Published in final edited form as:

Res Soc Work Pract. 2018 ; 28(5): 523–531. doi:10.1177/1049731517718939.

25 Years of Complex Intervention Trials: Reflections on Lived and Scientific Experiences

Kelli A. Komro^{1,2}

¹Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory University, Atlanta, GA, USA

²Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA, USA

Abstract

For the past 25 years, I have led multiple group-randomized trials, each focused on a specific underserved population of youth and each one evaluated health effects of complex interventions designed to prevent high-risk behaviors. I share my reflections on issues of intervention and research design, as well as how research results fostered my evolution toward addressing fundamental social determinants of health and well-being. Reflections related to intervention design emphasize the importance of careful consideration of theory of causes *and* theory of change, theoretical comprehensiveness versus fundamental determinants of population health, how high to reach, and health in all policies. Flowing from these intervention design issues are reflections on implications for research design, including the importance of matching the unit of intervention to the unit of assignment, the emerging field of public health law research, and consideration of design options and design elements beyond and in combination with random assignment.

Keywords

commentary; complex intervention trials; intervention design; research design

I was trained as a behavioral epidemiologist at the University of Minnesota School of Public Health, where I had the good fortune of being exposed to some of the first seminal community-randomized trials, including the Minnesota Heart Health Program (Luepker et al., 1994; Perry, Kelder, Murray, & Klepp, 1992) and Project Northland, a community-wide youth alcohol use prevention trial (Komro et al., 2001; Perry et al., 1996, 2002). For the past 25 years, I have lived through many rich experiences leading multiple group-randomized trials funded by the U.S. National Institutes of Health (NIH). Each trial has evaluated health

Reprints and permission: sagepub.com/journalsPermissions.nav

Corresponding Author: Kelli A. Komro, Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory University, 1518 Clifton Rd NE, GCR 564, Atlanta, GA 30322, USA; Department of Epidemiology, Rollins School of Public Health, Emory University, 1518 Clifton Rd NE, GCR 564, Atlanta, GA 30322, USA. kkomro@emory.edu.

Declaration of Conflicting Interests

The author declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

effects of complex interventions designed to prevent high-risk behaviors among youth. Each trial has focused on underserved populations of youth, including rural populations, urban central-city ethnic minority youth, and Native American youth. My theoretical and methodological expertise is in the design, implementation, and analysis of multilevel intervention trials (e.g., children measured numerous times, nested within communities or schools). I welcome this opportunity to share with you reflections on intervention and research design as well as my own evolution toward increasingly addressing fundamental social determinants of health and well-being.

Complex interventions have been defined as those with (a) interacting components, (b) multiple groups or socioecological levels targeted, and (c) degree of flexibility or tailoring of the intervention permitted (Craig et al., 2008; Hawe, Shiell, & Riley, 2004; Petticrew, 2011). I was trained in epidemiology with a research focus on the development and implementation of complex interventions evaluated with rigorous group-randomized trial designs. The first trial that I was involved with during my training involved 20 school districts in rural Minnesota randomly assigned to intervention or delayed program control conditions (Perry et al., 1996). The multiple year alcohol prevention intervention, Project Northland, combined strategies at the family, school, and community levels and provided evidence for the effectiveness of a multilevel intervention in reducing alcohol use among middle and high school students (Komro et al., 2001; Perry et al., 1996, 2002). The intervention has been listed on national model program lists, including the U.S. National Registry of Evidence-based Programs and Practices; has been disseminated to thousands of schools throughout the United States; and was adapted for research and dissemination in other countries including Russia and Poland (Bobrowski, Pisarska, Ostaszewski, & Borucka, 2014; Williams et al., 2001).

Professor Cheryl Perry and I then used these effective intervention strategies as the foundation for the Minnesota Drug Abuse Resistance Education (D.A.R.E.) Plus trial, with the goal of improving the effectiveness of the D.A.R.E. middle school program. The D.A.R.E. program is a classroom-based program for young adolescents implemented by police officers, and at the time we initiated the study, there was mounting evidence that the program was not effective, yet was the most widely disseminated drug prevention program in the United States. Our rationale for conducting the trial was to incorporate multilevel and evidence-based strategies into the widely disseminated program. In the trial, we randomly assigned 24 schools and their surrounding neighborhoods to one of the three study conditions (Komro, Perry, Veblen-Mortenson, Stigler et al., 2004; Perry et al., 2003). Results of the D.A.R.E. Plus trial provided additional evidence for the effectiveness of theory-based family and community intervention programs and reinforced the mounting scientific evidence at the time that the D.A.R.E. program alone was not effective in reducing high-risk behaviors among youth (Komro, Perry, Veblen-Mortenson, Stigler et al., 2004; Perry et al., 2003).

During the late 1990s through 2006, I led a large and diverse team to culturally adapt, implement, and evaluate Project Northland for urban youth with a group-randomized trial that included 61 schools in the city of Chicago (Komro, Perry, Veblen-Mortenson, Bosma et

al., 2004; Komro et al., 2006, 2008). Within the urban environment, the Project Northland intervention did not achieve positive behavioral change.

Currently, I am partnering with the Cherokee Nation in Oklahoma. The Cherokee Nation is the second largest American Indian tribe in the United States. We conducted a community-randomized trial testing two theoretically distinct alcohol preventive interventions in rural towns within the jurisdictional service boundaries of the Cherokee Nation (Komro et al., 2015, 2017). We implemented a community environmental change intervention using community organizing called Communities Mobilizing for Change on Alcohol (CMCA) and a universally implemented individual-level intervention implemented within schools combining brief intervention with motivational interviewing called CONNECT and found that both interventions, alone and in combination, were effective in reducing past month alcohol use, heavy use, and alcohol consequences (Komro et al., 2017). Results of these preventive intervention trials conducted over the past two decades shape the prevention landscape in the United States, advancing theory, practice, and methods. Here I share with you some key lessons learned from implementing these trials.

