Jonathan B. VanGeest
Timothy P. Johnson
Sonia A. Alemagno *Editors*

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Editors
Jonathan B. VanGeest
Department of Health Policy and Management, College of Public Health
Kent State University
Kent, OH
USA

Timothy P. Johnson
Survey Research Laboratory, Department of Public Administration, College of Urban Planning and Public Affairs
University of Illinois at Chicago
Chicago, IL
USA

Sonia A. Alemagno
Department of Health Policy and Management, College of Public Health
Kent State University
Kent, OH
USA

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Preface

This monograph provides an introduction and overview of the most common research methods currently being employed to study substance use- and abuse-related behaviors, primarily in regards to alcohol and/or illicit drugs, with a focus on their application in advancing understanding, prevention and treatment. Substance abuse research draws both its theories and methods from a variety of other fields, and we have tried to incorporate insights from these various perspectives here. We acknowledge up front some variation in the definitions of key concepts used in the field, particularly with regard as to what constitutes substance "use," "misuse," and "abuse." Inconsistencies in terminology abound, with "misuse" and "abuse" even used interchangeably by researchers. Some even abandon theses terms all together to focus on clinical diagnostic criteria indicative of use disorders, such as those found in the latest edition of The Diagnostic and Statistical Manual of Mental Disorders. While definitional issues are addressed in the text, due to lack of consensus in the field, some discretion is given to the chapter author(s) with regard to their preference. The monograph is divided into six parts. In the first of these, two overview chapters are provided. In Chap. 1, we chronicle how research in the field has advanced over the past fifty-plus years and how multiple waves of innovation contributed to current standards and best practices. In Chap. 2, Jennifer Reingle and Timothy Akers introduce the transdisciplinary research framework known as epidemiological criminology, which is now considered a promising approach for innovation in substance abuse research.

Part II covers quantitative approaches, including randomized controlled trials in Chap. 3 (by James Swartz), sampling strategies in Chap. 4 (by Joseph Gfroerer, Arthur Hughs and Jonaki Bose), methods of primary and secondary statistical data analysis in Chap. 5 (by Adam King, Libo Li and Yih-Ing Hser), and longitudinal methods in Chap. 6 (by Brent Teasdale and Jerreed Ivanich). Qualitative and mixed methods are examined in Part III. Paul Draus presents an overview of qualitative methods in Chap. 7, followed by Henry Browstein's discussion of qualitative data analysis methods in Chap. 8. The use of geographic information systems in substance abuse research are presented by Jacqueline Curtis and Andrew Curtis in Chap. 9, and Sheryl Chatfield and Jeffrey Hallam investigate mixed methods research strategies for substance abuse research in Chap. 10.

Measurement issues are addressed in Part IV. A general overview of substance abuse assessment is provided by Timothy Grigsby, Steve Sussman, Chih-Ping Chou, and Susan Ames in Chap. 11. This is followed by Brian Perron, David Cordova, Christopher Salas-Wright and Michael Vaughn's consideration of measurement validity in Chap. 12. The use of surveys to measure substance use behaviors is reviewed by Timothy Johnson and Jonathan VanGeest in Chap. 13, and Michael Fendrich, Timothy Johnson and Jessica Becker provide an overview of the use of biological measures in Chap. 14. In Part V, challenges and special considerations in conducting substance abuse research with several subgroups of the general population are discussed. In Chap. 15, Dianne Kerr and Willie Oglesby consider issues in the conduct of adolescent substance abuse research. In Chap. 16, these same authors address substance abuse research in the LGBT Community. Sage Kim and Michael Puisis discuss the conduct of research with incarcerated populations in Chap. 17. Finally, Part IV examines policy analysis methods. John Carnevale outlines the role played by research in the formulation of substance abuse policy in Chap. 18. The economic evaluation of substance abuse and prevention programs is examined, in Chap. 19, by Willie Oglesby and Lauren Birmingham, and the general evaluation of substance abuse prevention and treatment programs is discussed by Peggy Stephens, Zili Sloboda, and Deric Kenne in Chap. 20.

As we acknowledged earlier, substance abuse research draws ideas, theories, and methods from a variety of other disciplines. As such, we found it necessary in organizing this volume to similarly reach out to experts across a variety of fields in an effort to provide a comprehensive overview of current knowledge and practices. We are sincerely grateful for the contributions of all authors whose contributions are presented in this monograph, and thank them for their patience in working through multiple drafts with us over the past several years. We are hopeful that you, the reader, will agree.

Kent, OH, USA — Jonathan B. VanGeest
Chicago, IL, USA — Timothy P. Johnson
Kent, OH, USA — Sonia A. Alemagno
November 2016

Acknowledgments

This book is made up of contributions from a talented group of academics and practitioners. Collectively, they provide insights on some of the unique challenges (and solutions) associated with the conduct of research on substance abuse. It has been a pleasure working with this group of scholars and they have our deep appreciation for their contributions to this effort. We would also like to thank our colleagues who have contributed valuable insights and recommendations to improve our final product. Specifically, we thank Peggy and Richard Stephens for their helpful edits and contributions. Additionally, we thank Carissa Smock and Matthew Nichols (Kent State University, College of Public Health) for their help in editing text. We also thank the team at Springer for their support and seemingly endless patience as we put this volume together.

Lastly, we would like to thank our spouses—Sarah VanGeest, LuEllen Doty and Tom Alemagno for their unwavering support throughout this project.

Jonathan B. VanGeest
Timothy P. Johnson
Sonia A. Alemagno

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Editors and Contributors

About the Editors

Jonathan B. VanGeest, Ph.D., is a Professor in the Department of Health Policy and Management at Kent State University. His main areas of expertise include racial and ethnic disparities in health care, limited health literacy, and care outcomes associated with structural changes in medicine. He also has extensive experience in survey research methodology, program evaluation, and research on substance abuse issues among homeless persons and other marginalized risk groups.

Timothy P. Johnson, Ph.D., is the Director of the Survey Research Laboratory and a Professor in the Department of Public Administration at the University of Illinois at Chicago. His main areas of expertise include health disparities, survey methodology, and health behaviors in disadvantaged populations. Within the field of survey methodology, his work has focused primarily on sources of measurement and nonresponse error. Johnson has also invested considerable effort in examining the health behaviors of disadvantaged populations. Among the disadvantaged populations he has worked with are homeless persons, immigrants, cultural minorities, criminal justice populations, and mental health populations. Some of the health behaviors he has examined among these populations include cancer screening, nutrition, physical activity, tobacco use, alcohol consumption, and drug abuse.

Sonia A. Alemagno, Ph.D., is the Dean of the College of Public Health and a Professor in the Department of Health Policy and Management at Kent State University. She has focused her research on substance abuse and HIV/STD prevention, particularly examining public health services delivered within criminal justice settings such as prisons and detention centers. Her awards include a National Institutes of Health Career Development Award from the National Institute on Drug Abuse and the University of Akron Outstanding Researcher Award in 2005. In addition, she has been the principal investigator on several projects including research funded by the National Institutes of Health, the Centers for Disease Control, the National Institute of Justice, and the SAMHSA Center for Substance Abuse Treatment.

