during the heating/aerosolization process. The health impacts of frequent exposure to the toxicants in e-cigarette aerosol are not well understood, though several are known carcinogens. As highlighted previously in this chapter, the detection and level of these carcinogens depend on several factors, including the concentration of the e-liquid and the strength of the heating device. Although e-cigarettes have been used as a cessation device, the evidence supporting the effectiveness of e-cigarettes as an aid for quitting conventional cigarettes remains extremely weak for adults (Bullen et al. 2013; Caponnetto et al. 2013; Grana et al. 2014; Kalkhoran and Glantz 2016) and untested and nonexistent among youth.

Further research is warranted to focus on the characteristics of e-cigarette devices, the constituents of e-liquids, and the user behaviors that can influence the yield of nicotine and other toxicants (Shihadeh and Eissenberg 2015). This close focus includes providing details of devices (e.g., voltage of the power supply, heating element resistance) and components of e-liquids (e.g., propylene glycol, vegetable glycerin, other additives), and measuring user puff topography. Standardization of procedures for producing and delivering the aerosol is likely a necessary component of at least some in vivo and in vitro work. Preclinical work examining the effects of e-cigarette aerosols is a clear research need and, again, the standardization of procedures for production and delivery of the aerosol is necessary. To enhance relevance, the parameters of aerosol production should span the range of those seen with humans (Shihadeh and Eissenberg 2011).

The huge variety of products of different origin and design, the rapid emergence of new products, and the varied ways in which consumers use these products make the development of standard measurement conditions challenging (Famele et al. 2015). Accordingly, research is needed to understand how different design features relate to potential toxicity—for example, if the compounds in e-cigarettes are affected by heating, changes in chemical composition, or pH; if these compounds are absorbed into the bloodstream; and how additives to the e-liquid affect the bioavailability of these compounds, among other considerations. Research is also needed to understand whether potential health risks may be ameliorated by changes in product engineering.

Conclusions

1. Nicotine exposure during adolescence can cause addiction and can harm the developing adolescent brain.

2. Nicotine can cross the placenta and has known effects on fetal and postnatal development. Therefore, nicotine delivered by e-cigarettes during pregnancy can result in multiple adverse consequences, including sudden infant death syndrome, and could result in altered corpus callosum, deficits in auditory processing, and obesity.

3. E-cigarettes can expose users to several chemicals, including nicotine, carbonyl compounds, and volatile organic compounds, known to have adverse health effects. The health effects and potentially harmful doses of heated and aerosolized constituents of e-cigarette liquids, including solvents, flavorants, and toxicants, are not completely understood.

4. E-cigarette aerosol is not harmless "water vapor," although it generally contains fewer toxicants than combustible tobacco products.

5. Ingestion of e-cigarette liquids containing nicotine can cause acute toxicity and possibly death if the contents of refill cartridges or bottles containing nicotine are consumed.

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Chapter 4
Activities of the E-Cigarette Companies

Introduction

This chapter focuses on the companies that are active in the production, distribution, or marketing of e-cigarettes in the United States and examines the potential influence of these companies on the use of e-cigarettes, particularly among youth and young adults. The e-cigarette marketplace is complicated by the fact that some brands and devices are owned by tobacco companies, while others are independently owned. This chapter will refer to the e-cigarette companies as a whole but, when necessary, will distinguish between the e-cigarette brands that are owned by tobacco companies and others that are independently owned. The chapter covers manufacturing and price, marketing and promotional activities, the retail environments for e-cigarette products, exposure to marketing and receptivity to such activity, and the effects of e-cigarette marketing activities on consumer behavior.

Manufacturing and Price

As discussed in Chapter 1, although the concept of e-cigarettes was initially introduced in the 1960s, the first-generation version of e-cigarettes was not developed and commercialized until the mid-2000s (Grana and Ling 2014). In the short period since the first appearance of e-cigarettes, the exponential growth in awareness and use of these products (Centers for Disease Control and Prevention [CDC] 2015), the rapid product development (Zhu et al. 2014), and the rapid evolution of both the e-cigarette market and the industry itself (Huang and Chaloupka in press) have been unprecedented. E-cigarettes were recently named a "disruptive innovation" that may change the existing tobacco market and displace conventional (combustible) cigarettes in a foreseeable timeframe (Spielman and Azer 2013).

Consumer demand for a less harmful alternative to conventional cigarettes and the implementation of macro policies, such as those that restrict cigarette use or mandate clean indoor air, may influence the use of e-cigarettes (Pepper et al. 2014b; Rose et al. 2014). However, e-cigarette companies may play a critical role in shaping the market, affecting everything from the development and innovation of new products and brands to the manufacture, distribution, marketing, promotion, and pricing of the product—activities that parallel those in the cigarette industry.

This section describes and summarizes both the rapidly changing e-cigarette market and the activities of e-cigarette companies in the United States, providing a broad overview of the major players. These participants include the major tobacco companies and other manufacturers. The chapter also addresses how the companies influence the e-cigarette market in the United States, focusing on the impact of product development and innovation, distribution channels, product availability, and pricing strategies, as well as the role of e-cigarette trade organizations and partnerships.

Overview of the E-Cigarette Market in the United States

For 2014, the value of the e-cigarette market in the United States was estimated at $2.5 billion: 40% ($1.0 billion) was for cigarette-like e-cigarettes (cigalikes), and 60% ($1.5 billion) was for tank-style e-cigarettes, mods, and other types of "vaporizers" (Wells Fargo Securities 2015a) (Table 4.1). The market was projected to grow to $3.5 billion, a rise of 40%, in 2015 (Rose et al. 2014) (Table 4.2). Total sales of e-cigarettes in convenience, food, drug, and big-box stores (such as Walmart), which are tracked by commercial market research companies (such as Nielsen), were estimated to be $900 million in 2014. There was an additional estimated $500 million in online sales, and $1.1 billion in sales in "vape shops" and other channels, which are not currently tracked by commercial market research companies (Table 4.1) (Wells Fargo Securities 2015b).

Distribution and Purchase Channels

E-cigarettes entered the U.S. market around 2006–2007, and since that time the distribution and purchase channels for these products have evolved greatly. Initially they were sold exclusively by Internet retailers, but then selling activity expanded to shopping mall kiosks and conventional retail outlets and, more recently, to "vape shops" and some pharmacies (Rose et al. 2014; Lee and Kim 2015).

Some companies operating in the U.S. market have their own manufacturing facilities in this country, but companies generally import parts or even complete products from abroad, almost exclusively from China (Barboza 2014). Manufacturers and importers distribute their products via a wide number of channels, such as the companies'

Table 4.1 Estimated e-cigarette market size in 2014 ($ billion)

	Convenience, food, drug, and big-box stores	Online	Other channels ("vape shops" and other untracked retail channels)	Total
E-cigarettes	0.6	0.2	0.2	1.0
Vapors/tanks/mods	0.3	0.3	0.9	1.5
Total	0.9	0.5	1.1	2.5

Source: Wells Fargo Securities (2015a).

Table 4.2 Estimated e-cigarette market size in 2015 ($ billion)

	Convenience, food, drug, and big-box stores	Online	Other channels ("vape shops" and other untracked retail channels)	Total
E-cigarettes	0.7	0.4	0.4	1.5
Vapors/tanks/mods	0.4	0.4	1.2	2.0
Total	1.1	0.8	1.6	3.5

Source: Wells Fargo Securities (2015a).

own e-commerce websites and/or retail outlets. In 2010, the most popular channels for selling e-cigarettes and their accessories directly to consumers were websites and third parties, such as retail outlets (Linarch Information Solutions 2012). Many e-cigarette manufacturers and importers, including the big-brand companies and those supplying products to "vape shops," rely on distributors and retailers to deliver the products to the consumer (Linarch Information Solutions 2012).

The emergence of e-cigarette devices and products resulted from the endeavors of a few entrepreneurs and widespread Internet and television advertising (Grana et al. 2013; Rose et al. 2014). It is noteworthy that the product class took hold when e-commerce was rapidly expanding in the United States, and major social media platforms—such as Facebook (founded in 2004), YouTube (2005), and Twitter (2006)—were emerging. In such an environment, information about a new product like e-cigarettes could be rapidly disseminated across geographic boundaries, and new products and technologies could be speedily adopted. This process is partly reflected by the Google search volume of queries related to e-cigarettes; the volume of queries surpassed those for nicotine replacement therapy products and snus by 2008 (Ayers et al. 2011).

Manufacturers noticed the fast rise in consumer interest in e-cigarettes, so they quickly pushed to expand the sale of their products to brick-and-mortar retail stores. Sales of cigalikes and related products were first observed in Nielsen's store-scanner database in 2007, and between 2009 and 2012, retail sales of e-cigarettes expanded to all major markets in the United States (Huang and Chaloupka in press). This growth coincided with a surge in marketing expenditures by the e-cigarette companies across all media platforms (Kim et al. 2014; Kornfield et al. 2015). The products sold in these conventional channels were predominantly disposable and rechargeable cigalikes (Giovenco et al. 2015; Huang and Chaloupka in press), but retail stores started to carry tank-style e-cigarette devices as well (CSP Daily News 2014; Giovenco et al. 2015).

Today, e-cigarette brands, such as MarkTen (manufactured by Altria) and VUSE (manufactured by Reynolds American Inc.), are available in more than 70,000 retail stores across the country, and their availability is expanding rapidly (Wells Fargo Securities 2014b). E-cigarettes were more likely to be available in retail locations in neighborhoods with a higher median household income and a lower percentage of African American and Hispanic residents; these sales patterns are consistent with patterns of use of these products observed among youth, young adults, and adults more generally (see Chapter 2). Notably, the price of conventional cigarettes and the existence of comprehensive smokefree laws were inversely associated with the availability of e-cigarettes (Rose et al. 2014).

Through growth in their sales, tank-style e-cigarettes (also known as mods) and advanced personal vaporizers (APVs) have begun to play an increasingly important role in the e-cigarette market (Wells Fargo Securities 2015a). "Vape shops," which provide a range of e-cigarette devices and products, have emerged as the primary retail channel for consumers seeking such products (Lee and Kim 2015). Unlike conventional retail outlets, "vape shops" sell a wide range of more complex and powerful tank-style e-cigarettes and many different types of liquids for e-cigarette devices (e-liquids or e-juices) (Sussman et al. 2016).

The rise of "vape shops" can be attributed to a number of factors. First, in the past, most of these establishments offered a wide range of e-cigarettes and e-liquids, allowed users to sample different types of flavored e-liquids at no cost, and permitted the trial use of various types of e-cigarettes. Most of these establishments sell products made by independent companies, as opposed to products manufactured by the major conventional tobacco companies (Kamerow 2014; Sussman et al. 2016). As a result, "vape shops" can serve as an information hub where consumers can easily obtain knowledge about (and gain experience with) a wide range of e-cigarettes and related products (Sussman et al. 2016). However, the information provided may be misleading or misinterpreted (Cheney et al. 2016). Second, unlike traditional retail outlets, "vape shops" are usually equipped to provide consumers with individualized information about how e-cigarette products can be used to best satisfy the user's preferences; this capability may be important as e-cigarette products become more diversified and sophisticated. Because of the diversity of these products, some of these establishments provided free samples of different flavored e-liquids and allowed trial use of different e-cigarettes before actual purchase in an attempt to compete with traditional retail outlets. Under the deeming rule published in May 2016, free samples of e-liquids containing nicotine were banned (*Federal Register* 2016). Third, "vape shops" serve as a place for e-cigarette users to socialize.

Some "vape shops" also host various events, including competitions (also known as cloud chasing), that build loyal customer bases by creating a sense of community and camaraderie among customers (Sussman et al. 2014; Cheney et al. 2015; Lee and Kim 2015). Additionally, a 2015 study of "vape shop" owners found that customers view the owners as important sources of health information, which could include information related to cessation (Cheney et al. 2016). However, the owners reported (a) obtaining their information from YouTube or industry sources but finding the research hard to understand and (b) looking for government sources but not finding them.

Estimates of the number of "vape shops" in the United States have varied greatly due to the lack of a clear definition of what constitutes such an establishment. The low end of these estimates puts the number around 3,500 (Klein 2013; Lee and Kim 2015), while intermediate estimates indicate that there are about 6,000–15,000 "vape shops" in this country (Bour 2015; Wells Fargo Securities 2015b). One high estimate is that in 2014 there were as many as 35,000 such shops in the United States (Kamerow 2014).

Product Evolution

E-cigarette products have evolved and diversified rapidly since they entered the U.S. market (see Chapter 1). Detailed information about different types of e-cigarette products has been presented elsewhere (Grana et al. 2014). Over time, with consolidation of e-cigarette companies and technological improvements, the manufacturing process has become more standardized, enabling the production of e-cigarette products with a more effective and more consistent dose and delivery of nicotine and flavorings, and a more consistent generation of aerosol (Goniewicz et al. 2013a,b; Farsalinos and Polosa 2014; Saitta et al. 2014).

Many e-cigarette manufacturers make multiple types of e-cigarette products. For example, the NJOY brand has not only disposable and rechargeable cigalikes but also tank-style e-cigarette devices, which are larger than cigalikes and include options for refills and batteries. In addition, NJOY sells a variety of flavored e-liquids, although in California, flavors appealing to minors (e.g., strawberry and cookies and cream) are prohibited (*State of California v. Sottera, Inc.* 2010). Within each product type, there are many different brands, albeit the brands are often very similar. For example, NJOY, blu, Logic, Mistic, and many other brands of rechargeable e-cigarettes differ very little from each other with regard to the flavors and types of products offered (e.g., cigalike, tank style) (Zhu et al. 2014). A study examining the growth of brands and flavors between 2012 and 2014 found that older brands were more likely to involve cigalikes, while newer brands were more likely to offer tank-style devices and mods (Zhu et al. 2014).

As tank systems and mods become more popular, the distinction between a closed system and an open system becomes more important. In a closed system, components cannot be customized. In this case, the e-liquid is "locked in"; the amounts of e-liquid, level of nicotine, and flavors are dictated by the manufacturer. Because users cannot mix their own e-liquids or refill the cartridges or tanks, there is less risk of spillage, nicotine overdose, and accidental ingestion. In addition, users cannot change the power source, adjust the voltage, or customize the atomizers. Many brands offer only closed-system devices (e.g., Vype, Vapestick, and FIN). Most cigalikes are closed systems, sold primarily online or in conventional retail outlets, and are favored by the larger e-cigarette companies, likely because of the high profit margins from the e-liquid refill cartridges and the nature of the distribution paths.

Open systems, in contrast, allow for personalization and customization: Users can mix their own e-liquid, choosing different e-liquid bases, flavors, and nicotine concentration levels. Users can also adjust the voltage, customize the atomizers, and/or modify the aesthetics and shapes/sizes of their devices (Popken 2014; Richtel 2014c; Lee and Kim 2015). Tanks and mods/APVs are open systems sold primarily in "vape shops" or online. While research has demonstrated that more-experienced e-cigarette users prefer open system mods (Farsalinos et al. 2014), one analyst has suggested that closed systems may better facilitate consistent and enforceable product and manufacturing standards (Wells Fargo Securities 2014a).

Beyond the increased variety over time of products, their components, and related products (including accessories such as carriers, lanyards, stickers, and sleeves), the products continue to appeal to consumers through the incorporation of increasingly complex technologies—including location tracking; Bluetooth connectivity; social networking functions and integration with users' social media accounts; and entertainment functions, such as playing music and videos (Bauld et al. 2014; Brown and Cheng 2014; Honig 2014).

The terminology for e-cigarettes has also expanded. Terms such as e-cigars, e-hookahs, vaping pens, hookah pens, and personal vaporizers are used interchangeably (or preferentially) by some users (Richtel 2014b). In addition, the spectrum of use has broadened, as some e-cigarettes that involve open systems are also used for the aerosolization of marijuana and cannabis oil (Bryan 2014; Morean et al. 2015) and could be adapted for other illicit substances (see Chapter 2).

Worldwide, more than 95% of e-cigarettes sold are thought to have been manufactured in China (Jourdan 2014), most in one city—Shenzhen (Barboza 2014). A few large manufacturers (e.g., Joyetech, Kimree, and First Union) dominate the market (see Appendix 4.1 for descriptions of the major e-cigarette manufacturers).[1] Most of these manufacturers provide supplies to many different e-cigarette companies, including American companies marketing conventional cigarettes, as well as independent e-cigarette companies. Some companies (e.g., Gamucci) have an exclusive manufacturer in Shenzhen.

Some e-cigarette companies have begun to locate their manufacturing base in the United States. Reynolds American, for example, has a factory in Tobaccoville, North Carolina, to manufacture its VUSE brand and strongly emphasizes this location as part of its marketing strategy (CSP Daily News 2015). White Cloud, another U.S.-based company, moved its cartridge-filling production from China to Tarpon Springs, Florida, in May 2014 (McConnell 2014), and the U.S.-based brand Mistic has announced plans to move its manufacturing from China to Greenville, North Carolina (Bettis 2014).

Evolution of Market Share in the E-Cigarette Market

Although the e-cigarette market in the United States has changed significantly since its emergence, these changes have not been studied extensively. This section documents market share by brand for e-cigarette sales in retail outlets tracked by Nielsen, using data from the forthcoming study by Huang and Chaloupka (in press) and supplemented with data from industry reports issued by a number of investment banks. These data, available in Appendix 4.5, clearly show the dynamic changes in the e-cigarette market, and these changes are important to understand in terms of access to and marketing of these products to youth and young adults.

E-Cigarette Sales in Tracked Retail Outlets

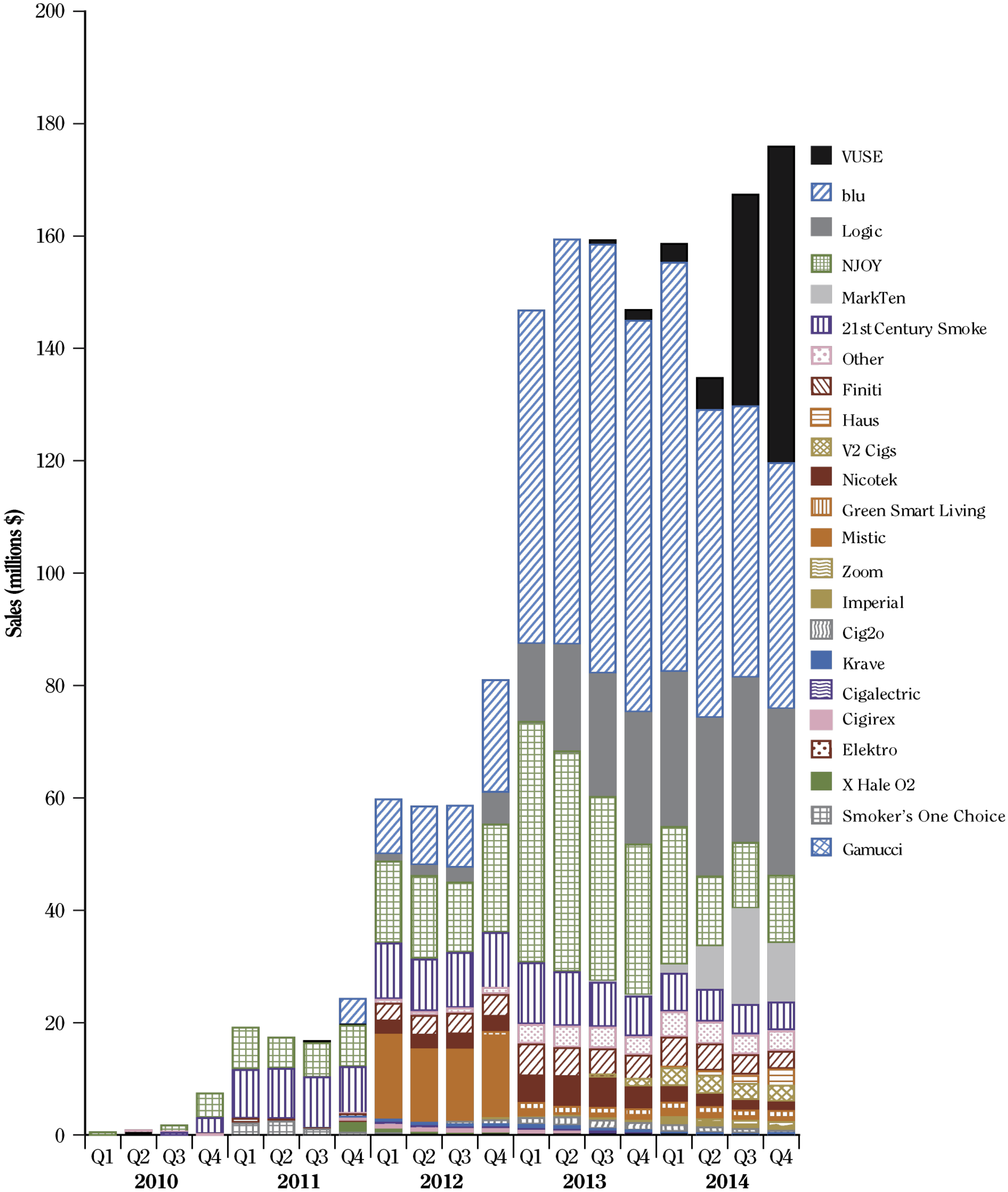
Total sales of e-cigarettes in tracked retail channels have surged exponentially since 2010, increasing from only a few million dollars per quarter in 2010 to more than $170 million in the last quarter of 2014 (Figure 4.1). Although Reynolds American's VUSE brand did not enter the market until late 2013, its sales climbed rapidly in 2014 because of heavy promotion and price discounts. At the end of 2014, VUSE had become the market leader with the highest quarterly sales at $56 million. Blu (owned by Lorillard and thus now by Imperial Tobacco) was the market leader for most of 2013 and 2014, with an average $60 million in quarterly sales. During this time the number of its distribution points rose from 60,000 to more than 150,000 because of its acquisition by Lorillard and subsequent marketing and promotion efforts.

After doubling every year between 2010 and 2013 (Figure 4.2) in the tracked retail channels, rates of increase in the sales of e-cigarettes decelerated significantly, with total sales actually declining in the second quarter of 2014. The deceleration may reflect, in part, the shift away from cigalikes to tank-style devices, mods, and other e-cigarette products among users; the sales of these devices are not tracked as well, which makes it difficult to know the true trends in sales (see Tables 4.1 and 4.2).

Figure 4.2 presents sales data by product type. Sales of disposable e-cigarettes trended upward from 2010 to 2013, increasing from a minimal amount in 2010 to almost $100 million in the second quarter of 2013, but 2014 showed a substantial decline, with the value only about $50 million for the final quarter of that year. The figure shows a clear pattern of seasonality in sales for disposables: sales usually rose in the first quarter of the

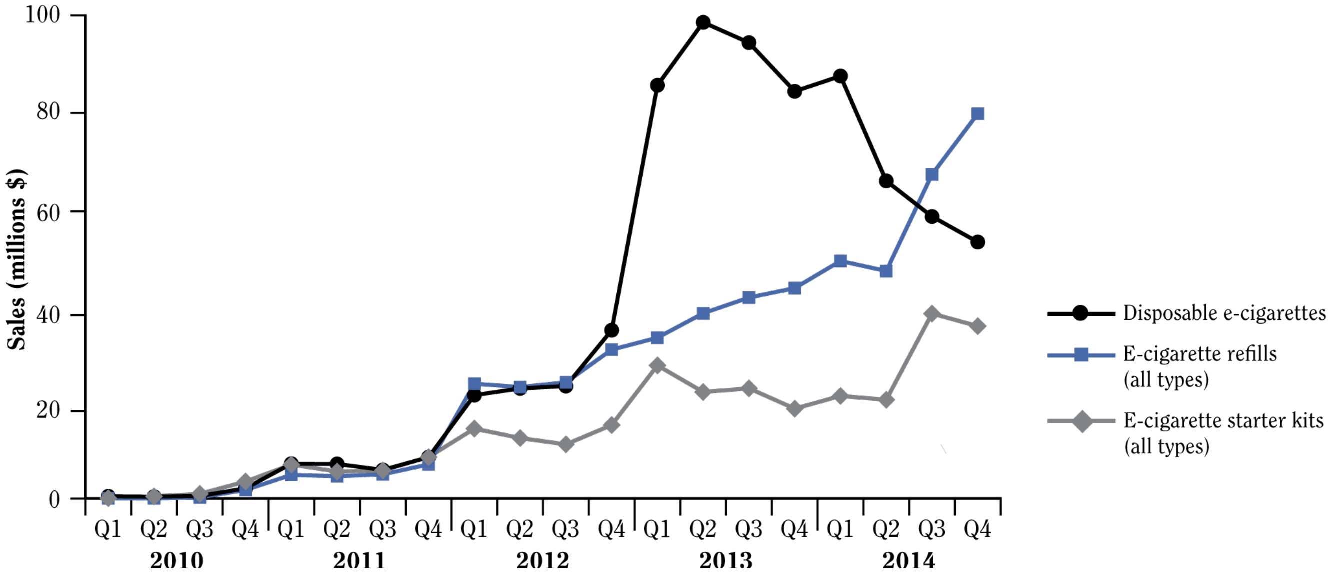
[1]All appendixes and appendix tables that are cross-referenced in this chapter are available only online at http://www.surgeongeneral.gov/library/reports/.

Figure 4.1 E-cigarette sales in tracked channels by brand, 2010–2014



Source: Huang and Chaloupka (in press).
Note: Data points for this figure are shown in Table A4.4-1 in Appendix 4.4.

Figure 4.2 E-cigarette sales in tracked channels by product type, 2010–2014



Source: Huang and Chaloupka (in press).

year—potentially reflecting the effect of New Year's resolutions among smokers who seek to use rechargeable e-cigarettes as a way to quit conventional cigarettes—but had subsequently declined during the rest of the year. Sales of e-liquid refills increased steadily over the 4-year period between 2010 and 2014 and reached $80 million in the final quarter of 2014, representing approximately half of the total e-cigarette sales in the tracked retail channels.

In 2014, more than 85% of e-cigarette sales occurred in the tracked retail and online channels, including certain convenience stores and food, drug, and big-box stores (Wells Fargo Securities 2015a; see Table 4.1). It was estimated that 20% of *all* e-cigarette sales (including e-cigarettes and tanks/mods) in 2014 occurred online, while 44% of *all* e-cigarette sales occurred in "vape shops" and other untracked retail channels (Wells Fargo Securities 2015a; see Table 4.1).

Another important trend in e-cigarette sales is the growth of flavored products. Although some brands, such as NJOY, initially did not sell flavored e-cigarette products, most companies now offer some form of flavored varieties. Giovenco and colleagues (2015) found that sales of menthol-flavored e-cigarettes in traditional U.S. retail channels (e.g., convenience stores, grocery stores, pharmacies, and mass merchandisers) more than doubled between 2012 and 2013, increasing from $96.4 million in 2012 to $215.7 million in 2013. Sales of fruit-flavored e-cigarettes more than tripled during the same period, from $4.9 million to $16.7 million.

Sales of different types and brands of e-cigarettes likely differ by demographic group. For example, anecdotal evidence suggests that youth and young adults prefer pen-style devices, those that come in various shapes and styles, and devices that may be used interchangeably with e-hookahs (Richtel 2014b). Research also suggests that users may eventually graduate to more complex systems; more specifically, experienced users may be more likely to use tanks and mods (Farsalinos et al. 2014). Unfortunately, sales data by demographics are very limited, and studies have not yet examined how sales of e-cigarette products differ by demographic classification.

Production of E-Liquids

E-liquids used in closed-system devices usually are produced in the United States and then shipped to China to be included in the assembly process. For example, MarkTen, blu, and NJOY manufacture their own e-liquids in the United States, which then are sent to China before the final product is assembled there.

In the United States, one of the biggest players in the premixed e-liquid market for refillable e-cigarettes is Johnson Creek Vapor Company (2011), which claims to be the world's leading manufacturer of e-liquid and the first company to produce and manufacture e-liquid in the United States. Johnson Creek has not disclosed the suppliers of its nicotine solution.

Impact of E-Cigarette Price on Sales and Use of These Products

This section summarizes the limited evidence on the impact of e-cigarette prices on the sales and consumption of these products. The sizable body of research examining the effects of taxes and prices on the sale and use of conventional cigarettes (Chaloupka and Tauras 2011; International Agency for Research on Cancer 2011) leads to the conclusion that price increases resulting from higher excise taxes are effective tools for reducing cigarette consumption, especially among youth.

Trends in E-Cigarette Prices over Time

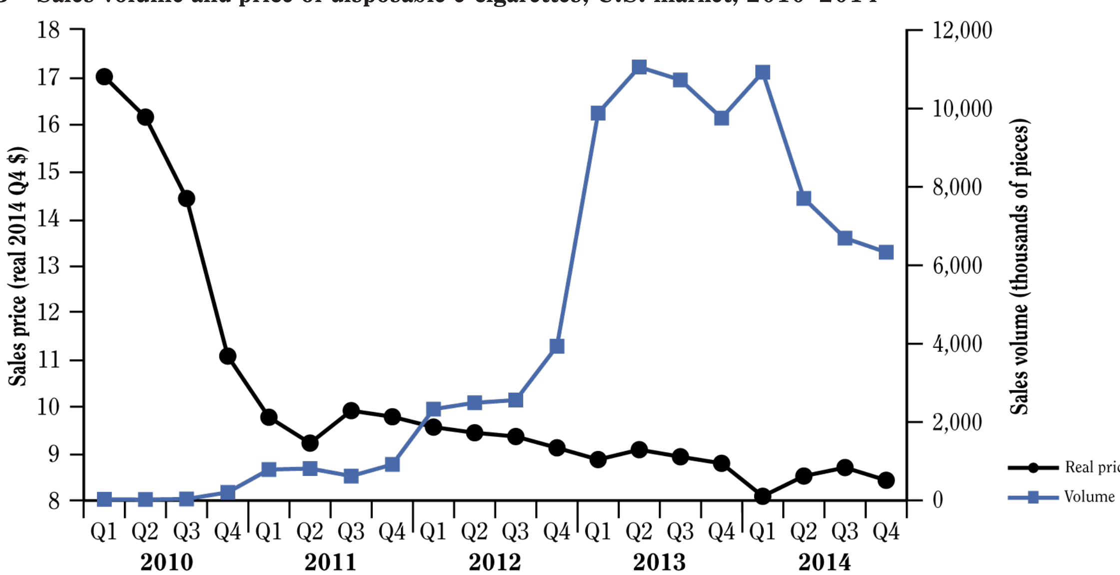
A study by Huang and Chaloupka (in press) documented and analyzed the relationship between real price and sales volume for both disposable and rechargeable e-cigarettes by using Nielsen data, which reflected the e-cigarette (predominantly cigalikes) sales and prices in retail stores tracked by Nielsen.