Each of these trials focused on one key risk behavior or a set of highly correlated risk behaviors, and the interventions were designed to target specific and relevant risk and protective factors for those behaviors. Recently, I had the opportunity to work with a diverse group of prevention scientists to take a very broad examination of determinants of child health and well-being. As chair of the policy team of the NIH-funded Promise Neighborhoods Research Consortium, I collaborated with a team of scientists from across the United States to provide a synthesis of research supporting intervention development to improve child outcomes in high-poverty environments. Important products from the project include over 100 policy briefs of evidence-based community-level policies as well as three scientific publications to help advance prevention science within high-poverty environments, covering theory, policy interventions, and research design (Komro, Flay, Biglan, & The Promise Neighborhoods Research Consortium, 2011; Komro, Flay, Biglan, & Wagenaar, 2016; Komro, Tobler, Delisle, O'Mara, & Wagenaar, 2013). The initial product from this collaboration, based on a synthesis of research from diverse fields, was a conceptual framework of potent and malleable influences of child health and well-being (Komro et al., 2011). We define key developmental outcomes within the cognitive, social/emotional, psychological/behavioral, and physical health domains and stress that outcomes across domains often correlate at one point in time and influence subsequent developmental outcomes over time within and across domains. We conceptualize three of the six chief domains as proximal (immediate) influences (including family, school, and peers) and three as distal influences (those important conditions in a child's environment, including income and resources, social cohesion, and the physical environment). We conclude that cognitive, social-emotional, psychological, behavioral, and health outcomes are interrelated and have an interacting set of key influences within the family, school, peer, and neighborhood environments. And since negative health and developmental outcomes are concentrated among children living in high-poverty and disadvantaged environments, community-wide efforts—integrating strategies to improve the social and physical environments within families, schools, peer groups, and neighborhoods—are vital to promoting optimal child

health and well-being. This comprehensive framework has influenced my thinking and the direction that I have taken recently in my current line of research.

Throughout my intervention trial research endeavors, I have partnered with many low-income communities, with an average household income well below the U.S. median, in rural communities and in inner-city neighborhoods, with majority White or multiple ethnic minority populations. In these trials, we experienced successes and failures. Through these experiences, I have been enormously enriched both personally and intellectually, with my inherent optimism enhanced by the many dedicated professionals and citizens that I have worked with. But, I also have been deeply dismayed by the conditions of many schools and communities—the context in which many children in the United States live, learn, and grow. I am frustrated by what we expect from, and the limits of, microlevel approaches to protect and promote health. Throughout my academic and personal journey, each year I become more motivated and inspired to keep moving further “upstream” to address more fundamental determinants of health. As Dr. Tom Frieden, who served as director of the U.S. Center for Disease Control and Prevention (CDC) from 2009 through January 20, 2017, clearly and simply portrayed in the Health Impact Pyramid (HIP; Frieden, 2010), we will have the largest health impact by addressing determinants of socioeconomic status and the context in which people live, work, and play. I have therefore recently embarked on a new line of research to examine the effects of family economic security policies on child health, recently funded by NIH (Komro, Burris, & Wagenaar, 2014; Spencer & Komro, 2017). This new area of research has extended my collaborations outside of public health to include legal scholars and economists—stretching my research endeavors to new areas, but always with the common theme of child health promotion. My interest has never been to simply explain health disparities but to be engaged in the science of how to achieve community-level change.

In reflecting on the past quarter century, I have seven conclusions to share related to intervention and research design, the importance of fundamental determinants of health, and what it means for complex intervention science. The seven reflections emphasize the importance of consideration of (a) theory of causes *and* theory of change, (b) theoretical comprehensiveness versus fundamental determinants of population health, (c) how high to reach, (d) health in all policies (HiAPs), (e) matching the unit of intervention to the unit of assignment, (f) public health law research, and (g) design options and design elements beyond and in combination with random assignment.

Intervention Design

Theory of Causes and Theory of Change

In response to concerns about the suitability or feasibility of conducting randomized controlled trial designs with complex interventions implemented in the real world, Hawe, Shiell, and Riley (2004) published an important editorial in the *British Medical Journal*, entitled, “Complex interventions: how “out of control” can a randomized controlled trial be?” They argue that complex interventions are suitable to be meaningfully evaluated using randomized controlled trial designs but emphasize that the standardized element to be evaluated is the mechanism of change or steps in the change process, rather than a

standardization of exact intervention components that may “take on different forms according to local context, while achieving the same objective” (Hawe et al., 2004). The issue, they argue, is to allow the form to be adapted while standardizing the process and function, not the components themselves. Integrity of the intervention is defined functionally, rather than compositionally, with a focus on the change process.

However, in the fields of prevention science, public health and health promotion minimal attention seems to be given to the distinction between theory of *causes* and theory of *change*. Most behavioral and social theories importantly delineate causal factors that influence health behaviors and health outcomes. Equally important, yet often not differentiated, are theories that address processes or mechanisms of *change*. Leading theories in prevention science, public health and health promotion fields include the Health Belief Model at the individual level, Social Cognitive Theory (SCT) at the interpersonal or group level, and ecological models at the societal level (Glanz, Rimer, & Viswanath, 2008). These influential theories have described multiple causes of health behaviors and health outcomes.