Contributors

Timothy A. Akers Division of Research and Economic Development, Morgan State University, Baltimore, MD, USA

Susan L. Ames School of Community and Global Health, Claremont Graduate University, Claremont, CA, USA

Jessica Becker School of Social Work, University of Connecticut, West Hartford, CT, USA

Lauren Birmingham Department of Health Policy and Management, College of Public Health, Kent State University, Kent, OH, USA

Jonaki Bose Substance Abuse and Mental Health Services Administration, Rockville, MD, USA

Henry H. Brownstein Center for Public Policy, The Wilder School for Government and Public Affairs, Virginia Commonwealth University, Richmond, VA, USA

John T. Carnevale Carnevale Associates, LLC, Gaithersburg, MD, USA

Sheryl L. Chatfield Department of Social and Behavioral Sciences, College of Public Health, Kent State University, Kent, OH, USA

Chih-Ping Chou Institute for Health Promotion and Disease Prevention Research, University of Southern California, Los Angeles, CA, USA

David Cordova School of Social Work, University of Michigan, Ann Arbor, MI, USA

Andrew Curtis GIS Health & Hazards Laboratory, Department of Geography, Kent State University, Kent, OH, USA

Jacqueline W. Curtis GIS Health & Hazards Laboratory, Department of Geography, Kent State University, Kent, OH, USA

Paul Draus Department of Behavioral Sciences, The University of Michigan-Dearborn, Dearborn, MI, USA

Michael Fendrich School of Social Work, University of Connecticut, West Hartford, CT, USA

Joseph Gfroerer Substance Abuse and Mental Health Services Administration, Rockville, MD, USA

Timothy J. Grigsby Department of Kinesiology, Health, and Nutrition, University of Texas, San Antonio, TX, USA

Jeffrey S. Hallam Department of Social and Behavioral Sciences, College of Public Health, Kent State University, Kent, OH, USA

Yih-Ing Hser University of California, Los Angeles, CA, USA

Arthur Hughes Substance Abuse and Mental Health Services Administration, Rockville, MD, USA

Jerreed Ivanich Department of Sociology, University of Nebraska-Lincoln, Lincoln, NE, USA

Deric Kenne Department of Health Policy and Management, College of Public Health, Kent State University, Kent, OH, USA

Dianne L. Kerr College of Education, Health, and Human Services, Kent State University, Kent, OH, USA

Sage Kim School of Public Health, University of Illinois at Chicago, Chicago, IL, USA

Adam King University of California, Los Angeles, CA, USADepartment of Mathematics and Statistics, California State Polytechnic University, Pomona, CA, USA

Libo Li University of California, Los Angeles, CA, USA

Willie H. Oglesby College of Population Health, Thomas Jefferson University, Philadelphia, PA, USA

Brian E. Perron School of Social Work, University of Michigan, Ann Arbor, MI, USA

Michael Puisis Correctional Consultant, Chicago, IL, USA

Jennifer M. Reingle Gonzalez Department of Epidemiology, Human Genetics, and Environmental Sciences, University of Texas School of Public Health, Dallas, TX, USA

Christopher Salas-Wright School of Social Work, The University of Texas at Austin, Austin, TX, USA

Zili Sloboda Applied Prevention Science International, Inc., Ontario, OH, USA

Peggy Stephens Department of Social and Behavioral Sciences, College of Public Health, Kent State University, Kent, OH, USA

Steve Sussman Institute for Health Promotion and Disease Prevention Research, University of Southern California, Los Angeles, CA, USA

James A. Swartz Jane Addams College of Social Work, University of Illinois at Chicago, Chicago, IL, USA

Brent Teasdale Department of Criminal Justice and Criminology, Georgia State University, Atlanta, GA, USA

Michael G. Vaughn School of Social Work, Saint Louis University, Saint Louis, MO, USA

Part I

Overview

History of Substance Abuse Research in the United States

1

Jonathan B. VanGeest, Timothy P. Johnson, and Sonia A. Alemagno

1.1 Introduction

Substance abuse is a global problem of epidemic proportions (Degenhardt and Hall 2015; Gowing et al. 2015; Griffiths et al. 2008). In the United States alone, an estimated 17 million people are dependent upon or have abused alcohol in the past year, with males at greatest risk, as well as young adults aged 18–25 years compared to other age groups (CBHSQ 2015). An estimated 7.1 million people aged 12 or older are dependent on or abused illicit drugs in the past year, with rates of abuse highest for males, young adults (18–25 years of age), and African Americans (CBHSQ 2015). While rates have been somewhat stable over the past five years, some analysts indicate that in 2014, past month illicit drug use and alcohol dependence were at the highest rate in more than a decade, with the increase driven primarily by escalations in marijuana use, nonprescription drug abuse, and heroin use among adults 25 years of age and older (ASAM 2015).

Prescription drug abuse, in particular, has exploded in the U.S. over the past two decades, especially among older teenagers and young adults (Dart et al. 2015; Lankenau et al. 2012; Maxwell 2011; Paulozzi et al. 2011; Sung et al. 2005; Young et al. 2012). Recent increases in heroin use and the emergence of new synthetic drugs—some of which are 10,000 times more powerful than morphine—have also been problematic (Abbott and Smith 2015; Palamar et al. 2015; Palamar and Acosta 2015). With regard to tobacco use, current national prevalence rates hover around 25%, despite declines in cigarette smoking among adults, with use varying by geography and sociodemographic factors, such as gender, age, race, ethnicity, and socioeconomic status (Agaku et al. 2014; King et al. 2012). Progress has also slowed in recent years due in part to the expanded use of alternative tobacco products, such as smokeless tobacco, cigars, hookah, and e-cigarettes, especially among youth and young adults (Agaku et al. 2014; Lee et al. 2014; McMillen et al. 2012; Singh et al. 2016).

The individual and public health implications of substance abuse are significant, with adverse consequences including, but not limited to, overdose death, education and vocation impairment, accidents, violence, developmental harms to children, and increased rates of a number of diseases, including HIV infection, heart disease, cancer, and tuberculosis (Paulozzi et al. 2011). In many instances, those suffering either directly or

J.B. VanGeest (✉) · S.A. Alemagno
Department of Health Policy and Management, College of Public Health, Kent State University, Kent, OH 44240, USA
e-mail: jvangees@kent.edu

S.A. Alemagno
e-mail: salemagno@kent.edu

T.P. Johnson
Survey Research Laboratory, College of Urban Planning and Public Affairs, University of Illinois at Chicago, Chicago, IL 60607, USA
e-mail: timj@uic.edu

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indirectly from the consequences of substance abuse are at additional risk themselves of developing further addictions to alcohol and/or drugs. In addition to the aforementioned health implications, substance abuse also represents a significant economic burden to society. In the U.S., the estimated economic costs associated with heavy alcohol consumption alone are in excess of $200 billion annually (Bouchery et al. 2011; NIDA 2016). Tobacco and drug addiction are also costly, with overall annual costs estimated to exceed $480 billion (NIDA 2016). The estimated total cost of just one emergent problem—the nonmedical use of prescription opioids—amounts to $50 billion annually (Hansen et al. 2011).

A snapshot of the substance abuse issue globally and in the U.S. would be impossible without ongoing research and public health surveillance. Worldwide, a variety of primary data sources inform substance abuse and dependence prevalence rates, respectively, with considerable variation in quality and coverage of available data across countries (Degenhardt et al. 2011, 2014; Gowing et al. 2015). In the U.S., large-scale representative surveys, such as the household-based National Survey on Drug Use and Health and the school-based Monitoring the Future (MTF) studies, provide rich data on substance abuse in the United States; pointing to ongoing shifts in trends of abuse critical for an informed and effective public health response. Additional methodological approaches, primarily social surveys and epidemiological studies, further inform our understanding of substance abuse, the nature and mechanisms of addiction, and an appropriate solution. The appropriateness of this response is largely dependent upon the quality of data provided, which is in turn based on the soundness of the methodological approaches employed in its collection.

At various times, substance abuse research has produced conflicting conclusions, due in part to inherent limitations in the methods employed (Turner and Miller 1997; Westermeyer 1990). Thus, the historical context of addiction research is critical to our understanding of how to address this problem. While not necessarily linear, advancements in substance abuse research methodology build upon one another, expanding our understanding of addiction, while informing treatment and policy solutions. It has even been argued that methodological advances in this one area of inquiry—research on tobacco particularly—have advanced and shaped the field of epidemiology generally (Samet 2016). Throughout this chapter, we explore the history of substance abuse research in the U.S. while noting some promising recent developments in the methods employed.