Figure 4.3 presents U.S. data on real price (determined by adjusting the prices to the value of the U.S. dollar in the fourth quarter of 2014) and sales volume for disposable e-cigarettes between 2010 and 2014 based on data from Huang and Chaloupka (in press). The average price for a single disposable e-cigarette declined from approximately $17 in the first quarter of 2010 to less than $9 in 2014. In terms of volume, the estimate for disposables increased from far below 100,000 in the first quarter of 2010 to almost 11 million in the first quarter of 2014, before dropping to about 6.3 million in the final quarter of 2014. This graph reveals an association between real price and the sales volume for disposable e-cigarettes from 2010 to the second quarter of 2013: As real price declined over time, sales volume increased. Looking back, the rapid decline in the price of disposable e-cigarettes between 2007 and 2011 (Huang and Chaloupka in press) may have occurred because of improvements in product technology and industry promotion, which significantly cut the costs of producing such products (Bhatnagar et al. 2014; Wells Fargo Securities 2015c). The rather modest declines in prices since 2011 may reflect the fact that further technological improvements became less feasible (Wells Fargo Securities 2015c).

In terms of volume, the substantial decrease in 2014 may be partly attributable to consumers shifting away from cigalikes to tanks, mods, and other more powerful devices, for which sales were not tracked well.

An inverse relationship is also evident between real price and sales volume for rechargeable e-cigarettes. Figure 4.4 demonstrates that when the real price went down, the sales volume increased, particularly after 2012. Between 2010 and 2014, the average unit price for rechargeables decreased markedly, dropping from $37 in the first quarter of 2010 to $12 at the end of 2014. However, there were more price fluctuations than were found for disposable e-cigarettes (Figure 4.3). The price fluctuations for rechargeables were likely because of the

Figure 4.3 Sales volume and price of disposable e-cigarettes, U.S. market, 2010–2014



Source: Huang and Chaloupka (in press).

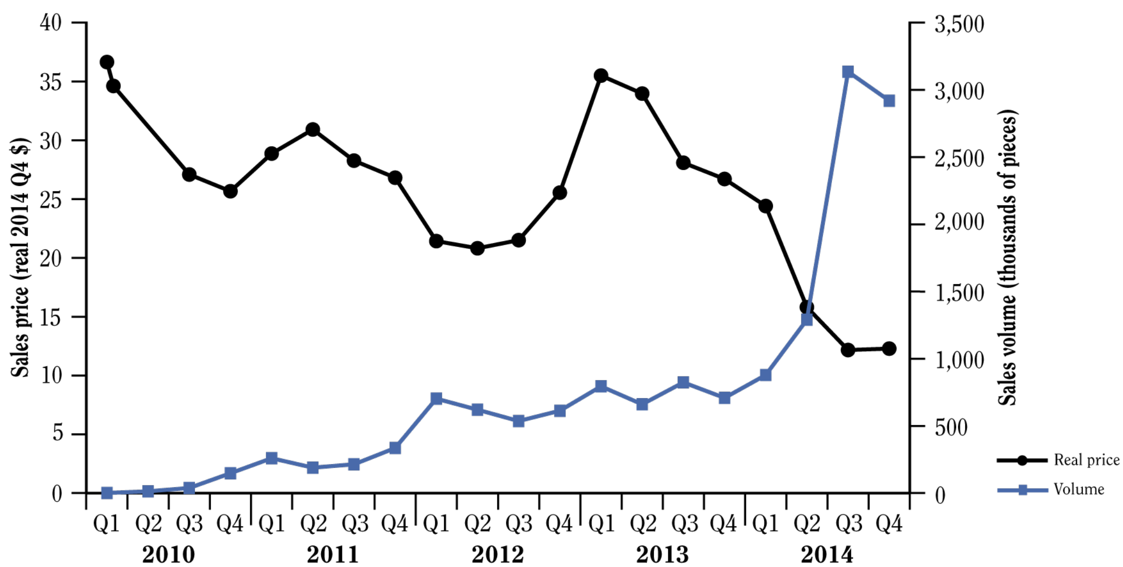
change in product mix and the influx of various new types and brands of these devices during this period (Bhatnagar et al. 2014; Wells Fargo Securities 2015c). Sales volume increased dramatically between 2010 and 2014, rising from a minimal amount at the beginning of 2010 to about 3 million units in the last quarter of 2014.

Impact of E-Cigarette Prices on E-Cigarette Sales

In one of the first studies to explore the effects of e-cigarette prices on the sales of these products, Huang and colleagues (2014b) estimated, from Nielsen data, both the own-price elasticity and the cross-price elasticity of demand for e-cigarettes (disposable or rechargeable) and studied the impact of conventional cigarette prices and smokefree policies on e-cigarette sales. Own-price elasticity is a measure showing how much demand for a product will change given a change in its price, while cross-price elasticity is a measure showing how much demand for a product will change given a change in another product's price. Using data from Nielsen's commercial retail store scanning service, this study employed fixed-effects models to estimate elasticity of demand and associations between e-cigarette sales and either the prices of conventional cigarettes or smokefree policies from 2009 to 2012. Results demonstrated (a) that e-cigarette sales were quite responsive to own-price changes (estimated own-price elasticities for disposable e-cigarettes centered around –1.2 [a 10% increase in price would decrease sales by 12%], while those for rechargeable e-cigarettes were approximately –1.9 [a 10% increase in price would decrease sales by 19%]) and (b) that disposable e-cigarettes appeared to be emerging as substitutes for rechargeables (a 10% increase in rechargeable e-cigarette prices increased sales of disposable e-cigarettes by about 5%). This study concluded that policies increasing the retail prices of e-cigarettes—such as imposing taxes or limiting rebates, coupons, and discounts—could potentially lead to significant reductions in e-cigarette sales and that variations in tax policy by product type could lead to substitution between product categories. It is important to note that "vape shops" were not included in these data, as Nielsen collects data only from convenience, food, drug, and big-box stores.

Although these results provide evidence that changing the price of e-cigarettes affects the number sold, the potential effects of the price of conventional cigarettes on the purchase of e-cigarettes are less clear. Huang and colleagues (2014b) found no consistent or statistically significant relationship between the price of conventional cigarettes and the sale of e-cigarettes. In contrast, Grace and colleagues (2015), who measured the cross-price elasticity of e-cigarettes and conventional cigarettes using simulated demand for the latter in a sample of New Zealand smokers, found that the cross-price elasticity of e-cigarettes was significantly positive, suggesting that e-cigarettes may be partially substitutable for conventional cigarettes. Thus, the use of e-cigarettes may increase as the price of conventional cigarettes increases.

Figure 4.4 Sales volume and price of rechargeable e-cigarettes, U.S. market, 2010–2014



Source: Huang and Chaloupka (in press).

Other evidence suggests that the potential impact of price changes on the use of e-cigarettes may differ by demographic characteristics. Relationships between the smoking of conventional cigarettes and socioeconomic status (SES) are well documented in the literature, and additional evidence has demonstrated that youth and young adults, and those with low SES, tend to exhibit higher sensitivity to changes in the price of conventional cigarettes (International Agency for Research on Cancer 2011; U.S. Department of Health and Human Services [USDHHS] 2012). Therefore, youth and young adults, as well as low-SES persons, may be more price-sensitive in the purchase of e-cigarette products, and thus they may be more likely to stop using e-cigarettes as their price increases. These potential connections between the price of e-cigarettes and their use should be examined carefully as more data become available.

Marketing and Promotion of E-Cigarettes

Marketing is an important tool for industries to use in influencing consumer preferences, and the potential for marketing to influence smoking behaviors has been a source of public health concern for many years (DiFranza et al. 1991; USDHHS 2000, 2012; National Cancer Institute [NCI] 2008). Research has demonstrated a causal relationship between tobacco marketing and smoking, with the majority of research focusing on the impact of tobacco marketing on the initiation of smoking by youth (Biener and Siegel 2000; USDHHS 2012). For adolescents, studies have found cross-sectional and longitudinal associations between the intensity of cigarette marketing and initiation of smoking, brand awareness, brand preferences, attitudes toward smoking, susceptibility to smoking, and smoking behaviors (O'Connell et al. 1981; Chapman and Fitzgerald 1982; McNeill et al. 1985; Charlton 1986; Potts et al. 1986; Aitken et al. 1987; Goldstein et al. 1987; Aitken and Eadie 1990; Botvin et al. 1991; DiFranza et al. 1991; Klitzner et al. 1991; Pierce et al. 1991; Botvin et al. 1993; Hastings et al. 1994; Pierce et al. 1994; Coeytaux et al. 1995; Evans et al. 1995; Pierce and Gilpin 1995; Richards et al. 1995; Slade et al. 1995; Unger et al. 1995; Pollay et al. 1996; Schooler et al. 1996; Gilpin and Pierce 1997; Lam et al. 1998; Feighery et al. 2006). A review of these and other studies led the 2012 Surgeon General's report to conclude that exposure to advertising causes the initiation of smoking (USDHHS 2012).

In general, product marketing is designed to inform people about the products being offered (and thus develop brand "awareness") and to persuade people to buy particular brands (i.e., develop brand "preference"). Branding is particularly important for products considered to be "commodities," such as conventional cigarettes and e-cigarettes, where the offerings are similar and branding differentiates the products (Rossiter and Bellman 2005; NCI 2008). Marketing is particularly critical for e-cigarettes, as new products must be introduced to potential users (Sethuraman et al. 2011).

Like marketers of conventional cigarettes, marketers of e-cigarettes use a number of channels and tactics to advertise and promote their products. These channels have included extensive marketing on the Internet and advertising in mainstream media, including popular magazines, retailer point-of-sale ads, product placement on popular media, and even television commercials—an advertising option unavailable to cigarette manufacturers because of regulatory policies (Legacy for Health 2014; Ganz et al. 2015). E-cigarette brands also use websites to interact directly with their customers through direct-to-consumer marketing (e.g., direct mail and direct e-mail) and social media channels, such as Facebook, Twitter, and Instagram (Huang et al. 2014a; Richardson et al. 2014; Ganz et al. 2015).

Marketing Expenditures

E-cigarette manufacturers currently are not required to report marketing expenditures to any regulatory agency (Boxer et al. 2013; *Federal Register* 2015). Using proprietary data from Kantar Media, however, Kornfield and colleagues (2015) tracked marketing expenditures (television, print, radio, and Internet) back to 2008 for approximately 130 e-cigarette brands (note that many e-cigarette products are not branded, and thus these data are not complete). Kornfield and colleagues (2015) found minimal spending through 2010, followed by an acceleration in spending from $12 million in 2011 to $125 million in 2014 (Figure 4.5). Not shown in the figure is that in 2012, more than 60% of advertising expenditures were for blu (then owned by Lorillard, now Imperial Tobacco), which was the market leader (Kornfield et al. 2015). The trajectory for spending was consistent with the pattern for product sales, particularly for the most dominant brands (Figures 4.1 and 4.5).

Annual marketing expenditures for conventional cigarettes ($9.2 billion in 2012) dwarf the $125 million in 2014 for e-cigarettes (Federal Trade Commission 2015a,b;

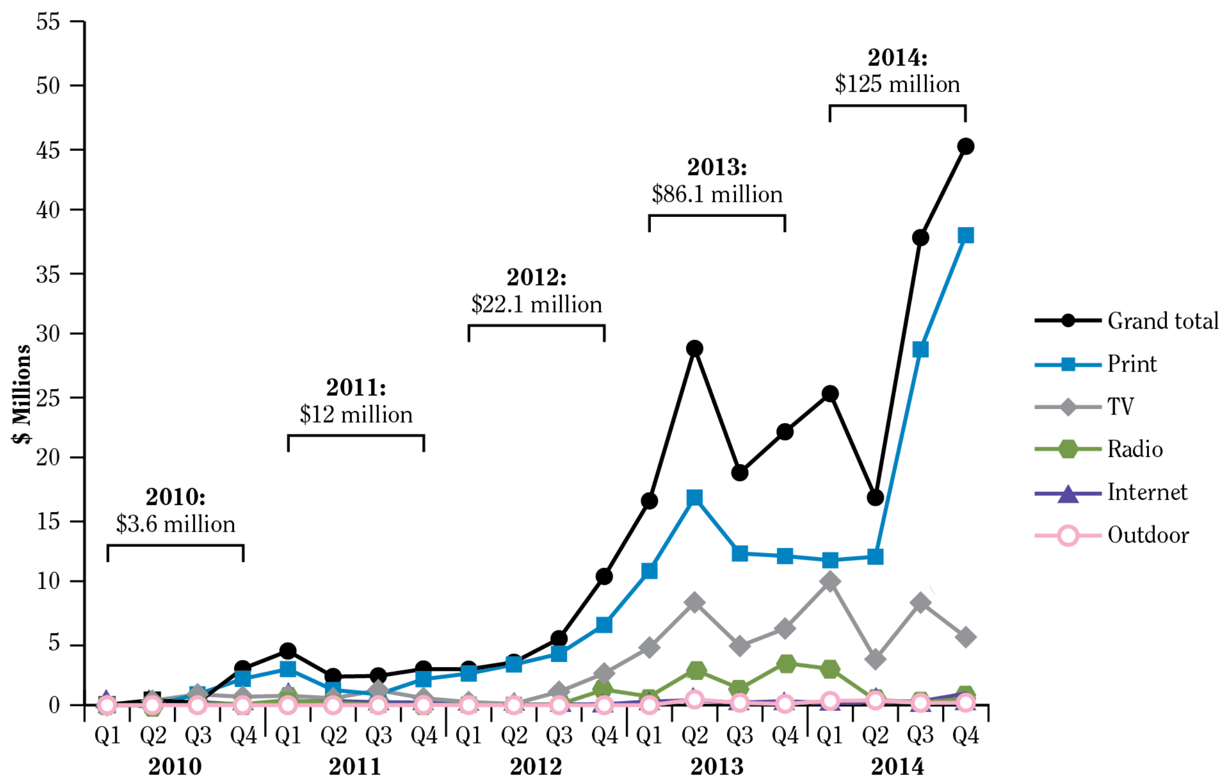
Kornfield et al. 2015). However, the available data about e-cigarette marketing also underestimate total marketing expenditures. Not included are expenditures for retail marketing, social media, and sponsored events, all of which are essential components of the industry's integrated marketing strategy. In the absence of regulation, television advertising for e-cigarettes will continue, as the two largest tobacco companies moved promotions of MarkTen (Altria) and VUSE (Reynolds American) from test markets to national distribution in 2014 (Kornfield et al. 2015; Truth Initiative 2015; Cantrell et al. 2016).

Tobacco marketing and surveillance systems—including the Trinkets & Trash archive maintained by the Rutgers University School of Public Health and the Stanford Research into the Impact of Tobacco Advertising (SRITA) research group—collect examples of e-cigarette advertising and promotions and make these available to users through image-rich websites (see Trinkets & Trash [http://www.trinketsandtrash.org] and Stanford Research into the Impact of Tobacco Advertising [http://tobacco.stanford.edu/tobacco_main/index.php]).

Magazine and Print Advertising

Print has been the dominant channel for tracked expenditures of traditional e-cigarette advertising, representing 84% of annual expenditures in 2014 (Kornfield et al. 2015; Figure 4.5). A study by Richardson and colleagues (2014) collected U.S. advertisements for all noncombustible tobacco products (i.e., e-cigarettes, snus, dissolvables, and chew/dip/snuff) for a 3-month period in 2012 through Mintel, which tracks direct mail and opt-in e-mail ads, and Competitrack, which monitors 21 other media sources. Metadata for identified ads showed advertising for e-cigarettes in print, television, radio, online, direct mail, and e-mail. The three most common media were print, television, and e-mail, and spending was highest for print ads (Richardson et al. 2014). An analysis of industry marketing data by the American Legacy Foundation (now called Truth Initiative) reported that 47% of U.S. teens (12–17 years of age) and 82% of young adults (18–21 years of age) were exposed to magazine advertising for e-cigarettes in 2014; popular venues

Figure 4.5 Quarterly promotional spending for e-cigarettes, 2010–2014



Source: Data for 2010–2013 (Q2) from Kornfield and colleagues (2015, p. 110) and adapted with permission from BMJ Publishing Group Limited. Data for 2013 (Q3)–2014 from Kantar Media (unpublished data).

included tabloids, entertainment weeklies, and men's lifestyle magazines (Truth Initiative 2015).

Research indicates that e-cigarette advertising in magazines with high teen readership is on the rise (U.S. Congress 2014). From 2012 to 2013, the number of e-cigarette advertisements in magazines with high youth readership was four times the number in magazines with high adult readership (U.S. Congress 2014). Recent studies using data from Kantar Media and GfK MRI (the latter measures media audiences and consumer insights; see http://www.mri.gfk.com) on e-cigarette advertisements show that blu led all e-cigarette brands in magazine advertising and that respondents had the highest recall of blu advertisements (Legacy for Health 2014).

A content analysis by Banerjee and colleagues (2015) of print magazine tobacco ads for 2012–2013, using data collected from Kantar Media, identified 171 e-cigarette ads over this period, 27 of which were unique. Ads were found in 24 magazines, 11 of which had been identified in prior studies as having youth and young adult readerships greater than 2 million per year or for which the teen portion of the audience was more than 10%. By number, ads for e-cigarettes were second only to those for conventional cigarettes and higher than the numbers for moist snuff, cigars, and snus. Eighty-five percent of the content in e-cigarette ads focused more on a theme of logos (i.e., logic or facts to support a position) than on a theme of emotional appeal.

In examining persuasive themes, the study found that ads used several approaches, including highlighting the conventional advantages of the product—such as a focus on customer satisfaction—and emphasizing the quality of the product or price (85.2%) (Banerjee et al. 2015). The ads also used the comparative approach, such as portraying the product as being different from other products, being smokefree, or being exempt from use in areas where conventional cigarettes are prohibited. Figure 4.6 shows examples of the claims in e-cigarette marketing. In terms of images, 100% of the ads included the brand name and an image of the product. In addition, ads were most frequently full-page advertisements (89.9%), usually placed the product in a way that drew attention to it (92.6%), and most often used six or more colors (85.2%), which the authors noted increases the attention-grabbing ability of the ads (Banerjee et al. 2015).

A different content analysis of magazine ads for e-cigarettes, this one for a 3-month period in 2012 (Richardson et al. 2014), found health-related themes and non-health-related attributes—such as romantic, sexual, or sociability content, with the highlighting of taste as the most frequent selling proposition (see Figure 4.6, parts B–D for examples). All ads in this analysis were found to contain links to a product's website. When examined by readership, e-cigarette ads were found to have run in magazines with mostly White-male readers and, to a lesser extent, magazines targeting White women. The analysis noted that ads were targeted to a magazine's readership, with different ads shown in the White, male-oriented *Rolling Stone* publication as compared with the female-dominated *Us Weekly*.

Television Advertising to Youth and Young Adults

The increasing frequency and reach of advertising on television raises concerns about the potential impact of promoting nicotine products and renormalizing smoking through that medium, particularly for youth (Hodge Jr 2013; Duke et al. 2014; Grana and Ling 2014). At least 40 unique advertisements for e-cigarettes appeared on U.S. television in 2013 and early 2014 (Farrelly et al. 2015). For example, e-cigarette ads were featured in the Super Bowl broadcast, which reached an estimated audience of more than 100 million persons in 2012 (Deans 2012). The Truth Initiative (formerly the American Legacy Foundation) found that in 2014, television advertising reached similar proportions of youth (62% of 12- to 17-year-olds) and young adults (64% of 18- to 24-year-olds) (Truth Initiative 2015). Using proprietary data from Nielsen, Duke and colleagues (2014) estimated that 50% of U.S. youth were exposed to e-cigarette ads on television in 2013 and that 80% of this advertising was for blu (Lorillard, now Reynolds American). On average, those exposed saw 21 ads between October 2012 and September 2013. Between 2011 and 2013, exposure to e-cigarette advertising on television increased dramatically, by 321% for young adults (18–24 years of age) and 256% for adolescents (12–17 years of age) (Duke et al. 2014).

The same study (Duke et al. 2014) found that more than 75% of the exposure of youth to e-cigarette ads occurred on cable networks. The study found television ads for several different brands—including blu, FIN, Starfire, and NJOY—during a 9-month period in 2013. The most widely aired ad was for blu, featuring a celebrity and closing with the tagline "we're all adults here. It's time to take back your freedom" (Duke et al. 2014, p. 6).

Sponsorships

After the Master Settlement Agreement in 1998, sponsorship of events with a significant youth audience, such as concerts and athletic events, was banned for conventional cigarettes. However, e-cigarettes do not fall under these parameters, and recalling the early marketing of conventional cigarettes, e-cigarette brands have used sponsorships to increase the awareness and appeal of their label and product. For example, in 2011 blu sponsored a NASCAR driver and had its own car in some races (PRNewswire 2011). Additionally, blu has handed out free

Figure 4.6 E-cigarette marketing claims

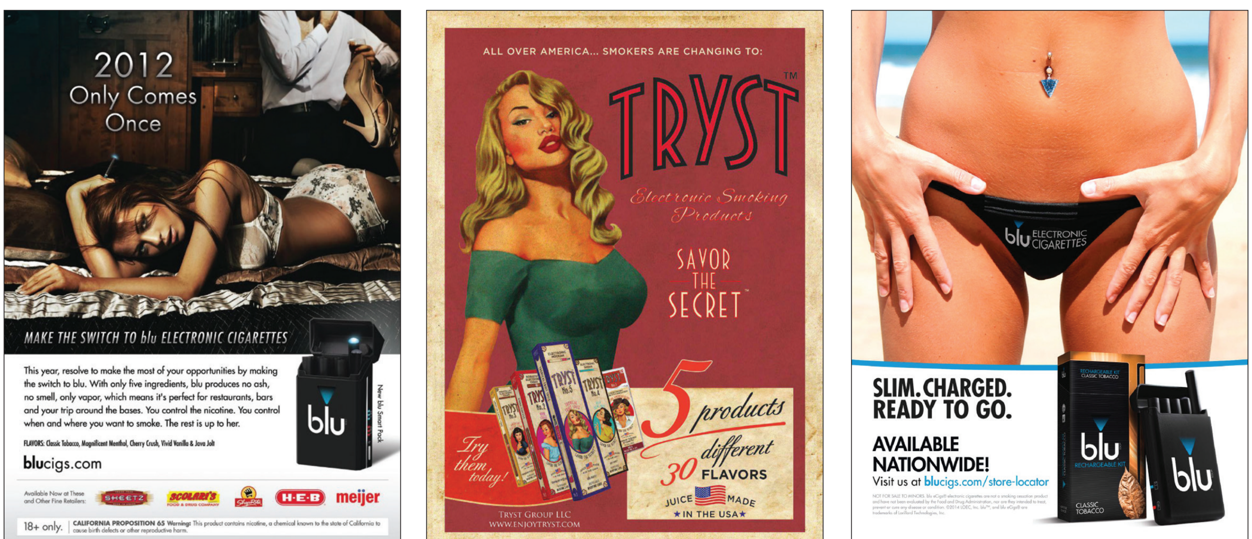
A. Freedom

Source: Esquire (2014).

B. Health

Source: Stanford Research into the Impact of Tobacco Advertising (n.d.b.).

C. Romance, sexuality, or sociability



Source: (Left) *Maxim* (2012), (middle) *Men's Journal* (2014), and (right) *Sports Illustrated* (2014).

Figure 4.6 Continued

D. Taste

Source: Soap Opera Digest (2013).

E. Smoking cessation

Source: Rolling Stone (2013).

F. Use in smokefree environments

Source: Rolling Stone (2012).

G. Product engineering

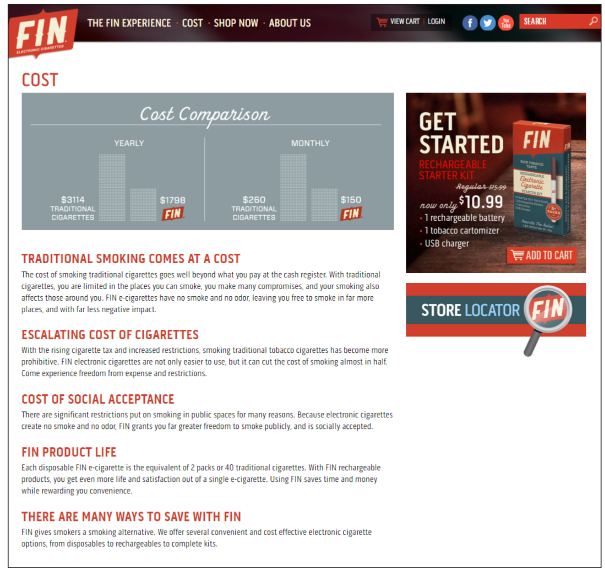
Source: Rolling Stone (2015).

Figure 4.6 Continued

H. Cleaner than cigarettes

Source: *Car and Driver* (2014).

I. Save money



Source: FIN Electronic Cigarettes (n.d.).

J. Circumvent smokefree policies

Source: Spin (2012).

samples during large events and has even sponsored events at music festivals (PRNewswire 2013; blu eCigs 2014). Further, conservative estimates indicate that in 2012 and 2013, free samples were provided by six companies at 348 events, most of these events having high participation by youth (Durbin et al. 2014). Under the deeming rule published in May 2016 (currently under litigation), free samples were banned (*Federal Register* 2016).

Digital Landscape for E-Cigarettes

The Internet has been widely used to promote cigarettes, cigars, and smokeless products (Ribisl 2003; Freeman and Chapman 2007; USDHHS 2012). This medium—through websites, message forums, and social media—has been heavily used to sell and glamorize e-cigarettes and their use. Nearly all teens 13–17 years of age (92%) use the Internet daily, and 73% of teens access the Internet via smartphones (Lenhart 2015). In 2015, a study conducted by the Truth Initiative indicated that 40% of youth (13–17 years of age) and 57% of young adults (18–21 years of age) had seen e-cigarette advertising online (Truth Initiative 2015).

Price promotions are not just involved in sales at brick-and-mortar stores; they are also offered by online stores and through social media. Grana and Ling (2014) found that 80% of websites indicated a sale price or discount, while Huang and colleagues (2014a) found that 34% of commercial tweets mentioned the words "price" or "discount." Both Facebook and Twitter provide opportunities for brands and companies to offer online coupons and discounts (Discount Coupons for blu n.d.; Vapor4Life n.d.). In a study of online e-cigarette retailers, 28% of the websites offered a promotion, such as a discount, other free items, or a loyalty program (Williams et al. in press). Without age restrictions or age verification, youth can access these websites easily and thus obtain the discount or coupon (Williams et al. in press). However, under the deeming rule, websites cannot sell e-cigarettes to youth under the age of 18, so access will likely be curtailed as a result (*Federal Register* 2016). The following sections review three basic categories of online e-cigarette content: websites that sell e-cigarettes, manufacturer-sponsored brand name websites, and e-cigarette promotions on social media websites (including Facebook, Twitter, and YouTube).

Websites Selling E-Cigarettes

Tobacco industry analysts estimate that online sales accounted for approximately 30% of e-cigarette sales volume in the first quarter of 2015 (Wells Fargo Securities 2015a). Some Internet vendors sell their own brands exclusively (e.g., Mistic, Green Smoke), while a large number are online stores that sell many brands and varieties of products (Zhu et al. 2014; Williams et al. in press).

Although the marketers of e-cigarettes have made claims that differ from those made for conventional cigarettes (such as use for smoking cessation, which is illegal without being an approved cessation drug or device), a content analysis of e-cigarette marketing (Grana and Ling 2014) and the observations of tobacco marketing surveillance systems point to several similarities, including the use of young, attractive models; lifestyle claims; and celebrities. Other claims made in e-cigarette advertising have been used in the past by conventional cigarette brands (such as having fewer carcinogens, lower risk of tobacco-related disease) or by smokeless tobacco products (such as the ability to use them where smoking is prohibited) (Grana and Ling 2014). However, under the deeming rule that was published in May 2016, after August 8, 2016, e-cigarette manufacturers cannot make modified risk claims (*Federal Register* 2016) (although this provision has been challenged in pending lawsuits).

Formal analyses of marketing claims of branded e-cigarette sites that both promote and sell e-cigarettes provide details on the types of claims made in these channels. The study by Grana and Ling (2014) analyzed claims from 59 English-language websites over a 2-month period in 2011 and found four major thematic content areas: health- and cessation-related benefits, avoiding smokefree policies, lifestyle benefits, and product-engineering claims. Ninety-five percent of websites made explicit or implicit health-related claims, and 64% made claims related to cessation, often through the use of testimonials. Almost all (98%) included a comparison of the risks and benefits of e-cigarettes and conventional cigarettes; 95% included claims that e-cigarettes are cleaner; and 93% said they were cheaper. Claims regarding where e-cigarettes could be used were also common—with 88% claiming e-cigarettes can be used anywhere, and 71% pointing to e-cigarette use as a means of circumventing clean air policies. Figure 4.6 shows advertising that exemplifies these marketing claims for e-cigarettes.

Grana and Ling's (2014) analysis also points to the common use of lifestyle-related claims, a hallmark of traditional tobacco marketing: 73% of websites contained images or claims of being modern or glamorous. Websites also pointed to social advantages for users of their particular brand: 44% of claims pointed to increased social status and 32% to enhanced social activity, 31% suggested romantic advantages, and 22% used celebrities. Claims of increased social status, opportunity, and romance as well as the use of celebrities may resonate especially with youth and young adults (Grana et al. 2011).