Yet theory of change, or mechanism for change, is less often explicitly addressed in the health promotion field, especially at community or societal levels. The Project Northland intervention was designed within the framework of SCT and defined three main tiers of intervention targets including environmental, social, and personal risk and protective factors (Perry et al., 1996, 2002). Change strategies were not explicitly defined but included a complex mix of strategies including facilitative, educational, persuasive, and regulatory or power strategies (Harper & Leicht, 2011). In the prevention trial in the Cherokee Nation, the theory of community change was explicitly tested and defined as a process of citizen-led and direct-action community organizing (Komro et al., 2015, 2017). The direct-action community organizing *process* was the *standard intervention* delivered across communities, yet specific intervention components and their dosage varied based on local contexts (Komro et al., 2017). We hired local citizens to serve as community organizers and provided ongoing training and support in community organizing processes and strategies. The organizers were also provided educational materials on evidence-based community strategies as a menu of options for their communities to select based on each community’s needs. A standardized measurement system was used to assess the community organizing process and outcomes (i.e., operational goals). Explicit definition, implementation, and monitoring of change processes will provide stronger evidence of how to achieve community-level change that can then be adapted for other communities and other health issues.

Theoretical Comprehensive Versus Fundamental Determinants

The field of health promotion has many health issues to tackle, including, but not limited to mental health; the obesity epidemic; alcohol, tobacco, and other drug use and misuse; sexual and reproductive health; pollution and respiratory health; and poverty. Each certainly can be considered a “wicked” problem. In 1973, two professors of design and urban planning at the University of California at Berkeley provocatively coined the term “wicked” to describe messy and multilayered challenges that defy simple, straightforward solutions (Rittel & Webber, 1973). There is no doubt that many of the issues we are concerned with are “messy

and multilayered.” Yet, is it necessary to target all the messiness or multilayers simultaneously? Is there not a more efficient way to tackle “wicked” problems?

If interventions focus solely on more proximal layers of risk factors, are they not inherently de-emphasizing more antecedent determinants of population health (such as environmental contextual conditions and social class)? An intervention may temporarily reduce proximal risk factors for those individuals exposed to a particular intervention (e.g., health education, screening); however, new people continue to enter the at-risk population at the same rate. Only if the intervention intervenes on the forces in the community that cause the problems in the first place is the long-term rate of new cases reduced (Syme, 2004). Importantly, the more antecedent determinants of population health influence many proximal risks, and they maintain an association with disease outcomes even when a few proximal risks improve (Link & Phelan, 1995). Link and Phelan (1995) defined such social conditions as *fundamental* causes of health inequalities.

Reflecting on trial experiences, I provide two examples to demonstrate varying approaches to the design of multiyear preventive interventions; both interventions had the goal of delaying early onset of alcohol use among adolescents. The first trial, Project Northland, was implemented in rural communities in Minnesota with high rates of alcohol-related problems (Perry et al., 1996, 2002). The goals of the multilayered intervention were to change environmental, social, and personal risk and protective factors related to youth alcohol use and involved four intervention strategies, including a series of school-based curricula to develop skills and shift peer norms, parent education to influence parenting practices, student-led activities to shift peer norms and the social environment, and community change strategies to reduce youth access to alcohol. The original trial, implemented in 20 counties in rural Minnesota, was conducted in two phases following a cohort of youth from ages 12 to 18. The first 3-year intervention phase reduced alcohol use among young adolescents through age 14, but when the intervention ended, within 2 years, the rates of alcohol use were the same among students who received the intervention compared with students in the control condition. We then reimplemented similar, yet developmentally appropriate, interventions when the students were ages 16–18, and again reductions were observed in alcohol use among students exposed to the intervention compared with the control students. As one example, there was a 22% relative reduction in alcohol use reported during the past week among youth in the intervention condition compared to the control condition.

In comparison, my most recent prevention trial in partnership with the Cherokee Nation in rural Oklahoma included an intervention condition that solely focused on community environmental change (Komro et al., 2015, 2017). We implemented CMCA, which uses community organizing strategies to galvanize adults to take actions to reduce youths’ access to alcohol through social and commercial sources. Youths, ages 15–18, were followed over 3 years and those who lived in the CMCA community were compared to those who lived in two control communities. Reductions in past month alcohol use, past month heavy use (five plus drinks in a row), and alcohol-related consequences of 22–25% were observed among youth exposed to CMCA. The results of these two multiyear trials, one a complex multicomponent intervention and the other an implementation of solely a community organizing strategy, both resulted in similar reductions in alcohol use.

Given the results from these two trials, I pose the following questions: (a) How comprehensive do interventions need to be? (b) How does a team decide how many layers of multilayer influences need to be addressed? (c) How does a team decide on the minimum number of layers that are feasible and necessary to address for sustaining long-term benefits to health?

How High to Reach?