1.2 Definition of Key Terms

Various definitions with regard to what constitutes substance "use," "abuse," and "misuse" are common in the research literature. This variation must be addressed in any discussion of the history of research in this area, as these inconsistencies have muddied the waters some in terms of research on alcohol and drug-related problems. For instance, "use" typically refers to the use of drugs or alcohol without consideration or assessment of frequency of use, risk of dependence and/or health-related consequence. Substance "abuse," on the other hand, generally refers to the use of any substance that may be unlawful and/or detrimental to the user. Frequency of use (e.g., regular or persistent use) or user intent to obtain psychotropic effects are also considerations in some definitions of abuse. Lastly, "misuse" is generally defined by emphasizing the use of substances in a manner contrary to medical indication or prescription (Smith et al. 2013). The concept of misuse gained traction, particularly in the 1980s, following concern by some that the term "substance abuse" represented an overly pejorative label and with the consideration that abusive action was not actually perpetuated on the drugs themselves (substances are

used or *misused* in terms of time- and place-bound values, but living organisms can be *abused*).[1] Over time, however, the concepts of abuse and misuse have often been used synonymously by researchers, as both involve use that contradicts medical advice (Smith et al. 2013). Choice of terminology is not simply an issue of semantics, as there are potential measurement implications associated with the construction utilized. As a result, researchers have periodically sought to better clarify and/or standardize the terminology employed in the field. In the mid 1980s, a four-stage Delphi survey of experts was conducted seeking to gain greater clarity and uniformity in terminology associated with drug/alcohol-related problems (Rinaldi et al. 1988). Achieving distinctions between misuse and abuse has been particularly important for researchers examining nontherapeutic use of prescription drugs, with the Analgesic, Anesthetic, and Addition Clinical Trials, Translations, Innovations, Opportunities, and Networks (ACTTION) public-private partnership convening an expert panel to develop mutually exclusive classifications (Smith et al. 2013). Despite efforts, definitional tensions and inconsistencies have persisted. For the purposes of this chapter, we follow the more general convention of referring to substance abuse, with additional reference to misuse, particularly related to research on prescription drugs.

1.3 History of Substance Abuse Research in the United States

1.3.1 Early Addiction Research

Due to the interdisciplinary nature of substance abuse research, establishing an accurate historical timeline for the field's development is somewhat difficult. However, there are some clear benchmarks that can be reasonably ascertained. For instance, most scholars would agree that addiction research was in its infancy during the late nineteenth and early twentieth century. Moreover, research activity during this period was sporadic, initially focused on understanding and addressing the observed associations between substance abuse and crime, thereby informing the progressive era reforms that aimed to rid society of the social problems associated with the consumption and abuse of alcohol and drugs (Campbell 2007). Research was typically conducted in private clinical settings, and was largely uncoordinated in any meaningful fashion. Often taking cues from the work of Sigmund Freud and others, early scientific investigations probed as to whether there were physiological and/or psychological markers capable of differentiating addicts from non-addicts (Acker 2002; Campbell 2007).

Utilizing a variety of research methodologies, ranging from laboratory experiments involving humans and animals to surveys and clinical chart reviews, scientists and practitioners sought to better understand the mechanisms of addiction. While advanced for their time, not all of the methodologies employed would be considered scientifically rigorous by today's standards. The work was also oriented by multiple and often competing explanatory models of addiction, many of which viewed the condition somewhere on a continuum between vice (a moral issue, with addiction resulting from emotional or psychological defects) and disease (the medical model of abuse and addiction) (Campbell 2007). In the U.S., much of the early research was funded by the Public Health Service (PHS) and the Rockefeller Institute's Bureau of Social Hygiene. The latter was established in 1913 principally as a grant-making agency emphasizing research and education. The Bureau was charged with "the study, amelioration, and prevention of those social conditions, crimes, and diseases which adversely affect the well-being of society" (Rockefeller Archive Center). While both alcohol and drug addiction fell within this charge, the Bureau specifically focused on narcotics, a choice driven largely by changing social attitudes toward the substantial rise in opium consumption (and later morphine, heroin, and cocaine) for

[1]Personal communication with Stanley Einstein, Founding Editor (1965–2013) of *Substance Use & Misuse*, November 2016.

medicinal and nonmedicinal purposes (Acker 1995; Musto 1997). Concurrently, mainstream alcohol and alcoholism studies, despite having a relatively strong scientific focus in the latter part of the nineteenth and the early twentieth centuries, were virtually halted following the passage of prohibition (Roizen 2000).

In 1921, the Bureau of Social Hygiene established the Committee on Drug Addictions, in order to stimulate research for new drugs possessing reduced addiction liabilities that might be substituted for opium-derived analgesics in medical practices. The Committee expanded their work, initially agreeing on a three-pronged effort that combined educational efforts for clinicians with sociological and laboratory research (May and Jacobson 1989). While the latter was dedicated to the search for alternate drugs, which ultimately became the focus of much of the committee's work, the sociological research sought to better understand the extent of the problem, as well as mechanisms of drug distribution and the economic implications of addiction, often utilizing surveys (Acker 1995, 2002). Shifting government policy towards a view of addiction from a criminological standpoint increasingly stifled research on addiction from a more medical/disease orientation for fear that it would undermine government policy and the criminal justice solutions being enacted (Acker 2002; Musto 1996, 1997). Both the PHS and Bureau of Social Hygiene supported this shift, with leadership increasingly framing addiction as a problem of criminology and/or vice, consistent with federal policy (Acker 2002). As such, the subsequent orientation clearly located the etiology of addiction in an individual's psychopathology (Acker 1997).

Research funding by the Bureau and the PHS also helped galvanize consensus on the status of addiction research through the formation of networks of scientists oriented toward research that might best improve the understanding and control of social problems associated with the abuse of alcohol and other drugs (Acker 2002). Although academic in nature, this research had very practical applications consistent with the focus on social reforms that emerged during this period (Acker 2002). Despite advancements in funding and corresponding sophistication in the research methodologies employed, including new city-wide surveys and advanced physiological studies, overall consistency in the quality of methods employed in the field as a whole remained elusive.

While researchers were active, overall scholarly productivity remained relatively low until 1929, when research on drug addiction was first mandated by the United States Congress (Campbell 2007; Musto 1996, 1997). That same year, the Committee on Drug Addiction was established by the National Research Council (NRC), in order to provide a more strategic and systematic approach to addiction research, including plans for a coordinated program of chemical, pharmacological, and clinical research. The Bureau of Social Hygiene also decided to transfer its support of research to the NRC, furthering this strategic reorganization. The NRC initially sought to identify key gaps in biological knowledge regarding addiction, and while both alcohol and other drugs were included under this broad charge, the Committee initially focused on morphine, in part to continue the search for an alternative to the drug that was not habit forming (Acker 1995; Musto 1996). Despite the passage of the Harrison Narcotics Act in 1914, which restricted morphine use, and the banning of all domestic manufacture of heroin in 1924, the drug remained one of the most commonly abused narcotics. Studies were conducted in both laboratories and clinical settings involving human subjects, initially at Yale and the University of Virginia. Animal studies were also initiated in a newly developed pharmacology unit at the University of Michigan (Acker 2002; Musto 1996).

Additional clinical facilities were set up in Lexington, Kentucky and Ft. Worth, Texas in the mid- to late-1930s. Christened "narcotic farms," they were actually special prisons for drug addicts, which were maintained under the supervision of the Public Health Service (Acker 1997; Musto 1996). At these prisons, clinical studies were conducted on prisoners to examine the compounds developed and produced in the new laboratories. This shift from a three-pronged

strategy to exclusively focusing on clinical and laboratory studies was done largely at the expense of sociological studies, which the Committee did not view as particularly helpful in addressing the drug situation (Musto 1996). However, social science research continued during this period albeit outside of the Committee, focusing on understanding the behavior, as well as the social determinants, that influence the abuse of drugs and alcohol.

Ultimately, the work of the NRC Committee on Drug Addiction gave birth to the Addiction Research Center (ARC) located in Lexington, Kentucky (Musto 1996). The ARC was established in 1935 as one of the first research laboratories in the National Institute of Mental Health. At the time of its establishment, the ARC was the only laboratory in the world devoted solely to the study of addiction, and one of the earliest explicitly multidisciplinary laboratories in existence (Campbell 2010). While the ARC was primarily charged with the study of the clinical neurophysiology of drug dependence, it also produced innovative research methods to examine potential public health problems associated with addiction (Campbell 2006, 2010; National Institute on Drug Abuse 1995). Still affiliated with a Federal prison in Lexington, the ARC provided treatment and conducted research on prisoners and others who voluntarily admitted themselves to the facility. Among the many successes attributed to the ARC is furthering the understanding of relapse behavior and the profiling of the physiological and psychological effects of different drug classes. Pharmacological research also provided major contributions to the understanding of opiate and alcohol dependence and withdrawal, as well as expanded opportunities for the advancement of new drug development, with new research methods devised in partnership with industry and academic partners to test the pharmacological effects of novel compounds (Acker 1995).

