EVALUATING THE COST-EFFECTIVENESS OF REAL-WORLD PREVENTION:
APPROACHES FOR ESTIMATING THE EFFICIENCY OF EVIDENCE-BASED
PROGRAMMING

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Abstract

Successful demonstrations of evidence-based preventative interventions (EBPIs) have led to a growing interest in prevention’s capacity to reduce major public health problems with greater efficiency. In response—just as prevention scientists once distinguished between the efficacy and effectiveness of prevention programs—now researchers are considering the distinction between program effectiveness and efficiency (i.e., contextualizing impact in terms of cost). This inquiry into the benefits and costs of EBPIs presents an opportunity to demonstrate prevention’s impact as well as its greater value to society. To accurately evaluate the efficiency of prevention efforts, program cost-effectiveness must be gauged in real-world contexts. In turn, new methodological approaches are needed to account for potential confounders that may reduce researcher’s ability to draw causal inferences about program impact. For instance, selection bias is introduced when local communities adopt one program over another and when the decision to enroll in multiple programs is left up to participants.

This work demonstrates an innovative approach for assessing the efficiency of evidence-based preventive interventions delivered in everyday settings. Using data from the PROSPER dissemination trial (over 12,000 youth; 28 Communities), this project applies propensity and marginal structural models to strengthen causal inference within cost-effectiveness analyses of community prevention efforts. Using these analytic techniques, I evaluated the effectiveness and cost-effectiveness of three school programs (Life Skills Training, All Stars and Project Alert) and a family program (SFP 10-14) to reduce prescription opioid misuse (e.g., Vicodin, OxyContin). Findings indicated that universal school-based EBPIs can on their own reduce prescription opioid misuse in a cost-effective manner and that the efficiency of a prevention effort employing such school programs can be enhanced by deploying an additional family-based program.

This methodological approach provides an opportunity to increase the relevance of prevention impact analyses by allowing researchers to better contextualize program effectiveness in terms of program costs. Specifically, this method provides a more refined approach for understanding the impact of combining interventions and may expedite the development of more efficient prevention efforts. Further, analyses such as these can provide important information to not only researchers, but to multiple stakeholders who seek to translate prevention science into practice.
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Chapter 1:

Introduction

Successful demonstrations of evidence-based preventative interventions have led to a growing interest in prevention’s capacity to manage major public health problems with greater efficiency (Cohen, Neumann, & Weinstein, 2008; Compton et al., 2005; Foster, Dodge, & Jones, 2003; Haddix, Teutsch, & Corso, 2003; Johnson et al., 2011; Miller & Hendrie, 2008; O’Connell, Boat, & Warner, 2009; Wang, Yang, Lowry, & Wechsler, 2003). In response—just as prevention scientists once delineated between the efficacy and effectiveness of prevention programs—now researchers are considering the distinction between program effectiveness and efficiency (i.e., contextualizing impact in terms of cost; Crowley, Greenberg, & Jones, under review; Doll, 2010; O’Connell et al., 2009; Wolfenstetter, 2011). This inquiry into the benefits and costs of prevention presents an opportunity to illustrate not only prevention’s impact, but also its greater value to society (Foster et al., 2003; O’Connell et al., 2009). In order to facilitate increased evaluation of prevention efficiency, methodologists are building upon existing tools from economics, engineering, and information science (Collins, Murphy, Nair, & Strecher, 2005; Foster, Jones, & CPPRG, 2006; Hansen, Bishop, & Bryant, 2008; Holtgrave, 2002; Swendeman & Rotheram-Borus, 2010). Of particular significance, some of these approaches are already being employed in state and federal policy-making (Aos et al., 2011; Aos, Lieb, Mayfield, Miller, & Pennucci, 2004).