What is the minimum number of layers of intervention that are feasible and necessary to address for sustaining long-term benefits to health? What is the most efficient societal level to intervene upon? Over the years, there have been three main theoretical perspectives that have influenced my thinking. First and foremost, the work of the late Professor Geoffrey Rose (Rose, 1992), who compellingly made the case for a population perspective and approach for disease prevention, rather than an individual-level medical strategy of “responding to the needs of sick individuals.” He summarized research depicting the continuous population distribution of risk, and when comparing across populations, the distribution is seen to shift up or down as a coherent whole. He concludes:

The essential determinants of the health of society are thus to be found in its mass characteristics: the deviant minority can only be understood when seen in its societal context, and effective prevention requires changes which involve the population as a whole. (Rose, 1992, preface)

Second, Professor Albert Bandura’s SCT (1986), a dominant theory applied to public health intervention development when I was working on my doctorate. SCT is a model of causation based on triadic reciprocal determinism where behavior, cognition and other personal factors, and environmental influences all operate as interacting determinants that influence each other. Professor Brian Flay’s Theory of Triadic Influence (Flay & Petraitis, 1994) expanded on SCT by incorporating other health behavior theories to highlight multiple *levels* of influences on behaviors from ultimate to most proximal within the personal, social, and environmental streams of influence. More proximal influences, including self-efficacy, social normative beliefs, and attitudes, are often the target of health education and behavior interventions. Focusing on these proximal influences, while ignoring more distal and ultimate influences of the societal systems that drive behavior, points to a serious limitation that impedes sustainability of effects. Long-term efficacy can rarely be attained without change in the more distal factors that shape health behaviors.

More recent theoretical frameworks consequential to my current thinking include socioecological approaches, highlighting the importance of more ultimate levels of influence not only on health behaviors but more importantly on population health outcomes and health equity. Two pieces of work, both published in 2010, were especially influential in my thinking and of making sense of what I was experiencing during my field trials. The World Health Organization’s Commission on the Social Determinants of Health Socio-Ecological Framework (2010) conveys how

social, economic and political mechanisms give rise to a set of socioeconomic positions ...; these socioeconomic positions in turn shape specific determinants of health status (intermediary determinants) ...; based on their respective social status,

individuals experience differences in exposure and vulnerability to health-compromising conditions. (World Health Organization, Solar, & Irwin, 2010, p. 5)

This framework clearly emphasizes social, economic, and political mechanisms as fundamental determinants of population health. Also in 2010, Dr. Tom Frieden, who served as director of the CDC from 2009 through January 20, 2017, presented the HIP, making a case that the largest health impact will be achieved by addressing determinants of socioeconomic status and the physical and social context in which people live, work, and play (Frieden, 2010). The HIP simply portrays a pyramid with five tiers, starting at the base with (a) socioeconomic factors, then with (b) changing the context to make individuals' default decisions healthy ones, (c) long-lasting protective interventions, (d) clinical interventions, and finally the smallest population-level effects of (e) counseling and education. The visual highlights that tiers at the base of the pyramid have the potential greatest population impact and least individual effort needed. Correspondingly, the smaller tiers of the pyramid have less population impact and greater individual effort needed.

These theoretical perspectives challenge us to consider “how high to reach?” when addressing social and public health needs of populations. Even the most complex interventions will have limited effects if they are focused on individual and interpersonal influences, without addressing more distal and complex sociocontextual determinants. As we grapple with “how high to reach?,” a key consideration is at what level of intervention do we hypothesize that sustained change can be achieved? Will sustained change be achieved if an intervention is delivered at the individual level? Interpersonal level? Family or school level? Community level? Based on theoretical and empirical evidence, as we determine that more macro-level interventions are necessary, what implications does this have for intervention and research design? For the feasibility of use of random assignment? For the appropriate level of intervention delivery?

HiAPs

Developing and evaluating intervention strategies that alter socioeconomic factors and contextual determinants of health often involves policy and policy outcome research. Altering the context in which people live, work, and play has received attention, with long-standing examples from the fields of injury, tobacco, and alcohol control (Burris et al., 2010). Lessons learned from these fields have been and are being applied to healthy eating and exercise initiatives (Institute of Medicine, 2012). Theoretically, similar strategies and methods can also be applied to addressing socioeconomic determinants of health, and there is growing recognition of the importance of doing so, importantly by the World Health Organization's Commission on Social Determinants of Health and its HiAPs initiative. The roots of HiAP are reflected in the early history of public health and its focus on environmental change around sanitary conditions for the protection of health. The actual HiAP term was first used in the late 1990s and became a major health theme during the second Finnish European Union Presidency in 2006 (Leppo & Tangcharoensathien, 2013). HiAP emphasizes the consequences of public policies on health determinants and the power of policy across sectors to improve population health and health equity.

In the United States, the federal government, including the CDC and NIH, initiated policy and health equity initiatives under President Obama's administration (CDC, 2016; National Institute on Minority Health and Health Disparities, 2014; NIH, 2017). The Robert Wood Johnson Foundation, one of the major nongovernmental funders of public health research in the United States, has had a long-standing interest in public health policy approaches. The American Public Health Association has been an active promoter of HiAP. Recently, the Association of Schools & Programs of Public Health (ASPPH) in the United States has sponsored roundtable discussions nationwide to bring together public health, health care, community, and business leaders in frank discussions around population health improvement. A major trend highlighted during the round tables was that "successful efforts to improve population health within and across communities require cross-sector understanding, connections, leadership, and engagement and the shared implementation of a 'health in all policies' strategy" (ASPPH News, 2017).

Globally, there is a growing understanding and emphasis on HiAP, with important implications for the design of complex interventions. My reflections have led to more questions than answers, including weighing the importance of theoretical comprehensiveness versus targeting just one of the fundamental determinants of health, how high of a level in society to intervene upon, and explication of both theory of causes and theory of change.

With greater attention to community or societal-level change comes important implications for research design. In the next section, I have three main reflections to share on research design, including matching the unit of intervention to the unit of assignment, public health law research methods, and consideration of design options and design elements beyond and in combination with random assignment.