A different content analysis, this one of the marketing messages of English-language branded e-cigarette retail sites, examined and compared websites for two different time periods (May–August 2012 and December 2013–January 2014) and found differences in claims between the two timeframes (Zhu et al. 2014). In comparing claims for brands available during both time periods with those that were newly available in 2013–2014, the authors found that products and advertising messages varied between the two samples. Brands analyzed from 2012 were significantly more likely than those in the later period to (a) claim that their products were healthier and less expensive than conventional cigarettes and could be used where smoking is prohibited and (b) indirectly claim their products were effective for smoking cessation through testimonials and other methods (Zhu et al. 2014). The study also found an increase from one period to the next in the number of branded retail websites and the number of flavors per brand advertised on a website, as well as the likelihood of a website offering e-cigarette hardware and such other products as e-liquids and e-hookahs or other products that did not resemble cigalikes (Zhu et al. 2014). The study's findings suggested that the emphasis for newer brands had shifted from comparing them with conventional cigarettes to a focus on their role as new nicotine delivery systems.

Williams and colleagues (in press) used a standardized search strategy employed in their earlier study of websites selling cigarettes (Ribisl 2003) to identify 995 English-language websites selling e-cigarettes in 2014. The authors performed a content analysis on the 281 most popular websites, as judged by data on traffic. Most of the websites were based in the United States (71.9%), the United Kingdom (16.7%), and China (5.3%), and they offered a variety of products, but more sold e-cigarette starter kits (92.5%) than disposables (55.2%). Most offered flavors, with the most popular being fruit (79.4%), candy (75.2%), coffee (68.0%), and alcohol (45.6%). Although 71.5% featured some type of health warning, 69.4% claimed health advantages over other tobacco products, and 32.7% claimed that the product helped people to quit smoking conventional cigarettes. The sites also featured endorsements or mentions of celebrities using the products (Stanford Research into the Impact of Tobacco Advertising n.d.a.). Physicians and other health professionals provided endorsements as well.

Elsewhere, Cobb and colleagues (2015) conducted a forensic analysis of websites that sold e-cigarettes and participated in affiliate advertising on the Internet. In addition to identifying multiple layers of redirection between online advertising by affiliates and websites selling e-cigarettes, the authors found that online advertisements and affiliate websites included cessation claims.

Research suggests Internet e-cigarette vendors have not routinely verified the age and identity of website visitors or blocked sales to minors. However, after August 8, 2016, due to the deeming rule, it has become illegal for online retailers to sell e-cigarettes to those under 18 (*Federal Register* 2016). In a survey of purchasing by youth, Williams and colleagues (2015) identified 98 websites selling e-cigarettes on which youth, 14–17 years of age, made purchase attempts using prepaid credit cards. In all, 18 (of 98) order attempts failed because of technical problems with the website or the payment system, all of which were unrelated to age verification. Of the remaining 80 orders, 75 (93.8%) were filled. Five vendors claimed to use a service offered by shipping companies to verify age at delivery, but none actually did. Although data are not available on the proportion of youth who purchase their e-cigarettes online versus buying them at retail outlets, this study suggests that youth would have ready access if they tried to purchase e-cigarettes online. The *Prevent All Cigarette Trafficking Act of 2009* requires Internet sellers of cigarettes and smokeless tobacco to, among other provisions, verify age of customers at the time of purchase and ensure that the deliverer checks identification at the time of delivery; stop Internet sales to minors; and pay applicable local, state, federal, and territorial taxes to reduce the price advantage of online sales. FDA regulation now prohibits the Internet sales of e-cigarettes to minors. However, there are currently no federal requirements for Internet vendors of e-cigarettes to check identification upon delivery or pay applicable taxes (Campaign for Tobacco Free Kids 2016).

The marketing of candy and fruit flavors may be one of the reasons that e-cigarettes appeal to youth (Grana and Ling 2014; Richtel 2014a; Zhu et al. 2014). Young adults (18–24 years of age) are more likely to use flavored tobacco products than are adults in the next age group (25–34 years of age) (Villanti et al. 2013). Zhu and colleagues (2014), who used three search engines (Google, Yahoo!, and Bing) and various keywords from May 2012 to January 2014 to identify a wide variety of e-cigarette brands and flavors, found 466 brands and 7,764 unique flavors, with 242 new flavors appearing each month. Other than tobacco flavor, the most popular flavors were menthol (92.1%), fruit (84.2%), dessert/candy (79.9%), and alcohol/drinks (77.5%). Additionally, in their content analysis of e-cigarette retail websites, Grana and Ling (2014) found that such flavors as coffee, fruit, and candy were offered on most sites. Further, flavors were being sold under brand names similar to cereal and candy products that appeal to youth, such as Wrigley's Big Red Gum (Daniels 2015).

Tobacco Industry Corporate and Brand Websites

Three categories of e-cigarette brands have emerged within the U.S. market: brands developed by cigarette manufacturers (i.e., MarkTen, VUSE), brands acquired by cigarette manufacturers (i.e., blu, Green Smoke) (Table 4.3), and brands that have no affiliation with a cigarette manufacturer (e.g., NJOY, FIN). A content analysis of websites for these three types of brands suggested that those *developed* by cigarette manufacturers may be marketed more cautiously than brands *acquired* by cigarette manufacturers or brands that have no affiliation with a cigarette manufacturer (Seidenberg et al. 2016). Table 4.4 compares and contrasts some key features of the websites by manufacturer affiliation. It shows, for example, that access to websites of brands developed by cigarette manufacturers (or a subsidiary) was restricted to users 21 years of age and older (MarkTen), and user registration was required (i.e., the user needed to input personal information such as name, address, and birthdate) for VUSE. In contrast, websites for brands with no affiliation

Table 4.3 Mergers, acquisitions, partnerships, and other agreements in the e-cigarette industry

Date	Purchaser	Acquisition target	Partnerships and other agreements	Deal size[a]	Geography[b]
December 2011	Japan Tobacco	—	Ploom (partnership)	Not disclosed	United States
December 2012	BAT	CN Creative	—	£40 million	United Kingdom
April 2012	Lorillard	blu	—	$135 million	United States
April 2013	National Tobacco	—	V2 Cigs (partnership)	Not disclosed	United States
August 2013	Imperial	Dragonite	—	$75 million	China
October 2013	Lorillard	SKYCIG	—	£60 million	United Kingdom
January 2014	ECIG	VAPESTICK	—	$70 million	United Kingdom
January 2014	Gilla	Drinan	—	Not disclosed	Ireland
February 2014	Altria	Green Smoke	—	$110 million	United States
March 2014	ECIG	FIN	—	$170 million	United States
April 2014	ECIG	VIP	—	$58 million	United Kingdom
June 2014	ECIG	Ten Motives	—	$104 million	United Kingdom
June 2014	PMI	Nicocigs	—	Not disclosed	United Kingdom
July 2014	ECIG	Hardwire	—	$30 million	Internet
November 2014	Japan Tobacco	E-Lites	—	Not disclosed	United Kingdom
January 2015	BreatheEcigs/DNA	Breathe LLC	—	Not disclosed	United States
February 2015	Japan Tobacco	—	Ploom (purchased the intellectual rights to some Ploom technology)	Not disclosed	United States
March 2015	Gilla	An undisclosed Florida e-liquid company	—	$1.5 million	United States
April 2015	Japan Tobacco	Logic	—	Not disclosed	United States
June 2015	Imperial	blu	—	$7.1 billion	United States and United Kingdom
December 2015	Gilla	The Mad Alchemist	—	$500,000	United States, Canada, Europe, and United Arab Emirates

Source: Various news sources and companies' websites, SEC (Securities and Exchange Commission) reports, and press releases as of January 25, 2016.

[a]Deal size refers to prices at the time of the announcement, not necessarily the final transaction price.

[b]Geography refers to the country in which the acquisition target was registered.

with a cigarette manufacturer and those acquired by cigarette manufacturers were accessible to users 18 years of age and older via self-reporting of age, with the exception of 21st Century Smoke. In addition, VUSE e-cigarettes were not sold online (they were sold only in retail outlets), and they were available in a single nicotine level with limited flavor options (except for forthcoming tank versions), while MarkTen could be purchased online. The websites for both MarkTen and VUSE mentioned selling flavored e-cigarettes. As far as e-cigarette brands not having an affiliation with a cigarette manufacturer or that were acquired by a cigarette manufacturer, all brands except Logic offered fruit, candy, or other flavors. Further, all of the unaffiliated brand websites sold e-cigarettes online and offered multiple nicotine levels. Most websites offered nicotine-free options and flavored e-cigarettes as well (Seidenberg et al. 2016). The Green Smoke website even provided a link to guide customers in finding the proper nicotine level for their cartridges (Green Smoke E-Vapor n.d.).

Social Media Promoting E-cigarettes

E-cigarettes have been widely promoted on social media platforms such as YouTube, Twitter, Instagram, and Facebook; most of these social media sites do not require age verification. YouTube is the most popular video-sharing website globally and features many e-cigarette videos. Luo and colleagues (2014) used various search terms to identify 196 unique videos in February 2013 that were portraying e-cigarettes and found that 94% of the videos were “pro” e-cigarettes, 4% were neutral, and

Table 4.4 Comparison of website access restrictions, online sales, nicotine levels, and flavors among e-cigarette brands with no cigarette manufacturer affiliation, brands acquired by cigarette manufacturers, and brands developed by cigarette manufacturers

	E-cigarette brands (10)		
	Not affiliated with a cigarette manufacturer: NJOY, Logic, 21st Century Smoke, FIN, Nicotek, and Mistic (6)	**Acquired by a cigarette manufacturer: blu and Green Smoke (2)**	**Developed by a cigarette manufacturer (or subsidiary): MarkTen and VUSE (2)**
Website access	All websites (except 21st Century Smoke) have one-click access[a] or age verification to restrict initial access to people 18 years of age and older; 21st Century Smoke does not have any website restrictions for initial access.	Both sites have one-click access or age verification to restrict initial access to people 18 years of age and older (blu) and 21 years of age and older (Green Smoke).	MarkTen has age verification to restrict initial access to people 21 years of age and older. Before initial access, VUSE requires people 21 years of age and older to register first with the website.
Online sales	All brands can be purchased online.	Both brands can be purchased online.	MarkTen can be purchased online; VUSE cannot.
Multiple levels of nicotine	Among all brands, the level of nicotine varies by product. Some (e.g., blu, Logic Zero, 21st Century Smoke, Nicotek) offer products with 0% nicotine (by volume).	Among both brands, the level of nicotine varies by product.	For MarkTen, the level of nicotine varies by product. VUSE e-cigarettes contain 4.8% nicotine (by weight). VUSE tanks, set to come out in February 2016, will have different levels of nicotine (Kress 2015).
Flavors (other than tobacco and/or menthol)	All brands offer a variety of flavors, such as fruit and candy.	Both brands offer a variety of flavors.	MarkTen offers two flavors: fusion and wintermint. VUSE offers four flavors: crema, chai, berry, and mint (Kress 2015).

Source: Unless cited otherwise, information was obtained from the companies’ websites (January 2016): https://www.njoy.com/; http://store.logicecig.com/; https://www.21stcenturysmoke.com/; https://www.fincigs.com/; http://www.nicotekecigs.com/; http://www.misticecigs.com/; http://www.blucigs.com/; https://www.greensmoke.com/; https://www.markten.com/; and https://vusevapor.com/.

[a]With “one-click access,” visitors to a website self-report on their age by identifying their age from a clickable pop-up box. For example, persons 18 years of age and older can browse the website, but those younger than 18 cannot.

2% were "anti" e-cigarettes. Those authors found that the three most common genres were advertising of products, user sharing, and product reviews. Of the "pro" e-cigarette videos, 84.3% featured links to websites selling e-cigarettes, and 71.4% claimed that e-cigarettes were a healthier alternative to conventional cigarettes. Finally, the "pro" videos received more visits and were rated more favorably than were the small number of "anti" videos.

The authors of another study, this one a content analysis of 365 e-cigarette videos on YouTube that ran at some time from June 2007 to June 2011, estimated that more than 1.2 million youth and a total of 15.5 million people worldwide were exposed to these videos (Paek et al. 2014). In addition to looking at viewership, the content analysis examined the type, sponsorship, and health claims of the videos. Just 16% of the videos were formal advertisements or news clips, and 79.2% of the content was coded as appearing to have been generated by users. Videos emphasized economic, psychological, and social benefits, and health claims included e-cigarettes being less harmful than conventional cigarettes, healthy, and providing help in quitting smoking. Most (85.2%) videos in the sample were sponsored by e-cigarette companies or their associates, with an additional 10% coming from individuals who did not mention a specific website or company. Interestingly, videos sponsored by marketers contained a significantly lower level of health claims than did those from laypeople (users) and, not surprisingly, contained a higher level of information cues (e.g., product contents, price, distribution channel).

A cross-sectional study of Twitter, a microblogging platform, that examined more than 74,000 tweets accessed through a licensed Twitter data provider over a 2-month period in 2012, found extensive marketing of e-cigarettes (Huang et al. 2014a). The majority of e-cigarette content during this period was advertising and promotion. In fact, 89.6% of the tweets contained commercial content (e.g., presence of branded promotional messages or hyperlinks to commercial websites), and only 11% identified as being non-sponsored or independent, reflecting individual opinions or experiences, or being linked to non-promotional content. Commercial tweets most commonly contained price promotions and discounts (34.3%), with cessation-related claims included in 10.8% and lower percentages for health or safety (Huang et al. 2014a).

Jo and colleagues (2016), in a study of 2,847 tobacco-related tweets about price promotions and coupons, found that e-cigarettes, not conventional cigarettes, were the most frequently mentioned product (90.1%), and about one-third of all e-cigarette-related tweets included a discount code. The tweets also touted the relatively low price of e-cigarettes and made comparative claims about the health risks of the product.

Sponsored Online and Video Advertising

The study by Richardson and colleagues (2015) used information from the monitoring service Competitrack to analyze the volume and characteristics of industry-sponsored tobacco and e-cigarette online banner/video advertisements in the United States and Canada in 2012–2013. This study found that online banner/video advertising—which embeds an ad or video on a website—was more commonly used for e-cigarettes than for conventional cigarettes. E-cigarette ads were often placed on music or entertainment (39.1%) sites, which the authors noted attract a sizeable number of youth and young adults. The most frequent theme for the 24 online banner or video e-cigarette ads (promoting five e-cigarette brands) analyzed was that the product was more "green" or environmentally friendly than conventional cigarettes (54.2%), followed by less harmful than cigarettes (37.5%), and being an alternative to conventional cigarettes when someone could not smoke (33.3%).

E-Cigarettes in the Retail Environment

Conventional Tobacco Retailers (Convenience Stores, Pharmacies, Tobacco Shops)

As of December 2015, 48 of the 50 states prohibited sales of e-cigarettes to minors (National Conference of State Legislatures 2015), but compliance of retailers with youth-access laws has not yet been studied. FDA is actively enforcing the federal minimum age requirements. As of August 8, 2016, the federal deeming rule bans the sale of e-cigarettes to minors under the age of 18 and requires photo identification for those under age 27 (*Federal Register* 2016). In the past few years, brick-and-mortar retailers have surpassed the Internet as the dominant distribution channel for e-cigarettes. For example, after Lorillard acquired blu in 2012, the number of retailers selling this brand increased from 13,000 to 127,000 in just 1 year (Esterl 2012; Bannon 2013). In California, the proportion of licensed tobacco retailers that sold e-cigarettes increased from 12% in 2011 to 67% in 2014 (Chapman 2015).

E-cigarettes are widely available in convenience stores, a type of establishment that 4.1 million U.S. teenagers visit at least once per week (Rose et al. 2014; Sanders-Jackson et al. 2015a). According to a 2013 state-sponsored survey that included a sample of approximately 7,300 licensed tobacco retailers in California, e-cigarettes were sold in more than half of convenience stores, pharmacies, and liquor stores and in nearly all tobacco shops

(California Department of Public Health and California Tobacco Control Program 2014).

Only three studies have examined the retail availability of e-cigarettes near schools. In a 2012 nationally representative sample of tobacco retailers, the presence of a public school within 1,000 feet was not related to the availability of e-cigarettes (Rose et al. 2014). In a study that examined a much larger buffer zone in Kentucky, 88% of schools in two counties were located within 1 mile of a retailer that sold e-cigarettes (Hahn et al. 2015). As for colleges, disposable and/or rechargeable e-cigarettes were available at 60% of tobacco retailers near campuses in North Carolina and Virginia in 2013, a more than two-fold increase from the previous year (Wagoner et al. 2014).

A pilot study examining tobacco point-of-sale advertising and promotion in the central Harlem neighborhood of New York City found that 26% of stores had e-cigarette advertising on the building's exterior (Ganz et al. 2015). External ads included those located less than 3 feet above the ground at the eye level of children—a placement that was outlawed for conventional cigarettes by the Master Settlement Agreement—and featured flavored products (Ganz et al. 2015).

Unlike conventional cigarettes, e-cigarettes appear to be relatively less prevalent at stores in economically disadvantaged communities. In an analysis that examined data from two studies that had used representative samples of U.S. tobacco retailers, e-cigarettes were less likely to be sold than conventional cigarettes at stores located in economically disadvantaged neighborhoods and in neighborhoods with a higher proportion of African American residents (Rose et al. 2014). These patterns are consistent with evidence that e-cigarette marketing in other channels targets higher income non-Hispanic White males (Emery et al. 2014). However, the retail availability of e-cigarettes has changed at different rates in different neighborhoods. In a study of U.S. food stores, only 3% of stores located in non-Hispanic White and Hispanic neighborhoods sold e-cigarettes in 2010; none of the stores in predominantly African American neighborhoods sold them (Khan et al. 2014). Three years later, the figures were 36% in predominantly non-Hispanic White neighborhoods, 18% in Hispanic-majority neighborhoods, and 19% in African American-majority neighborhoods. Notably, these data were collected before the two largest U.S. tobacco companies launched MarkTen (Altria) and VUSE (Reynolds American) in late 2013. Thus, the industry's current influence on disparities in the retail availability and marketing of e-cigarettes cannot be readily estimated from the studies reviewed.

Two studies examined retail data about e-cigarettes as a function of state and/or county smokefree air laws (Huang et al. 2014b; Rose et al. 2014). In one of the studies, which used data collected in two studies that used independent samples of U.S. tobacco retailers, the odds of selling e-cigarettes were greater for retailers in states with weaker smokefree air policies, even after controlling for store type, price of conventional cigarettes, and neighborhood demographics (Rose et al. 2014). A similar inverse relationship was found between sales of disposable e-cigarettes (as measured by retail scanner data in 52 U.S. markets from 2009 to 2012) and the proportion of the population protected by 100% smokefree policies covering all indoor areas of bars, restaurants, and workplaces (Huang et al. 2014b). Taken together, these results suggest that e-cigarettes are, at least initially, more likely to be sold in communities with weaker smokefree policies.

Few retail surveillance studies have characterized promotion, placement, or price for e-cigarettes (Hsu et al. 2013; Wagoner et al. 2014; Ganz et al. 2015). In a study of licensed tobacco retailers in Florida, advertising for e-cigarettes was more prevalent on the exterior than the interior (50% vs. 11%) (Kim et al. 2015). In the study by Wagoner and colleagues (2014), the presence of e-cigarette advertising near college campuses in North Carolina and Virginia tripled on store exteriors and quadrupled in store interiors in just 1 year. Although the price of rechargeable units decreased significantly, there was little evidence of price discounting for any e-cigarettes (Wagoner et al. 2014). The low visibility of price discounts at the point of sale suggests that marketing for e-cigarettes favors a "pull" strategy, relying on direct mail and e-mail coupons and special offers to entice customers to retail locations.

"Vape Shops"

"Vape shops" specialize in the sale of refillable devices and tank systems, typically offer a tasting menu of flavors, and sometimes feature a lounge area where customers can "vape" while socializing (Lee and Kim 2015; Sussman et al. 2016). "Vape shops" have been excluded from most studies about the retail marketing of e-cigarettes, in part because the environment is so different from that of conventional tobacco retailers (Lee and Kim 2015) and because so few states require these establishments to obtain a tobacco retailer license, effectively keeping them out of the sampling frame for many studies and making the monitoring and enforcement of laws difficult (Lee et al. 2014).

Anecdotal evidence suggests that "vape shops" currently do not have readily visible branded signs and displays that characterize the retail marketing of other tobacco products. Even though the relationship between the "vape shop" industry and the tobacco industry can be adversarial (Sussman et al. 2016), one study found that the marketing practices of these establishments closely resemble the current and former strategies that tobacco companies have used to market other tobacco products (Cheney et al. 2015). According to this study, “vape shop” owners and managers in Oklahoma used free samples, loyalty programs, sponsored events, direct mail, advertising through social media, and price promotions targeted at particular consumers, such as college students (Cheney et al. 2015). No other study about marketing by “vape shops” has been published.

Numerous gaps exist in research about “vape shops,” including information on consumer behavior, the use of tracking systems for sales data, marketing surveillance, purchases by youth, and the opinions of retailers and the general public about regulations. Spatial analyses are needed to determine whether “vape shops” are clustered near schools or college campuses, whether other neighborhood demographics are correlated with the location of these establishments, and how such associations, if present, have changed over time and in response to state and local policy interventions. The proportion of “vape shops” where workers mix solutions of liquid nicotine on site is not known, and the absence of uniform safety precautions regarding handling and spills poses additional concern for regulation (ChangeLab Solutions 2014). Under the deeming rule that was published in May 2016, “vape shops” that mix and sell e-liquids are both retailers and manufacturers and, therefore, are subject to the provisions in the deeming rule and the Tobacco Control Act that apply to both (*Federal Register* 2016).

Exposure and Receptivity to Advertising for E-Cigarettes

Exposure

Given industry data about increasing expenditures for e-cigarette advertising and extending its reach, the high levels of advertising awareness reported in studies of youth and/or young adults are not surprising. An online panel of U.S. youth (13–17 years of age) and young adults (18–21 years of age) conducted in February 2014 found that awareness of e-cigarette advertising was greatest for retail advertising, followed by awareness of advertising on television and online (Truth Initiative 2015). In this study, and compared with the entire population, awareness among current smokers of e-cigarette advertising was higher across all channels and higher for online ads than for television ads (Legacy for Health 2014).

In school-based surveys of middle and high school students in Connecticut, gas stations and television were the dominant channels in which students reported recently seeing e-cigarettes advertised or sold (Krishnan-Sarin et al. 2015). A different pattern was observed in a convenience sample of college students in Hawaii, where the figures for seeing ads were 59%, online; 58%, television; 71%, malls; 41%, gas stations; and 47%, convenience stores (Pokhrel et al. 2015). Elsewhere, in an online experiment, 56% of adolescents (13–17 years of age) who had never used e-cigarettes reported seeing at least one televised advertisement previously, and there were modest, but statistically insignificant differences in exposure by smoking status and race/ethnicity ($p<.10$) (Farrelly et al. 2015).

The National Youth Tobacco Survey reported that in 2014, 18.3 million middle and high school students were exposed to e-cigarette advertising from at least one source (CDC 2016b). In this nationally representative sample of U.S. middle and high school students, nearly 7 out of 10 reported seeing an e-cigarette advertisement in that year. The most common places for exposure among middle school students were retail stores (52.8%), the Internet (35.8%), television and movies (34.1%), and newspapers and magazines (25.0%). Similarly, high school students reported the highest exposure at retail stores (56.3%) and then the Internet (42.9%), television and movies (38.4%), and newspapers and magazines (34.6%). Among both middle school and high school students, exposure through retail stores was higher among non-Hispanic Whites than non-Hispanic Blacks. However, non-Hispanic Blacks had higher exposure to e-cigarette advertisements on television and in movies than non-Hispanic Whites. Females had higher exposure than males to advertisements on the Internet and in newspapers and magazines.

Receptivity to Advertising

Receptivity to tobacco marketing is a well-established risk factor for tobacco use by adolescents and young adults (NCI 2008; USDHHS 2012), and two studies adapted measures of receptivity to the marketing of tobacco in research on e-cigarettes. In one study, college students from a southwestern state who watched three advertisements for different brands of e-cigarettes in an online survey used a 7-point scale to rate how enjoyable, likable, and appealing the ads were; results suggested moderate receptivity (mean of 51 on a scale ranging from 7 to 126) and significant differences between brands (Trumbo and Kim 2015). In the other study, Pokhrel and colleagues (2015), using a sample of college students from Hawaii, adapted a multi-item scale of liking advertisements from studies about alcohol (Unger et al. 2003) and two items from the most commonly used measure of receptivity to tobacco marketing (Pierce et al. 1998). This study observed low levels of liking advertisements (all below the scale midpoint) (Pokhrel et al. 2015). The extent to which youth and young adults who are receptive to e-cigarette marketing are also receptive to tobacco marketing has not been studied. However, the extent to which advertising strategies for e-cigarettes mimic strategies used by tobacco companies suggests that the two measures of receptivity could be highly correlated.

Effect of E-Cigarette Advertising on Behavior

Associations with E-Cigarette Use and Intentions to Use

Evidence that advertising for conventional cigarettes increases product initiation among never users, discourages quit attempts in current users, and encourages relapse in those trying to quit is well established (NCI 2008; USDHHS 2012). However, while fewer studies have focused on e-cigarette advertising in particular, the available evidence suggests that e-cigarette advertising has similar effects, although additional research is recommended. A search for studies of youth or adults that either (a) manipulated exposure to e-cigarette advertising or measured self-reported recall of advertisements, (b) assessed the frequency of exposure to advertising in one or more channels, or (c) measured receptivity to e-cigarette advertising yielded 10 studies that addressed the impact of advertising on the use of or intentions to use e-cigarettes.

One experiment tested whether seeing television advertising for e-cigarettes predisposed adolescents to try these products (Farrelly et al. 2015). Among adolescents (13–17 years of age) who had never used e-cigarettes, a single exposure to a set of four televised advertisements for popular brands resulted in significantly greater intention to try e-cigarettes—more than 50% higher in the treatment group than the control group (Farrelly et al. 2015). Another study examined responses to e-cigarette advertisements among young adults (Trumbo and Kim 2015); among a convenience sample of college students who watched three television ads for e-cigarettes, greater receptivity to e-cigarette advertising was associated with significantly higher odds of intending to use e-cigarettes in the future, but the analysis did not adjust for prior use or individual demographics (Trumbo and Kim 2015).

Very few cross-sectional or longitudinal surveys have examined associations between adolescents' exposure to e-cigarette advertising and either trial or regular use of such products. An analysis of the 2011 National Youth Tobacco Survey found that adolescents who reported frequent exposure to protobacco advertising at the point of sale and on the Internet (e.g., seeing ads most of the time or always) had significantly higher odds of ever using e-cigarettes, and there was a dose-response association between the number of marketing channels to which they were exposed and ever use (Agaku and Ayo-Yusuf 2014).

Surveillance research that differentiates exposure to advertising for e-cigarettes from exposure to ads for conventional tobacco products would be useful to establish whether exposure to e-cigarette advertising is correlated with product use and contributes to product initiation and product use among young people who were not tobacco users to start. It bears mentioning here that a generation of U.S. youth has grown up without any television or billboard ads for conventional cigarettes. In this context, research is needed to understand at what age young people understand that e-cigarette advertising depicts the use of e-cigarettes rather than the smoking of conventional cigarettes and to examine whether there are spillover effects of marketing for e-cigarettes on the use of conventional tobacco products.

In the study from Hawaii (Pokhrel et al. 2015), researchers examined the association between exposure to e-cigarette advertising and product use using a convenience sample of approximately 300 college students in that state. The study found that more frequent exposure to e-cigarette advertising—as measured by exposure in any of multiple channels (e.g., newspapers, magazines, Internet, television billboards, sporting/cultural events, convenience stores, gas stations, grocery stores, and malls)—was associated with significantly higher odds of ever using e-cigarettes, and receptivity to e-cigarette advertising was associated with higher odds of past-month use, even after adjustments for smoking status and individual demographics.

Two studies strongly support the association between exposure to e-cigarette advertising and youth susceptibility to and use of e-cigarettes (CDC 2016a; Mantey et al. 2016). Both studies examined data from the 2014 National Youth Tobacco Survey, a survey of more than 20,000 U.S. middle and high school students. The studies assessed self-reported levels of exposure to e-cigarette ads on the Internet, in newspapers and magazines, at retail stores, and on television or in movies, and used multivariate logistic regression models to examine the relationships between marketing exposure and e-cigarette susceptibility and use. Exposure to each type of e-cigarette marketing was significantly associated with increased likelihood of ever having used and current use of e-cigarettes among middle and high school students (CDC 2016a; Mantey et al. 2016). Exposure was also associated with susceptibility to use e-cigarettes among current nonusers. In multivariate models, as the number of channels of e-cigarette marketing exposure increased, the likelihood of use and susceptibility also increased (Mantey et al. 2016).

One concern is that e-cigarette advertising may perpetuate dual use of conventional cigarettes and e-cigarettes, a concern that comes from the visual depictions of e-cigarette use that may serve as smoking cues to current and former smokers of conventional cigarettes, increasing the urge to smoke and decreasing intentions and efficacy to quit or abstain from smoking (Glynn 2014; Grana and Ling 2014; Maloney and Cappella 2016). Consistent with cue-reactivity studies about conventional cigarettes, exposure to e-cigarette use in a laboratory was associated with increased urge to smoke conventional cigarettes among smokers and an urge to use e-cigarettes among users of that product (King et al. 2015). Whether exposure to depictions in advertising of the use of e-cigarettes triggers urges to begin or continue to smoke conventional cigarettes or weakens users' resolve to quit has received little attention. This is particularly important because rates of cigarette smoking among youth in the United States are at an historic low (CDC 2014).