Unfortunately, these transdisciplinary methods are being applied within trials that often fail to capture the complexity of real-world prevention efforts—potentially overestimating program effects and underestimating program costs (Aos et al., 2004; Chatterji, Caffray, Jones,
Lillie-Blanton, & Werthamer, 2001; Crowley, Jones, Greenberg, Feinberg, & Spoth, 2012; Foster, Porter, Ayers, Kaplan, & Sandler, 2007; O’Connell et al., 2009). Specifically, these evaluations may neglect important factors that impact program delivery outside research settings (e.g., community capacity, program receipt, implementation quality). For instance, when prevention efforts are deployed in everyday contexts, participants are often given the opportunity to receive not a single program, but instead multiple programs delivered across ecological levels (e.g., within schools, families, the workplace; Elias, Gara, Schuyler, Branden-Muller, & Sayette, 1991; Ringwalt et al., 2002; Sarason & Sarason, 1996). This raises a variety of questions including: What factors influence participants’ receipt of different programs? How can researchers evaluate the impact of receiving multiple programs when randomization would greatly reduce the findings’ generalizability? Further, is receiving multiple programs an efficient use of scarce prevention dollars?

To address these questions, I propose a novel methodological approach for estimating the effectiveness of real-world prevention efforts in terms of their economic costs. This method entails the use of cost-effectiveness analyses (CEA) employing innovative methods for statistical control to evaluate prevention efforts delivered in everyday contexts. Within this proposal, I first provide general background on cost-effectiveness analyses. Then, I consider current approaches for evaluating how prevention programs perform in the real world. Finally, I outline an example for applying this approach to estimate the cost-effectiveness of receiving different prevention programs within the PROSPER (PROmoting School-community-university Partnerships to Enhance Resilience) dissemination trial. While this method could be used to study many of the factors that impact the success of prevention efforts (e.g., community capacity, implementation
quality), this work exclusively focuses on evaluating the cost-effectiveness of program receipt (e.g., receiving different programs within school and family settings).

**Cost-Effectiveness Analysis & Productive Efficiency**

Cost-effectiveness analysis (CEA) is an analytic tool that has long facilitated efficient decision making (Pigou, 2002; Quade, 1971) and remains the predominant approach within the United States for evaluating healthcare efficiency (Haddix et al., 2003). Researchers from economics, decision analysis, and operations research have developed increasingly rigorous methods for broadly employing CEA (Carande-Kulis et al., 2000; Drummond, 2005; Russell, Gold, Siegel, Daniels, & Weinstein, 1996). Contemporary CEAs calculate incremental cost-effectiveness ratios (ICERs) that estimate the incremental cost of a gain in a single unit of benefit (e.g., the cost of a 1% drop in underage drinking arrests; Haddix et al., 2003). CEAs are used to compare the same outcome across programs and can provide insight into what is known as a program’s productive efficiency (Gold, Stevenson, & Fryback, 2002; Palmer & Torgerson, 1999).

A program is considered productively efficient if it attains the maximum possible effect (i.e., output) from a specified set of resource inputs\(^1\) (Palmer & Torgerson, 1999). Alternatively, if a program produces an effect below this maximum level—known as the production possibility frontier—then it is considered to be productively inefficient (Drummond, 2005; Lovell, 1993). Different programs can be compared with CEA if they target the same outcome (Haddix et al., 2003). By making these comparisons, CEAs can inform decisions regarding where resources

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\(^1\) Note: This maximum effect is generally set by the best available program and increases as more effective programs are developed.
should be allocated to make the greatest impact on the outcome of interest (Drummond, 2005; Petitti, 2000).