Research Design

Unit (Level) of Intervention → Unit of Assignment

The design of interventions, including the highest organizational or structural level of intervention delivery, determines the appropriate level of randomization to study condition (Murray, 1998). Therefore, if theory suggests that modifiable risk at the level of community is important and can be achieved, then the community becomes the unit of intervention delivery. Such designs are often called community-, group-, or cluster-randomized designs, where the entire higher order cluster is randomized to study condition (rather than individual persons). Studies of the effects of interventions on higher order units, such as families, schools, work sites, and even whole communities, are now common (Murray, Pals, Blitstein, Alfano, & Lehman, 2008; Murray, Varnell, & Blitstein, 2004).

Key characteristics of group-randomized trials include (a) unit of assignment to study condition is an identifiable group, (b) different groups are allocated to each condition, (c) units of observations are members of groups, and (d) typically involve only a limited number of assignment units to each study condition (e.g., 10–15; Murray, 1998; Shadish, Cook, & Campbell, 2002). There is a unique hierarchical nature to group-randomized designs with units of observations nested within units of assignment nested within study condition. The

analysis strategy must match the multilevel nature of the design to avoid biased statistical analyses and misinterpretation of study results. Individuals within group are not independent and will have something in common, due to commonalities in selection, exposure, or interaction. The commonality, reflected in the intraclass correlation (ICC), violates the statistical assumption of independent errors. If the ICC, or lack of independent residual errors, is ignored, the Type I error rate is increased (and an effect might be incorrectly deemed to be statistically significant when in fact it is simply by chance). Therefore, analysis must take into account the multilevel nature of the design of nesting of individuals within groups (Murray, 1998, 2016).

A key challenge of group-randomized designs is the limited number of higher order units available to randomize and the balance of planning for adequate statistical power while constraining costs at feasible levels (Shadish et al., 2002). In most typical group-randomized trials, it is only possible to randomize a small number of units per condition. Therefore, there may be limited opportunity for randomization (under the laws of large numbers) to distribute confounders evenly. A priori matching or stratification becomes an important strategy to minimize potential confounding (and improve statistical power). Regression adjustment for covariates is another strategy to minimize confounding, while increasing statistical power by reducing residual variance and ICC (Murray, 2016). Statistical power is almost always improved more by increasing the number of aggregate units (e.g., adding more schools), rather than by increasing the number of individuals within units (e.g., adding more students within schools; for further information on design and analysis strategies for group-randomized designs, see Murray, 1998, 2016; Shadish et al., 2002).

During the design of our group-randomized trial in partnership with the Chicago Public Schools, adapting Project Northland for an urban population, we had to deal with several complex issues. One of the most important and consequential was redefining the level of the Project Northland alcohol prevention intervention from a whole city approach to a neighborhood-level approach. We did this to feasibly conduct a group-randomized trial within a large, urban area. It was not feasible, within the time and fiscal constraints of an NIH grant, to randomize and implement a multilevel intervention across 12 or more large metropolitan areas. However, in hindsight, by reducing implementation to a neighborhood level, we limited our options for creating sustainable community contextual change. City-defined neighborhoods within Chicago do not encompass a legally defined policy making jurisdiction. Therefore, the design at the neighborhood level altered the community intervention options to a focus on policies and practices of local institutions (stores that sell alcohol, schools, families) rather than policy-level changes at the level of a city or town (e.g., city ordinance to require routine age-of-sale compliance checks of alcohol outlets or a change in standard operating procedures of police departments). Randomization at the neighborhood level within large urban areas also increases risk of study participant exposure across neighborhood conditions, either intentional or not. For example, if it becomes difficult to obtain alcohol within one neighborhood, youth may find it easy to seek access in a contiguous neighborhood. The research design decision to move down to the level of the neighborhood may be one important reason why the beneficial intervention effects of Project Northland were not replicated in the adaptation for neighborhoods within the City of Chicago (Komro et al., 2008). An important lesson learned from this experience is the

critical early study phase of thinking through both theory of causes (e.g., easy access to alcohol for underage youth) and theory of change (direct-action community organizing for policy change) to clearly define the structural level or levels of intervention hypothesized as necessary for sustained health improvement. Once the level of intervention implementation is defined, the intervention level determines the level of assignment to study condition.

If higher level change (e.g., community contextual change through policy change) is hypothesized to be necessary for sustained health improvement, the level of intervention may not, feasibly, be under the control of scientists. Given these constraints, there have been calls for greater partnership between policy makers and researchers to work together to (randomly or with a known assignment algorithm) roll out and rigorously evaluate policy innovations (Buck & McGee, 2015).

Public Health Law Research Methods

The growing recognition of the social determinants of health (Marmot, 2005; World Health Organization et al., 2010) and the need for structural interventions signify that public health increasingly is returning to its classic emphasis on environmental and social conditions. Because law and policy are such important influences shaping environmental and social conditions, elevating empirical research on law's public health effects is an increasingly recognizable field of study (Komro, O'Mara, & Wagenaar, 2013; Wagenaar & Burris, 2013).

Changing the physical and social contexts in which people live, work, and play, and certainly changing socioeconomic determinants of health, will necessarily involve policy-level change. As I have described, the majority of my research has been conducting group-randomized trials evaluating efforts to change school and community contexts to better promote child and adolescent health. I have recently shifted focus to public health law research. Through this process, I am applying methods long used in the areas of tobacco, alcohol, and injury control to the core social determinants of health.