Corresponding abuse liability studies were developed, again utilizing innovative experimental methods, to assist scientists in determining whether new pharmaceutical products were addictive, or whether they might have the potential for treating addiction and abuse (Acker 1995). Use of prisoners allowed for the development of closely comparable research protocols to test for addictiveness. All of this work coalesced around a model of addiction stressing the psychoneurotic individual possessing preexisting defects of personality that predisposed them to intractable addiction, emerging as the dominant explanatory model of the period. The continued linkage between addiction research and social reform, as noted earlier, reintroduced opportunities to pursue disciplinary agendas beyond exclusively pharmacological approaches, including new and innovative multidisciplinary addiction research incorporating biomedical sciences, social sciences, and public health (Campbell 2010).

Given the expansion of focus and resources, research on alcohol and tobacco use developed apace with drug research during the 1920s and 1930s. Studies on alcohol and alcoholism commenced again following the repeal of prohibition in 1933 (Roizen 2000), with early research focusing primarily on the metabolism and physiology of alcohol consumption (Candon et al. 2014). In 1938, the American Association for the Advancement of Science founded the Research Council on the Problems of Alcohol, an association of scientists and doctors whose goal was to raise support for multidisciplinary research on the effects of alcohol on the body, in addition to studying the extent of alcoholism in U.S. society. In 1939, the Council hired E.M. Jellinek to conduct the first comprehensive review of the literature on the effects of alcohol on the individual (Candon et al. 2014; Weglarz 1987).[2]

Dissemination of research findings was also a key component of the Research Council's activities. Their official journal, the *Quarterly Journal of Studies on Alcohol*, was founded in 1940 by Howard W. Haggard, M.D., director of Yale University's Laboratory of Applied Physiology, as the only scientific periodical at the time

[2]Initial funding for the review was from a grant from the Carnegie Corporation. Designated as the Classified Abstract Archive of Alcohol Literature (CAAAL), the collection was maintained and updated until 1978 and is comprised of approximately 20,000 abstracts.

devoted solely to the study of alcohol and alcoholism. The Laboratory was already heavily involved in alcohol research when, in 1943, it established the Section of Studies on Alcohol to further expand its body of work, made up of a multidisciplinary research team of sociologists, psychologists, physicians, biochemists, and economists (Candon et al. 2014; Page 1988, 1997; Roizen 2000). Research methods were a major focus of this new section, with statistical methods explored to produce improved, and oftentimes controversial, measures of the prevalence of alcohol-related phenomena, including measures of use and new alcoholic typologies (Page 1997). This work was also instrumental in achieving the recognition of alcoholism as a major public health problem, as well as a treatable illness, in the face of open social hostility toward both the alcoholic and the addict (Page 1997; Roizen 2000; Warren and Hewitt 2010).[3]

On the tobacco front, early epidemiologic studies linking tobacco use and cancer were occurring largely outside of the United States (Cummings 2002; Proctor 2012; Samet 2016). By the 1930s, experimental studies in South America and Europe had led many researchers and clinicians to conclude that smoking was indeed a potential cause for a number of cancers (Doll 1998; Proctor 2012). These initial studies were often case-control designs, implemented in cooperation with clinics and hospitals. Tobacco use was typically ascertained using questionnaires, and while advanced compared to previous designs, many of these studies had methodological limitations (Doll 1998; Proctor 2012; Samet 2016). These limitations led many in the U.S. to ignore or dismiss the results. Also important was public opinion, which was shifting as most state and local prohibitions against tobacco use were being lifted in favor of taxation policies, opening up opportunities to market tobacco products to wider audiences and ultimately contributing to a period of unprecedented growth in the prevalence of smoking (U.S. Centers for Disease Control and Prevention 1999, Cummings 2002).

Despite clear methodological and scientific advances in addiction research in the 1920s and 1930s, a non-habit-forming analgesic had still not been found. While many drugs had been tested, the methodologies employed were still quite simple by today's standards, often involving merely substituting the test drug for a regular dose of morphine in a morphine-addicted person, with subsequent observations failing to address the molecular level where dependence actually occurs (Musto 1996). Without the driving need to identify a non-habit forming alternative for medical purposes, alcohol research languished alongside treatment and support programs, which remained underfunded and underdeveloped during this period (Warren and Hewitt 2010). Tobacco use was even encouraged by the government, which was including cigarettes in the rations for soldiers during World War II. However, a foundation for future addiction research had been laid, and notable advances in substance abuse research achieved. Methods had been improved as researchers began to move toward more sophisticated designs; documenting the pitfalls of drug testing and, by all accounts, making significant progress in advancing addiction research methods along multidisciplinary lines. While addiction research was still in its infancy, the progress was striking, especially considering its rather modest beginnings as a more coherent science just a few decades previous.

1.3.2 Post War to 1965—A New Beginning in Substance Abuse Research

Addiction research during the war years was largely on a hiatus, although some clinical studies supporting new drug development continued in Lexington. After the war, the Committee on Drug Addiction and Narcotics (CDAN) was established by the NRC in 1947 to replace the Committee on Drug Addiction. Research again focused on drug development, with initial studies

[3]This shift recognizing alcoholism as a treatable medical condition occurred despite the corresponding loss of faith that narcotics addicts could be similarly treated; a view that persisted into the 1960s, with implications for research.

concentrating on methadone, a synthetic analgesic developed by German scientists (May and Jacobson 1989). Researchers' considerable interest in methadone's possibilities prompted requests to pharmaceutical manufacturers to contribute to a designated research fund that the Committee would administer (Musto 1996). University science departments also contributed some of their own resources, along with other outside agencies, including the Veterans Administration and the World Health Organization. This fund grew quickly, allowing for the sponsoring of a variety of research, including studies of methadone as well as other synthetic opioids and opiate antagonists, the latter referring to drugs that block opioids by attaching to the opioid receptors without activating them (May and Jacobson 1989).[4]

Still, no analytical techniques were developed that were sufficiently sensitive or specific to measure levels of opiates and/or similar compounds in blood or urine, forcing researchers to rely primarily on clinical observation. However, within these limitations, advanced research methods were employed, including double-blinded techniques, to compare the effects of new drugs with those of a placebo and the standard drug, which was often morphine, ultimately serving as models for future clinical drug trials. The pharmacological research at the Lexington facility provided major contributions to the understanding of opiate and alcohol dependence and withdrawal, building upon what amounted to decades of baseline data by the early 1950s (Campbell 2007, 2010; May and Jacobson 1989). Much of the Lexington research was still conducted using prisoners during this period, although pending legislation was poised to fundamentally alter the relationship between the larger prison-hospital and the research unit (Campbell 2010). Aside from research, the Committee served in an advisory role to agencies, such as the Federal Bureau of Narcotics and the Food and Drug Administration (FDA), informing on the potential abuse liability of marketable drugs.

In addition to the work of the CDAN, a number of other factors contributed to a resurgence of post-war addiction research. In 1949, the National Institute of Mental Health (NIMH) was established as one of the National Institutes of Health, providing additional coordination and funding opportunities for substance abuse research.[5] By the early 1960s, private foundations had also begun to fund addiction research, prompted by an increasing concern over the rise of illicit drug use. This concern also prompted Federal action, including the 1962 White House Conference on Drug Abuse and the subsequent report of the President's Commission on Narcotics and Drug Abuse released the following year (Musto 1996). The result was an expansion of work far beyond the more narrow focus on drug development that characterized much of the research in previous decades.

Expanding illicit drug use also spurred more localized research initiatives, especially in large urban centers where community-level solutions were sought to counter the emergent drug culture. This included social (community-based) research, such as ethnographic studies which sought to understand drug addiction within the context of culture, as well as pharmacological and clinical examination (Neale et al. 2005). For instance, in New York, concern over heroin addiction prompted Rockefeller University to partner with the New York City Health Research Council to conduct pharmacological research, with the goal of developing appropriate classifications for

[4]For a discussion of the various drugs tested by the CDAN, as well as Committee composition, see the detailed narrative history of the Committee on Problems of Drug Dependence by May and Jacobson (1989).