CEAs in prevention science are increasingly common for a variety of reasons. First, data constraints within prevention often limit researchers’ conducting full benefit-cost analyses (BCA)—an analytic approach that places a monetary value on both program costs and benefits (Foster et al., 2003; Kilburn & Karoly, 2008). Second, CEAs provides an estimate of a program’s productive efficiency. This approach can estimate the relative efficiency of one intervention to another by comparing different programs’ ICERs. This is particularly useful for advocacy work with funders seeking to improve a specific outcome by adopting new programs (Hoffmann et al., 2002). CEAs may also be used to estimate a program’s absolute efficiency by comparing the program’s ICER to a societal willingness to pay threshold. This threshold is an estimate of what society would be willing to give up in order to avoid a specific outcome (e.g., what society would pay to decrease underage drinking arrests by 1%). Third, because prevention efforts often aim to improve health and educational outcomes, CEAs avoid many of the ethical pitfalls that befall more comprehensive economic analyses (e.g., BCA; Donaldson, Birch, & Gafni, 2002; Russell et al., 1996). For instance, BCAs tend to undervalue the impact of programs that increase educational attainment in minorities. This is because markets tend to value minorities’ time less than that of other populations due to discrimination in the labor market (i.e., distributional issues; Frank, 2000; Mishan & Quah, 2007). Since CEAs do not monetize participants’ outcomes, these inequities are less likely to influence estimates of program efficiency.

In this manner, CEAs are not only more targeted than other efficiency analyses, but also more focused in their scope. In many cases, understanding a program’s efficiency to reduce a specific problem is valuable for informing prevention efforts. Sometimes, a broader perspective
is needed and BCAs are more useful. While some disagreement exists, where groups advocate one method over another, a growing group of researchers and decision makers acknowledge the benefit of multiple forms of efficiency analyses to provide a more complete understanding of the value that can be obtained from intervening in a variety of areas (Drummond, 2005; Haddix et al., 2003).

Within medical settings, CEA is frequently used to evaluate preventive interventions (Ginsberg, Edejer, Lauer, & Sepulveda, 2009; Tengs et al., 1995). CEAs within mental, emotional and behavioral (MEB) prevention are less common (e.g., Belani & Muennig, 2008; Foster et al., 2006; Jones et al., 2009; O’Connell et al., 2009). Unfortunately, as mentioned earlier, the problem with current applications of CEA to MEB prevention programs is that they rarely evaluate efforts operating in real-world contexts. To understand why CEAs are seldom undertaken in these settings, I next consider current practices for evaluating prevention performance in the real world.

Evaluating Prevention Program Performance in Real-World Settings

As researchers built the science of prevention, increasingly tight experimental controls were deployed to evaluate whether interventions could avert poor developmental outcomes (i.e., efficacy trials—Flay, 1986; Flay et al., 2005). These trials greatly improved researchers’ confidence in the impact of prevention (Coie, Watt, West, Hawkins, & et al, 1993; O’Connell et al., 2009). However, as researchers sought to disseminate programs into general practice, intervention potency appeared to diminish based upon the influence of numerous factors (e.g., community capacity, program receipt, implementation quality; Chinman et al., 2005; Dodge, 2001; Glasgow, Lichtenstein, & Marcus, 2003). Consequently, standards of evidence were
developed that articulated the difference between what is known as program efficacy and as program effectiveness (Flay et al., 2005). Efficacy describes a program’s impact under “optimal conditions” while effectiveness describes its impact in “real-world settings” (Greenberg, 2004; Kellam & Langevin, 2003). In turn, the criteria believed necessary for broad program dissemination includes intervention effectiveness as well as a capacity to be adopted, implemented and sustained (Elliot & Mihalic, 2004; Sussman, 2006).

**Difficulties in Estimating Program Impact in Real-World Settings.** Despite efforts to evaluate MEB prevention programs as discrete interventions (as researchers traditionally evaluate pharmaceuticals), these programs naturally operate within a systemic community context (Chinman et al., 2008; Abraham Wandersman et al., 2008). Notwithstanding the intentions of researchers, successful prevention efforts are born into, supported by, and discontinued within social service systems (e.g., health service, education, cooperative extension, criminal justice; Dunworth, Mills, Cordner, & Greene, 1999; Green, 2006; Olds, Hill, Obrien, Racine, & Moritz, 2003; Spoth, Greenberg, Bierman, & Redmond, 2004). Unfortunately, as increasingly recognized by the scientific community, because of the complex relationships that exist between many systemic factors, the study of service systems is challenging (Flood, 1993; Mabry, Olster, Morgan, & Abrams, 2008; Madon, Hofman, Kupfer, & Glass, 2007; Spohrer, Maglio, Bailey, & Gruhl, 2007).