Feasible research design options for evaluating new laws and policies rarely include randomization, given that passage and implementation are not under the control of researchers. Rigorous empirical evaluations have been conducted on many important laws that have had significant effects on population health (Burris et al., 2010; Wagenaar & Burris, 2013). Such designs are commonly called natural, or quasi experiments. Random assignment is only one of a dozen or more important design elements that increase confidence in causal interpretation of an observed difference (Shadish et al., 2002). When evaluating effects of laws and policies, under which random assignment is rarely feasible, careful attention to full use of many other design elements is warranted (Wagenaar & Komro, 2013). Moreover, effectively combining many design elements into a single study can produce real-world legal evaluations with high levels of internal and external validity (Wagenaar & Komro, 2013). Design elements (Shadish et al., 2002) for strong legal evaluations are similar to those used in experimental and quasi-experimental designs, including (a) many repeated measures; (b) comparison jurisdictions not exposed to the law; (c) comparison groups, within jurisdictions, not expected to be affected by the law; (d) comparison outcomes related to the primary outcome but are not affected by the law or

policy under study; (e) replications; and (f) dose–response analyses (Wagenaar & Komro, 2013).

Design Options and Design Elements

Methods and design options keep expanding with an emphasis on creatively combining design elements for maximum rigor. Complex intervention research, with or without policy change, poses multiple challenges for scientific control and precision. My colleagues and I recently contributed a paper for a special issue of *Translational Behavioral Medicine* (Fishbein, Ridenour, Stahl, & Sussman, 2016) on research design issues for complex intervention trials and translational research (Komro et al., 2016). We first provided a summary of research designs in order of scientific rigor, including (a) randomized controlled trials, (b) regression discontinuity designs, (c) matched control group designs, (d) designs involving repeated measures, (e) interrupted time-series designs, and (f) staggered introduction of intervention across units, such as a stepped wedge design. Second, we describe a hierarchical approach to study design, again based on design elements as described in Shadish et al. (2002). Our recommendations for strengthening any research design, with or without randomization, include (a) addition of more waves of measurement, both before and after an intervention starts, to enhance understanding of the pattern of health outcome over time and the ability to detect changes in the point estimate or slope due to the initiation of an intervention or package of interventions; (b) inclusion of multiple settings to increase power and generalizability of results; (c) inclusion of multiple dependent variables (measuring both intermediate and primary outcomes) hypothesized to be affected by the intervention; (d) inclusion of comparison-dependent variables that are not expected to change due to the intervention; and (e) careful use of sophisticated analytical approaches to improve interpretation of results, including casual inference.

Pertinent to complex and higher order structural interventions is consideration of new pragmatic approaches to research design including staggered introduction of interventions across units, such as the stepped wedge design (Hemming, Haines, Chilton, Girling, & Lilford, 2015) and time-series designs long used for the rigorous evaluation of policy-level interventions (Wagenaar, 1983; Wagenaar & Holder, 1991; Wagenaar, Maybee, & Sullivan, 1988). As we suggest in our translation research paper (Komro et al., 2016), it is unlikely that the first attempt to implement a complex package of interventions will be totally successful; adjustments will be necessary. Therefore, a stepped-wedge or time-series design with routine and frequent assessments of implementation and intermediate outcomes could simultaneously address the needs for a rigorous evaluation and for a practical way of implementing, refining, and improving the intervention. In this way, continuous evaluation and refinement of the intervention (including implementation strategies and intervention components) can occur within one community and lessons learned applied to implementation in subsequent communities (Komro et al., 2016). As the complexity and higher order level of response continues to develop, so too do the research design options that need to be considered for rigorous evaluation in real-world settings.

Summary

I have shared seven thematic reflections from my 25 years of experience conducting complex intervention trials. Related to intervention design, I discussed the importance of considering the theory of *causes* and the theory of *change*, pondered the priority of theoretical *comprehensiveness* versus *fundamental determinants* of population health, posed what I hope is a persuasive study design question of “*how high in the social structure to reach?*,” and summarized the influential conceptualization of *HiAP*. Emerging from these intervention design issues are implications for research design. I summarized the importance of thinking through the level of intervention and *matching the unit (level) of intervention to the unit of assignment*, introduced the emerging field of *public health law research*, and summarized research *design options and design elements*, beyond and in combination with random assignment, for consideration for future complex intervention research.

Acknowledgments

Funding

The author received financial support for research summarized in this publication (NIH Award 5R01AA02069; NIH Award R01MD010241), and financial support from the Swedish Council for Working Life and Social Research, the Swedish Agency for Health Technology Assessment and Assessment of Social Services, the Public Health Agency of Sweden, and the National Board of Health and Welfare, to attend and present at the Stockholm Conference on Behavioral and Social Intervention Research, May 11–12, 2017.

References

- ASPPH News. ASPPH sponsored roundtables on population health held in Atlanta and Nashville. 2017. Apr 6. Retrieved from <http://www.aspph.org/aspph-sponsored-roundtables-on-population-health-held-in-atlanta-and-nashville/?c=1>
- Bandura, A. Social foundations of thought and action. Englewood Cliffs, NJ: Prentice Hall; 1986.
- Bobrowski KJ, Pisarska A, Ostaszewski K, Borucka A. Effectiveness of alcohol prevention program for pre-adolescents. *Psychiatry Poland*. 2014; 48:527–539.
- Buck, S., McGee, J. Why government needs more randomized controlled trials: Refuting the myths. Houston, TX: Laura and John Arnold Foundation; 2015.
- Burris S, Wagenaar AC, Swanson JW, Ibrahim JK, Wood JW, Mello MM. Making the case for laws that improve health: A framework for public health law research. *Milbank Quarterly*. 2010; 88:169–210. [PubMed: 20579282]
- Centers for Disease Control and Prevention. Strategies for reducing health disparities. 2016. Oct 3. Retrieved from <https://www.cdc.gov/minorityhealth/strategies2016/index.html>
- Craig P, Dieppe P, MacIntyre S, Michie S, Nazareths I, Petticrew M. Developing and evaluating complex interventions: The new Medical Research Council Guidance. *British Medical Journal (Clinical Research Edition)*. 2008; 337:a1655.
- Fishbein DH, Ridenour TA, Stahl M, Sussman S. The full translational spectrum of prevention science: Facilitating the transfer of knowledge to practices and policies that prevent behavioral health problems. *Translational Behavioral Medicine*. 2016; 6:5–16. [PubMed: 27012249]
- Play BR, Petraitis J. The theory of triadic influence: A new theory of health behavior with implications for preventive interventions. *Advances in Medical Sociology*. 1994; 4:19–44.
- Frieden TR. A framework for public health action: The health impact pyramid. *American Journal of Public Health*. 2010; 100:590–595. [PubMed: 20167880]
- Glanz, K.Rimer, BK., Viswanath, K., editors. Health behavior and health education: Theory, research, and practice. San Francisco, CA: John Wiley; 2008.