[5]The new agency adopted a model approach to mental disorders, including addiction, which stressed the interrelatedness of research, training, and services. As a result, the research portfolio of the NIMH differed significantly from other NIH institutes. In addition to basic and clinical biomedical research, NIMH strongly supported behavioral research and some social science research. The three-pronged approach, however, did create inherent tension, as the combination of research and service in a single agency left advocates for each side concerned that they may not be receiving equal prioritization of funding and support. This tension would remain until being resolved in later decades.

addicts and improved options for managing the problem (Kreek et al. 2004). These initiatives helped refine the methods of inquiry; both in terms of study designs employed, and also in the community-based translational research projects that followed as scientists sought an effective pharmacotherapy for heroin addiction that could be combined with behavioral care (Kreek et al. 2004). Central in this expansion and search for novel treatments was an emerging shift in orientation toward narcotic addiction. As noted previously, most scientists at this time still considered drug addiction as either deviant behavior or the result of a personality disorder (Campbell 2007). However, community-based researchers, experienced in working with addicts in New York and elsewhere, realized that arrest and incarceration were not effective methods of management, and began to thus reframe narcotic addiction once again as a disease.

Alcohol research also accelerated in the 1950s and early 1960s, with new methods employed to better understand abuse. For example, an early longitudinal study conducted between 1949 and 1952 collected data on 16,000 college students from 27 colleges and universities in the United States explored the etiology of addiction within this population (Fillmore and Marden 1977). Prospective and longitudinal study designs were also improved and used to examine the stages and patterns of alcohol abuse, with attention to potential antecedents of change signaling transitions from non-problematic to problematic drinking behavior (Burgheim 1953; Fillmore and Marden 1977). Qualitative inquiry, in particular, was resurgent in this era, as sociologists, social psychologists, and anthropologists sought to better understand addiction in the context of culture, bringing with them various ethnographic methods and approaches to studying alcohol abuse (mirroring what was happening in drug addiction research; see also Chap. 6 in this volume).

In the 1950s, the Yale Laboratory of Applied Physiology's Section of Studies on Alcohol was rebranded as the Center of Alcohol Studies, the first multidisciplinary research institution focusing explicitly on alcohol problems (Campbell 2007; Page 1997). Initial consideration was given primarily to the sociological aspects of abuse, with the physiological and psychological aspects the purview of a new section within the Laboratory of Applied Physiology, the Laboratory of Applied Physiology, and Biodynamics (Candon et al. 2014); in 1961, the Center moved to Rutgers University. At the same time, there was an emergent view of alcohol dependence as a separately recognized medical disorder, reinforcing the "disease concept of alcoholism" and shaping future research (Jellinek 1960). Alcoholism research itself was also emerging as a legitimate science, with a move afoot to create an institute within NIH solely dedicated to the alcohol field (Israel and Lieber 2002; Page 1997). Still lacking urgency, progress was still slow by the mid-1960s, with the NIMH beginning a small grants program in the area of alcohol research, and establishing the Center for Prevention and Control of Alcohol Problems, though these initiatives had limited budgets and/or authority (Warren and Hewitt 2010). Overall, stable support for alcohol research was summarily lacking, with funding for studies often cobbled together from a variety of sources, including government agencies, charitable organizations, and industry, slowing the overall progress as a coherent field of inquiry (Candon et al. 2014; Warren and Hewitt 2010).

Major breakthroughs in tobacco research did occur in the early 1950s and 1960s when scientists from the United States and elsewhere began to publish their research linking smoking and cancer, thereby birthing the modern era of tobacco control (Doll 1998; Parascandola 2001; Proctor 2012; Samet 2016). By the end of 1953, thirteen epidemiologic studies linking smoking to cancer had been completed, most of which utilizing case-control methods (Parascandola 2004). Advances in methodological rigor were evident in this work, including the development of new statistics to assess risk. Results sparked critical debate among researchers, with some concluding that there was sufficient evidence to conclude a cause and effect relationship, while others remained skeptical in the face of available evidence. In a review of this debate,

Parascandola (2004) notes that methodological weaknesses of the case-control method played an important role in this dialogue.[6]

Parascandola further mentions that improved study methods, including the first large-scale prospective cohort studies, ultimately strengthened the body of evidence against tobacco use, but that the debate continued, as these new methods also had weaknesses, including selection bias and an inability to control for potential hidden confounders (Parascandola 2004). Anomalies in the mass of evidence, such as the lack of association between cigar and pipe smoking and cancer, were likewise problematic. While not fully resolved among all investigators, the growing tide of evidence, including new randomized controlled trials, began to overwhelm the argument. In a 1964 groundbreaking report, the Surgeon General's Advisory Committee on Smoking and Health concluded, based on the consistency, strength, and coherence of the available evidence, that "Cigarette smoking is causally related to lung cancer in men; the magnitude of the effect of cigarette smoking far outweighs all other factors. The data for women, though less extensive, point in the same direction" (Advisory Committee to the Surgeon General of the Public Health Service 1964).

Despite being an era of new beginnings for substance abuse research, the period between 1950 and the mid-1960s has been characterized by some as the infancy of substance abuse research (Campbell 2007). Specifically, the continued prioritization of criminalization over treatment, especially with regard to drug addiction, hindered individual and private research. Other factors also played significant roles, including computational and methodological study limitations, resulting in the continued reliance on largely observational study methods, as well as the failure of a stable funding base to emerge from which to launch addiction research on a larger scale. Moreover, most studies were only conducted on men. Lastly, studies were hampered by an over-reliance on unitary models of dependence that failed to fully articulate the mechanisms of addiction (Nathan and Lansky 1978). Where significant advances were noted, such as in the establishment of the tobacco-cancer link, they were largely foundational, setting the stage for major future advances.

1.3.3 1965—Today

Funding for drug abuse research expanded dramatically in the 1960s and early 1970s, due to increases in grants by NIMH. Also facilitating this increase were evolving public attitudes around drug addiction, which began to support treatment research with individuals struggling with addiction as opposed to punishment (Musto 1996). The Committee on Drug Addiction and Narcotics changed its name to the Committee on Problems of Drug Dependence (CPDD) in 1965 to meet the new definition of "addiction" promulgated by World Health Organization and others, which explicitly viewed illicit drug abuse as a disease (May and Jacobson 1989; Musto 1996).[7] In 1967, the Center for Studies of Narcotics and Drug Abuse was formed within NIMH to administer the rapidly growing portfolio of grants and contracts dedicated to the study of problems related to drug abuse. A year later, NIMH's new Division of Narcotic Addiction and Drug Abuse assumed administrative responsibilities for all of the agency's research activities. Further abandonment of the punitive-deterrent

[6]Also contributing were favorable research studies funded by tobacco companies and/or comments by scientific experts discounting the evidence that were part of a broader marketing and public relations campaign designed to challenge evidence that smoking caused disease (Cummings et al. 2007).

[7]The WHO's new definitions facilitated their increased responsibility, as established by international treaties, to control narcotics. In the 1950s, the presence of physical dependence was emphasized, with the WHO primarily concerned with differentiating between psychic dependence and physical dependence. In 1969, the WHO abandoned efforts to differentiate habits from addictions and adopted terminology designating as dependence "those syndromes in which drugs come to control behavior." They further recognized that dependencies on different classes of drugs (such as alcohol, opiates, cocaine) can differ significantly.

philosophy in the U.S. followed the report of the President's Commission on Narcotics and Drug Abuse, which advocated adoption of approaches in line with the view of illicit drug abuse as a disease. Congress followed by enacting the Comprehensive Drug Abuse and Control Act of 1970, establishing the National Commission on Marijuana and Drug Abuse, which would report on a range of issues linked to drug use, arguably the most important (from a researcher's perspective) being the Commission's second report, as it promulgated strong recommendations for the expansion of government-sponsored research and for the continuance of newly implemented national surveillance surveys on drug use, including the National Household Survey on Drug Abuse (Musto 1996).[8]

The Commission further conceived a wider range of research relevant to drug issues to be incorporated into the research programs of the NIMH. This research, along with all of the NIMH intra- and extramural treatment and research activities was transferred to the National Institute on Drug Abuse (NIDA) following its formation in 1974 (Kreek et al. 2004; Musto 1996).[9] Today, NIDA supports most of the world's research on the health aspects of drug abuse and addiction, with strategic research and treatment priorities focused on priority areas that include better understanding of the factors influencing drug use trajectories, accelerating the developments of new treatments, and supporting translational research to ultimately improve individual and public health (NIDA 2015; Sloboda 2012).