Associations with Knowledge, Risk Perceptions, and Other Attitudes

Advertising is an important source of information about e-cigarettes for youth and adults (de Andrade et al. 2013; Pepper et al. 2014a), and there is emerging evidence about how unregulated advertising for e-cigarettes may influence consumer perceptions about product safety. One study of adolescents (Farrelly et al. 2015) and three studies of adults (Pokhrel et al. 2015; Sanders-Jackson et al. 2015b; Tan et al. 2015a) examined the associations between exposure to e-cigarette advertising and knowledge or perceptions of these products.

Among U.S. adolescents (13–17 years of age) who had never used e-cigarettes, a single exposure to a set of four televised advertisements was associated with significantly higher odds of agreeing that the products can be used without affecting those around you and with lower odds of agreeing that the products are harmful (Farrelly et al. 2015). Compared with the control group, the treatment group reported significantly more positive attitudes about the benefits of using e-cigarettes. Elsewhere, in an online survey representative of U.S. households, 57% of young adults (18–34 years of age) were aware that some e-cigarettes contain nicotine, but more frequent exposure to e-cigarette advertising at point of sale, in mass media, and in social media (the three variables combined) was associated with a significantly higher likelihood of answering this question incorrectly (Sanders-Jackson et al. 2015b).

In the previously cited study of college students in Hawaii (Pokhrel et al. 2015), greater receptivity to e-cigarette marketing—but not more frequent exposure to the advertising of these products—was associated with significantly greater endorsement of beliefs about harm reduction for e-cigarettes (e.g., safer, improves health, helps to quit). A different study referred to an online survey of U.S. adults (the Annenberg National Health Communication Survey [ANHCS]) in which surveyors measured the frequency of exposure to e-cigarette advertising (point of sale, mass media, and social media) and the degree to which participants perceived those messages as negative or positive (Tan et al. 2015a). Compared with those who reported no exposure to advertising, those who held negative perceptions of these messages reported significantly greater perceptions of harm from breathing e-cigarette vapor. Taken together, the available evidence suggests that continued exposure to unregulated advertising likely promotes reduced perceptions of harm and toxicity and increased perceptions of the efficacy of e-cigarettes for quitting conventional cigarettes.

Whether the increasing amount of advertising and promotional activities for e-cigarettes serves to renormalize the smoking of conventional cigarettes—that is, to shift public norms back to acceptance of cigarette smoking—is also not known. In focus groups of adult smokers 45 years of age and older, participants expressed almost unanimous agreement, after seeing selected ads, that e-cigarette advertisements promote smoking as a socially desirable behavior (Cataldo et al. 2015). The analysis by Farrelly and colleagues (2015) also looked at outcomes for conventional cigarettes. After exposure to e-cigarette advertising, there were no significant differences between the treatment and control groups on intentions to smoke conventional cigarettes, attitudes toward those products, or perceived harm from cigarettes (even though there were differences between groups on their perceptions of e-cigarettes, as noted previously).

The study that used data from the ANHCS also tested the hypothesis that greater exposure to e-cigarette advertising was associated with weaker support for restricting cigarette smoking in public spaces (Tan et al. 2015b). Both more frequent exposure to e-cigarette advertising and the degree to which participants perceived those messages as positive correlated negatively with support for smoking restrictions. However, in models adjusted for demographic variables, neither measure predicted support for restricting smoking. Further research is needed to address whether the large amount of advertising for e-cigarettes weakens support for smokefree air laws and other tobacco control policies or supports other potential indicators of renormalizing smoking, particularly those indicators that are known risk factors for tobacco use by adolescents and young adults, such as descriptive norms (e.g., perceived prevalence), injunctive norms (e.g., peer acceptance or social acceptability), outcome expectations (e.g., perceived benefits), and attitudes toward the tobacco industry. Additional research is also needed to assess whether e-cigarette advertising that draws comparisons to conventional cigarettes could serve to undermine antismoking messages.

Evidence Summary

Although the e-cigarette marketplace is complicated by the differences in brands that are owned by tobacco companies versus independent brands, e-cigarette companies continue to change and to influence the manufacturing, price, marketing and promotion, and distribution of e-cigarette products and accessories. The e-cigarette market continues to grow, with projected sales of $3.5 billion in 2015. Consolidation of e-cigarette companies has been rapid, with the first major merger taking place in 2012. These mergers and acquisitions are likely to continue, but the rate of consolidation may slow down as sales of cigalikes decelerate, and "vape shops" could have the potential to influence the e-cigarette marketplace based on the current structure of the marketplace and a regulatory landscape where federal regulation is just beginning to be implemented. All of these factors create additional uncertainties and risks for both the existing independent e-cigarette companies and the large cigarette companies. This chapter has shown that many of the marketing techniques used by e-cigarette companies are similar to those used by the tobacco industry for conventional cigarettes, and that awareness by youth and young adults of this marketing, and their levels of exposure to it, is high. Further, tracking marketing expenditures and product sales is difficult because of the rapidly changing venues, including "vape shops," use of social media, and online advertising.

Conclusions

1. The e-cigarette market has grown and changed rapidly, with notable increases in total sales of e-cigarette products, types of products, consolidation of companies, marketing expenses, and sales channels.

2. Prices of e-cigarette products are inversely related to sales volume: as prices have declined, sales have sharply increased.

3. E-cigarette products are marketed in a wide variety of channels that have broad reach among youth and young adults, including television, point-of-sale, magazines, promotional activities, radio, and the Internet.

4. Themes in e-cigarette marketing, including sexual content and customer satisfaction, are parallel to themes and techniques that have been found to be appealing to youth and young adults in conventional cigarette advertising and promotion.

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Chapter 5
E-Cigarette Policy and Practice Implications

Introduction

The previous chapters have set out what is currently known and not known about e-cigarettes. Despite the identified gaps in evidence and the dynamic, evolving patterns of the use of e-cigarettes, policy options are needed. These policy options are particularly important as they affect the use of e-cigarettes by youth and young adults. As this report has demonstrated, e-cigarettes are widely used by youth and young adults and are particularly risky for these age groups, and efforts to prevent their use by young people are needed. This chapter explores the policy landscape of e-cigarettes and sets forth recommendations that should protect the public's health, particularly as these policies relate to the short- and long-term health of youth and young adults.

The *Family Smoking Prevention and Tobacco Control Act of 2009* (or Tobacco Control Act) (2009) is meant to protect the health of the public, including young people. As previously discussed, on May 10, 2016, FDA published a final rule which deemed all other products, including e-cigarettes, meeting the definition of a tobacco product, except accessories of such products, to be subject to the *Federal Food, Drug, and Cosmetic Act.* This rule went into effect on August 8, 2016 (Federal Register 2016). Under the Tobacco Control Act, FDA likely will be required to consider the consequences of e-cigarette use for those who do not use tobacco products (as well as for those who do).

It can be stated that public health will be harmed *if* the availability of e-cigarettes:

- Increases exposure to nicotine among youth and young adults;
- Leads to the initiation of combustible tobacco smoking;
- Slows or prevents cessation of combustible products by nicotine-addicted smokers; or
- Increases the likelihood that former smokers will again become addicted to nicotine and/or use combustible products after being reintroduced to nicotine by e-cigarettes.

Potential harm also comes from secondhand exposure to the vapor or aerosol expelled from e-cigarette users. Secondhand exposure comes from inhaling the aerosol or contacting vapor-contaminated surfaces. Each of the potential negative consequences of the availability of e-cigarettes could lead to additional disease and premature mortality (Chapter 3).

Relative to efforts in cigarette and smokeless tobacco use prevention and control, a polarized debate has been in progress for several years over the role of e-cigarettes. There is general agreement that exclusive use of e-cigarettes poses a lower health risk to the individual than the extremely high health risks of using conventional, combustible tobacco products (Farsalinos and Polosa 2014; Grana et al. 2014a,b), although more research is needed on this as more becomes known about the harmful constituents of e-cigarettes (Sleiman et al. 2016). The controversy reflects the relative degree of emphasis given to the potential harm to adolescents and young adults from using e-cigarettes at one pole compared with the potential for reduced risk for established adult users of conventional cigarettes at the other (if they transition completely to e-cigarettes). Although this characterization does not reflect the complexity of the situation, it is useful in defining the potential tradeoffs that are implicit: increased numbers of young people who are exposed to nicotine (and who may go on to conventional tobacco products) versus reduced health risks to individuals who completely switch from conventional, combustible tobacco products with their extremely high health risks. The discussion has become increasingly complicated as e-cigarette use has increased, and still-incomplete evidence potentially supports the views of those holding to both poles of the argument about reducing harm for the overall population. However, the majority of currently available scientific evidence does not support the recommendation to use e-cigarettes for the cessation of cigarette smoking (Hartmann-Boyce et al. 2016). Additionally, the use of e-cigarettes does not pose benefits to youth and young adults, and some data suggest that use of e-cigarettes could lead to the more harmful use of conventional cigarettes. In the context of young people, the precautionary principle should apply. The precautionary principle is defined by the United Nations Educational, Scientific and Cultural Organization (2005) as appropriate "when human activities may lead to morally unacceptable harm that is scientifically plausible but uncertain, actions shall be taken to avoid or diminish that harm" (p.14).

Critical Issues Related to Policies on E-Cigarettes in 2016

The E-Cigarette Landscape Is Dynamic and Evolving

Considerations of policy approaches to e-cigarettes offered in this report are made in the context of a rapidly changing marketplace for nicotine-containing products that now includes primarily conventional cigarettes, cigars, smokeless products, hookahs, and e-cigarettes (see Chapter 2). The manufacture and sales of nicotine-containing products, once dominated by a few large companies selling conventional cigarettes, have been transformed and now include many smaller companies that manufacture and sell through stores and "vape shops." E-cigarettes are also sold through websites and in places where conventional cigarettes have long been available—convenience stores, pharmacies, gas stations, and grocery stores. Currently, hundreds of different e-cigarette products are on the market: designs are evolving rapidly, and major tobacco companies have their own lines of e-cigarette products. However, unlike the situation in the past in which the marketing of conventional tobacco products changed relatively slowly and there were limited media outlets, information about e-cigarettes is now promoted quickly through new media, as well as television, in part to reach key target groups, including youth and young adults.

As documented in Chapter 2, patterns of use are rapidly changing among adolescents and young adults, and likely among other groups within the population. For some of the most critical issues related to e-cigarettes, longitudinal data are not yet available because the use of these products is recent and constantly changing, and whether and when the patterns of use will stabilize is uncertain. Additionally, surveillance data and research on the wide-ranging consequences of e-cigarette use, including such key issues as the likelihood of addiction and other health problems for users and those passively exposed, are lagging behind the highly dynamic changes in the nicotine-product marketplace and the impact of these changes on the use of tobacco products, including e-cigarettes.

With regard to the potential health consequences of using e-cigarettes, estimates can be made based on knowledge of the characteristics and components of the aerosols that are then inhaled. Unfortunately, evidence on short-term risks is limited, and long-term risks have not yet been identified because this would require monitoring users for years. For example, the impact of long-term inhalation of flavorings is not yet known. While some of the flavorings used in e-cigarettes are generally recognized as safe for ingestion as food, the health effects of their inhalation are generally unknown, and some flavorings have been shown to cause a serious lung disease, bronchiolitis obliterans, when inhaled (Kreiss et al. 2002; Barrington-Trimis et al. 2014). Whether the risk of lung disease or other disorders is truly substantial will require longer term epidemiologic and other research (Allen et al. 2016).

Thus, policy approaches must support control measures that (a) are as dynamic as the rapidly changing marketplace for e-cigarettes; (b) are supported by surveillance data; and (c) document in timely fashion the current status of the use of multiple types of tobacco products (including e-cigarettes); the emergence of state, local, tribal, and territorial policies; and the strategies being used to market these products.

Risk Tradeoffs Are Inherent for E-Cigarettes

Policy discussions about e-cigarettes have highlighted the potential tradeoffs in risk that could occur, particularly if e-cigarettes are positioned as a harm-reducing alternative to combustible tobacco products. Some have characterized these products as new technologies that might lead to a dramatic decline in the use of more dangerous forms of nicotine delivery, particularly conventional cigarettes and other combustible tobacco products (Abrams 2014; Cobb and Abrams 2014; Fagerström and Bridgman 2014; Grana et al. 2014a; Hajek et al. 2014; Henningfield 2014; Schraufnagel et al. 2014; West and Brown 2014; Lindblom 2015). Correspondingly, e-cigarettes have been proposed by some as a harm-reduction strategy and as a tool for smoking cessation, but the data to date do not support e-cigarettes for harm reduction or cessation (Siegel et al. 2011; Abrams 2014). By contrast, others are concerned that the availability of these new products will expand the number of youth and young adults who are exposed to nicotine and will eventually lead to exclusive use of other conventional tobacco products or dual use of both (e-cigarettes and conventional cigarettes) (Leventhal et al. 2015; Primack et al. 2015). Early longitudinal evidence provides some support for these concerns, although further research on this issue is still warranted.

As reviewed in Chapter 3, uncertainty remains about the health effects of e-cigarettes, particularly in the long term. Such effects will remain unknown until sufficient observations can be made over time. However, current knowledge of the characteristics of the inhaled aerosol from e-cigarettes suggests that if a current adult smoker of conventional cigarettes or other combustible tobacco products would use e-cigarettes exclusively instead of combustibles as a substitute nicotine delivery system, either en route to quitting tobacco completely or even as a long-term alternative, the risks of tobacco-related diseases would be reduced substantially compared with the risk imparted by continued smoking of conventional cigarettes (Fiore et al. 2014; USDHHS 2014; McNeill et al. 2015).

Still, as documented in Chapter 3, immediate and future health risks for youth and young adults who use e-cigarettes can be anticipated from exposure to nicotine, including addiction and harmful effects on brain development. Research must continue to characterize and quantify the full spectrum of potential health risks. Thus, in formulating policies related to the role of e-cigarettes in tobacco control and reducing the burden of tobacco-related disease, particularly among youth and young adults, e-cigarette products that deliver nicotine cannot be considered a risk-free alternative to conventional cigarettes or other combustible tobacco products.

Any analysis of the potential increased risks and reduced harms of e-cigarette use also needs to consider data on the actual patterns of use because more of the risks affect youth and young adults and most of the potential benefits from reduced risk to health largely accrue to older cigarette smokers (Chapter 2). However, the reports of the tobacco industry to investors indicate the industry's interest in maintaining a broad pattern of use of nicotine-containing products, including conventional cigarettes, for decades to come (Calantzopoulos 2015). When considered in the context of the tobacco industry's past changes to product design (e.g., the creation of so-called "low-tar" cigarettes), the broader array of tobacco products now being discussed within the tobacco industry's plans (e.g., "Heat-Not-Burn" products) could slow cessation (because smokers have historically been drawn to reduced-harm products) and thus the overall decline of tobacco-related diseases (USDHHS 2014).

The dynamic balancing between risks and potential benefits of e-cigarette use will be swayed by the impact of such use on the use of other tobacco products by youth and young adults over time. The availability of e-cigarettes could adversely affect the use of tobacco products in this group by slowing the decline of smoking because this population will be exposed to nicotine and possibly become addicted to that substance. Indeed, data reviewed in Chapter 2 show evidence of such trends. Although the decline in rates of smoking conventional cigarettes and other combustible tobacco products is viewed universally as positive, the increasing number of youth and young adults who use e-cigarettes is a serious concern for all the reasons cited above. West and Brown (2014) and McNeill and colleagues (2015) suggest that the limited evidence from the United Kingdom does not support the concern that using e-cigarettes leads to the use of other tobacco products, and they maintain that the new adolescent users of these e-cigarette products include very few never smokers. However, the marketing of e-cigarettes is quite different between the United Kingom and the United States, and the patterns of use, particularly among youth, are also quite different (European Parliament and Council 2014; England et al. 2015; Klein 2015; Leventhal et al. 2015; Primack et al. 2015; Barrington-Trimis et al. 2016; Wills et at. 2016; Institute for Global Tobacco Control n.d.). This pattern is also evident in some U.S. survey data from early in the era of e-cigarette use (as reviewed in Chapter 2), but not in more recent data, which indicate that e-cigarette products may contribute to nicotine addiction in a new generation of young people and thereby lead to increased use of a variety of nicotine delivery products, including combustible tobacco (Bauld et al. 2016; CDC 2016).

Fundamentally, the public health challenge and the charge to policy development can be framed as balancing the potential use of e-cigarettes as a new technology to reduce the use of combustible tobacco products against the possibility of expanding tobacco use among non-using youth and young adults, long-term former smokers, and other vulnerable populations (e.g., women of reproductive age and individuals with significant comorbidities, including those with mental health problems). Already, the e-cigarette companies are increasing the appeal of their offerings by enhancing the efficiency of nicotine delivery and using flavorings while they continue to advertise and promote their products aggressively.

Additional Evidence Suggested for Future Research

To characterize the critical balance for public health between the harms and potential benefits of e-cigarettes, more evidence on each of the elements that determine that balance would be useful (Table 5.1). The needed data would come from surveillance of patterns of adoption of e-cigarettes and their use among the population generally, and particularly among the most critical populations for uptake: youth and young adults, former smokers, smokers, and other populations that are particularly at risk for adverse outcomes. Few studies have been done on the health risks posed by e-cigarettes and their potential effectiveness for smoking cessation (Hartmann-Boyce et al. 2016). However, as discussed in Chapter 2, there are still no standardized questions for research on

Table 5.1 Comparative risk assessment: Potential harms and benefits of e-cigarettes

Harms	Benefits
Increased youth exposure to nicotine and potentially greater initiation of conventional cigarettes	Reduced disease risk for current smokers who completely switch to e-cigarettes
Slowing cessation by smokers due to nicotine addiction	Reduced disease morbidity for smokers with existing heart or lung disease who switch to e-cigarettes
Nicotine addiction in former smokers who begin to use e-cigarettes and possibly transition back to smoking	Potential for cessation of combustible products
Renormalization of nicotine use and smoking as acceptable	Fewer users of combustible products in the entire population
Future disease risks for youth who are exposed to nicotine	
Increasing the dual use of e-cigarettes with combustible products	
Serving as a "gateway" to the initiation of tobacco smoking	
Increased disease risk vs. complete cessation among those who use both e-cigarettes and combustible products	
Exposure to secondhand aerosol and lack of clean air	

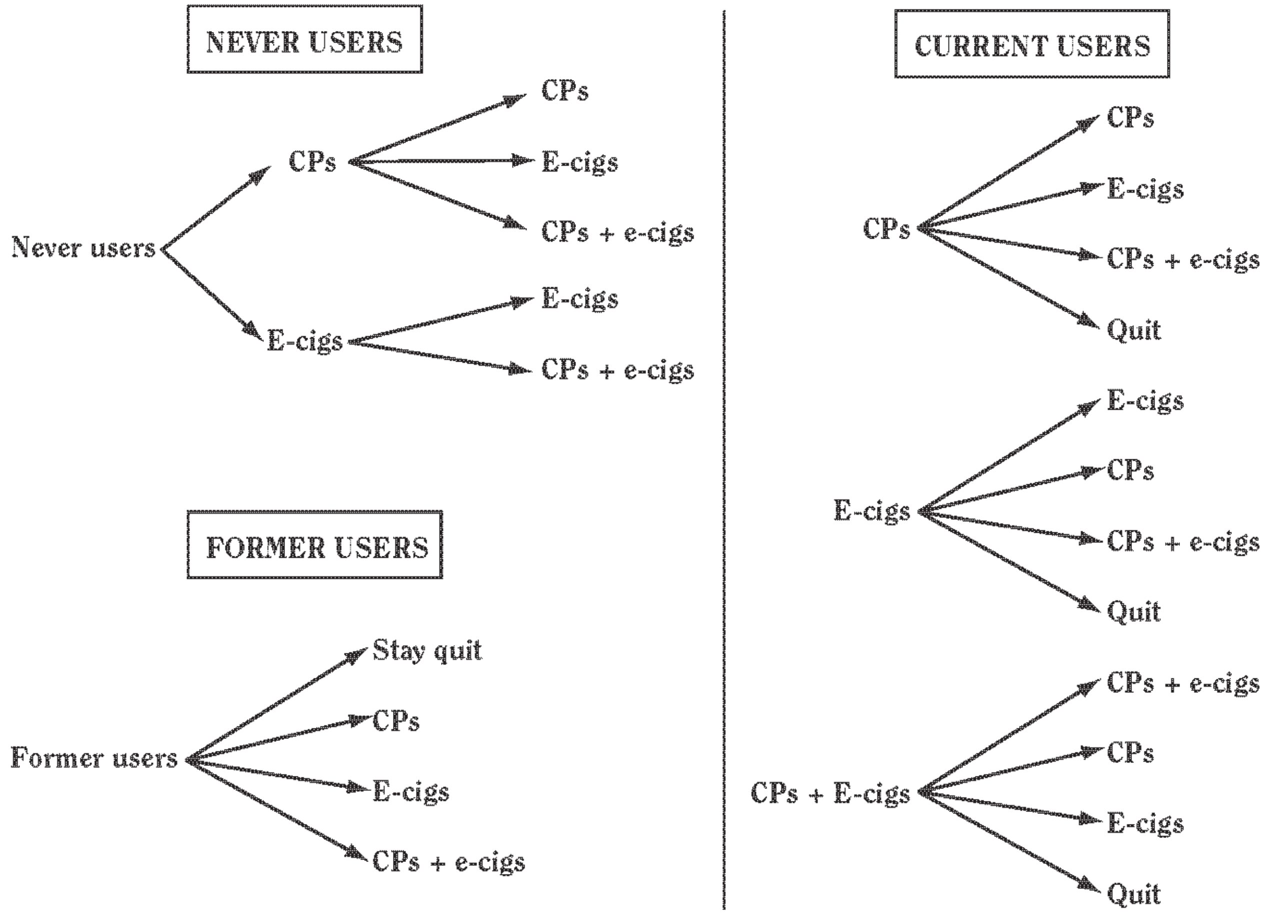
e-cigarettes, and there is a need for further testing and development of e-cigarette questions and measurements.

To characterize the harms and benefits of e-cigarettes to public health, models are used to project their overall impact on public health (Levy et al. 2016). The use of modeling was described in detail in the 2014 Surgeon General's report (USDHHS 2014). Conceptual models are needed to define the potential scenarios of changes in patterns of use among youth, young adults, adult smokers, former smokers, and other significant vulnerable populations. Figure 5.1 displays the range of patterns that are emerging with the wider adoption of e-cigarettes (Cobb et al. 2015; Vugrin et al. 2015). Researchers and public health officials can use dynamic population models (Mejia et al. 2010; Kalkhoran and Glantz 2015; Vugrin et al. 2015; Levy et al. 2016) to analyze the potential impact on population health of the relative probabilities of these various paths. Initial modeling has shown that the potential population health benefits are very sensitive to several factors: the levels of product risk, particularly those of e-cigarettes; patterns of initiation and switching; and the extent of dual use (Mejia et al. 2010; Cobb et al. 2015; Kalkhoran and Glantz 2015; Vugrin et al. 2015). The benefits of smoking cessation, particularly as early in life as possible, are well documented, but the epidemiologic evidence that reducing (but not quitting) cigarette consumption can lower the risk of all-cause mortality, or mortality from cardiovascular diseases, remains inconclusive (USDHHS 2014). Thus, more research is needed to better characterize the health consequences of dual use, in particular, in comparison to the recognized health benefits of complete smoking cessation (or potentially only e-cigarette use). Similarly, the health risks to former smokers who become exposed again to nicotine through e-cigarettes are uncertain. Data are still limited on the risk of starting (or not starting) to smoke conventional cigarettes again (after successful cessation) following exposure to nicotine via e-cigarettes.

As reviewed in Chapter 3, the long-term health risks of e-cigarettes will not be known for decades, although evidence to date suggests that they are generally less harmful than combustible products. However, less harmful is not the same as harmless. A substantial amount of evidence is available on some components of the aerosols inhaled by e-cigarette users. For many people, exposure to aerosol could occur across much of the life span, beginning in adolescence and even in childhood, when the lungs and brain are still developing. Flavorings are of particular concern with regard to pulmonary toxicity, as are the various effects of nicotine on the brain. Although the National Institutes of Health is now supporting a growing program of research on e-cigarettes, critical questions have not yet been answered. Given experiences with conventional cigarettes, long-term studies will be needed to identify the full health consequences of using e-cigarettes.

Thus, policies related to e-cigarettes will necessarily be made in the context of accumulating but incomplete evidence. The landscape is changing rapidly and, inevitably, research cannot keep pace. Quoting Sir Austin Bradford Hill's landmark paper on environment and disease: "All scientific work is incomplete—whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer on us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to demand at a given time" (Hill 1965, p. 300).

Figure 5.1 Potential patterns of use of combustible products (CPs) and e-cigarettes (e-cigs)



Source: USDHHS (2014). Adapted for this report.

Potential Public Policy Approaches

In formulating public policies related to e-cigarettes, the context and possibilities vary across the national, state, local, tribal, and territorial governments and public entities. At the national level, progressive steps are being taken by FDA under the Tobacco Control Act. In 2010, the U.S. Court of Appeals for the D.C. Circuit determined that e-cigarettes and other products made or derived from tobacco may be regulated by FDA as tobacco products under the Tobacco Control Act and are not drugs or devices unless marketed for therapeutic purposes, such as being an aid to smoking cessation (*Sottera, Inc. v. Food and Drug Administration* 2010). In May 2016, FDA released its deeming rule to regulate the sale and distribution of e-cigarettes as a tobacco product (see Chapter 1) (*Federal Register* 2016). The rule is currently under litigation. The rule restricts the age of sale to those 18 years of age and older and requires retailers to check the age identification of young people under age 27, restricts vending machines to adult-only facilities, prohibits free samples, requires a health-warning statement about nicotine on packaging and in advertisements, requires domestic manufacturers to register their products and disclose the ingredients of their products, requires the reporting of the levels of harmful and potentially harmful constituents to FDA, allows FDA to review any new or changed products before being sold, and requires manufacturers to show scientific evidence that demonstrates the overall public health benefit of any product before it can be marketed as a modified risk tobacco product (*Federal Register* 2016). The Tobacco Control Act does not provide FDA with authority to impose taxes on tobacco products (Bhatnagar et al. 2014; Huang et al. 2014; Tobacco Control Legal Consortium 2015) or regulate indoor air quality (Schripp et al. 2013; Bam et al. 2014; Bhatnagar et al. 2014; Brandon et al. 2015a), occupational health and safety (USDHHS 2015; Whitsel et al. 2015), or hazardous waste disposal (Chang 2014; Krause and Townsend 2015).

FDA is not the only federal agency with potential jurisdiction over some aspect of e-cigarettes (Table 5.2). For example, the U.S. Department of Defense and U.S. Department of Veterans Affairs relate to specific populations, and other agencies relate to regulatory activities, such as the U.S. Federal Trade Commission, U.S. Department of Transportation, and the U.S. Environmental Protection Agency. Some agencies have coverage over specific areas, such as the General Services Administration and the National Park Service.

State, local, tribal, and territorial governments, as well as private entities, may also address these and other matters that are covered by the Tobacco Control Act (Freiberg 2012), and since 2010 many actions have been taken at the nonfederal level. State and local governments may utilize effective interventions that would also be expected to apply to e-cigarettes: increasing the price of tobacco products through taxation (Community Preventive Services Task Force 2012); creating and enforcing clean air policies (Hopkins et al. 2010); and passing comprehensive laws prohibiting sales to minors, combined with active enforcement (Community Preventive Services Task Force 2001). In addition, based on evidence that new e-cigarette products may addict a generation of young people to nicotine (Bunnell et al. 2015; CDC 2015b) and on mounting indications about potential harm from the use of these products in this population (Flouris et al. 2013; Barrington-Trimis et al. 2014; Goniewicz et al. 2014; Grana et al. 2014a; Pisinger and Dossing 2014; Goniewicz and Lee 2015), numerous health organizations have called for the extension of smoking-related policies to e-cigarettes (Association of State and Territorial Health Officials 2014; Bam et al. 2014; Bhatnagar et al. 2014; Offermann 2014; Schraufnagel et al. 2014; World Health Organization 2014a; Brandon et al. 2015a; USDHHS 2015). In the absence of causal findings that have guided evidence-based tobacco control for decades, the “precautionary principle” is relevant to decision makers as a guide to action to address e-cigarettes among youth and young adults. This principle supports intervention to avoid possible health risks when the potential risks remain uncertain and have been as yet partially undefined (Bialous and Sarma 2014; Saitta et al. 2014; Hagopian et al. 2015). However, the interventions should be appropriate to the currently perceived risk for future health consequences, in this case from e-cigarette use by youth, young adults, and pregnant women, as well as from the secondhand exposure of nonusers to e-cigarette vapor.

Clean Indoor Air Policies

Clean indoor air or smokefree policies prohibit the use of conventional tobacco products in indoor public places, such as worksites, restaurants, bars, and casinos. Because most of these policies predate the rise of e-cigarettes, their language does not necessarily cover emissions from these products. To protect the public from both secondhand smoke and secondhand aerosol, smokefree air policies should be modernized to include e-cigarettes. Such policies will maintain current standards for clean indoor air, reduce the potential for renormalization of tobacco product use, and prevent involuntary exposure to nicotine and other aerosolized emissions from e-cigarettes (Ingebrethsen et al. 2012; Schripp et al. 2013; Goniewicz et al. 2014; Offermann 2014; Schober et al. 2014). Updating existing policies to cover e-cigarettes (and all electronic nicotine delivery systems) will eliminate the introduction of airborne toxins into enclosed spaces and establish a uniform standard for preventing the use of both combustible and electronic tobacco products in public and private spaces, including schools, offices, restaurants, bars, casinos, and airplanes.