- Harper, CL., Leicht, KT. Exploring social change: America and the world. 6. New York, NY: Routledge; 2011.
- Hawe P, Shiell A, Riley T. Complex interventions: How “out of control” can a randomised controlled trial be? *British Medical Journal*. 2004; 328:1561–1563. [PubMed: 15217878]
- Hemming K, Haines TP, Chilton PJ, Girling AJ, Lilford RJ. The stepped wedge cluster randomised trial: Rationale, design, analysis, and reporting. *British Medical Journal*. 2015; 350:h391. [PubMed: 25662947]
- Institute of Medicine. Accelerating progress in obesity prevention: Solving the weight of the nation. Washington, DC: National Academies Press; 2012.
- Komro KA, Burris S, Wagenaar AC. Social determinants of child health: Concepts and measures for future research. *Health Behavior and Policy Review*. 2014; 1:432–445. DOI: 10.14485/hbpr.1.6.1
- Komro KA, Flay BR, Biglan A. The Promise Neighborhoods Research Consortium. Creating nurturing environments: A science-based framework for promoting child health and development within high-poverty neighborhoods. *Clinical Child and Family Psychology Review*. 2011; 14:111. [PubMed: 21468644]
- Komro KA, Flay BR, Biglan A, Wagenaar AC. Research design issues for evaluating complex multicomponent interventions in neighborhoods and communities. *Translational Behavioral Medicine*. 2016; 6:153–159. [PubMed: 27012263]
- Komro KA, Livingston MD, Wagenaar AC, Kominsky TK, Pettigrew DW, Garrett BA. Cherokee Nation Prevention Trial Team. Multilevel prevention trial of alcohol use among American Indian and White high school students in the Cherokee Nation. *American Journal of Public Health*. 2017; 107:453–459. DOI: 10.2105/AJPH.2016.303603 [PubMed: 28103073]
- Komro, KA., O’Mara, RJ., Wagenaar, AC. Understanding how law influences environments and behavior: Perspectives from public health. In: Wagenaar, AC., Burris, S., editors. *Public health law research*. San Francisco, CA: John Wiley; 2013. p. 307-324.
- Komro KA, Perry CL, Veblen-Mortenson S, Bosma LM, Dudovitz BS, Williams CL, ... Toomey TL. Brief report: The adaptation of Project Northland for urban youth. *Journal of Pediatric Psychology*. 2004; 29:457–466. [PubMed: 15277588]
- Komro KA, Perry CL, Veblen-Mortenson S, Farbachsh K, Kugler KC, Alfano KA, ... Jones-Webb R. Cross-cultural adaptation and evaluation of a home-based program for alcohol use prevention among urban youth: The “Slick Tracy Home Team Program. *Journal of Primary Prevention*. 2006; 27:135–154. DOI: 10.1007/s10935-005-0029-1 [PubMed: 16502143]
- Komro KA, Perry CL, Veblen-Mortenson S, Farbachsh K, Toomey TL, Stigler MH, ... Williams CL. Outcomes from a randomized controlled trial of a multi-component alcohol use preventive intervention for urban youth: Project Northland Chicago. *Addiction*. 2008; 103:606–618. [PubMed: 18261193]
- Komro KA, Perry CL, Veblen-Mortenson S, Stigler M, Bosma LA, Munson KA, Farbachsh K. Violence-related outcomes of the D.A.R.E. plus project. *Health Education and Behavior*. 2004; 31:335–354. [PubMed: 15155044]
- Komro KA, Perry CL, Williams CL, Stigler MH, Farbachsh K, Veblen-Mortenson S. How did Project Northland reduce alcohol use among young adolescents? Analysis of mediating variables. *Health Education Research*. 2001; 16:59–70. [PubMed: 11252284]
- Komro KA, Tobler AL, Delisle AL, O’Mara RJ, Wagenaar AC. Beyond the clinic: Improving child health through evidence-based community development. *BMC Pediatrics*. 2013; 13:1471–2431.
- Komro KA, Wagenaar AC, Boyd M, Boyd BJ, Kominsky T, Pettigrew D, ... Maldonado-Molina MM. Prevention trial in the Cherokee Nation: Design of a randomized community trial. *Prevention Science*. 2015; 16:291–300. DOI: 10.1007/s11121-014-0478-y [PubMed: 24615546]
- Leppo, K., Tangcharoensathien, V. The health sector’s role in HiAP. In: Leppo, K.Ollila, E.Pena, S.Wismar, M., Cook, S., editors. *Health in all policies*. Ministry of Social Affairs and Health, Finland; National Institute for Health and Welfare; European Observatory on Health Systems and Policies; United Nations Research institute for Social Development; Ministry for Foreign Affairs of Finland; 2013. p. 309-324.
- Link BG, Phelan J. Social conditions as fundamental causes of disease. *Journal of Health and Social Behavior*. 1995; 35:80–94.