While NIDA is the dominant funder, other Federal agencies, such as the U.S. Centers for Disease Control and Prevention and the U.S. Department of Justice, also fund drug research, with the latter focusing on drug use in relation to violence and crime (Sloboda 2012).[10] In addition to government funding, foundation support for drug abuse research and treatment also emerged in the 1960s and 1970s. An early example is The Ford Foundation's Drug Abuse Survey Project, which sought to identify gaps in basic knowledge of drug addiction and the role of drugs in society, resulting in the Foundation's creation of a Drug Abuse Council, which funded studies on illicit drug abuse from 1972 to 1978 (Musto 1996). Although relatively few foundations focus exclusively on substance abuse research, compared to its modest beginnings, foundation backing of drug abuse research overall helped to stabilize research support, as well as promote the integration of evidence into treatment in subsequent decades as new drug-related issues emerged, such as the Crack epidemic of the 1980s or today's extra-medical use of prescription drugs (Acker 2002; Musto 1996; Sloboda 2012).

Acknowledging the need for more information on problem drinking, President Nixon signed the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment, and Rehabilitation Act in 1970, authorizing a comprehensive Federal program to address prevention and treatment of alcohol abuse and alcoholism, including the expansion of alcohol addiction research (Warren and Hewitt 2010). Alcoholism was also acknowledged as a serious, but curable, public health problem. Moreover, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) was established as a component of the NIMH; subsequently becoming a separate institute alongside NIDA in a move that further increased targeted funding for alcohol research

[8]The National Commission on Marijuana and Drug Abuse's second report is entitled Drug Use in America: Problem in Perspective (NCMDA 1973).

[9]The creation of NIDA in 1974 was a major step forward in the promotion of addiction research, as previous work had been folded into the larger portfolio of the National Institute on Mental Health (Kreek et al. 2004; Sloboda 2012). The new institute focused exclusively on drug research. In 1992, NIDA became part of the National Institutes of Health.

[10]NIDA also funds drug and crime research. Examples include the NIDA funded research conducted by the National Development and Research Institutes examining the relationship between drugs and criminality (Lipton and Johnson 1998). Today, NIDA is increasingly focused on medical interventions and brain science research.

(Candon et al. 2014; Israel and Lieber 2002; Warren and Hewitt 2010).[11]

As the lead Federal agency addressing problems associated with alcohol abuse and alcoholism, NIAAA primarily supported research to improve understanding of the scope and nature of alcohol addiction and its effects on the body, as well as exploration of new alcoholism treatments (Lieber 1989; NIAAA 2011; Warren and Hewitt 2010; Willenbring 2010). The agency also backed efforts to prevent alcohol-related problems through policy research and scientific support for advocacy, including targeted efforts addressing underage drinking, college drinking, and parental alcohol exposure, among others (Voas and Fell 2010; NIAAA 2011). What followed was a proliferation of new research and research centers across the country, such as the Research Society on Alcoholism, thus furthering the organization and expansion of alcohol and alcoholism research (Israel and Lieber 2002; Lieber 1989).

Tobacco research also grew in recent decades. However, unlike other areas where one or (at most) two agencies were primarily responsible for spearheading the federal response, numerous agencies promoted research on nicotine addiction and tobacco use, including the National Cancer Institute (NCI), the FDA, the U.S. Centers for Disease Control and Prevention (CDC), the Office of the Surgeon General, NIDA, and the Agency for Healthcare Research and Quality (AHRQ), each with different focuses and priorities.[12] Much of this work has focused on better understanding general patterns and determinants of use, as well as developing more comprehensive epidemiologic models for understanding tobacco addiction and its impact on health (Doll 1998; Giovino 2002). Additional topics included tobacco use by women, adolescents, and other minority and underserved populations, better understanding patterns of addiction and related health risks, and addressing key deficiencies in the knowledge base noted in earlier reviews and reports. Most notably, the Surgeon General's reports in 1980 and 2001 dealt specifically with the health risks of smoking for females.[13] Reports in 1998 and 1994 addressed tobacco use among adolescents.[14]

Important in our most recent era of substance abuse research was a split in the structure and funding of Federal research support, distinguishing between research and treatment (Sloboda 2012). This change, anchored in a new definition of addiction that emerged in the 1980s focusing on behavior (as opposed to unalterable personality characteristics), facilitated a shift of professional focus on an emerging addiction treatment enterprise, fostering development of new treatment approaches and applied research examining the success and dissemination of these new initiatives. Until the early 1990s, and consistent with the original "three-legged stool" approach supporting research, training, and services, addiction services and research were principally funded through the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA), which was established in 1973 as the successor to the NIMH (Sloboda 2012). However, in 1992, bowing to inevitable tensions associated with this arrangement, the research components were moved to NIH and the service components were organized under the newly establish Substance Abuse and Mental Health Services Administration (SAMHSA), whose mission was to lead public health efforts to advance behavioral health, such as reducing the impact of substance abuse and mental illness on

[11]Prior to the establishment of NIAAA, research on alcohol addiction was conducted within the National Institute of Mental Health (NIMH). Since 1974, NIAAA has been an independent Institute of the National Institutes of Health (Warren and Hewitt 2010).

[12]NIDA supports research on nicotine addiction and funds some studies of cessation programs. The CDC's Office of Smoking and Health is the lead Federal agency for comprehensive tobacco prevention and control. The AHRQ supports Cochrane Collaboration Reviews, as well as systematic reviews and meta-analyses.

[13]In 2001, Surgeon General David Satcher stated that, "Women not only share the same health risk as men, but are also faced with health consequences that are unique to women, including pregnancy complications, problems with menstrual function, and cervical cancer."

[14]Overall, expansion of addiction research occurred in recent decades to include a broader range of target at-risk populations than previously studied, including women, veterans, homeless, LGBTI populations, and the elderly.

America's communities. SAMHSA was also charged with conducting applied research to evaluate service programs, as well as the support of ongoing national surveillance systems, such as the National Survey on Drug Use and Health (Sloboda 2012).[15]

Prevention also became a major focus in the 1980s, with the prevention branch at NIDA created in 1982 within the Division of Epidemiology and Prevention Research (Cázares and Beatty 1994; Bell and Battjes 1985). This NIDA Division supports research on the development, testing, and implementation of prevention interventions across a variety of contexts, including early intervention and drug abuse prevention services research, systems and methodology research, along with a full range of drug abuse epidemiology (including nicotine addiction), and services research.[16] Similar structures exist within NIAAA, charged with reducing alcohol-related mortality and morbidity and other alcohol-related problems and consequences through the integration and application of epidemiology and prevention science. SAMHSA also took a leading role in pioneering efforts to catalog knowledge and evaluate the application of evidence-based prevention with aims to further policy and program development (Brounstein et al. 2006; Condon et al. 2008; Marsh et al. 1996). Prevention research, consequently, emerged as a new area of inquiry with its own unique methodological challenges (Botvin 2004; Brounstein et al. 1997; Cázares 1994; Elliott and Mihalic 2004; Hersch et al. 2000; Renes et al. 2007). Also strengthened was the focus on health services research related to both substance abuse prevention and treatment, as efforts were made to improve translation of research into practice, progress in improving community-based care, as well as efforts to offset the social costs of addiction (Compton et al. 2005; Delany et al. 2008). Private foundation funding, such as the Robert Wood Johnson Foundation's support of policy, prevention, and treatment research/programs, also played an important role in advancing substance abuse research opportunities, distinguishing funding along similar lines.

Coinciding with the expansion of resources dedicated to addiction research in recent decades, the nature of investigation also fundamentally changed, largely by way of methodological advances in laboratory, clinical, and community-based research. The reviews conducted by the Surgeon General's Office, for instance, were in and of themselves, methodological advances, serving as precursors to today's complex comprehensive systematic reviews and meta-analyses (Samet 2016). Transformations were also noted in laboratory and clinical research, almost too numerous to mention. An early change was the discontinuation of prisoner research in the early 1970s.[17] This development spurred the creation of new loci of addiction research beyond Lexington and the ARC, the latter of which moved to Baltimore in 1979 to become part of NIDA (Campbell 2010; Kreek et al. 2004). These new centers and institutes collaborated with Federal agencies, such as NIAAA and NIDA, in development and application of innovative research strategies to better understand addiction, including research on special populations (Compton et al. 2005;

[15]State governments also support research; however, most of this funding also comes from the Federal government, which is passed through state agencies.