This complexity extends to estimating the cost-effectiveness of prevention programs operating within systems. Fortuitously, the goal here is not to study the system as a whole, but instead to model the influence of these systemic factors on prevention efforts within CEAs (Haddix et al., 2003). These systemic factors are confounders in that they impact or predict the intervention received. By modeling the influence of these confounding factors, researchers can
control for selection effects and draw stronger causal inferences about program impact (Pearl, 2000; Robins, Hernán, & Brumback, 2000). For instance, in the case of program receipt, there are a variety of confounders that influence whether or not participants are actually (1) offered and (2) enroll in a program (Durlak & DuPre, 2008; Prinz & Miller, 1994; Spoth, Redmond, & Shin, 2000). These include participant factors (e.g., time, distance), family factors (e.g., family structure, willingness to participate), organizational factors (e.g., capacity, training), infrastructure factors (e.g., school resources, buy-in) and community factors (e.g., local support and awareness). For each participant, these factors influence the likelihood they will be offered and enroll in a prevention program. Consequently—in order to evaluate how the program will perform—researchers must first account for the impact of these confounders (Rubin, 1997).

Program Delivery in Real-World Settings. Approaches for evaluating prevention program performance in everyday settings include large-scale, longitudinal efforts known as dissemination trials (e.g., Andreasson, 2000; Garber et al., 2009; Rohrbach, Gunning, Sun, & Sussman, 2009). These trials test the capacity of prevention programs to be adopted, implemented, and sustained in real-world contexts (Rohrbach et al., 2009; Sanders, 2003). To evaluate how a program and system interact, these trials are often randomized at the school- or community-level (e.g., Brown, Hawkins, Arthur, Briney, & Abbott, 2007; Spoth et al., 2004; Swaim & Kelly, 2008). Within these programming units, different decisions regarding what programs to offer are often left up to local efforts (e.g., recruitment, sustainability planning) and participants’ choice (e.g., program enrollment and attendance). This is largely to increase the generalizability of results into non-research contexts. Characteristic of dissemination trials is intensive monitoring of systemic factors that influence program adoption, implementation, and sustainability as well as participant outcomes (e.g., Feinberg, Chilenski, Greenberg, Spoth, &
Redmond, 2007; Greenberg, Feinberg, Meyer-Chilenski, Spoth, & Redmond, 2007). By monitoring these systems-level factors in addition to participant effects, these trials provide an opportunity to account for the impact of confounders that would otherwise interfere with the ability to draw causal inferences.

One early attempt to estimate the impact of prevention efforts in a real-world setting occurred within a large-scale prevention trial known as Project Northland (Perry et al., 1996). This trial was a community-wide implementation of five preventive interventions designed to reduce underage alcohol use (i.e., classroom curricula, peer leadership, participation in or planning of extracurricular activities, parenting programs, and community activism). One evaluation of the trial estimated the impact of participants’ receipt of the different programs (Stigler, Perry, Komro, Cudeck, & Williams, 2006). While this analysis was able to detect a significant effect for receiving different program combinations, the authors acknowledge the analytic design could not account for many systemic confounders that most likely influences whether participants received the different programs—nor did it consider program effectiveness in terms of cost.

Project Northland is an example of how the methods used by prevention scientists to account for confounders generally include carefully constructed study designs (Flay, 1986). In particular, randomized-control trials are generally considered the ‘gold standard’ design when seeking to estimate the impact of a program (Concato, Shah, & Horwitz, 2000; Shadish, 2001). By employing randomization to minimize participant selection effects, an estimate of a program’s total effect may be interpreted with a high degree of confidence. Outside tightly controlled evaluations—such as dissemination trials—systemic confounders may obscure the impact of different programs within a prevention effort and make drawing such inferences using
methods of *design control* alone difficult (McCall & Green, 2004). Fortunately, with the rise of dissemination trials that carefully monitor these factors, researchers can employ more sophisticated methods for *statistical control* to account for these confounders—allowing for less biased causal inferences. These methods fall under the potential outcomes framework for causal inference (Rubin, 1974).