Prohibiting the use of e-cigarettes in enclosed spaces eliminates potential health risks to nonusers and ensures their right to clean air; may discourage the dual use of electronic and combustible tobacco products; simplifies public compliance with and enforcement of existing clean indoor air laws; facilitates reduced consumption of these products; and maintains clear, comprehensive nonsmoking norms (Richardson et al. 2014; World Health Organization 2014a). As of January 1, 2016, six states (Delaware, Hawaii, New Jersey, North Dakota, Oregon, and Utah) had passed comprehensive smokefree indoor air laws that include e-cigarettes (CDC 2015a). These laws prohibit smoking and the use of e-cigarettes in indoor areas of private worksites, restaurants, and bars. Sixteen additional states had prohibited the use of e-cigarettes on some or all state property, and 475 local laws restricted e-cigarette use in 100% smokefree venues (Americans for Nonsmokers’ Rights Foundation 2015). Nationwide, more than 400 local jurisdictions prohibit e-cigarette use in 100%-smokefree workplaces (Americans for Nonsmokers’ Rights Foundation 2015). Major cities that have addressed e-cigarettes include Austin, Boston, El Paso, Chicago, Los Angeles, Minneapolis, San Francisco, and New York City.

Table 5.2 Principle federal policies and regulations of tobacco that emphasize e-cigarettes

Agency	Authority and description	Current	Potential
Executive Office of the President (EOP) and Office of Management and Budget (OMB)	—	Executive Order 13058, issued on August 9, 1997 (EOP 1997), generally prohibits the smoking of tobacco products in all interior space owned, rented, or leased by the executive branch of the federal government, and in any outdoor areas under executive branch control in front of air intake ducts. The Executive Order carves out an exception to its smoking prohibition for any residential accommodation for persons voluntarily or involuntarily residing, on a temporary or long-term basis, in a building owned, leased, or rented by the federal government.	—
Executive Office of the President (EOP) and Office of the U.S. Trade Representative (USTR)	—	Executive Order 13193, issued January 18, 2001 (EOP 2001), prohibits all U.S. executive branch agencies from promoting the sale or export of tobacco. It also prohibits using U.S. trade initiatives to restrict tobacco marketing and advertising regulations in other countries, unless those regulations discriminate against U.S. tobacco products in favor of that country's domestic tobacco products.	—
Federal Communications Commission (FCC)	Has broad regulatory power over commercial communication, including television, radio, and the Internet.	15 U.S.C. § 1335 (the "Broadcast Ban"), 15 U.S.C. § 4402(f): Prohibits advertising for cigarettes, little cigars, smokeless tobacco, and chewing tobacco on radio, TV, or any other medium of electronic communication under FCC's jurisdiction.	Prohibit the advertising of smoking accessories, cigars, pipes, pipe tobacco, or cigarette-making machines on television; prohibit the advertising of e-cigarettes on television; and regulate the advertising of tobacco products on the Internet.
Federal Trade Commission (FTC)	Publishes annual report on tobacco products. Reviews tobacco manufacturer-proposed schedules to rotate mandatory package warnings. Protects consumers. Enforces antitrust laws.	15 U.S.C. § 46 authorizes FTC to require entities to file special reports. On an annual basis, FTC collects and publishes information on the practices of the largest manufacturers of cigarettes and smokeless tobacco in the United States. Among other things, the information collected includes sales and, in several categories, expenditures for marketing. 15 U.S.C. § 45: FTC has broad authority to prevent "unfair or deceptive" business practices. It is an unfair and deceptive act or practice for a firm to make unsubstantiated claims, express or implied, about such matters as a product's efficacy, safety, or health benefits (FTC 1983). FTC is broadly authorized to prevent companies from using "unfair methods of competition" that affect commerce. FTC uses its antitrust authority to review and impose conditions on those proposed mergers of tobacco companies that raise anticompetitive concerns.	Collect sales, advertising, and information on promotion expenditures from e-cigarette companies and issue reports on same. Take enforcement action against unfair or deceptive advertising of tobacco products or e-cigarettes.

Table 5.2 Continued

Agency	Authority and description	Current	Potential
General Services Administration (GSA)	In its role as an independent agency, GSA manages and maintains more than 1,550 federally owned buildings and leases space in an additional 7,100 buildings in the United States. GSA manages the federal government's automobile fleet and is the acquisition arm of the federal government.	GSA Order ADM, 5800. 1C: Smoking in GSA-occupied space and government-owned or -leased vehicles assigned to GSA is prohibited "to protect GSA employees, GSA contractors, and the visiting public from exposure to tobacco smoke in the Federal workplace." The Order prohibits smoking in or on all "interior GSA-occupied space, exterior GSA-occupied space, including courtyards, garages, loading docks, stairwells, rooftops and balconies, and other outdoor areas under GSA control within 25 feet of doorways and building air intake ducts; and government-owned or leased vehicles assigned to GSA" (U.S. General Services Administration 2009).	Clarify that existing policies include e-cigarettes. Implement a tobacco-free campus policy in GSA-occupied space.
Office of Personnel Management (OPM)	—	While not regulatory in nature, OPM and GSA coordinate standard responses to frequently asked questions about the use of e-cigarettes in government facilities.	—
U.S. Department of Agriculture (USDA)	Commodity and inspection standards for agricultural products. Administers SNAP and WIC programs.	7 U.S.C. § 30: USDA provides commodity standards for tobacco. 7 U.S.C. § 2012: Under the *Food and Nutrition Act of 2008,* tobacco products cannot be purchased with SNAP benefits. ENDS are included in the policy because the USDA interprets ENDS to be tobacco products. 7 CFR 246.10: USDA identifies requirements for WIC-eligible foods.	—

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Defense (DoD)	May issue general instructions and restrictions in regulating the sale and/or use of tobacco products. Individual service branches may expand these regulations. Individual bases may also draft regulations. These typically are based on DoD instructions, directives, or service policies. DoD has authority over TRICARE.	DoD follows the smoking policy in federal facilities covered in 41 CFR 102-74.315, which states, "pursuant to Executive Order 13058, 'Protecting Federal Employees and the Public From Exposure to Tobacco Smoke in the Federal Workplace' it is the policy of the Executive Branch to establish a smokefree environment for federal employees and members of the public visiting or using federal facilities. The smoking of tobacco products is prohibited in all interior space owned, rented or leased by the Executive Branch of the federal government" (*Federal Register* 2008, p. 77518). Each of the armed services has issued statements clarifying that the prohibition on smoking tobacco products extends to the use of e-cigarettes. The 2015 NDAA directs the sale of cigarettes, cigars, and chewing tobacco at military commissaries. These items cannot be sold on military bases at prices lower than the most competitive prices in the local community. The NDAA replaced Directive 1330.09 (U.S. Department of Defense 2005), which established that tobacco prices on U.S. military bases should be no lower than 5% below the most competitive commercial price in the local community. Branches of the armed services have tobacco policies: • U.S. Navy and Marines, Instruction 5100.13E (U.S. Navy 2002) • U.S. Army, Army Health Promotion Policy Regulation 600–63 (U.S. Army 1996) • U.S. Air Force, Instruction 40-102, Air Force Tobacco Policy (U.S. Air Force 2013) TRICARE covers limited tobacco cessation counseling from any TRICARE-authorized provider in the United States. This coverage includes up to 18 counseling sessions per quit attempt, with up to 4 individual counseling sessions per quit attempt. Two quit attempts per fiscal year are automatically covered, with coverage extending to a third with a doctor's justification and pre-authorization. TRICARE also covers tobacco cessation products, including prescriptions and over-the-counter products, with 120 days' use of a tobacco cessation product per quit attempt.	DoD-unified regulations on tobacco use in common housing. Increased restrictions on commissary sales.

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Education (ED)	Funding for tobacco control programs	In FY 2014, pursuant to 20 U.S.C. § 7131, *Safe and Drug-Free Schools and Communities Act,* ED awarded the first round of 5-year grant awards under the School Climate Transformation Grant—Local Educational Agency Grants program. These FY 2014, Year 1 grant awards provided more than $35.8 million to 71 school districts in 23 states; Washington, DC; and the U.S. Virgin Islands. The funds should be used to develop, enhance, or expand systems of support for implementing evidence-based, multitiered behavioral frameworks for improving behavioral outcomes and learning conditions among students. The goals of the program are to connect children, youth, and families to appropriate services and supports; improve conditions for learning and behavioral outcomes for school-aged youth; and increase awareness of mental health issues and the ability to respond to such issues among school-aged youth. School districts can also use the funds to implement models for reform and evidence-based practices. Drug prevention, including preventing tobacco use by youth, is an allowable activity. Grantees are encouraged, as part of their local needs assessment, to measure drug use among students along with other relevant issues and problems. This assessment of local needs will also be used by grantees to help identify and select the most appropriate evidence-based programs and practices. If the needs assessment indicates that drug abuse is an issue for students, prevention of drug abuse should be addressed by a multitiered behavioral framework.	—
U.S. Department of Education (ED)	Restrictions on tobacco use	20 U.S.C. § 7181: *The Pro-Children Act of 2001* prohibits smoking in any indoor facility that provides routine or regular kindergarten, elementary, or secondary education and library, health, or day care services to children, if such services and/or facilities are funded by the federal government, whether directly or through state or local governments, by federal grant, loan, loan guarantee, or contract programs.	—

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Health and Human Services, Centers for Medicare & Medicaid Services (CMS) (continues on next page)	Sets policies regarding Medicaid coverage for tobacco cessation products and counseling.	42 U.S.C. § 1396r–8(d)(7): Tobacco cessation medications cannot be excluded from coverage under Medicaid prescription drug benefits. Section 2502 of the *Affordable Care Act* amends section 1927(d)(2) of the *Social Security Act* by removing barbiturates, benzodiazepines, and agents used to promote smoking cessation from the list of drugs that a state Medicaid program may exclude from coverage or otherwise restrict. 42 U.S.C. §§ 18021(a)(1)(B), 18022(b)(1): Tobacco use screening and cessation must be provided at no cost as an essential health benefit and a preventive benefit. This includes Medicaid expansion plans, plans sold on insurance exchanges, and private plans. For youth: Tobacco cessation services are coverable as part of EPSDT, the Medicaid benefit for children and adolescents. EPSDT provides a comprehensive array of prevention, diagnostic, and treatment services for low-income infants, children, and adolescents under age 21, as specified in Section 1905I of the *Social Security Act*. For pregnant women: Section 4107 of the *Affordable Care Act* amends section 1905 of the *Social Security Act* to require coverage of counseling and pharmacotherapy for cessation of tobacco use by pregnant women. Section 1905(bb)(2) of the *Social Security Act* defines the new tobacco cessation coverage services for pregnant women as services recommended in the 2008 PHS Guideline, or any subsequent modification of this Guideline, and such other services that the Secretary recognizes to be effective for cessation of tobacco use by pregnant women. *Affordable Care Act,* Section 4108, Medicaid Incentives for Chronic Disease Prevention Program: This is a grant program in which states apply for funds to incentivize Medicaid recipients to prevent chronic disease, including through tobacco cessation.	—

Table 5.2 Continued

Agency	Authority and description	Current	Potential
(continued from previous page) U.S. Department of Health and Human Services, Centers for Medicare & Medicaid Services (CMS)	—	42 U.S.C. § 1395x (ddd): Medicare covers tobacco cessation programs (Centers for Medicare & Medicaid Services 2010): Effective for claims with dates of service on or after August 25, 2010, CMS will cover tobacco cessation counseling for outpatient and hospitalized Medicare beneficiaries: • Who use tobacco, regardless of whether they have signs or symptoms of tobacco-related disease; • Who are competent and alert at the time that counseling is provided; and • Whose counseling is furnished by a qualified physician or other Medicare-recognized practitioner. Intermediate and intensive tobacco cessation counseling services are covered under Medicare Parts A and B when the above conditions of coverage are met, subject to frequency and other limitations. Medicare covers two individual tobacco cessation counseling attempts per 12-month period. Each attempt may include a maximum of four intermediate or intensive sessions, with a total benefit covering up to eight sessions per 12-month period per Medicare beneficiary who uses tobacco. The practitioner and patient have the flexibility to choose between intermediate (more than 3 minutes, up to 10 minutes) and intensive (more than 10 minutes) cessation counseling sessions for each attempt. Medicare beneficiaries also have access to smoking cessation prescription medication through Medicare Part D.	—
U.S. Department of Health and Human Services, Centers for Medicare & Medicaid Services (CMS)	Sets policies regarding private and marketplace health plan coverage of tobacco cessation products and counseling.	42 U.S.C. §§ 18021(a)(1)(B), 18022(b)(1): Tobacco cessation must be provided at no cost as an essential health benefit. This includes Medicaid expansion plans, plans sold on insurance exchanges, and private plans. 42 U.S.C. § 300gg-6 (Public Law 114-38): Tobacco cessation must be covered in employer plans. Plans should cover two cessation attempts per year, including (1) all FDA-approved cessation medications (both prescription and over-the-counter) and (2) four tobacco cessation counseling sessions, including telephone, group, and individual counseling. 42 U.S.C. § 300gg(a)(1(iv)): Tobacco users may be charged 50% more for insurance than nonusers of tobacco. 42 U.S.C. § 300gg–4(j)-(k): Employers may reward or penalize employees by up to 50% of the cost of health care coverage based on their tobacco use, if the employer offers a health-contingent wellness program designed to prevent or reduce tobacco use.	—

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Health and Human Services, National Institutes of Health (NIH)	NIH is a tobacco-free campus.	NIH's policy specifically includes e-cigarettes. In accordance with the tobacco-free initiative from HHS, the use of cigarettes, e-cigarettes, cigars, pipes, smokeless tobacco ("snuff"), and any other tobacco product is prohibited on the NIH campus in Bethesda, MD (NIH 2016).	—
U.S. Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse (NIDA), National Advisory Council on Drug Abuse (NACDA)	The mission of NIDA is to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health. NACDA serves crucial roles in advising NIDA on research priorities and policy and in providing a secondary level of review for applications under consideration for federal funding.	NIDA (2016) urges grantees to recognize that: • Receiving funding from the tobacco industry may compromise the perceived objectivity of their research results, which in turn could impact the overall credibility of their research findings, including its interpretation, acceptance, and implementation; • Acceptance of tobacco industry funds is viewed by many as contributing directly or indirectly to the industry's interests, and thus harmful to the public health; and • Any connection between tobacco industry-supported research (or tobacco industry scientists) and NIDA could negatively impact NIDA's credibility and the public's trust in NIDA-funded research.	—

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration (SAMHSA)	Implements the Synar Amendment, which requires states, in order to receive their full Substance Abuse Prevention and Treatment Block Grant awards, to enact and enforce laws that prohibit the sale or distribution of tobacco products to individuals under the age of 18.	More information about the Synar Program is available online: http://www.samhsa.gov/synar/about	SAMHSA is exploring opportunities to align the Synar regulation with the federal statutory definition of tobacco products, which includes e-cigarettes.
U.S. Department of Homeland Security (DHS)	Sales and use restrictions for the U.S. Coast Guard. DHS Management Directorate-Directive No. 06603 Smoking Policy.	COMDTINST M6200.1B limits smoking to designated outdoor areas, prohibits use of tobacco by recruits, and prohibits tobacco use in any Coast Guard-controlled living quarters, including common areas. This policy includes extensive sales and advertising restrictions, but it does not consider NRT to be a tobacco product.	Implement a policy to enforce a ban on e-cigarette use on federal property.
U.S. Department of Homeland Security (DHS), Bureau of Immigration and Customs Enforcement (ICE)	Issues standards for facilities housing immigration detainees	Detainee smoking is prohibited in all buildings, including detainee-housing units. If smoking is permitted at a particular facility, the only designated smoking areas are outside of all buildings (Immigration and Naturalization Service 2000).	—

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Housing and Urban Development (HUD)	Resident health in assisted housing	Public and Indian Housing (PIH) Notice 2009-21 strongly encourages HUD-funded public housing agencies to adopt smokefree policies in some or all of their public housing units. Housing Notice 2010-21 encourages owners and management agents of HUD-assisted multifamily housing to implement smokefree housing policies in one or all of the properties they own or manage. Both notices focus on cigarettes that "burn" as their mechanism for generating smoke, and so their applicability to e-cigarettes is uncertain. Regarding its Weaver Building headquarters (the only building for which GSA has designated HUD as the facility management authority), HUD follows GSA Order ADM 5800.1C, GSA's smoking policy for federal offices (U.S. General Services Administration 2009). This GSA policy permits smoking in exterior space under GSA control that is beyond "25 feet of doorways and building air intake ducts," except for "courtyards, garages, loading docks, stairwells, rooftops, and balconies." The management of HUD's other facilities, federally owned or leased, is not delegated to the Department, and so GSA makes the decision on smoking policy for those campuses.	HUD's Office of PIH published its proposed rule on Instituting Smoke-Free Public Housing (80 FR 71762) on November 17, 2015, accepting comments through January 19, 2016 (*Federal Register* 2015). In addition to inviting comments on all aspects of the proposed rule, the notice specifically solicited public comments on nine questions (e.g., should the policy extend to electronic nicotine delivery systems, such as e-cigarettes, and/or to waterpipe tobacco smoking?). Based on responses to HUD's Request for Information on Adopting Smoke-Free Policies in PHAs and Multifamily Housing (77 FR 60712) (Federal Register 2012), HUD may consider drafting a regulation or notice that could prohibit smoking in some or all HUD-assisted multifamily housing. Such a proposal could cover e-cigarettes. HUD is beginning to prepare for the adoption and implementation of a campus-wide tobacco-free policy, which would include e-cigarette use, at the Weaver Building headquarters by January 1, 2017.

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Justice, Bureau of Alcohol, Tobacco, Firearms and Explosives (ATF)	ATF is given primary jurisdiction to combat cigarette trafficking and administration (via the CCTA) and to stop tobacco diversion (via the PACT).	18 U.S.C. § 2342: Under the CCTA, it is illegal to possess more than 10,000 unstamped cigarettes in a state that requires a tax stamp. 18 U.S.C. § 2343: Any person who distributes more than 10,000 cigarettes must keep accurate records pertaining to the shipment, receipt, sale, and distribution of cigarettes. 18 U.S.C § 2320: Trafficking in counterfeit cigarettes. 15 U.S.C. § 375: It is illegal to ship cigarettes to a non-licensee in a state without notifying the state taxation authority. 15 U.S.C. § 375–377: Requires online retailers to check the identification of customers at purchase and delivery: section 375 covers definitions; section 376 covers reports to state tobacco administrators; and section 377 covers penalties. The *Smuggled Tobacco Prevention (STOP) Act* amends the IRC to restrict the sale, lease, export or import, or delivery of tobacco production machines to persons lawfully engaged in (1) the sale, lease, export or import, or delivery of such machines; (2) the manufacture or packaging of tobacco products or processed tobacco; or (3) the application of unique identification markings onto tobacco products or processed tobacco packages.	—
U.S. Department of Justice, Bureau of Prisons (BOP)	BOP has authority to govern the control and management of federal penal and correctional institutions.	28 C.F.R. § 551.162: Smoking is generally prohibited in and on the grounds of BOP institutions and offices, with exceptions for smoking as part of an authorized inmate religious activity, and for smoking only in smoking areas designated by the warden, for BOP staff and official visitors. 28 C.F.R. § 551.163: Possession of smoking apparatus and tobacco in any form is prohibited for inmates, unless as part of an authorized inmate religious activity.	BOP Operations Memorandum 006-2015 (BOP 2015) sets out guidelines for e-cigarette use. Guidelines state that e-cigarette use is to be limited to designated outdoor areas that are reasonably accessible to employees and provide a measure of protection from the elements. These areas may only be used by employees, but must be separate from the areas presently designated as “smoking areas” for use of tobacco products. Indoor use of e-cigarettes shall not be permitted in BOP facilities, except in perimeter towers and perimeter patrol vehicles when occupied by one person.

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Labor, Occupational Safety and Health Administration (OSHA)	Sets standards for indoor air quality.	29 CFR 1910.1000, Air Contaminants: This policy restricts employee exposure to several of the main chemical components found in tobacco smoke. OSHA rules apply to tobacco smoke only in rare and extreme circumstances, such as when contaminants created by a manufacturing process combine with tobacco smoke to create a dangerous air supply that fails OSHA standards for the workplace. In normal situations, exposures would not exceed permissible exposure limits and, as a matter of prosecutorial discretion, OSHA will not apply the General Duty Clause to environmental tobacco smoke.	Have smokefree workplaces. In the 1990s, OSHA proposed a regulation setting indoor air quality standards for environmental tobacco smoke, but this rulemaking was terminated (*Federal Register* 2001).
U.S. Department of Transportation (DOT)	Sets restrictions on tobacco use on commercial and personal aircraft.	49 U.S.C. § 41706: Prohibits smoking on passenger flights. 14 CFR Part 252: DOT rule implementing 49 U.S.C. § 41706, and prohibiting smoking on most passenger flights. DOT interprets current Part 252 to include e-cigarettes in smokefree policies. Note: FAA regulations also prohibit smoking on most aircraft from an aircraft safety perspective, not from a health perspective (see notes to 14 CFR Part 252).	In early 2016, DOT issued a final rule (RIN 2105-AE06). In keeping with section 41706, the rule amends Part 252 to prohibit smoking on charter flights where a flight attendant is a required crew member. The rule also makes explicit the determination that the use of e-cigarettes falls within the definition of smoking. DOT's Pipeline and Hazardous Materials Safety Administration has proposed a rule to prohibit the charging of e-cigarettes in an aircraft cabin, and to prohibit stowage of e-cigarettes in the cargo hold of an aircraft (this is a hazardous material/safety rule, not a health/tobacco rule).

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Treasury, Alcohol and Tobacco Tax and Trade Bureau (TTB)	TTB administers the provisions of the Internal Revenue Code (IRC) of 1986, as amended, that impose federal excise taxes on tobacco products and cigarette papers and tubes, and it establishes a comprehensive civil and criminal framework to protect the revenue. Among other issues, TTB investigates illegal production, underreporting of production, smuggling or unlawful importation, and diversion of domestic tobacco products intended for export.	26 U.S.C. 26 § 5701–5763, Tobacco Products and Cigarette Papers and Tubes: Under the IRC, the tobacco products that are subject to tax and TTB regulation are cigars, cigarettes, smokeless tobacco (chewing tobacco and snuff), pipe tobacco, and roll-your-own tobacco. Each of these tobacco products is defined with reference to "tobacco." TTB also has regulatory authority over processed tobacco, which is not subject to tax. TTB regulations define processed tobacco to mean any tobacco that has undergone processing but that does not include tobacco products. The processing of tobacco includes, but is not limited to, stemming (i.e., removing the stem from the tobacco leaf); fermenting, threshing, cutting, or flavoring the tobacco; or otherwise combining the tobacco with nontobacco ingredients. To protect revenue, the IRC and its implementing regulations establish qualification criteria to engage in businesses related to manufacturing, importing, or exporting tobacco products or in manufacturing or importing processed tobacco, and they require that persons obtain permits to engage in these activities. Under the IRC, manufacturers of tobacco products and export warehouse proprietors must file a bond that relates to the tax liability for the tobacco products on the premises covered by the permit. The IRC and implementing regulations also include recordkeeping and reporting requirements designed to ensure that TTB can verify that the tax on tobacco products is paid or determined or that adequate documentation exists to confirm that a tax exemption applies. The IRC also provides TTB with certain enforced-collection options (e.g., liens and levies), civil and criminal penalties, permit suspension and revocation procedures, and forfeiture provisions to ensure that the tax is collected. ENDS that do not contain nicotine derived from tobacco are not tobacco products under the IRC and are not subject to taxation or TTB regulation. ENDS containing nicotine derived from tobacco may meet the definition of a tobacco product under the IRC, in which case they would be regulated by TTB and taxed accordingly.	TTB will collaborate with foreign-counterpart tax administrators to share information and best practices in the administration of tobacco excise taxes and their enforcement. Areas of possible technical assistance include setting up an auditing system and permitting regimen and conducting investigations. TTB's tobacco laboratory provides technical assistance to TTB program offices on tobacco products for regulatory compliance and enforcement purposes. TTB's tobacco laboratory develops and validates analytical methods and protocols on tobacco products. It also collaborates with national and international tobacco regulatory federal agencies and has established a collaborative partnership with the World Health Organization's Tobacco Laboratory Network and the North America Tobacco Regulatory Laboratory Network.

Table 5.2 Continued

Agency	Authority and description	Current	Potential
U.S. Department of Veterans Affairs (VA)	Can restrict the use of e-cigarettes and combustible cigarettes on facility grounds of the Veterans Health Administration to designated outdoor smoking areas only.	Public Law 102-585: Requires medical centers, nursing homes, and domiciliary care facilities of the Veterans Health Administration to establish smoking areas for patients and residents in a way that is consistent with medical requirements and limitations.	Include language about restrictions on the use of e-cigarettes in local and national guidance regarding smokefree policies.
U.S. Department of Veterans Affairs (VA)	Provides evidence-based tobacco cessation treatment to veterans receiving care in the VA health care system.	38 CFR Part 17: Eliminated in 2006 the copayment for smoking cessation counseling for veterans in care facilities of the Veterans Health Administration (*Federal Register* 2006).	Continue to provide clinical guidance for the health care professionals and patients in facilities of the Veterans Health Administration on the evidence base of (a) potential health effects of e-cigarettes and (b) comparisons to FDA-approved NRT for cessation treatment.
U.S. Environmental Protection Agency (EPA)	Sets policies regarding the hazardous waste status of e-cigarettes under the RCRA.	Nicotine is a commercial chemical product listed in 40 CFR 261.33(e) and is an acute hazardous waste (EPA waste code P075) when disposed. EPA has concluded that nicotine is the sole active ingredient of the e-liquid in e-cigarettes and thus a commercial chemical product, that e-cigarettes are not manufactured articles, and that e-cigarette cartridges are considered containers of nicotine. Therefore, e-cigarettes may be regulated as acute hazardous waste code P075 when disposed. If the nicotine e-liquid is legitimately recycled, it is not considered a solid waste under 261.2 because it is considered a commercial chemical product, and therefore it is not subject to hazardous waste regulation. E-cigarettes that are disposed of by consumers at their residences are considered exempt household hazardous waste under 261.4(b)(1) and are not subject to regulation as hazardous waste under the federal RCRA regulations. • Regulatory Citation(s): 261.2, 261.4(b)(1), 261.33. • Statutory Citation(s): 3006 Read U.S. Code 42, Chapter 82.	—

Note: **ATF** = Bureau of Alcohol, Tobacco, Firearms and Explosives; **BOP** = Bureau of Prisons; **CCTA** = *Contraband Cigarette Trafficking Act;* **CFR** = Code of Federal Regulations; **CMS** = Centers for Medicare & Medicaid Services; **DHS** = U.S. Department of Homeland Security; **DoD** = U.S. Department of Defense; **DOT** = U.S. Department of Transportation; **ED** = U.S. Department of Education; **ENDS** = electronic nicotine delivery systems; **EOP** = Executive Office of the President; **EPA** = U.S. Environmental Protection Agency; **EPSDT** = Early and Periodic Screening, Diagnosis and Treatment; **FAA** = Federal Aviation Administration; **FCC** = Federal Communications

Table 5.2 Continued

Commission; **FDA** = Food and Drug Administration; **FTC** = U.S. Federal Trade Commission; **FY** = fiscal year; **GSA** = General Services Administration; **HUD** = U.S. Department of Housing and Urban Development; **ICE** = Bureau of Immigration and Customs Enforcement; **IRC** = Internal Revenue Code; **NACDA** = National Advisory Council on Drug Abuse; **NDAA** = *National Defense Authorization Act;* **NIDA** = National Institute on Drug Abuse; **NIH** = National Institutes of Health; **NRT** = nicotine replacement therapy; **OMB** = Office of Management and Budget; **OPM** = Office of Personnel Management; **OSHA** = Occupational Safety and Health Administration; **PACT** = *Prevent All Cigarette Trafficking Act;* **PHS** = Public Health Service; **PIH** = Public and Indian Housing; **RCRA** = *Resource Conservation and Recovery Act;* **SAMHSA** = Substance Abuse and Mental Health Services Administration; **SNAP** = Special Supplemental Nutrition Program; **TTB** = Alcohol and Tobacco Tax and Trade Bureau; **U.S.C.** = United States Code; **USDA** = U.S. Department of Agriculture; **USTR** = U.S. Trade Representative; **VA** = U.S. Department of Veterans Affairs; **WIC** = Women, Infants, and Children.

Prevent Youth Access

Ensuring that laws on youth access include e-cigarettes is intended to protect youth from exposure to nicotine, which can lead to addiction and other health problems. Additionally, ensuring that these laws include e-cigarettes helps to capture the full diversity of the tobacco product landscape, including combustible, noncombustible, and electronic tobacco products. Effective strategies to deter access to e-cigarettes by youth and the use of these products in this population include restricting sales of e-cigarettes to minors, requiring verification of age, mandating clear signage about minimum age where sales take place, prohibiting the sale of e-cigarettes from vending machines, eliminating self-service displays of e-cigarettes, and actively enforcing existing laws with a focus on retailers. Compliance with laws that regulate the sale and distribution of e-cigarettes is facilitated by requiring retailers to be licensed. To date, 46 states have prohibited the sale of e-cigarettes to minors younger than a specified age (National Conference of State Legislatures 2015; The Council of State Governments 2015). Federally, aligning youth tobacco access control regulations with the statutory definition of tobacco products in the Tobacco Control Act, which includes e-cigarettes, could provide consistent framework to help ensure that restrictions on youth access to e-cigarettes are prioritized and enforced (*Federal Register* 2016). This could include modifications to the Synar regulation, which requires states, U.S. territories, and jurisdictions to enact and enforce laws prohibiting the sale or distribution of tobacco products to youth. Substance Abuse Prevention and Treatment Block Grant recipients must comply with the Synar amendment and implement regulations in order to receive their full awards (U.S. Food and Drug Administration, Center for Tobacco Products n.d.).