- Luepker RV, Murray DM, Jacobs DRJ, Mittelmark MB, Bracht N, Carlaw R, ... Blackburn H. Community education for cardiovascular disease prevention: Risk factor changes in the Minnesota Heart Health Program. *American Journal of Public Health*. 1994; 84:1383–1393. [PubMed: 8092360]
- Marmot M. Social determinants of health inequalities. *Lancet*. 2005; 365:1099–1104. [PubMed: 15781105]
- Murray, DM. Design and analysis of group-randomized trials. New York, NY: Oxford University Press; 1998.
- Murray, DM. Group-randomized trials in public health and medicine [Webinar]. 2016. Aug 16. Retrieved from <https://prevention.nih.gov/docs/about/presentations/murray-sct-webinar-2016.pdf>
- Murray DM, Pals S, Blitstein JL, Alfano CM, Lehman J. Design and analysis of group-randomized trials in cancer: A review of current practices. *Journal of the National Cancer Institute*. 2008; 100:483–491. [PubMed: 18364501]
- Murray DM, Varnell SP, Blitstein JL. Design and analysis of group-randomized trials: A review of recent methodological developments. *American Journal of Public Health*. 2004; 94:423–432. [PubMed: 14998806]
- National Institute on Minority Health and Health Disparities. NIMHD Funding opportunities: System-level health services and policy research on health disparities. 2014. May 5. Retrieved from <https://grants.nih.gov/grants/guide/rfa-files/RFA-MD-15-001.html>
- National Institutes of Health. National Institutes of Health funding opportunity: Education and health: New frontiers. 2017. Apr 6. Retrieved from <https://grants.nih.gov/grants/guide/pa-files/PA-16-079.html>
- Perry CL, Kelder SH, Murray DM, Klepp KI. Community-wide smoking prevention: Long-term outcomes of the Minnesota heart health program and the class of 1989 study. *American Journal of Public Health*. 1992; 82:1210–1216. [PubMed: 1503159]
- Perry CL, Komro KA, Veblen-Mortenson S, Bosma LM, Farbakhsh K, Munson KA, ... Lytle LA. A randomized controlled trial of the middle and junior high school D.A.R.E. and D.A.R.E. *Plus programs*. *Archives of Pediatrics and Adolescent Medicine*. 2003; 157:178–184. [PubMed: 12580689]
- Perry CL, Williams CL, Komro KA, Veblen-Mortenson S, Stigler MH, Munson KA, ... Forster JL. Project Northland: Long-term outcomes of community action to reduce adolescent alcohol use. *Health Education Research*. 2002; 17:117–132. [PubMed: 11888042]
- Perry CL, Williams CL, Veblen-Mortenson S, Toomey TL, Komro KA, Anstine PS, ... Wolfson M. Project Northland: Outcomes of a communitywide alcohol use prevention program during early adolescence. *American Journal of Public Health*. 1996; 86:956–965. [PubMed: 8669519]
- Petticrew M. When are complex interventions “complex”? When are simple interventions “simple”? *European Journal of Public Health*. 2011; 21:397–398. [PubMed: 21771736]
- Rittel HW, Webber MM. Dilemmas in a general theory of planning. *Policy Science*. 1973; 4:155–169.
- Rose, G. The strategy of preventive medicine. New York, NY: Oxford University Press; 1992.
- Shadish, WR., Cook, TD., Campbell, DT. Experimental and quasi-experimental designs for generalized causal inference. New York, NY: Houghton Mifflin; 2002.
- Spencer RA, Komro KA. Family economic security policies and child and family health. *Clinical Child and Family Psychology Review*. 2017; doi: 10.1007/s10567-017-0225-6
- Syme SL. Social determinants of health: The community as an empowered partner. *Preventing Chronic Disease*. 2004; 1:1–5.
- Wagenaar, AC. Alcohol, young drivers, and traffic accidents: Effects of minimum age laws. Lexington, MA: Lexington Books; 1983.
- Wagenaar, AC., Burris, S. Public health law research: Theory and methods. Hoboken, NJ: John Wiley; 2013.
- Wagenaar AC, Holder HD. A change from public to private sale of wine: Results from natural experiments in Iowa and West Virginia. *Journal of Studies on Alcohol*. 1991; 52:162–173. [PubMed: 2016877]

- Wagenaar, AC., Komro, K. Natural experiments: Research design elements for optimal causal inference without randomization. In: Wagenaar, AC., Burris, S., editors. Public health law research: Theory and methods. San Francisco, CA: Jossey-Bass; 2013. p. 307-324.
- Wagenaar AC, Maybee RG, Sullivan KP. Mandatory seat belt laws in eight states: A time-series evaluation. *Journal of Safety Research*. 1988; 19:51–70.
- Williams CL, Grechanaia T, Romanova O, Komro KA, Perry CL, Farbakhsh K. Russian-American partners for prevention: Adaptation of a school-based parent-child programme for alcohol use prevention. *European Journal of Public Health*. 2001; 11:314–321. [PubMed: 11582613]
- Solar, O., Irwin, A. World Health Organization. The World Health Organization Discussion Paper Series on the Social Determinants of Health, 2. Geneva, Switzerland: World Health Organization; 2010. A conceptual framework for action on the social determinants of health. Social determinants of health discussion paper 2 (Policy and Practice).