[16]Within the NIDA Division of Epidemiology and Prevention Research, areas of emphasis include, but are not limited to (1) development of new theoretical approaches to epidemiology, services, and prevention research, (2) determination of intrapersonal, environmental, and genetic factors important in the development of drug abuse/addictions, and (3) development of effective strategies to ensure that evidence-based practices are optimally utilized in the development of services to prevent and treat drug abuse/addictions (Cázares 1994).

[17]While conclusion of prisoner studies is often linked to the release of the Tuskegee Report in 1972, research in prisons was still possible. It did become increasingly difficult, however, following the American Correctional Association's (ACA) release of its first informed consent protocol for correctional institutions in 1972 and the placing of prisoners in the category of vulnerable dependents (Campbell 2010). The ACA later moved to eliminate prison research entirely by withholding accreditation from facilities where it was conducted (Campbell 2010).

Leshner 2000; Millstein 1994; NIDA 2015; Thomas and Conway 2010).

Other changes were directly linked to improved technology. Clinical studies, for instance, were enriched by the proliferation of increasingly sophisticated electronic medical record systems, which allowed researchers to better track subjects and understand drug response (Roden et al. 2012). Increasingly sensitive and specific measurement and analytical techniques allowed for new pharmacokinetic and metabolism studies in humans, furthering understanding of the absorption, distribution, metabolism, and elimination of drugs (including nicotine) and/or alcohol from the body, as well as their impact. These advances ultimately paved the way for an improved understanding of the molecular and cellular mechanisms/genetics of addiction, with wide implications for both policy and practice, such as treatment strategies tailored for high-risk populations (Benowitz 2008; Berrendero et al. 2010; Gorini et al. 2013; Koob et al. 2004; Koob 2006; Kreek et al. 2004; Litten et al. 2010; Riggs et al. 2007). Traditional research tools were also enhanced; particularly substance use surveys, to better control for the biases associated with the reports of sensitive topics such as substance abuse (Gfroerer et al. 1997; Johnson and Fendrich 2005; Kypri et al. 2004; Meiklejohn et al. 2012; Richardson et al. 2003; Weisner et al. 1995; see also Chap. 13 in this volume). Methodological options were also developed to improve self-report. These options now include innovations such as Audio Computer-Assisted Self Interviews (ACASI), or the use of multimedia, specifically pre-recorded audio, in addition to the on-screen text, to facilitate improved substance use data reporting, including reporting by high-risk populations (Currivan et al. 2004; Gribble et al. 2000; Lessler and O'Reilly 1997; Mullany et al. 2013; Turner et al. 1998).[18]

ACASI has also shown promise in clinical study applications (McNeely et al. 2016; Perlis et al. 2004). Biological measures, including urine, hair, and oral fluid testing have further improved epidemiological studies of addiction, including population-based studies (Cook et al. 1997; Fendrich et al. 2004; Palamar et al. 2016; Turner and Miller 1997; see also Chap. 11 in this volume).[19] Public health surveillance was also enhanced by way of improved sampling and the use of new tools, such as geospatial mapping and cellphone/online data-gathering methods to collect information pertaining to substance use and related community-level factors (Kuntsche and Lebhart 2014; Mazumdar et al. 2015; see also Chap. 12).

Lastly, methodologies for treatment outcome studies were improved, including behavioral research and economic evaluation methods (Robinson et al. 2014; see, for example, Chaps. 12 and 14 in this volume). While not all-encompassing, the list of innovative research examples could go on and on, with advances in one area applicable to research in many other areas of inquiry within the substance use field, including program/intervention assessment and epidemiological studies (Greenfield and Kerr 2008; Leshner 2000).

1.4 Increasing Interdisciplinary and Transdisciplinary Research

One major innovation was the evolution of interdisciplinary and transdisciplinary substance abuse research. Due to its complexity, substance abuse research has spanned many disciplines, including but not limited to pharmacology, medicine, the neurosciences, public policy, and the social and behavioral sciences (Sussman and Unger 2004; Sussman et al. 2004). However, historically, work (as well as methodological traditions) from diverse disciplines has not

[18]Not all studies support the use of ACASI to improve self-report. For example, a study by Fendrich et al. (2005) found self-report sensitivity estimates for tobacco use in a drug use survey to be well below the 90% level. Other studies have noted mixed effects of ACASI (Couper et al. 2003; Gribble et al. 2000; Turner et al. 2005).

[19]According to Fendrich et al. (2004), the utility of testing for surveys depends on both the type of substance being examined and the type of test employed, with multiple tests generally having more utility than a single test.

always been well integrated in substance abuse research (Abrams and Clayton 2001; Westermeyer 1990). While challenging, improved communication, statistical approaches, and technology have facilitated the integration of research in new and innovative ways, resulting in a concerted move toward research crossing disciplinary lines. Very specifically, this trend has supported transdisciplinary research, as scientists sought to move beyond simply recognizing inputs by different disciplines to actively establishing—and building upon—connections across disparate research traditions (Kessel and Rosenfield 2008; Klein 2008). Transdisciplinary research is problem focused, collaborative, and differs significantly from interdisciplinary scholarship in that it is characterized by a full integration of epistemologies in the development of study methodology, effectively breaking down disciplinary boundaries (Wickson et al. 2006).

As compared to more traditional lines of scholarship, teams of transdisciplinary collaborators can advance science as they bring to bear and integrate different theories, methodologies, statistical approaches, data, and research traditions; resulting in better quality science, increased innovation, and accelerated translation of evidence into practice (Bozeman and Corely 2004; Chou et al. 2004).[20] Driving factors in this transition include the recognized need to understand the complex array of individual and contextual factors influencing both the use and misuse of drugs and alcohol (Mermelstein et al. 2007; Turner et al. 2004). This realization extends even to fields such as genetic research, where context remains critical to understanding the mechanisms of addiction, thereby necessitating a broader perspective (Giovino 2002; Turner et al. 2004). Transdisciplinary research perspectives have also been integrated into all areas of inquiry, such as prevention as well as intervention and treatment design and evaluation (see also Chap. 2), particularly due to their ability to support tailored interventions (Alemagno 2009; Baker et al. 2003; Compton et al. 2005; Lieber 1989; Sloboda et al. 1998; Sussman et al. 2004). They have also become an important element in the research agendas of government agencies such as the National Cancer Institute, as well as private foundations such as the Robert Wood Johnson Foundation (Kessel and Rosenfield 2008). These agendas have supported transdisciplinary research/prevention/treatment initiatives as well as new research centers, such as Transdisciplinary Tobacco Use Research Centers (Kobus and Mermelstein 2009; Mermelstein et al. 2007; Turkkan et al. 2000) or the NIDA-funded Transdisciplinary Prevention Research Centers, which supports both research that translates theories to practice and policies that prevent substance use.

Transdisciplinary research has also been a major thematic element at professional conferences, such as the "Reflections on 40 Years of Drug Abuse Research" meeting in Key Largo, Florida in 2006, resulting in a special issue of the *Journal of Drug Issues* (Sloboda et al. 2009a, b). Despite this progress, the promise of a fully transdisciplinary approach to addiction research has not yet been fully realized, and the need for better integration of data systems, theoretical and analytical models, and intentional connections crossing disciplinary silos persists. The latter, in particular, is not easy, as these collaborations require considerable effort and time (Mermelstein et al. 2007; Provan et al. 2008).

1.5 Continued Challenges and New Opportunities

Collectively, the methodological advances in substance abuse research did not happen overnight, and, even today, remain a work in progress. An early comprehensive review of common methodological problems associated with addiction research by Nathan and Lansky (1978) identified a number of ongoing concerns, including selective or biased reviews of the literature, reliance on incomplete diagnostic criteria for study inclusion, inadequately accounting for

[20]The Institute of Medicine has broadly called for a shift to research that engages investigators from multiple fields and disciplines to better capitalize on rapidly expanding knowledge of how genetic, social, and environmental factors impact health (Hernandez and Blazer 2006).

study dropouts, and failure to follow subjects for adequate lengths of time. Even today, despite noted advancements, there remain a number of methodological issues that have yet to be resolved. Surveys, for example, while being the primary source for much of what we know about drug and alcohol abuse, are plagued by methodological failures, including sampling, coverage, nonresponse, measurement, and processing errors (Fendrich et al. 2005; Gfroerer and Kennet 2015; Gfroerer et al. 1997; Giovino 2002; Grucza et al. 2007; Johnson and Fendrich 2005; Johnson 2012, 2014, 2015; Kremling 2013; Midanik et al. 2013; Sevigny and Fuleihan 2015) see also Chap. 13 this volume. As these methodological and conceptual failures continue to hinder understandings of substance abuse, improving the collection and use of data is critical to the value of the information and the conclusions produced (Johnson 2012). Treatment and prevention researchers face similar issues related to study design, principally related to studies utilizing addicts as subjects (Booth and Watters 1994; Flay and Petraitis 1991; Sloboda et al. 1998).