Licensing

Licensing is used to regulate professional practice and business operations and represents one strategy to control the rising use of e-cigarettes among youth. In general, in the case of tobacco-related licensing, a business is authorized to manufacture, distribute, or sell tobacco products as long as it complies with all relevant laws (McLaughlin 2010). Typically, tobacco-related licensing requirements for retailers and/or manufacturers help to prevent evasion of excise taxes, ensure that licensees comply with tobacco-related laws, and promote safe manufacturing practices (ChangeLab Solutions 2012). Repeat violators of relevant laws may be subject to suspension or permanent revocation of their license, an outcome that provides a strong incentive to comply with existing requirements. As in the conventional cigarette industry, licensing of e-cigarette retailers and manufacturers is designed in part to prevent the use of these products by youth and to facilitate safe manufacturing practices. Unlike traditional tobacco products, for which retailers sell prepackaged products and the number of manufacturers is limited, a growing number of businesses engage in both the retail sale and manufacturing of devices and liquids used in the devices (e-liquids). Stores devoted exclusively to the sale of e-cigarettes are known as "vape shops." These shops frequently offer a social environment for using products, and they may also sell food and beverages (Sussman et al. 2014).

As of April 2015, 99 cities and counties in California required a retailer to obtain a license to sell e-cigarettes. The majority of these jurisdictions did so by broadening the definition of tobacco products to include "electronic smoking devices" (ChangeLab Solutions 2015a). The definition was purposely broadened to include products that do not include nicotine to decrease the complexity of enforcement and in recognition of the fact that e-cigarette devices are sometimes used with liquids that do not contain nicotine but may contain marijuana oil (The Center for Tobacco Policy & Organizing 2015a). Licensing requirements also may be used to restrict the sale of flavored products or to address issues of consumer and worker safety relative to the mixing of e-liquids.

Imposing a moratorium is another potential approach that has been used in some communities to stop new "vape shops" from entering the market while a more comprehensive approach was being considered. A moratorium is a land-use law that takes effect immediately to stop temporarily the issuance of a business license, building permit, or use permit. Typically, a moratorium is enacted to provide a jurisdiction with time to research and study how to regulate a type of business (ChangeLab Solutions 2015b). In California, several communities enacted moratoria that are initially 45 days but can be extended for up to 2 years (ChangeLab Solutions 2014, 2015b). A four-fifths vote, however, is required to establish a moratorium in California. Hayward and Union City, California, are examples of cities that have enacted moratoria and later adopted both retail licensing requirements for existing e-cigarette retailers and zoning restrictions to prohibit new vapor and hookah bars and lounges from opening within city limits (ChangeLab Solutions 2014; The Center for Tobacco Policy & Organizing 2015b).

Taxation and Other Price Policies

Taxation and other price policies directed at making e-cigarettes more expensive may be implemented at multiple levels of government, from local to federal. Increasing the price of conventional cigarettes, including those increases resulting from excise taxes, significantly prevents and reduces tobacco use, particularly among youth and young adults (USDHHS 2014), and has potentially more impact on prevalence of current use in this population than on first use (Bader et al. 2011). Similarly, price policies are likely to reduce the use of e-cigarettes: a 10% increase in the price of e-cigarettes has been estimated to reduce sales of disposable e-cigarettes by approximately 12% and reusable products by about 19% (Bader et al. 2011; Huang et al. 2014). Data are currently lacking on the potential effects that taxing e-cigarettes might have on conventional cigarettes. Tobacco products are taxed in two main ways:

1. A "specific" excise tax is levied based on the quantity of the product sold (e.g., as measured by number of cigarettes, weight, or volume). This type of mechanism applies the same tax across low-end and premium brands and is generally simple to administer. The disadvantages to specific excise taxes are that the real value of the tax declines over time with inflation, making products more affordable, and that super-lightweight products—such as snus, orbs, sticks, and dissolvables—are grossly undertaxed if the tax is based on weight (Freiberg 2012; Boonn 2013; Shang et al. 2015).

2. The second tax mechanism is an ad valorem excise tax, which is levied on a percentage of the value of the tobacco product (e.g., the retailer's, wholesaler's, or manufacturer's price). This type of tax keeps up with inflation and establishes a flat tax rate across all brands, product types, weights, and packaging. The disadvantages to this kind of tax include the potential for tax evasion through predatory (below-cost) or anticompetitive pricing; increasing the price differential between products with different pretax prices, leading to greater price variability and more opportunity for tax avoidance; a government-provided subsidy for manufacturers' price cuts; and more expensive brands being subjected to a larger tax (Freiberg 2012; Boonn 2013; Shang et al. 2015).

Governments use uniform, tiered, and mixed-tax approaches to implement specific and ad valorem tobacco excise taxes. Uniform systems apply the same tax rate across all products; tiered systems levy taxes based on such product characteristics as toxicity, nicotine content, type of production (handmade versus machine made), sales volume, packaging, or whether the products are domestic or imported; and mixed systems use a combination of uniform and tiered-tax approaches (Shang et al. 2015). Tiered-tax approaches, such as those based on nicotine content, could steer consumers to a less toxic product or one with lower nicotine (Benowitz 2014). Tiered-tax approaches are more complex to administer and may provide greater opportunity for tax evasion as a result of manipulation of the product or its packaging by the manufacturer (Shang et al. 2015). In recognition of nicotine's toxicity, particularly to youth, several health groups have endorsed imposing excise taxes on e-cigarettes to discourage their use by youth (American Thoracic Society 2013; Association of State and Territorial Health Officials 2014; Bhatnagar et al. 2014; Brandon et al. 2015a; Crowley and Health Public Policy Committee of the American College of Physicians 2015; National Association of County and City Health Officials 2014). E-cigarettes are likely less toxic than combustible products (such as conventional cigarettes), and therefore, some contend should be taxed at a lower rate (Benowitz 2014; Bhatnagar et al. 2014). Yet others argue that e-cigarettes should be taxed at the same rate as other tobacco products (Freiberg 2012; American Thoracic Society 2013; National Association of County and City Health Officials April 2014).

As of January 2016, four states (Kansas, Louisiana, Minnesota, and North Carolina) and six localities (Juneau, Matanuska-Susitna, Petersburg, and Sitka, Alaska; Montgomery County, Maryland; and Chicago, Illinois) had enacted e-cigarette taxation policies. Minnesota's ad valorem tobacco tax equates to 95% of the wholesale cost of any product containing or derived from tobacco (Minnesota Revenue 2014; Tobacco Control Legal Consortium 2015). It taxes e-liquids and e-cigarettes sold with nicotine cartridges that cannot be removed (i.e., disposables). In Minnesota, devices without a nicotine cartridge are not taxed as a tobacco product. On the other hand, North Carolina applies a specific excise tax, taxing e-liquids based on volume at 5 cents per milliliter (National Conference of State Legislatures 2015).

The Tobacco Control Legal Consortium, which is based at William Mitchell College of Law in St. Paul, Minnesota, recommends using an ad valorem tax for e-cigarettes applied at the retail level to the "essential" components of these devices. The tax is simple, captures both disposable and refillable devices, and could exclude accessories and universal parts sold separately, such as batteries or charging cords (Tobacco Control Legal Consortium 2015).

Numerous major health organizations support raising the price of e-cigarettes through non-tax options, such as limiting rebates, discounts, and coupons (Freiberg

2012; Association of State and Territorial Health Officials 2014; Bhatnagar et al. 2014; Huang et al. 2014; Brandon et al. 2015a).

Finally, Chaloupka and colleagues (2015) have proposed that differential taxation of tobacco products can be used to incentivize a move away from combustible products to less hazardous noncombustible products, including e-cigarettes. They have argued that taxation could be part of a harm-reduction system. In their view, future determinations by FDA as to whether a product poses a substantially reduced risk would be one criterion in determining the relative rate of taxation.

Restrictions on Marketing

As described in Chapter 4, the marketing of e-cigarettes drives consumer demand for these products. Such marketing also may promote misperceptions about the safety and efficacy of these products for use as cessation devices (Choi and Forster 2014; Mark et al. 2015; Pokhrel et al. 2015). For some populations—such as pregnant women, adolescents, former smokers, and young adults—the adverse health consequences of nicotine intake are substantial. Several groups have supported extending marketing restrictions that apply to conventional cigarettes and other tobacco products to e-cigarettes (Association of State and Territorial Health Officials 2014; Bam et al. 2014; Bhatnagar et al. 2014; Partnership for Prevention 2014; Brandon et al. 2015a). Significant barriers still exist to regulating commercial speech, including the First Amendment rights of the e-cigarette companies (Laird-Metke 2010).

Additionally, for traditional tobacco products, partial advertising bans and voluntary agreements have generally been ineffective in reducing consumption because the tobacco industry circumvents the restrictions by shifting the marketing platforms used to unregulated platforms (National Cancer Institute 2008). This response would be expected to be similar with regard to e-cigarettes. Therefore, despite the numerous barriers, public health groups and state, local, tribal, and territorial governments should take steps to stem the proliferation of e-cigarette marketing likely to appeal to young people by using tools designed to curb youth-oriented tobacco marketing and expanding evidence to inform future restrictions on the marketing of e-cigarettes to youth and young adults.

Surveillance of e-cigarette marketing, performing content analyses of the messages used, and conducting studies to assess the link between exposure to e-cigarette marketing and the use of e-cigarette products, particularly among youth and young adults, will facilitate the development of an evidence base of the type that informed prior federal and Master Settlement Agreement restrictions on tobacco advertising. Observations of retailers' practices, assessments of outdoor advertising, and identification of event sponsorships and promotional activities at bars and community events are actions that state, local, tribal, and territorial public health agencies have taken related to traditional tobacco products. Many of these actions can be adapted to monitor and document the presence of e-cigarette marketing in communities (Pucci et al. 1998; Feighery et al. 2001; Rigotti et al. 2005; Roeseler et al. 2010; Rose et al. 2014).

In the absence of legal restrictions on e-cigarette marketing, and apart from the issue of the previous promulgation by some companies of unsubstantiated health and cessation claims, public health groups can advocate for television and radio broadcasters, print and outdoor media companies, the management of event venues and sports events, digital media outlets, retailers, and others to voluntarily refuse to air or place e-cigarette advertising, offer sponsorships, or give out free samples at fairs and festivals. Although the impact of a voluntary approach may be low, such actions raise awareness, build concern, and help to denormalize the proliferation of e-cigarette marketing. In California, surveillance plus voluntary efforts to promote restrictions on sponsorship of events by the tobacco industry facilitated a modest decline in tobacco industry-sponsored events and youth-oriented activities at those events that promoted the interests of the tobacco companies, and it led to a productive partnership with the tobacco litigation unit of the California attorney general's office that resulted in several settlements with tobacco companies (Roeseler et al. 2010).

State, local, tribal, and territorial public health agencies may be able to contribute to the stimulation of enforcement and compliance with existing rules that constrain marketing. Some states have brought lawsuits against e-cigarette companies, alleging that distributors of these products violated state law by selling to minors or making unsubstantiated health claims; some of those lawsuits resulted in financial damages and agreements to stop making claims that e-cigarettes are safer than conventional cigarettes unless confirmed by rigorous science (Center for Public Health and Tobacco Policy 2013).

Finally, another area to address is the use of "advertorials" employed by e-cigarette retailers to promote cessation and health claims. Advertorials are paid advertisements designed to look like an independent editorial. Although there are no specific rules for how a publisher should distinguish actual editorial content from paid editorial content in terms of their appearance, the Federal Trade Commission (FTC) stated in an advisory opinion that disclosure of the source is necessary when content "uses the format and has the general appearance of a news feature and/or article for public information which purports to give an independent, impartial and unbiased view" (*Federal Register* 1972, p. 154). Additionally, paid advertising must be disclosed clearly and conspicuously in a manner that is understandable to consumers (FTC 1984). State and local public health agencies can play an important role by monitoring and providing substantiation to their state attorney general or FTC regarding advertising that makes improper claims or is not clearly identified as advertising.

Educational Initiatives

The extensive data reviewed in Chapter 2 highlighted the limited knowledge that members of the general public, particularly adolescents and young adults, have about e-cigarettes and their potential for nicotine addiction and other adverse health consequences. FDA has jurisdiction for product warnings that can reach users, but that agency, along with other federal entities and state and local governmental and nongovernmental organizations, can also carry out educational campaigns to enhance such limited knowledge levels. Potentially effective initiatives with youth and young adults to prevent smoking were reviewed in the 2012 Surgeon General's report and may be applicable to preventing e-cigarette use. That report concluded that sufficient evidence exists to conclude that mass media campaigns, comprehensive community programs, comprehensive statewide tobacco control programs, and school-based programs that have shown evidence of effectiveness, if they contain specific components, can produce at least short-term effects and reduce the prevalence of tobacco use among school-aged youth (USDHHS 2012).

Implications for Health Care Practice

Although the issues are not well documented, health care practitioners face questions about e-cigarettes from their patients and their communities, including what are the risks of using e-cigarettes, how do these risks compare with those of cigarettes or other combustible products, and is e-cigarette use an effective way to quit smoking? Chapter 3 set out the limited evidence base related to these questions. Clinicians need to respond to these questions and guide their patients in the context of considerable uncertainty. At this time, practitioners can turn to the various statements from medical organizations, which generally urge caution regarding e-cigarettes and do not find the evidence to be supportive of their use for cessation or for formal harm-reduction strategies (Table 5.3). In fact, any recommendation to use e-cigarettes for the cessation of smoking is not supported by the bulk of the available scientific evidence (Hartmann-Boyce et al. 2016). Both the American Association of Cancer Research and the American Society of Clinical Oncology recommend against advising the use of e-cigarettes for cessation (Brandon et al. 2015b). The U.S. Preventive Services Task Force found that there is insufficient evidence that e-cigarettes are an effective smoking cessation tool in adults, including pregnant women (Agency for Healthcare Research and Quality 2015).

The clinical care setting is a critical venue for taking evidence-based approaches for enhancing smoking cessation and increasing the protection of susceptible groups against exposure to secondhand smoke (USDHHS 2014). However, research on e-cigarettes in relation to this set of venues is lacking and urgently needed. Regardless, some pragmatic approaches have been proposed. For example, the American Academy of Pediatrics (AAP) gives advice on how pediatricians can approach questioning about the use of e-cigarettes. As of October 2015, the AAP's position on e-cigarettes is that sales to minors should be prohibited; flavors that appeal to youth should be prohibited; and measures against the use of e-cigarette products need to be included in requirements for maintaining smoke-free environments, such as in restaurants and workplaces (AAP 2015a).

Table 5.3 Medical organizations

A. Positions of professional organizations

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
American Academy of Pediatrics (2015b)	—	• "Concentrated nicotine solution for electronic nicotine delivery systems should be sold in child-resistant containers with amounts limited to that which would not be lethal to a young child if ingested." • "Prohibitions on smoking and use of tobacco products should include prohibitions on use of electronic delivery systems."	• "The promotion and sale of electronic nicotine delivery systems to youth should be prohibited by federal, state, and local regulations." • "Prohibitions on promotion should include all media that can be viewed by youth, including broadcast, print, and electronic (Web- or Internet-based) media." • "Prohibitions on promotion should include prohibitions on sponsorships, such as sports, cultural event, and entertainment sponsorships. Any promotional activities that can be accessed by children and/or adolescents should be considered promoting to children." • "Electronic nicotine delivery systems should be subject to the same restrictions on advertising and promotion at least as restrictive as that on combustible cigarettes. Until government agencies institute these prohibitions, media companies, entertainment companies, sports teams, and promoters should voluntarily institute these prohibitions." • "Celebrities should not use their privileged position to model tobacco product use, including electronic nicotine delivery systems and other existing or emerging tobacco products."	—

Table 5.3 A Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (2015) (continues on next page)	• FDA has not approved e-cigarettes as smoking cessation aids, and current data are inconclusive with regard to their efficacy as quit-smoking products. • "Oncologists would be wise to refrain from recommending e-cigarettes to patients as a first-line therapy for smoking cessation."	• "The evidence regarding the risks and benefits of e-cigarettes is difficult to interpret, and data on the long-term consequences of e-cigarette use are not yet available." • "Chemicals and ultrafine particles known to be toxic and carcinogenic and/or to cause respiratory and heart distress have been identified in e-cigarettes." • "Studies find the levels of the toxicants in e-cigarette aerosol to be significantly lower than in cigarette smoke and, in many cases, comparable with trace amounts found in a medicinal nicotine inhaler. It is unclear what effects these toxicants might have on e-cigarette users after chronic and frequent use." • "The vast majority of e-cigarette users use products containing nicotine. Nicotine is an addictive chemical, adversely affects maternal and fetal health during pregnancy, has adverse consequences for fetal brain development, and may adversely affect the adolescent brain. It is unclear what effect nicotine intake via e-cigarettes has on health or on the addictiveness of these products."	• "The FDA CTP should regulate all ENDS that meet the statutory definition of tobacco products and their component parts. ENDS delivery systems and e-liquids containing tobacco-derived nicotine should be regulated whether they are sold together or separately." • "ENDS manufacturers should be required to register with FDA and report all product and ingredient listings, as well as the nicotine concentration in the ENDS solution." • "ENDS packaging and advertising should be required to carry health warnings and safety labels—including a warning regarding nicotine addiction." • "Youth-oriented ENDS advertising and marketing should be prohibited, including: self-service ENDS displays, the provision of gifts and other giveaways with purchase of ENDS, the sale and distribution of items such as hats or t-shirts with ENDS brand logos, brand name sponsorship of social or cultural events, or of any team entry into those events, and youth-oriented advertising of tobacco products." • "Internet and other mail-order sellers of ENDS should be required to check the age and identification of customers at the point of purchase and delivery; to comply with all laws in the purchaser's state or local jurisdiction; and pay all applicable federal, state, and local taxes." • "Childproof caps should be required for all e-liquid containers." • "ENDS and ENDS liquid containing candy and other youth-friendly flavors should be banned unless there is evidence demonstrating that these products do not encourage youth uptake." • "ENDS use should be prohibited in places where combustible tobacco product use is prohibited by federal, state, or local law until the safety of second- and thirdhand aerosol exposure is established."	• "There are insufficient data on health consequences of e-cigarette use, their value as tobacco cessation aids, and their effects on the use of combustible tobacco products by smokers and nonsmokers." • "Oncologists should advise all smokers to quit smoking combustible cigarettes, encourage use of FDA-approved cessation medications, refer patients for smoking cessation counseling, and provide education about the potential risks and lack of known benefits of long-term e-cigarette use."

Table 5.3 A Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
(continued from previous page) American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (2015)	—	• "Data from the [CDC] showed a significant increase in e-cigarette-related calls to poison centers between 2010 and 2014 as a result of accidental ingestion or absorption of e-cigarette liquid." • "Secondhand exposure to toxicants and nicotine from e-cigarette aerosol has been documented, though there are not current data suggesting that exposure to the aerosol has adverse health effects." • "There are no published studies evaluating thirdhand (i.e., residue that builds up on surfaces over time) exposure to e-cigarette aerosol in indoor environments, although preliminary data suggest that nicotine from e-cigarettes can stick to surfaces."	• "Funding generated through tobacco product taxes, including any potential taxes levied on ENDS, should be used to help support research on ENDS and other tobacco products, but should not preclude the allocation of federal funding for this research." • "All data related to ENDS composition, use, and health effects should be disclosed for dissemination and independent review as well as to enhance policy decisions for ENDS product regulation." • "Tobacco products should be taxed proportionate to their harm; therefore, ENDS should not be taxed at equal or higher rates than combustible cigarettes." • "State and local governments should implement ENDS regulations within their authorities that are appropriate for protecting the public health, including restricting the sale, distribution, marketing, and advertising of ENDS to youth." • "International cooperation is needed to develop standards for the regulation of ENDS, and these regulations should prioritize protection of the public's health and draw upon the best available scientific evidence whenever possible."	—
American Association for Respiratory Care (AARC) (2015)	• "Even though the concept of using the e-cigarettes for smoking cessation is attractive, they have not been fully studied and the use among middle school children is increasing year after year."	• "There is no evidence as to the amount of nicotine or other potentially harmful chemicals being inhaled during use or if there are any benefits associated with using these products."	—	• Date effective: April 2014 • "The [AARC] opposes the use of the electronic cigarette (e-cigarette)."

Table 5.3 A Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
American College of Physicians (ACP) (Crowley and Health Public Policy Committee of the ACP 2015)	• "ENDS, which include electronic cigarettes, or e-cigarettes, are growing in popularity, but their safety and efficacy as a smoking cessation aid are not well understood."	• "[There is concern] that the health effects of ENDS use are unknown, that they may appeal to young people, and that they may encourage dual use of ENDS and traditional tobacco products."	• "The Food and Drug Administration [should] extend its regulatory authority granted through the *Family Smoking Prevention and Tobacco Control Act* to cover electronic nicotine delivery systems (ENDS)." • "Characterizing flavors should be banned from all tobacco products, including ENDS." • "The [ACP] supports taxing tobacco products, including ENDS devices and nicotine liquids, to discourage use among children and adolescents. Local governments should be permitted to establish higher tax rates for ENDS and related products than state levels." • "The [ACP] supports legislative or regulatory efforts to restrict promotion, advertising, and marketing for ENDS products in the same manner as for combustible cigarettes, including a prohibition on television advertising." • "Youth tobacco prevention efforts, such as antismoking media campaigns and school-based interventions, should include information about the potential risks of ENDS use." • "The federal, state, and local regulators should take action to extend indoor and public place clean air laws that prohibit smoking in public places, places of employment, commercial aircraft, and other areas to ENDS products." • "The federal government should authorize and appropriate funding to rigorously research the health effects of ENDS use, chemical content, and toxicity; effects of ENDS vapor exposure; dual-use rates; and effects of ENDS-derived nicotine on human health."	• "The [ACP] supports strong regulations to ensure product safety and transparency, policies that prevent use among young people, increased research to better determine their health effects, strong limits on marketing and promotion to discourage interest among young people, and application of indoor air laws to protect the health of bystanders." • "This paper is not intended to offer clinical guidance or serve as an exhaustive literature review of existing ENDS-related evidence but to help direct the [ACP], policymakers, and regulators on how to address these products."

Table 5.3 A Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
American Thoracic Society (2013, 2015) (continues on next page)	• “The new CDC data show that Big Tobacco is once again peddling a new product intended to get youth hooked on nicotine, and that e-cigarettes are not about harm reduction or smoking cessation, but about addiction.”	• “The short- and long-term health risks of these nicotine-delivery devices are largely unknown.”	• “States should regulate e-cigarettes as tobacco products. E-cigarettes should not be sold to those younger than 18, and regulations requiring identification and proof of age at the time of purchase should apply. Internet sales of e-cigarettes should be strictly regulated.” • “E-cigarettes should be taxed at rates equivalent with traditional cigarettes and other tobacco products.” • “E-cigarettes should be subject to the same restrictions regarding public use as combustible tobacco products, and e-cigarettes should not be used in smoke-free areas.” • “The FDA should deem regulatory authority over e-cigarettes.” • “Candy and menthol flavored e-cigarettes should be banned.” • “E-cigarette packaging should include warning labels, similar in size and scope to those required of combustible tobacco packaging. Where risks are known, the consumer should be informed of those risks in clear and direct language. Where data regarding risk is [*sic*] unavailable or inconclusive, the consumer should be informed of the lack of reliable safety testing data.” • “The FDA should regulate the form and content of e-cigarette advertising.” • “Both direct and implied health and safety claims by e-cigarette manufacturers should be subject to the same evidentiary review process currently required for other products making such claims.” • “The FDA should require e-cigarette manufacturers to adopt Good Manufacturing Processes similar to those that exist for other regulated products, including lot numbers, securing packaging, etc.” • “Given that nicotine is an addictive drug, with the dependence liability related to the pharmacokinetic characteristics of the delivery device, delivery characteristics of the e-cigarette should be evaluated and disclosed, and periodically monitored to ensure consistency of the product’s dependence potential over time.”	• “[E]-cigarettes need to be subject to the same marketing and manufacturing restrictions as tobacco products.” • “For the first time, e-cigarette use among young people is higher than for any other tobacco product.”

Table 5.3 A Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
(continued from previous page) American Thoracic Society (2013, 2015)	—	—	• "Content of e-cigarette cartridges should be disclosed and regulated." • "The nicotine content of the e-cigarette cartridge should not exceed that of similar user volume of combustible tobacco." • "Deliverable nicotine levels should be consistent between cartridges." • "Researchers and clinicians, along with scientific societies and publications, receiving funding from e-cigarette manufacturers should disclose this relationship and the potential for conflict of interest in a manner equivalent to disclosures required for funding from the remainder of the tobacco industry."	—

Table 5.3 A Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
European Respiratory Society (ERS) (2014)	• "Electronic cigarettes are designed for the purpose of direct nicotine delivery to the respiratory system, and they fall into a regulatory gap in most countries, escaping regulation as medicinal products and avoiding the controls applicable to tobacco products."	• "For ERS, the priority of the Revision of the Tobacco Products Directive is to protect children and youth from becoming smokers by preventing them from picking up their first cigarette." • "There is no adequate scientific research available on the overall health risk or the long-term effects of electronic cigarette use on humans."	• "Mandatory reporting system of ingredients used in tobacco products." • "Harmonised regulation of the ingredients of tobacco products." • "80% pictorial health warnings, covering the front and back of packages. Based on evidence, the larger the pictorial health warnings are, the more effective they are." • "Plain/standardised packaging of tobacco products." • "Introduction of both visible and invisible security features on tobacco packaging and ensuring that the storage and access to such data is [*sic*] independent from tobacco companies." • "Prohibition on the cross-border distance sale of tobacco products." • "Strong regulatory framework and independent research for electronic cigarettes. Any regulation of electronic nicotine delivery systems should be science based." • "Ensuring the adoption of delegated acts is not exposed to the interests of the tobacco industry, which would jeopardise the achievement of high level of health protection."	• "ERS supports the European Commission's Proposal for the Tobacco Products Directive and Rapporteur Linda McAvan's efforts to improve it." • "Introduction of standard packs with increased health warnings." • "Prohibition of characterizing flavours." • "Strengthening of traceability and security features for combating illicit trade." • "Prohibiting misleading features, including slim cigarettes." • "Approximately 700,000 EU citizens die prematurely every year because of tobacco consumption."

Table 5.3 A Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
Forum of International Respiratory Societies (American College of Chest Physicians 2014; Schraufnagel et al. 2014)	• "Studies looking at whether electronic cigarettes can aid smoking cessation have had inconsistent results."	• "The safety of electronic cigarettes has not been adequately demonstrated." • "The addictive power of nicotine and its untoward effects should not be under-estimated. • "Potential benefits to an individual smoker should be weighed against harm to the population of increased social acceptability of smoking and use of nicotine." • "Adverse health effects for third parties exposed to the emissions of electronic cigarettes cannot be excluded."	• "Health and safety claims regarding electronic nicotine delivery devices should be subject to evidentiary review." • "If ENDS devices are permitted, they should be regulated as tobacco products." • "Research, supported by sources other than the tobacco or electronic cigarette industry, should be carried out to determine the impact of electronic nicotine delivery devices on health in a wide variety of settings." • "The use and population effects of END devices should be monitored." • "All information derived from this research should be conveyed to the public in a clear manner."	• "ENDS should be restricted or banned, at least until more information about their safety is available."

Table 5.3 Continued

B. Voluntary health organizations

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
American Cancer Society (ACS) (2014)	• "Because the American Cancer Society doesn't yet know whether e-cigarettes are safe and effective, we cannot recommend them to help people quit smoking." • "There are proven methods available to help people quit, including pure forms of inhalable nicotine as well as nasal sprays, gums, and patches."	• "[E]-cigarettes are not labeled with their ingredients, so the user doesn't know what's in them." • "Inhaling a substance is not the same as swallowing it." • "Studies have shown that e-cigarettes can cause short-term lung changes that are much like those caused by regular cigarettes."	• "E-cigarettes need to be researched and regulated."	• "Until electronic cigarettes are scientifically proven to be safe and effective, ACS will support the regulation of e-cigarettes and laws that treat them like all other tobacco products."

Table 5.3 B Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
American Heart Association (AHA) (Bhatnagar et al. 2014) (continues on next page)	• "Current evidence evaluating the efficacy of these products as a cessation aid is sparse, confined to 2 randomized controlled trials and 1 large cross-sectional study, anecdotal reports, and Internet-based surveys." • "[R]eports are confounded by a self-selection bias in that the respondents are often e-cigarette enthusiasts." • "The AHA maintains that e-cigarette use should be part of tobacco screening questions incorporated into clinical visits and worksite/community health screenings that are tied into healthcare delivery."	• "Low levels of harmful or potentially harmful metals such as lead, nickel, and chromium are listed as having been detected." • "Trace levels of tobacco-specific N-nitrosamines, polycyclic aromatic hydrocarbons, and volatile organic compounds in the e-liquid and vapor have been reported." • "The FDA has issued warnings to several e-cigarette companies for selling e-cartridges with [diethylene glycol, weight-loss chemical rimonabant (Zimulti), and the erectile dysfunction medication tadalafil (active ingredient in Cialis)] contaminants." • "There are no reports of e-cigarette safety in patients with known cardiovascular disease."	• "The regulation should allow for quality-controlled products for adults who want to transition from conventional cigarettes to e-cigarettes or to quit or reduce smoking." • "Bottles containing nicotine refill liquids can be toxic if swallowed, so cartridges and bottles should have proper warning labeling and child-proofing packaging." • "It is important that the relevant government agency monitor whether these devices are used for delivery of other drugs and medications." • "Companies should not be able to claim that e-cigarettes are a cessation aid unless they are approved by the FDA for that purpose."	• "The [AHA] supports effective regulation that addresses marketing, labeling, quality control of manufacturing, and standards for contaminants." • "[It] also supports including e-cigarettes in smoke-free air laws and prohibiting the sales of e-cigarettes to youth."