**Propensity Models.** Within CEAs, and intervention research more broadly, each individual has an outcome under each level of the intervention, but only one of these outcomes can be observed for a given individual. Under the potential outcomes framework, causal effects are defined as contrasts between potential outcomes for an individual. Because only one of the potential outcomes is observed, causal inference is not possible without further assumptions, such as the need to account for all potential confounding relationships that would lead to differences between treatment groups not attributable to the intervention.

Traditionally, prevention researchers include confounders unaccounted for by experimental designs as covariates within outcome analyses (e.g., ANCOVA). These methods have a limited ability to account for a large number of confounders that span across multiple levels. An alternative method to accomplish this is propensity score models. These analyses employ the potential outcomes framework to estimate confounders’ impact on the likelihood of receiving or not receiving a treatment (Rosenbaum & Rubin, 1983; Rubin, 1974). From these models the propensity of treatment receipt for each participant is estimated. This *propensity score* may in turn be used to match or weight participants. The result is groups that are similar to what is achieved through randomization (i.e., to achieve balanced groups; Rosenbaum & Rubin, 1983, 1984; Sampson, Morenoff, & Gannon-Rowley, 2002). Specifically, propensity scores (\(\pi_i\)
are the probability that an individual \((i)\) received a program \((T_i)\) given measured confounders \((X_i;\)

\[
\pi_i = P(T_i = 1|X_i)
\]

By using propensity scores to balance different groups, what is known as the _average causal effect_ (ACE) of an intervention may be estimated. Interpreting this effect allows researchers to draw causal inferences about group differences with a greater degree of confidence (Luellen, 2005; Schafer & Kang, 2008). Further, confounders from across different ecological levels (e.g., family, schools, community) that influence potential outcomes may be modeled under the non-interference assumption where an individual \(j\) in Community A is not influenced by the treatment of individual \(i\) in Community B (i.e., stable unit treatment value assumption—SUTVA; Rubin, 1978).

This approach has previously been employed within behavioral and prevention science (e.g., Blechman, Maurice, Buecker, & Helberg, 2000; Coffman, Moore, & Lanza, 2011), particularly as an approach to facilitate compliance and dosage analyses (e.g., Foster, 2003; Stuart, Perry, Le, & Ialongo, 2008). Within dissemination trials, the potential outcomes framework may be used to account for the effect of confounders on the propensity to receive a program or treatment. For instance, recent work using data from the PROSPER trial demonstrated the ability to balance two groups of individuals, those who voluntarily enrolled in a school-based prevention program versus those who enrolled in both school- and family-based prevention programs. The ACE of receiving a family-program in addition to a school-based program on prevention of underage drinking was estimated (Crowley, Coffman, Feinberg, & Greenberg, in press).
Propensity models are often used in evaluations of medical intervention efficiency (Chow et al., 2007; Mitra & Indurkya, 2005; Shireman & Braman, 2002). Multiple examples are available within behavioral science (Caldwell, Vitacco, & Van Rybroek, 2006; Katon et al., 2005; Mojtabai & Zivin, 2003), but few are found within prevention (Foster, 2010). Building on earlier methodological work, I demonstrate the value of using the potential outcomes framework and propensity models in CEAs of dissemination trials. Specifically, this method was applied to the PROSPER dissemination trial described below.

The PROSPER Delivery & Support System

The PROSPER delivery and support system links stakeholders from the state and local cooperative extension service (CES) and local public school systems for the purpose of implementing school- and family-based preventive interventions (Spoth et al., 2004). An embedded CES agent and a school official comprise the core of community prevention teams that involve multiple members representing various community interests. The local teams are supported by prevention coordinators in the CES and by university prevention teams (for a review, see Spoth et al., 2004). The teams each select from a menu of school and family evidence-based programs and offer those programs to youth and families within the community. Within the PROSPER dissemination trial three school programs were delivered (each community only delivers one of these programs): Life Skills Training, Project Alert and All Stars. Additionally, all PROSPER communities chose to deliver the Strengthening Families Program: For Parents and Youth Ages 10-14.