While improving over time, key issues still include intervention exposure/compliance, implementation fidelity, assessment of exposure and outcome measures, sampling attrition, accuracy of subject reports, and the choice of analytic model; necessitating consideration of new and innovative designs, including those incorporating "real-world" contexts of service delivery (Alemagno 2009; Baker et al. 2011; Borders and Booth 2007; Clark and Winters 2002; Colby et al. 2004; Compton et al. 2005; Galea et al. 2004; Robinson et al. 2014; Sloboda et al. 1998, 2009a, b; Willenbring 2010). This includes economic evaluation of substance abuse services and interventions (French and Drummond 2005).

Also problematic are the several views that still exist regarding the etiology of substance use and abuse, each weighing somewhat differently the relative contributions of genetic, individual, cultural, and social influences. Resolution is not yet fully possible, as even recent advancements in neurobiological research on addiction, such as increasingly sensitive and specific analytical techniques, as well as improved information on the contributions of gene variations to vulnerability to addiction, cannot fully articulate all of the factors contributing to addiction across diverse populations (Foroud et al. 2010; Hall et al. 2008; Kalant 2009; Kreek et al. 2004; Obot et al. 2004; Trujillo et al. 2006; Volkow and Baler 2014). Additional research is also needed on the impact of misuse on individual function (Scott et al. 2007). Moreover, despite the promise of neuroscience research, caution is necessary when relying solely on a single explanation, so as to avoid overly deterministic causal models of addiction that mask the complex interaction between environment and individual, again making an argument for more of a transdisciplinary focus with all the inherent challenges therein.

With regard to the transfer of evidence into practice, there have again been noted improvements due, in part, to advances in the research process, which has compelled revisions of best practices implementation, especially with regard to preventive interventions attempting to maximize population impact (Millstein 1994; Sloboda 2014; Spoth et al. 2013).

Lastly, in examining progress made in addiction research, it is important to remember that the issue itself is a moving target, with new and emerging drugs and risk populations. Substance abuse research is also influenced by advances in research methods, further complicating the picture. For example, new research methodologies, such as web mapping, have been used to more rapidly identify new and emerging trends in substance abuse. One example is the Psychonaut Web-Mapping Project, a European collaboration which monitors discussion forums, social media, and other internet resources to rapidly identify emerging trends in novel psychoactive substances warranting public health response (Deluca et al. 2012). Similar web-mapping initiatives, as well as the use of other internet-based open-source tools, have been used elsewhere to better understand and respond to the changing array of emerging psychoactive substances entering the marketplace, as well as other trends in substance abuse (Brownstein et al.

2009; Bruno et al. 2013; Butler et al. 2007; Young et al. 2015).[21]

Each new trend that is discovered, in turn, creates its own methodological challenges for scientists seeking understanding and/or solutions, as shifts often involve unique risk populations as defined by geography, age, culture, socioeconomic status, and the like. Subsequent solutions take many forms, including the leveraging of new technologies and alternate forms of communication, which is evident in smartphone and other handheld technologies that have opened up opportunities for the assessment of substance use/misuse via text messaging and other forms of electronic contact, as well as providing for new intervention opportunities (Bernhardt et al. 2007; Kuntsche and Labhart 2012, 2014; Kuntsche and Robert 2009; Phillips et al. 2014; Sufoletto et al. 2012). This includes important advances in the collection of ecological momentary assessment (EMA) data on use, as well as daily factors associated with the abuse of substances such as alcohol and tobacco (Collins et al. 2003; Freedman et al. 2006; Minami et al. 2010; Shiffman 2009). While still an emerging area that is not without its challenges in substance abuse research, available studies have found these assessments to be both feasible and valid (Collins et al. 2003; Ferguson and Shiffman 2011; Galloway et al. 2008; Phillips et al. 2014; Serre et al. 2012; Shiffman 2009). Today, these technological advances, including the aforementioned GPS technologies, are increasingly used to collect real-time use and behavioral data associated with the use and abuse of alcohol, drugs, and tobacco. Overall improvements in informatics generally, as well as team science, have facilitated further integration of these data; allowing for more rapid analysis across diverse substances and risk populations.

Ethical concerns have been expressed related to the use of real-time data, but it remains possible to remove identifiers from the data and use of passwords can further reduce the risk of privacy violations (Beckjord and Shiffman 2014). The use of handheld technology is illustrative of new tool utilization for improved study design, including studies identifying or responding to an emergent trend. This cycle is ongoing, regardless of the substances under investigation, as the field constantly seeks to improve data that can be effectively utilized to more rapidly inform interventions as new problems arise.

[21]Web-based bioinformatics and other open-source research and development are also being used to spur drug discovery and assessment (Chen and Butte 2016; Wishart 2005).

1.6 Conclusion

The history of substance abuse research and treatment is complex, spanning multiple disciplines, each with their own research traditions. It also involves multiple substances, both alone and in combination. Still, advances in the methodologies employed in terms of conceptual sophistication, study design, measurement, and data analysis have built upon one another in a transdisciplinary manner; greatly expanding our knowledge of the mechanisms of addiction, as well as informing new and innovative solutions, including efforts to prevent abuse altogether (O'Brien 2003; Sloboda 2014; Treno et al. 2014). This has been especially true over the last several decades, as neurogenetic research methods and models, coupled with advances in technology and bioinformatics, have the potential to finally resolve, or at least reconcile, competing explanatory models of addiction that have dominated the scientific debate; historically defining addiction as either principally stemming from an individual's moral or medical state. Caution is necessary, however, lest we fall into the historical trap of trying to establish more simplified linear causal models, as there are inherent limitations to any scientific discipline. Despite the noted advances in neuroscience, addiction remains a behavioral disorder generated within exceedingly complex interactions of agent (e.g., drug, alcohol, or tobacco), user, and environment (Kalant 2009). The social sciences remain essential to our understanding of abuse, helping explain the need, mechanisms of distribution (access), economic implications

of addiction, and the like. There are certain aspects of addiction that simply cannot be explained by neurogenetic research. As elegantly stated by Kalant, "This [*sic*] is no longer the terrain of pharmacology or neurobiology or psychology or sociology, but an amalgam of them all" (2009). A transdisciplinary perspective is foundational to further progress.

There are other important considerations when assessing past progress in addiction research as a marker for future development. It is important, for instance, to remember that progress has been nonlinear; shaped, in part, by larger political and social forces. For instance, financial support for drug and alcohol research over the years has been impacted by a number of factors (Musto 1996; Sloboda 2012). Generally, when drug or alcohol abuse has been viewed as a major crisis, money flows in support of addiction research, thus spurring advances. However, support often wanes when abuse rates stabilize or shift away from high-priority substances. Additionally, as progress is made, especially with regard to the neuroscientific and genetic elucidation of the mechanisms of addiction, scientists must increasingly anticipate the ethical issues that arise from this work to identify individual biomarkers for risk, including the capacity of addicted persons to give consent to treatment, individual privacy, and risk of coercion (Hall et al. 2004).

Lastly, it is important to remember that much remains to be known. Most methodological advances in addiction research have largely occurred only in the last 50 years. This is especially true of research on key risk groups, such as women, children, LGBTI populations, and the elderly, that have often been historically neglected, both in the U.S. and globally. Also challenging is the noted fluidity of the subject matter, with new and emerging substances and risk populations changing constantly. As a result, there are calls for an urgent need to review and improve the quality and timeliness of substance abuse data, its implications, and intervention outcomes, theoretically facilitating an effective clinical and public health response (Degenhardt et al. 2011; Fischbein and Ridenour 2013; French and Drummond 2005; Gowing et al. 2015; Riggs et al. 2007).

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