Table 5.3 B Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
(continued from previous page) American Heart Association (AHA) (Bhatnagar et al. 2014)	• "Clinicians should be educated about e-cigarettes and should be prepared to counsel their patients who are using combustible tobacco products to use e-cigarettes as a primary cessation aid." • "For patients with existing cardiovascular disease and stroke, or at risk of a cardiovascular disease event, intensive cessation counseling should be offered as soon as possible."	—	—	—

Table 5.3 B Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
American Lung Association (2014, 2015)	• "Until and unless the FDA approves a specific e-cigarette for use as a tobacco cessation aid, the American Lung Association does not support any direct or implied claims that e-cigarettes help smokers quit."	• "There is currently no scientific evidence establishing the safety of e-cigarettes." • "FDA found detectable levels of toxic cancer-causing chemicals, including an ingredient used in anti-freeze, in two leading brands of e-cigarettes and 18 various cartridges." • "The lab tests also found that cartridges labeled as nicotine-free had traceable levels of nicotine." • "Nicotine is believed to contribute to increased incidence of premature birth, and low birth weight." • "Research has also shown a negative impact on pulmonary function in newborns."	• "The FDA has not approved any e-cigarettes as a safe or effective method to help smokers quit."	• "Including e-cigarettes in smokefree laws and ordinances." • "State laws that would prohibit the sale of any flavored e-cigarette product." • "Taxing e-cigarettes at a rate equivalent with all tobacco products, including cigarettes." • "Eliminating e-cigarette sales to youth, otherwise restricting youth access to e-cigarettes and requiring e-cigarette retailers to be licensed." • "E-cigarettes should be defined as tobacco products." • "Opposes creating new definitions for 'vapor products' and/or 'alternative nicotine products' in state laws."

Table 5.3 B Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
Americans for Nonsmokers' Rights (ANR) (n.d.a; n.d.b)	• "ESDs are not proven cessation devices." • "Many people become 'stable dual-users' who use both cigarettes and ESDs."	• "Americans for Nonsmokers' Rights recommends that e-cigarettes not be used in areas where people will be exposed to the vapors they emit." • "Electronic smoking device aerosol is not water vapor. . . . The aerosol (incorrectly called vapor) contains nicotine, hazardous ultrafine particles that lodge deeply in the lungs . . . and toxins known to cause cancer."	• "Electronic smoking devices are currently unregulated products." • "[ANR] . . . encourages municipalities and states to prohibit the use of ESDs in all smokefree venues."	• "Electronic cigarettes are not a safe alternative!"

C. World Health Organization

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
World Health Organization (WHO) (Bates 2014; WHO 2014b) (continues on next page)	• "Prohibit manufacturers and third parties from making health claims for ENDS, including that ENDS are smoking cessation aids." • "The regulatory standard for cessation claims and approval as cessation aids should remain an appropriate body of evidence, based on well-controlled clinical trials."	• "ENDS users should be legally requested not to use ENDS indoors, especially where smoking is banned until exhaled vapour is proven to be not harmful to bystanders and reasonable evidence exists that smoke-free policy enforcement is not undermined. If smoke-free legislation is not fully developed according to Article 8 of the WHO FCTC and the guidelines for its implementation, this should be done as soon as possible." • "Health warnings should be commensurate with proven health risks."	• "Parties should contemplate putting in place an effective restriction on ENDS advertising, promotion and sponsorship." • "Protection from vested commercial interests." • "Governments are recommended to use or strengthen their existing tobacco surveillance and monitoring systems to assess developments in ENDS and nicotine use by sex and age."	• "Overall, in its public communication WHO portrays e-cigarettes as a threat to public health." • "Encourage smoking cessation and provide a quitline number if one exists."

Table 5.3 C Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
(continued from previous page) World Health Organization (WHO) (Bates 2014; WHO 2014b)	• "For ENDS products to be approved for smoking cessation by the suitable regulatory agency, the appropriate balance should be reached between providing accurate scientific information to the public about the risk of ENDS use and its potential benefits as compared with smoking."	—	—	—

Table 5.3 Continued

D. Government health

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
European Union (EU) (European Parliament and Council 2014; WHO Framework Convention on Tobacco Control 2014)	—	• "Certain additives used to create the impression that tobacco products have health benefits, as well as those with [carcinogenic, mutagenic, or reprotoxic] properties in unburnt form, should be prohibited in order to ensure uniform rules throughout the Union and a high level of protection of human health." • "Electronic cigarettes and refill containers could create a health risk when in the hands of children—it is necessary to ensure products are child and tamperproof." • "Nicotine-containing liquid should only be placed on the market in electronic cigarettes or in refill containers that meet certain safety and quality requirements."	• "The prohibition of tobacco products with characterizing flavours does not preclude the use of individual additives outright, but it does oblige manufacturers to reduce the additive or the combination of additives." • "Electronic cigarettes and refill containers should be regulated by this Directive." • "Where the manufacturer of the relevant product is not established in the Union, the importer of that product should bear the responsibilities relating to the compliance of those products with this Directive." • "Nicotine-containing liquid should only be allowed to be placed on the market, where the nicotine concentration does not exceed 20 mg/ml." • "Only electronic cigarettes that deliver nicotine doses at consistent levels should be allowed to be placed on the market." • "The labeling and packaging of [e-cigarettes] should display sufficient and appropriate information on their safe use."	• New directive: May 2014. • New rules applied: First half of 2016. • "Aims at ensuring equal treatment across the EU for nicotine-containing e-cigarettes (products that do not contain nicotine are not covered by the Directive)." • "Electronic cigarettes can develop into a gateway to nicotine addiction and ultimately traditional tobacco consumption, as they mimic and normalize the action of smoking. For this reason, it is appropriate to adopt a restrictive approach to advertising electronic cigarettes and refill containers."

Table 5.3 D Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
CAP/BCAP (UK) (2014)	—	• "Ads cannot convey health benefits or claim that they are safer or healthier than smoking tobacco."	• "Ads must not be likely to appeal particularly to people under 18, especially by reflecting or being associated with youth culture." • "People shown using e-cigarettes or playing a significant role must neither be, nor seem to be, under 25." • "Ads must not be directed at people under 18 through the selection of media or the context in which they appear." • "Ads must not encourage nonsmokers or nonnicotine users to use e-cigarettes." • "Ads must make clear that the product is an e-cigarette and not a tobacco product." • "Ads on TV and radio will be subject to scheduling restrictions to reduce the chance of e-cigarette advertisements being seen or heard by children."	• Effective date: November 10, 2014. • "The rules place an emphasis on the protection of young people and ads must avoid containing anything that promotes the use of a tobacco product or that shows the use of a tobacco product in a positive light." • CAP: Write and maintain the UK advertising codes.
Public Health England (UK) (Britton and Bogdanovica 2014; CAMQUIT n.d.)	—	—	• "Under the terms of the new Tobacco Product Directive (TPD) . . . advertising of nicotine-containing devices that are not licensed as medicines will be prohibited, products will be required to carry health warnings, meet purity and emission standards that are yet to be defined."	• Effective date: 2016. • "The UK [Medicines and Healthcare products Regulatory Agency] announced that from 2016, it intended to regulate electronic cigarettes and other nicotine-containing products as medicines by function, and thus require manufacture to medicinal purity and delivery standards, and proactive controls on advertising."

Table 5.3 D Continued

Organization	Organizational position on cessation	Organizational position on harm	Organizational position on regulation	General comments
International Union Against Tuberculosis and Lung Cancer (2013)	• "The benefits of e-cigarettes have not been scientifically proven." • "Very few studies have assessed ECs/ ENDS as a harm reduction and cessation aid and with conflicting findings."	• "The safety of ECs or ENDS has not been scientifically demonstrated." • "Adverse health effects for [secondhand smoke] cannot be excluded because the use of electronic cigarettes leads to emission of fine and ultrafine inhalable liquid particles, nicotine and cancer-causing substances into indoor air."	• "A range of current and proposed legislative and regulatory options exists." • "Brazil, Norway, and Singapore have banned ECs/ENDS completely." • "ENDS could undermine the implementation of WHO FCTC Article 12 (de-normalisation of tobacco use)." • "Use of ENDS could also hamper the implementation of Article 8 (protection from exposure to tobacco smoke)."	• "The Union strongly supports the regulation of the manufacture, marketing and sale of Electronic cigarettes (ECs) or electronic nicotine delivery systems (ENDS); the preferred option is to regulate ECs or ENDS as medicines." • "The Union is concerned that the marketing, awareness and use of ECs or ENDS is growing rapidly."

Note: **AARC** = American Association for Respiratory Care; **ACP** = American College of Physicians; **ACS** = American Cancer Society; **AHA** = American Heart Association; **ANR** = Americans for Nonsmokers' Rights; **CAP/BCAP** = Committees of Advertising Practice/Broadcast Committee of Advertising Practice; **CDC** = Centers for Disease Control and Prevention; **CTP** = Center for Tobacco Products; **ECs** = electronic cigarettes; **ENDS** = electronic nicotine delivery systems; **ERS** = European Respiratory Society; **ESDs** = electronic smoking devices; **EU** = European Union; **FCTC** = Framework Convention for Tobacco Control; **FDA** = U.S. Food and Drug Administration; **UK** = United Kingdom; **WHO** = World Health Organization.

Case Studies

Case studies in California and North Dakota demonstrate how e-cigarette policies have been enacted at the local and state levels, and they provide potential models of how cities, counties, and other states might address e-cigarettes in their jurisdictions.

City of Hayward Takes Bold Steps to Address Tobacco Products Aimed at Kids

In response to the "D" grade that the city of Hayward received in 2011 from the American Lung Association in California for its efforts to protect youth from tobacco sales, the city council directed its staff to develop regulations to address the problem of youth tobacco sales. Draft regulations were presented at a city planning meeting in 2012, followed by a series of community meetings and hearings that culminated in the Hayward city council's adoption of a 45-day moratorium to begin in January 2014 on the issuance of business licenses or building permits for any new tobacco retailers. The following month, the moratorium was extended another 15 months to provide more time to research and consider the issue (City of Hayward 2014).

On July 1, 2014, the Hayward city council unanimously adopted an ordinance that requires sellers of tobacco products and "electronic smoking devices" to obtain annually a $400 tobacco retailer license that covers the cost of an annual inspection for compliance with federal, state, local, tribal, and territorial tobacco control laws. The ordinance allowed the city's existing 142 tobacco retailers, 8 e-cigarette retailers, and 2 hookah lounges to continue operating at their current locations; however, new sellers must obtain a conditional use permit, are restricted to special commercial zones, and may not locate within 500 feet of residential areas or child-sensitive areas (e.g., schools and parks) or within 500 feet of an existing tobacco seller. It also prohibits new hookah lounges or vaping lounges from opening within the city.

The ordinance also contains provisions to prohibit self-service displays of tobacco products and e-cigarettes and to regulate the sales of cigars, flavored products, and imitation tobacco products. Cigars selling for less than $5 each are required to be sold in pack sizes of five or more, and the sale of flavored traditional tobacco products, e-cigarettes, and imitation tobacco products (e.g., candy cigarettes, bubble gum chew) is prohibited within 500 feet of schools for any business not selling these products before July 1, 2014.

Penalties range from $1,500 for a first violation and possible suspension to a complete revocation of a license after three violations within a 3-year period (City of Hayward 2014; n.d.a.). Active enforcement of the ordinance began in April 2015 (City of Hayward n.d.b.).

Throughout the process, Hayward officials and staff relied heavily on materials from the American Lung Association, the Center for Tobacco Policy and Organizing, and ChangeLab Solutions to provide the public health and legal rationale for supporting the provisions. Hayward's tobacco retail licensing effort was also supported by the tobacco control program of the Alameda County public health department, which used monies from its Master Settlement Agreement to fund the Hayward police department to conduct youth decoy operations and local community and youth organizations to conduct educational outreach (City of Hayward 2014). Collectively, these resources informed the Hayward city council's decision-making process.

North Dakota's Statewide Clean Indoor Air Law Prohibits Conventional Tobacco Products and E-Cigarettes

In November 2012, North Dakota achieved a remarkable victory for statewide clean indoor air (BreatheND n.d.a.) despite major obstacles, including a harsh winter climate, an adult smoking rate of 21.9% (CDC 2013), and several prior failed legislative attempts to close exemptions in the state's 2005 clean indoor air law (CDC 2014). Despite these impediments, two-thirds of the state voted to prohibit both the smoking of conventional tobacco products and use of e-cigarettes in all non-hospitality workplaces; restaurants; bars; hotel guest rooms and communal areas; health care facilities; assisted living facilities; all licensed child and adult day care facilities; gaming facilities; indoor areas of sports arenas; and within 20 feet of entrances, exits, operable windows, air intakes, and ventilation systems of enclosed areas where smoking is not allowed (BreatheND n.d.b.). Additionally, the law provided no exemptions for tobacco-only retail or "vape shops" (Americans for Nonsmokers' Rights Foundation 2015, n.d.).

The 2012 ballot initiative on statewide clean indoor air resulted from the lack of progress in working with the legislature to try to close smoking exemptions in the state law. The initiative's sponsors, Tobacco Free North Dakota and the American Lung Association in North Dakota, worked closely with the Tobacco Control Legal Consortium to draft policy language, which included prohibiting the use of e-cigarettes anywhere smoking was prohibited. The sponsors approached stakeholders and assessed public support. Little opposition was encountered to prohibiting the use of e-cigarettes indoors. In addition to the sponsors' efforts, the North Dakota Center for Tobacco Prevention and Control Policy conducted a media campaign and worked with local partners to educate their communities, resulting in 11 smokefree ordinances prior to the issuing of the statewide ballot initiative. The landslide victory (66% vs. 33%) in favor of clean indoor air, with the initiative successfully carried in every one of North Dakota's 53 counties, demonstrated widespread public support for clean indoor air (Ballotpedia 2012).

Only a few years later, the law continues to enjoy strong public support from nonsmokers (84.4%) and smokers (58%) alike. Compliance with the law is comparable to cigarette smoking; just 16.8% of North Dakotans reported having observed smoking indoors in areas where it was prohibited, and 23.2% reported having seen e-cigarettes used indoors in such places. Local enforcement personnel confirm a high level of compliance, reporting violations primarily related to smoking within 20 feet of entrances. To date, the only prosecuted violation of the law involved the sampling of an e-cigarette product inside a "vape shop" (BreatheND 2014). In hindsight, the decision to include e-cigarettes in North Dakota's smokefree law was helpful, given increasing concerns about involuntary exposure to nicotine and other aerosolized e-cigarette emissions.

Summary and Recommendations

The Surgeon General has long played a leading role in identifying the harms of tobacco use and documenting the most effective ways to reduce them. This report comes amid the rising use of e-cigarettes among the nation's youth and young adults. It calls attention to this problem and the need to implement immediately a comprehensive strategy to minimize any negative public health impact now and in the future, giving consideration to the potential for youth to be harmed from e-cigarettes while, simultaneously, acknowledging that gains might be made if the use of combustible tobacco products fell among adult smokers. Chapters 1–4 documented the particular challenges posed by the rapid emergence and dynamic nature of e-cigarette use among youth and young adults. The marketplace is diverse, and although it includes the large tobacco companies, e-cigarettes are sold in thousands of "vape shops" and other small commercial locations and on the Internet. Marketing strategies exploit social media, reaching widely and with tailored targeting to consumers.

The differences notwithstanding, the principles and strategies articulated in the 2014 Surgeon General's report and prior reports remain relevant to e-cigarettes. The 2014 report was written not long after the use of e-cigarettes began to surge dramatically; that report commented on the need for rapid elimination of conventional cigarettes and other combustible tobacco products but did not specify a role for e-cigarettes or discuss strategies to minimize adverse effects among youth and young adults (USDHHS 2014). The report's final chapter, however, set out an evidence-based strategy for the future. The present report builds on this foundation, adding recommendations related to e-cigarettes.

Conclusions

1. The dynamic nature of the e-cigarette landscape calls for expansion and enhancement of tobacco-related surveillance to include (a) tracking patterns of use in priority populations; (b) monitoring the characteristics of the retail market; (c) examining policies at the national, state, local, tribal, and territorial levels; (d) examining the channels and messaging for marketing e-cigarettes in order to more fully understand the impact future regulations could have; and (e) searching for sentinel health events in youth and young adult e-cigarette users, while longer-term health consequences are tracked.

2. Strategic, comprehensive research is critical to identify and characterize the potential health risks from e-cigarette use, particularly among youth and young adults.

3. The adoption of public health strategies that are precautionary to protect youth and young adults from adverse effects related to e-cigarettes is justified.

4. A broad program of behavioral, communications, and educational research is crucial to assess how youth perceive e-cigarettes and associated marketing messages, and to determine what kinds of tobacco control communication strategies and channels are most effective.

5. Health professionals represent an important channel for education about e-cigarettes, particularly for youth and young adults.

6. Diverse actions, modeled after evidence-based tobacco control strategies, can be taken at the state, local, tribal, and territorial levels to address e-cigarette use among youth and young adults, including incorporating e-cigarettes into smoke-free policies; preventing the access of youth to e-cigarettes; price and tax policies; retail licensure; regulation of e-cigarette marketing that is likely to attract youth and young adults, to the extent feasible under the law; and educational initiatives targeting youth and young adults. Among others, research focused on policy, economics, and the e-cigarette industry will aid in the development and implementation of evidence-based strategies and best practices.

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The Call to Action

The Call to Action on E-Cigarette Use Among Youth and Young Adults

The Surgeon General issues this Call to Action on e-cigarettes, specifically focusing on youth and young adults, to accelerate policies and programs that can reduce e-cigarette use among young people. This Call to Action comes amid the dramatic increase in e-cigarette use among our nation's youth and young adults. It highlights the need to implement proven strategies that will prevent potentially harmful effects of e-cigarette use among young people. The previous chapters explained what we know and do not know about e-cigarettes and reviewed policy options. Gaps in scientific evidence still exist, and this Call to Action is being issued while these products and their patterns of use are changing quickly. However, policies and strategies are available that can clearly reduce the public health threat posed by e-cigarette use among young people.

Use of e-cigarettes is increasing rapidly among young people, even among those who have never smoked cigarettes.

This Call to Action presents six goals and related strategies that should guide efforts to reduce e-cigarette use among youth and young adults. To achieve these goals, we must work together, which means working with individuals and families; civic and community leaders; public health and health care professionals; e-cigarette manufacturers and retailers; voluntary health agencies; researchers; and other stakeholders.

Stakeholders Who Can Take Action

- Individuals, parents, and families
- Teachers, coaches, and other youth influencers
- Civic and community leaders
- Public health and health care professionals
- Researchers
- Federal government
- State, local, tribal, and territorial governments
- E-cigarette manufacturers, distributors, and retailers
- Voluntary health agencies, non-governmental organizations, and other community- and faith-based organizations

Goal 1. First, Do No Harm

Since 1964, reports from the U.S. Surgeon General have led the way in identifying the harms of tobacco use and detailing the most effective ways to reduce the dangerous effects of tobacco use. For example, reports from 1994 and 2012 outlined proven strategies to prevent and reduce tobacco use among youth and young adults (U.S. Department of Health and Human Services [USDHHS] 1994, 2012). Building on these and other past reports, this Call to Action considers the harms of e-cigarette use among youth and young adults and stresses the importance of strategies that will protect young people from the adverse consequences of these new products.

Strategy 1A.

Implement a comprehensive strategy to address e-cigarettes that will avoid adverse consequences and give careful consideration to the risks for youth and young adults. This can be done by including e-cigarettes in policies and programs related to conventional cigarette smoking at the national, state, local, tribal, and territorial levels.

We have many effective strategies to prevent tobacco use among youth and young adults (USDHHS 2012), and many of these strategies can also be applied to e-cigarettes. A strategy to address e-cigarette use among young people should be precautionary. A precautionary approach urges action to prevent harm when there is scientific uncertainty. That is, when there is inadequate or early knowledge, public health decisions should be made on the basis of precaution to prevent harm, rather than on certain risk. This approach requires proof that a product *is not* harmful—especially for youth—rather than proof that it *is* harmful. The burden of proof regarding product safety should be placed on those who wish to market and sell such tobacco products, rather than the public health community charged with protecting the public's health. The harms of nicotine exposure in youth and young adults are well-documented in this report and warrant this Call to Action (see Chapter 3). We must protect the health of our nation's young people by assuring that there will be no harm to youth from e-cigarettes. The stakeholders identified on the previous page should work together to prevent and reduce the use of all forms of tobacco products, including e-cigarettes, among our nation's youth and young adults. A comprehensive strategy includes:

- Implementing the U.S. Food and Drug Administration's (FDA's) authority to regulate tobacco products in order to provide oversight of the manufacturing, distribution, and marketing of e-cigarettes, particularly as they relate to youth and young adults;

- Funding comprehensive statewide tobacco control programs at levels recommended by the Centers for Disease Control and Prevention (CDC);

- Implementing comprehensive clean indoor air policies that protect people from exposure to secondhand tobacco smoke and the aerosol emitted from e-cigarettes;

- Raising and strongly enforcing minimum age-of-sale laws for all tobacco products, including e-cigarettes, to prevent initiation at young ages;

Use of e-cigarettes can expose young people to nicotine. Nicotine can be highly addictive and can harm brain development. Nicotine use may also lead to the use of other tobacco or nicotine-containing products.

- Setting price policies for e-cigarettes, which could include taxation policies;

- Restricting advertising and marketing that encourages youth and young adults to use e-cigarettes;

- Sponsoring high-impact media campaigns to educate the public using evidence-based information about the consequences of e-cigarette use among youth and young adults, including the harms of nicotine on the developing brain; and

- Expanding tobacco control and prevention research efforts to increase our understanding of the evolving landscape of e-cigarettes.

These components make up an evidence-based strategy. However, the e-cigarette marketplace is diverse and continues to evolve. Thus, ongoing efforts should rapidly and effectively track and adapt to such changes, thereby protecting our nation's young people from the consequences of e-cigarette use and exposure to secondhand aerosol.

Strategy 1B.

Provide consistent and evidence-based messages about the health risks of e-cigarette use and exposure to secondhand aerosol from e-cigarettes.

Research on e-cigarettes is ongoing, and the e-cigarette marketplace continues to evolve. Even so, a sufficient body of evidence justifies actions taken now to prevent and reduce the use of e-cigarettes and exposure to secondhand aerosol from e-cigarettes, particularly among youth and young adults. Most important, many health risks are already known, and sufficient information exists to take action to minimize potential harms. The evidence is most compelling for nicotine. As part of comprehensive reviews, previous Surgeon General's reports have provided causal findings on the development of addiction and other health consequences of exposure to nicotine (USDHHS 1988, 2014). Beyond addiction, intake of nicotine by young people can harm brain development (Chapter 3).

Additionally, aerosol from e-cigarettes contains toxins that can harm the body, and the flavorings used in these products cannot be considered safe for inhalation, either firsthand or secondhand (Chapter 3). For example, some flavorings have been known to be associated with pulmonary toxicity (Allen et al. 2016).

Messaging about the potential role of e-cigarettes in reducing the burden of tobacco-related diseases should note that e-cigarette products that deliver nicotine are not considered safe, particularly for youth and young adults, even before researchers fully characterize and quantify all of their health risks, including possible permanent changes to the adolescent brain and lungs.

The use of any tobacco product, including e-cigarettes, among young people is unsafe.

Goal 2. Provide Information About the Dangers of E-Cigarette Use Among Youth and Young Adults

Once youth and young adults start using products that contain nicotine, including e-cigarettes, they can become addicted. Such addiction has the potential to lead to long-term use of products that contain nicotine, such as cigarettes. Most adolescents who use tobacco already use more than one nicotine-containing product and are not just using e-cigarettes alone (Chapter 2). The majority of tobacco users start before they are 18 years of age, and almost no one starts after age 25 (USDHHS 2012). Therefore, the best way to protect young people from the harms of tobacco use, including e-cigarettes, is to prevent the use of these products altogether. Prevention should start with robust public policies that make it easy for youth not to use tobacco and harder for them to use any tobacco products. Parents, teachers, health professionals, and other influencers of youth should be educated about the risks of e-cigarette use. They can then help educate their own children as well as other young people about the harms of e-cigarettes and the risk of a potential lifetime of nicotine addiction.

Use of e-cigarettes and exposure to nicotine is particularly dangerous for pregnant women. Nicotine is toxic to the fetus and impairs fetal brain and lung development.

Strategy 2A.

Educate parents, teachers, coaches, and other influencers of youth about the risks of e-cigarette use among youth and young adults.

Parents, guardians, teachers, coaches, health professionals, faith leaders, and other persons whose advice and behavior influence youth play critical roles in protecting youth and young adults from the harms of e-cigarette use and exposure to the secondhand aerosol emitted from these devices. Most adults are familiar with some of the dangers of using tobacco products, especially conventional cigarettes, and of exposure to secondhand tobacco smoke. Because of these dangers, many adults have taken steps to keep children safe. However, most adults are not aware of the potential risks of using e-cigarettes and exposure to secondhand aerosol, and e-cigarette marketing often promotes these products as safe alternatives to smoking conventional cigarettes. But messaging about the dangers is essential. For example, the use of these products can lead to nicotine addiction, harm brain development, and lead to continued tobacco use.

Parents, teachers, coaches, and others can protect their children and other young people by educating them about e-cigarettes:

- Talk openly about the harms of nicotine and tobacco use.

- Express firmly the idea that young people should not use any tobacco products, including e-cigarettes.

- Do not let any individuals use e-cigarettes or other tobacco products around children.

- Ask health care providers, adults, and parents to discuss with children the health risks of using e-cigarettes, such as nicotine addiction.

- Patronize restaurants and other places that do not allow the use of e-cigarettes indoors, and let business owners that allow e-cigarette use indoors know that it is not as safe as clean air or even legal in many places.

- Make sure children's day care centers, schools, and universities are completely tobacco-free, including being free of e-cigarettes. A comprehensive tobacco-free campus policy prohibits any tobacco use, including e-cigarettes, on school property by anyone at any time. These policies should be expanded to include school events that are held off campus.

- Prohibit tobacco and e-cigarette company sponsorship of teams or events, promotional activities, and offers of educational materials for preventing tobacco use among youth.

- Make homes and cars completely tobacco-free, including the use of e-cigarettes. This means no use by family members, friends, or guests. Opening a window does not fully protect against exposure to secondhand cigarette smoke or from the secondhand aerosol from e-cigarettes. For youth and young adults to be fully protected from indoor exposure, all indoor environments must be 100% free from tobacco smoke and e-cigarette aerosol.

- Set an example by being tobacco-free.

- Provide positive support and encouragement to anyone who is trying to quit tobacco.

E-cigarettes are now the most common form of tobacco used by young people. High school students use e-cigarettes more than adults.

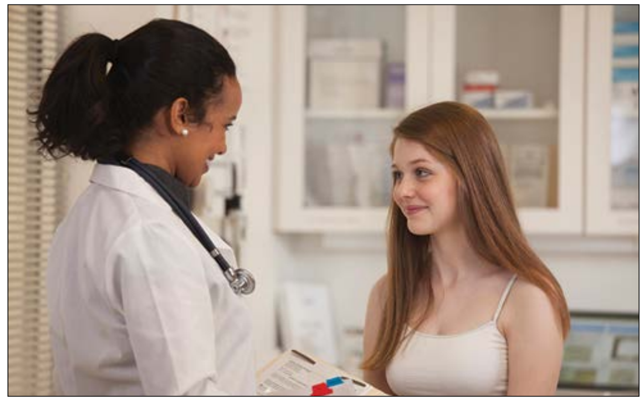
Research suggests that youth and young adults are not as aware of the health consequences of e-cigarette use as they are with the consequences of cigarette smoking (Chapter 2) (Pearson et al. 2012; Richardson et al. 2014; Tan and Bigman 2014). FDA has the authority to require health warnings on tobacco products and tobacco advertising. In addition, FDA and other federal entities, along with state and local organizations, can carry out educational campaigns to better inform the public, especially parents, and increase their understanding of the harms of e-cigarette use.

Strategy 2B.

Educate health professionals about the risks of e-cigarette use among youth and young adults.

The health care setting is an ideal place to educate people of all ages on the potential risks of e-cigarette use and exposure to secondhand aerosol from e-cigarettes. Because e-cigarettes are a relatively new product, health care professionals frequently face a lot of questions about them. These often include questions related to the risks of using e-cigarettes and whether these products can help people to quit smoking. No e-cigarettes have been approved as safe and effective cessation aids.

For youth, in particular, sufficient evidence shows that the use of nicotine is not safe regardless of the delivery device: combustible, non-combustible, or electronic (USDHHS 2014; see also Chapter 3). Thus, health care professionals should warn youth and youth influencers, such as parents, about the health risks of using any product that contains nicotine, including e-cigarettes. They should also warn youth about the dangers of using other substances, such as marijuana, in e-cigarette devices (American Academy of Pediatrics 2015).



Goal 3. Continue to Regulate E-Cigarettes at the Federal Level to Protect Public Health

In 2009, the *Family Smoking Prevention and Tobacco Control Act* (Tobacco Control Act) provided FDA with authority to regulate tobacco products in a manner that is "appropriate for the protection of public health" (e.g., §§ 906(d)(1), 907(a)(3)(A) & (a)(4)(A), and § 910(c)(2)(A) of the *Federal Food, Drug, and Cosmetic Act,* as amended by the Tobacco Control Act) (*Family Smoking Prevention and Tobacco Control Act* 2009, p. 1786). The Tobacco Control Act also requires FDA to consider in regulatory actions the health effects at the individual and population levels, including the impacts on the initiation of measures taken to quit tobacco use as well as effects on relapse among former tobacco users. But FDA is not the only federal agency that can address certain aspects of e-cigarettes (see Chapter 5, Table 5.2).

Strategy 3A.

Implement FDA regulatory authority over the manufacturing, marketing, and distribution of e-cigarettes.

A federal appellate court decision titled *Sottera, Inc. v. Food & Drug Administration* (2010) determined that FDA can regulate e-cigarettes and other products made or derived from tobacco under the Tobacco Control Act, and that these products are not drugs or devices under the *Food, Drug, and Cosmetic Act* unless marketed as therapeutic or smoking cessation products. In May 2016, FDA finalized a rule deeming most products meeting the definition of a tobacco product, including e-cigarettes, subject to regulation under the Tobacco Control Act. The regulation went into effect on August 8, 2016 (but is under litigation) (FDA 2016).

FDA's rule for e-cigarettes includes several provisions that can help protect youth and young adults from the harms of e-cigarettes, such as the following:

- Prohibiting the sale of e-cigarettes to youth who are under 18 years of age (both in person and online);
- Requiring proof of age at the point of purchase;

- Prohibiting vending machine sales in all facilities where children are allowed to enter;
- Prohibiting the distribution of free samples;
- Requiring health warnings about nicotine on packaging and in advertisements;
- Requiring manufacturers to register their e-cigarette products with FDA and disclose the ingredients and levels of harmful and potentially harmful constituents in those products to that agency;
- Requiring premarket review of new or changed tobacco products and authorization by FDA before they can be introduced into the marketplace; and
- Requiring manufacturers that intend to market e-cigarettes for use to reduce harm or risk of tobacco-related disease to receive authorization from FDA based on scientific evidence that the product is less harmful or presents less risk to the public.

This authority allows FDA to undertake future regulatory actions, if determined appropriate for the protection of public health, including:

- Within constitutional limitations, restricting promotion, marketing, and advertising of e–cigarettes;
- Restricting Internet sales and requiring age verification on websites and upon delivery;
- Prohibiting characterizing flavors;
- Promulgating product standards to reduce the toxicity, addictiveness, or appeal of tobacco products;

- Regulating packaging, including requiring minimum package sizes, mandating child-resistant packaging, and requiring health warnings; and
- Prohibiting self-service displays.

Despite gaining this broad authority, FDA does not have specific authority for certain regulatory actions. For example, FDA generally does not restrict tobacco use in public places, levy taxes on tobacco products, or restrict sales to only certain types of retailers (e.g., pharmacies); and FDA cannot completely eliminate nicotine in tobacco products, require prescriptions for tobacco products, or raise the minimum age for sale of tobacco products above 18.

Other complementary comprehensive tobacco control strategies at the state, local, tribal, and territorial levels include:

- Implementing comprehensive clean indoor air laws;
- Prohibiting sales to those under 21 years of age;
- Increasing prices of tobacco products; and
- Developing high-impact countermarketing campaigns.

Effective action at the state and local levels is critical to fully protecting young people from the harms of e-cigarettes.

Strategy 3B.

Reinforce other federal agencies as they implement programs and policies to address e-cigarettes.

Of the other federal agencies that play a role in implementing strategies to address e-cigarettes (see Chapter 5, Table 5.2), some target specific populations (e.g., the U.S. Department of Defense and the U.S. Department of Veterans Affairs); others cover specific areas (e.g., the General Services Administration, National Park Service); and some focus on certain aspects of e-cigarettes (e.g., the Federal Trade Commission, the U.S. Department of Transportation, and the U.S. Environmental Protection Agency). Specific strategies to address e-cigarettes could include those that protect employees, customers, and visitors from exposure to secondhand aerosol, support and encourage tobacco cessation, and curb youth-targeted or false advertising. For example, the National Park Service (2015) implemented a policy to protect employees and visitors from exposure to secondhand aerosol from e-cigarettes.

Goal 4. Programs and Policies to Prevent E-Cigarette Use Among Youth and Young Adults

Subject to certain exceptions, the Tobacco Control Act does not limit the authority of state, local, tribal, and territorial governments to enact any tobacco-related policies related to the sale, distribution, or possession of tobacco products; exposure to these products; or access to them. This broad preservation of authority enables states and localities to adopt many comprehensive tobacco control strategies that have been proven to prevent and reduce tobacco use among youth and young adults. That means that state, local, tribal, and territorial governments could act first in developing regulations, policies, and programs that minimize any individual- and population-level harms of e-cigarettes. The strongest, most innovative tobacco control policies typically have originated at the local level before eventually being adopted at the state level. However, it is important that these strategies are developed with evaluators and epidemiologists that can collect robust data to inform the implementation and sustainment of such strategies.

Strategy 4A.

State, local, tribal, and territorial governments should implement population-level strategies to reduce e-cigarette use among youth and young adults, such as including e-cigarettes in smokefree indoor air policies, restricting youth access to e-cigarettes in retail settings, licensing retailers, and establishing specific package requirements.

Over 50 years of research offers a strong body of evidence on the effectiveness of certain tobacco prevention and control measures. Much of this evidence can also be applied to e-cigarettes. And from this evidence, state, local, tribal, and territorial entities can take a variety of actions to address e-cigarettes, such as:

- Including e-cigarettes in smokefree indoor air policies;
- Restricting youth access to e-cigarettes in retail settings;
- Licensing retailers; and
- Establishing specific package requirements.

Including E-Cigarettes in Smokefree Indoor Air Policies

Most smokefree indoor air policies were put in place before the great rise in e-cigarette use. Because of that, these policies may not cover e-cigarettes or exposure to the aerosol they produce. Aerosol from e-cigarettes is not harmless (CDC 2014). Smokefree indoor air policies should be updated to prohibit the use of both conventional cigarettes and e-cigarettes, thereby preserving standards for clean indoor air. Efforts to include e-cigarettes in smokefree laws should also uphold or strengthen, not weaken, existing protections against exposure to secondhand smoke.

Including e-cigarettes in smokefree indoor air policies can:

- Eliminate health risks from exposure to secondhand aerosol from e-cigarettes;
- Discourage people from using both combustible and electronic tobacco products (dual use);
- Simplify compliance with and enforcement of existing smokefree laws;
- Help to reduce the use of e-cigarettes among youth and young adults; and
- Maintain tobacco-free norms.

Aerosol from e-cigarettes is not harmless.

To date, several states and several hundred communities include e-cigarettes in comprehensive smokefree laws that prohibit smoking in all indoor areas of public places, including worksites, restaurants, bars, and gambling facilities (Americans for Nonsmokers' Rights Foundation 2015; CDC n.d.).

Restricting Youth Access to E-Cigarettes

When laws prohibiting tobacco sales to youth are strong and actively enforced with the education of retailers, they successfully reduce tobacco use among youth (Task Force on Community Preventive Services 2001; Zaza et al. 2005). To date, all 50 states and the District of Columbia restrict the sale of tobacco products to minors (CDC n.d.). Extending such laws to include e-cigarettes can further protect youth from exposure to nicotine, which nearly all states have done. Specific strategies can be implemented to deter the access of youth to e-cigarettes and their use in this population:

- Restricting the sale of e-cigarettes to minors;
- Placing restrictions on Internet sales of all tobacco products and e-cigarettes, including requirements for verifying age and providing identification at the time of purchase and upon delivery;
- Requiring age verification at the point of purchase;
- Displaying clear signage in retail locations about required age for sale;
- Prohibiting the sale of e-cigarettes from vending machines;
- Eliminating self-service displays of e-cigarettes; and
- Enforcing laws on the retail sale of e-cigarettes to minors.

Nearly all states prohibit the sale of e-cigarettes to youth under 18 years of age. Some states have a higher minimum age for purchase (e.g., 19 or 21 years of age) (CDC 2014). Some e-cigarette manufacturers have supported state legislation to prevent minors from purchasing e-cigarettes (Healy 2014). Their actions may, to some extent, be responsible for why these age-of-sale laws have been adopted more quickly than laws that prohibit e-cigarette use in public indoor spaces. However, industry-supported, youth-access bills have contained provisions that undermine prevention efforts for youth, including preemption of stricter local policies and weak requirements for enforcement (USDHHS 2012). Additionally, laws prohibiting sales to minors are likely to have limited effectiveness as a prevention strategy if they are not aggressively enforced and are not coupled with proven interventions, such as comprehensive smokefree laws, pricing strategies, or public health campaigns (USDHHS 2012, 2014). Ensuring that e-cigarettes are regulated at the state and local levels can facilitate the application of additional tobacco control policies regarding e-cigarettes.

Many actions can help to protect young people from the harms of e-cigarettes, such as including e-cigarettes in smokefree indoor air policies, restricting youth access to e-cigarettes in retail settings, licensing retailers, and setting specific package requirements.

Licensing Retailers

Licensing is another strategy to control access to e-cigarettes among youth and young adults. A tobacco-related license can authorize a business to manufacture, distribute, or sell tobacco products (McLaughlin 2010). Licensing requirements help to prevent sales to minors, prevent evasion of tobacco excise taxes, ensure that licensees comply with tobacco-related laws, and promote safe manufacturing practices (ChangeLab Solutions 2012). Businesses that repeatedly violate these laws can have their right to engage in commercial activity suspended or their licenses permanently removed. The possibility of these outcomes provides a strong incentive to comply with license requirements. Licensing may also be used to restrict the sale of flavored products or to address consumer and worker safety issues involved with the mixing of liquids for e-cigarette products (e-liquids).

Establishing Specific Packaging Requirements

Federal, state, local, tribal, and territorial governments are actively considering the potential harms of e-liquids. Exposure to these liquids may lead to nicotine and other types of poisoning. Calls to poison control centers about e-cigarettes and e-liquids have been on the rise, and about half of these calls are for incidents involving young children (American Association of Poison Control Centers 2015). The most common adverse health effects of poisoning are vomiting, nausea, and eye irritation, but some deaths have occurred as well. Developing strategies to monitor and prevent future poisonings is critical.

Calls to poison control centers about e-cigarettes are on the rise. A large portion of these calls are for incidents involving young children.

Enacting laws that require e-liquids to be labeled and sold in childproof packaging is one way to reduce the incidence of poisonings, particularly among children. To date, in addition to the federal *Child Nicotine Poisoning Prevention Act of 2015* (2016) enacted in January 2016, more than a dozen states have enacted laws requiring childproof packaging for e-liquids (Tobacco Control Legal Consortium n.d.). Health care providers, the public health community, e-cigarette manufacturers and retailers, and the public should be aware that e-liquids pose a serious public health concern, particularly among young children.

Strategy 4B.

Coordinate, evaluate, and share best practices from state and local entities that have implemented programs and policies to address e-cigarette use among youth and young adults.

Many governments at the national, state, local, tribal, and territorial levels are involved in the regulation of e-cigarettes. To have the biggest impact on reducing the use and exposure of e-cigarettes among youth and young adults, it is integral for these governments to share best practices and coordinate and evaluate efforts as part of a comprehensive tobacco prevention and control strategy. FDA has asserted regulatory authority over e-cigarettes, and other agencies and governments, as discussed previously and in Chapter 5, also have relevant authorities.

Goal 5. Curb Advertising and Marketing that Encourages Youth and Young Adults to Use E-Cigarettes

Unconstrained marketing of e-cigarettes drives consumer demand for these products. E-cigarette manufacturers are using tactics similar to those used to market conventional cigarettes to youth, including offering candy-flavored products; employing youth-minded themes, such as rebellion, glamour, and sex; getting celebrity endorsements; and obtaining sports and music sponsorships (Chapter 4). Some groups have called for extending to e-cigarettes the same marketing restrictions that already apply to conventional cigarettes and other tobacco products (Association of State and Territorial Health Officials 2014; Partnership for Prevention 2014). But regulating commercial speech is typically met with significant barriers and complex legal issues (Laird-Metke 2010), and partial advertising bans and voluntary agreements generally have not been fully effective at reducing consumption because the tobacco industry adapts by shifting to other types of advertising that are not regulated (National Cancer Institute 2008). Despite these obstacles, public health organizations and state and local governments must take action to control the marketing of e-cigarettes to youth and young adults, including (a) seeking legally feasible interventions that are proven to curb youth-oriented tobacco marketing, including removing advertising from television; and (b) continuing to help build an evidence base that informs future potential restrictions on e-cigarette marketing.

Strategy 5A.

Curb e-cigarette advertising and marketing that are likely to attract youth and young adults.

In the absence or delayed implementation of government restrictions on the marketing of e-cigarettes, media outlets, the management staff of special event and sports venues, and retailers can voluntarily refuse to air or place youth- and young adult-oriented e-cigarette advertising; avoid sponsorships; and not offer free samples of these products at fairs, festivals, and other events.

E-cigarettes are aggressively marketed using tactics similar to those proven to lead to cigarette smoking among youth.

Finally, state and local public health agencies can stimulate enforcement of and compliance with existing rules that limit marketing. For example, they can monitor advertising and notify their state's attorney general or the Federal Trade Commission about improper claims or marketing that is not clearly identified as advertising (*Federal Register* 1972; FTC 1984; Center for Public Health and Tobacco Policy 2013).

Strategy 5B.

Urge the e-cigarette companies to stop advertising and marketing that encourages and glamorizes e-cigarette use among youth and young adults.

E-cigarette advertising has increased considerably over the years in multiple venues (Legacy for Health 2014; Ganz et al. 2015; see also Chapter 4), while the advertising for conventional cigarettes on television has been prohibited in the United States since 1971. But e-cigarettes are now marketed on television and other mainstream media channels, such as radio and magazines, which are main sources of information for youth and young adults. Emerging research suggests that exposure to television advertisements for e-cigarettes increases the likelihood that young people will use e-cigarettes in the future and will believe that e-cigarettes can be used in places where conventional cigarette smoking is not allowed (Farrelly et al. 2015). This is not surprising because e-cigarette marketing has previously included unproven claims about safety and smoking cessation, as well as statements that e-cigarettes are exempt from clean air policies that restrict smoking (USDHHS 2014). Visual depictions of e-cigarette use in advertisements may also serve as smoking cues to both current and former smokers, increasing their urges to smoke and undermining their efforts to quit (Maloney and Cappella 2015). Advertising for e-cigarettes that encourages and glamorizes the use of e-cigarettes among youth and young adults can harm public health by undermining:

- Clean indoor air standards;
- Enforcement of smokefree policies;
- Tobacco-free social norms; and
- Marketing restrictions that prohibit the advertising of cigarettes and smokeless tobacco on television and radio.

Discontinuing advertising and marketing by e-cigarette companies that intentionally or unintentionally encourages or glamorizes e-cigarette use among youth and young adults is essential. Responsible advertising by the e-cigarette companies is needed, including advertising that focuses directly on established adult smokers and features adults (not young adults), does not depict active use of e-cigarettes, does not use themes proven to appeal to youth and young adults, avoids media channels with high youth access, and does not undermine cessation efforts involving traditional tobacco products.

Goal 6. Expand Surveillance, Research, and Evaluation Related to E-Cigarettes

Tobacco control research focused on e-cigarettes has grown considerably in the past few years. Certainly, more detailed information is needed to better understand the use of e-cigarettes and its relationship to the use of other types of tobacco products. A comprehensive and evolving approach to research, surveillance, and evaluation is needed.

Strategy 6A.

Improve the quality, timeliness, and scope of e-cigarette surveillance, research, and evaluation.

Present surveillance systems show that e-cigarette use is increasing rapidly and that most regular e-cigarette users also use conventional tobacco products (see Chapter 2). Thus, further study can inform strategies that minimize harms and maximize the potential health benefits of these products at the individual and population levels. Data should be timely and focus on the patterns of e-cigarette initiation and use among the general public—including youth, young adults, and former smokers. Strategic and comprehensive research and evaluation must further characterize the health risks of e-cigarette use. A comprehensive package of surveillance, research, and evaluation should:

- Track patterns of e-cigarette use through cross-sectional surveys and through panels that follow the same people, including youth and young adults, over time;
- Monitor trends in the e-cigarette retail market by type of product;
- Examine the channels and messaging in the e-cigarette marketplace to inform proactive countermarketing strategies;
- Assess the short- and medium-term health effects of e-cigarette use by youth and young adults and track long-term consequences;
- Examine the risk factors and other risk behaviors that may be associated with using e-cigarettes; and
- Create a model to develop and track the public health impact of e-cigarettes.

The rapidly changing nature of the e-cigarette landscape calls for a comprehensive and evolving approach to research, surveillance, and evaluation.

For such a package, researchers, the public health community, and other key stakeholders must work together to address and overcome many challenges:

- The rapidly changing e-cigarette landscape and terminology;
- Limited resources for collecting timely information;

- The cross-sectional nature of existing surveys and their limited space for questions;
- The different populations that need to be studied;
- A lack of validated questions; and
- Different measures and definitions across surveys.

Strategy 6B.

Address surveillance, research, and evaluation gaps related to e-cigarettes.

Patterns of e-cigarette use are rapidly changing among youth and young adults, as well as among other groups in the population. Longitudinal data are not yet available to address some of the most critical issues related to e-cigarettes. The e-cigarette marketplace is changing so fast that surveillance data and research on the harms of e-cigarette use and the impact of these changes on traditional tobacco products are lagging behind. As they look to fill in gaps in scientific research, it is important for researchers to continue to seek more current and complete answers to many critical questions, such as:

- What are the risks of progressing to traditional tobacco use among youth and young adults who have used e-cigarettes?
- What are the health risks posed by e-cigarettes?
- Are e-cigarettes safer and more effective than current products at helping smokers with smoking cessation?
- What are the health consequences for youth and young adults of initiation of e-cigarettes and of dual use (conventional cigarettes plus e-cigarettes) compared with the health benefits of completely quitting smoking (or not starting at all)?
- What are the health risks to former smokers who are exposed to nicotine from e-cigarette use? Will these persons be more likely to resume smoking?

Additionally, surveillance of e-cigarette marketing and the advertising messages and strategies used is critical, as is the carrying out of more studies assessing the link between exposure to e-cigarette marketing and use of these products. With traditional tobacco products, state and local public health agencies have monitored retail settings, assessed outdoor advertising, and identified sponsorships of events by tobacco companies. These efforts should be adapted to e-cigarettes.

The health care setting has always been an important venue for exchanging information about evidence-based approaches to smoking cessation and for protecting susceptible groups from exposure to secondhand smoke. More research is needed on the role of e-cigarettes in facilitating or hindering cessation of conventional cigarettes and the potential hazards of exposure to secondhand aerosol from e-cigarettes so that e-cigarettes can also be a part of this exchange. But even without this research, there is sufficient evidence about the dangers that nicotine-containing cigarettes pose for youth and young adults that health care providers and professionals can act now to prevent the use of such products among their young patients.

Finally, existing research and surveillance efforts should include more detailed measures than just general use of e-cigarettes, including:

- Frequency and patterns of e-cigarette use;
- Type of e-cigarette and/or other tobacco product used;
- The natural history of e-cigarette use, including initiation, co-use with other tobacco products, and flavoring;
- Ingredients, such as nicotine and flavors;
- Brand;
- Reasons for using and quitting e-cigarettes;
- Exposure to e-cigarette advertising;
- Methods of obtaining e-cigarettes; and
- Exposure to secondhand aerosol from e-cigarettes.

Additionally, evaluation is critical to further assess the impact of policies on e-cigarette initiation, use, and other patterns of tobacco use.

Conclusions

E-cigarette use, particularly among youth and young adults, has become a public health concern that warrants immediate and coordinated action. The increase in e-cigarette use among youth and young adults in the past few years is cause for great concern. Many questions remain about e-cigarettes and their long-term impact, even as evidence on patterns of use and risks to health continue to emerge. But we know enough about these health risks to take action now to protect the health of our nation's young people. We cannot wait. Strategies to prevent and control the harms of e-cigarettes among youth and young adults need to be precautionary. Therefore, we must take a precautionary approach by implementing these strategies and protecting the health of our nation's young people.

We know what works to effectively prevent tobacco use among young people. Now we must apply these strategies to e-cigarettes—and continue to apply them to other tobacco products. To achieve success, we must work together, aligning and coordinating efforts across a wide range of stakeholders. We must protect our nation's young people from a lifetime of nicotine addiction and associated problems by immediately addressing e-cigarettes as an urgent public health problem. Now is the time to take action.

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List of Abbreviations

α4β2	alpha 4 beta 2-nicotinic acetylcholine receptor subtype
α7	alpha 7 nicotinic acetylcholine receptor subtype
α6	alpha 6 nicotinic acetylcholine receptor subtype
μg	microgram
5AP tLTP protocol	5 action potential timing-dependent long-term potentiation protocol
5-CSRTT	5-choice serial reaction time task
5-HIAA	5-hydroxyindole acetic acid, the primary metabolite of serotonin
5-HT_{1AR}	serotonin (5-hydroxytryptamine) receptor 1A
$5\text{-HT}_{2A/C}$	serotonin (5-hydroxytryptamine) receptor 2 A/C
86Rb+ efflux assay	measure of nicotinic acetylcholine receptor function via rubidium-86 ion efflux [125-I]α-Btx binding measurement of binding at α7 nAChRs using the antagonist alpha-bungarotoxin
$[^{125}I]\alpha$-CtxMII binding	measurement of binding at α6 nAChRs using the antagonist alpha-conotoxin MII
$[^{125}I]$A-85380 binding	measurement of binding at α4β2 nAChRs using the agonist A-85380
A1	primary auditory cortex
AAP	American Academy of Pediatrics
ACR	American Association of Cancer Research
AARC	American Association for Respiratory Care
ACP	American College of Physicians
ACS	American Cancer Society
ADHD	attention deficit hyperactivity disorder
ADI	acceptable daily intake
AEMSA	American E-Liquid Manufacturing Standards Association
AHA	American Heart Association
AMPA	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
AMPAR	AMPA receptor
ANHCS	Annenberg National Health Communication Survey
ANR	Americans for Nonsmokers' Rights
AOR	adjusted odds ratio
AP	acetyl propionyl
APA	American Psychiatric Association
APV	advanced personal vaporizers
arc	activity-regulated cytoskeleton-associated protein
ATF	U.S. Department of Justice, Bureau of Alcohol, Tobacco, Firearms and Explosives
A-V	atrial-ventricular
AVA	American Vaping Association
BART	Balloon Analogue Risk Task
BCAP/CAP	Committees of Advertising Practice (UK)
BLA	basolateral amygdala
BNST	bed nucleus of the stria terminalis
BOP	Bureau of Prisons
BP	blood pressure
CAD	cinnamaldehyde
CAM	cell-adhesion molecule
cAMP-PKA	cyclic AMP-protein kinase A, signaling cascade
CARDIA	Coronary Artery Risk Development in Young Adults
CASAA	Consumer Advocates for Smoke-free Alternatives Association
CCTA	Contraband Cigarette Trafficking Act
CDC	Centers for Disease Control and Prevention
CDER	Center for Drug Evaluation and Research
C-DISC-IV	Diagnostic Interview for Children–Version 4
cFos	protooncogene and immediate early gene used as a marker of neuronal activity
CFR	Code of Federal Regulations
CI	confidence interval
CMS	Centers for Medicare & Medicaid Services
CO_2	carbon dioxide
COMDTINST	Commandant Instruction
CPP	conditioned place preference
CPu	caudate putamen
CREB	cAMP response element-binding protein
CRF	corticotropin-releasing factor

CRP	C-reactive protein
CSI	Child Symptom Inventory
CTA	conditioned taste aversion
CTP	Center for Tobacco Products
D1R	dopamine D1 receptor
DA	diacetyl
DA	dopamine
DAT1	dopamine regulation genotype
DEHP	diethylhexyl phthalate
DEP	diethyl phthalate
DHS	U.S. Department of Homeland Security
DISC-YC	Diagnostic Interview Schedule for Children-Parent Scale-Young Child
DoD	U.S. Department of Defense
DOPAC	3,4-dihydroxyphenylacetic acid, metabolite of dopamine
DOT	U.S. Department of Transportation
DSM-III	Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
EC	electronic cigarette
ECIG Inc.	Electronic Cigarette Industry Group, Inc.
ECIG Ltd.	Electronic Cigarettes International Group, Ltd.
ED	U.S. Department of Education
ENDS	electronic nicotine delivery systems
ENNDS	electronic non-nicotine delivery systems
EOP	Executive Office of the President
EPA	U.S. Environmental Protection Agency
ERS	European Respiratory Society
EPSC	excitatory postsynaptic current
EPSDT	Early and Periodic Screening, Diagnosis and Treatment
EPSP	excitatory postsynaptic potential
ESD	electronic smoking device
EU	European Union
F1	first filial generation (and similar)
FAA	Federal Aviation Administration
FCC	Federal Communications Commission
FCLAA	Federal Cigarette Labeling and Advertising Act
FCTC	Framework Convention on Tobacco Control
FD&C Act	Federal Food, Drug, and Cosmetic Act
FDA	U.S. Food and Drug Administration
FEF	forced expiratory flow
FeNO	exhaled nitric oxide
FEV_1	forced expiratory volume in 1 second
fMRI	functional magnetic resonance imaging
FR	fixed ratio
FST	forced swim test
FTC	U.S. Federal Trade Commission
FVC	forced vital capacity
FY	fiscal year
G20	gestational day 20 (and similar)
g	gram
GABA	gamma-aminobutyric acid
GABAergic	any cell, especially any neuron, that releases GABA
GPCR	G-protein-coupled-receptor
GSA	General Services Administration
GTP	guanosine triphosphate
GTPase	large family of hydrolase enzymes that can bind and hydrolyze GTP
HONC	Hooked on Nicotine Checklist
HPLC-ECD	high-performance liquid chromatography electrochemical detection
HUD	U.S. Department of Housing and Urban Development
HVA	homovanillic acid
IARC	International Agency for Research on Cancer
ICD-10	International Statistical Classification of Diseases and Related Health Problems, 10th revision
ICE	Bureau of Immigration and Customs Enforcement
ICR mice	Institute for Cancer Research strain of mice
ICSS	intracranial self-stimulation
IOM	Institute of Medicine
i.p.	intraperitoneal
IQ	intelligence quotient
IRC	Internal Revenue Code
i.v.	intravenous
kg	kilogram
KO	knockout
L	liter
L&M	Liggett & Myers
LC-MS/MS	liquid chromatography-tandem mass spectrometry

LH	lateral hypothalamus
M&As	mergers, formations of partnerships, and acquisitions
m^2	square meter
m^3	cubic meter
MAOA	monoamine oxidase A
MAPK	mitogen-activated protein kinase
MCH	melanin-concentrating hormone
mFTQ	modified Fagerström Tolerance Questionnaire
mg	milligram
mGluR2	metabotropic glutamate receptor 2
mL	milliliter
mPFC	medial prefrontal cortex
mRNA	messenger ribonucleic acid
MSN	medium spiny neuron
MTF	Monitoring the Future
NAB	N-nitrosoanabasine
N_2	nitrogen
NAc	nucleus accumbens
NACDA	National Advisory Council on Drug Abuse
nAChR	nicotinic acetylcholine receptor
NAc-shell	nucleus accumbens shell
NAT	N-nitrosoanatabine
NATS	National Adult Tobacco Survey
NCI	National Cancer Institute
NDAA	National Defense Authorization Act
NDSS	Nicotine Dependence Syndrome Scale
NE	norepinephrine
ng	nanogram
NGFI-B	nerve growth factor-induced gene-B
NHANES III	Third National Health and Nutrition Examination Survey
NHSDA	National Household Survey on Drug Abuse
NIH	National Institutes of Health
NMDAR	*N*-methyl-D-aspartate receptor
NIDA	National Institute on Drug Abuse
NIOSH	National Institute for Occupational Safety
NJYTS	New Jersey Youth Tobacco Survey
NLSY	National Longitudinal Survey of Youth
nm	nanometer
NNN	N-nitrosonornicotine
NNK	4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone
NRT	nicotine replacement therapy
NYS	New York State Follow-Up
NYTS	National Youth Tobacco Survey
O_2	oxygen
ODD	oppositional defiant disorder
OMB	Office of Management and Budget
OPM	Office of Personnel Management
OR	odds ratio
OSH	Office on Smoking and Health
OSHA	U.S. Department of Labor, Occupational Safety and Health Administration
P3 (and similar)	postnatal day number
PACT	Prevent All Cigarette Trafficking Act
PAH	polycyclic aromatic hydrocarbon
PATH	Population Assessment of Tobacco and Health
PDAY	Pathological Determinants of Atherosclerosis in Youth
PFC	prefrontal cortex
PHS	Public Health Service
PIH	Public and Indian Housing
PVN	paraventricular nucleus of the thalamus
PG	propylene glycol
PM	particulate matter
$PM_{2.5}$	fine particulate matter
PNE	prenatal nicotine exposure
p.o.	per os (by mouth)
Postn	periostin, osteoblast-specific factor
PR	progressive ratio
PREP	potential reduced-exposure product
PVN	paraventricular nucleus of the thalamus
qRT-PCR	quantitative real-time polymerase chain reaction
RCRA	Resource Conservation and Recovery Act
SAC	saccharin
SAMHSA	Substance Abuse and Mental Health Services Administration
s.c.	subcutaneous
SCAN	Screening test for Auditory Processing Disorders
SD	standard deviation
SE	standard error
sec	seconds
SEC	Securities and Exchange Commission
SES	socioeconomic status

SFATA	Smoke Free Alternatives Trade Association
SIDS	sudden infant death syndrome
SMC	serial multiple choice
SNAP	Special Supplemental Nutrition Program
SNP	single-nucleotide polymorphism
SRITA	Stanford Research into the Impact of Tobacco Advertising
STOP	Smuggled Tobacco Prevention Act
TCR	trigeminocardiac reflex
TEOAEs	transient evoked otoacoustic emissions
TH	tyrosine hydroxylase
THC	tetrahydrocannabinol
TSNA	tobacco-specific nitrosamine
TTB	U.S. Department of Treasury, Alcohol and Tobacco Tax and Trade Bureau
TVECA	Tobacco Vapor Electronic Cigarette Association
UK	United Kingdom
U.S.C.	U.S. Code
USDA	U.S. Department of Agriculture
USDHEW	U.S. Department of Health, Education, and Welfare
USDHHS	U.S. Department of Health and Human Services
USP	U.S. Pharmacopeia
USTR	U.S. Trade Representative
V	voltage
VA	U.S. Department of Veterans Affairs
VG	vegetable glycerin
VOC	volatile organic compound
VTA	ventral tegmental area
WHO	World Health Organization
WIC	Women, Infants, and Children
Wnt	Wingless-Type MMTV Integration Site Family, member 1, intracellular signaling factors
WT	wild type
w/v	weight/volume
YRBSS	Youth Risk Behavior Surveillance System

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Executive Summary

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[1]The Executive Summary and appendixes are not a part of the main report. Instead, they are available online at http:/www.surgeongeneral.gov/library/reports/.

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