Evidence-Based Programs Delivered within the PROSPER System
**Project Alert.** Project Alert is a school-based program that attempts to reduce substance use by targeting negative social influences that encourage use and promote social norms that reduce the likelihood of substance use. The program is comprised of 11 sessions that involve interactive activities such as role-playing, skills rehearsal and small group activities (see Ellickson, McCaffrey, Ghosh-Dastidar, & Longshore, 2003; Ghosh-Dastidar, Longshore, Ellickson, & McCaffrey, 2004).

**All Stars.** All Stars is a school based program consisting of 13 sessions that seeks to promote healthy beliefs regarding drug use, create conventional norms against substance use, build strong personal commitments, facilitate school bonding, and increase parental monitoring. Activities are interactive, consisting of games, art activities, and small group discussions (Hansen, 1996; Harrington, Giles, Hoyle, Feeney, & Yungbluth, 2001; McNeal, Hansen, Harrington, & Giles, 2004).

**Life Skills Training.** Life Skills Training is a school based program that aims to prevent substance use and abuse by changing social influence and competencies. In particular, this program seeks to teach social skills that build personal competence as well as facilitate assertiveness and refusal of substances across 18 sessions (see Botvin, Griffin, & Nichols, 2006; Spoth, Randall, Trudeau, Shin, & Redmond, 2008; Trudeau, Spoth, Lillehoj, Redmond, & Wickrama, 2003).

**The Strengthening Families Program (SFP) 10-14.** SFP is a family-based program designed to reduce substance use and is grounded in a variety of family, resilience and biopsychosocial etiological theories. Families receive seven sessions (one per week) with parents and youth separated for an hour and then together (for an additional hour). The program seeks to
reduce risk factors such as poor parental monitoring and bonding as well as issues of socio-emotional health (see Spoth, 2006; Spoth, Redmond, & Shin, 2001).

**Effectiveness of the PROSPER System**

Previous evaluations of the PROSPER dissemination trial (17,701 adolescent participants in 28 communities) have demonstrated the system’s effectiveness in promoting evidence-based preventive interventions’ (EBPIs) adoption, implementation and sustainability (Spoth, Guyll, Lillehoj, Redmond, & Greenberg, 2007; Spoth, Guyll, Redmond, Greenberg, & Feinberg, 2011) as well as significantly reducing rates of adolescent alcohol and substance abuse (Spoth, Redmond, et al., 2011; Spoth et al., 2008). Further, researchers found that youth in PROSPER communities—compared to the control communities—were significantly less likely to report ever consuming alcohol, tobacco and other drugs four years after the programs were delivered (Spoth, Redmond, et al., 2011).

**Costs of the PROSPER System**

Recent work has estimated the economic cost of the PROSPER system to be between $81,488 and $106,244 annually per site to operate the local prevention teams and maintain successful community-university-school partnerships (Crowley et al., 2012). The cost analysis also provided evidence that delivery of school and family evidence-based preventive interventions may be lower than in settings outside of formal prevention delivery and support systems—with a $22-$40 per child reduction in the cost of delivering Life Skills Training, a $2-$20 per child reduction in delivery of the All Stars program and a $502-$572 reduction in the delivery of SFP 10-14. Additional work has begun to look at the general cost-effectiveness of the PROSPER program based upon these estimates (Guyll et al., in prep; Jones, Crowley, Guyll et
al., in prep). Despite these promising findings, the cost-effectiveness of receiving a particular school program and receiving the family program has yet to be evaluated.

**Outcome-of-Interest.** As a demonstration of the methodological approach described above, I focused on one form of substance misuse that has become a major public health concern: prescription opioid misuse. Prescription opioid misuse is the second most prevalent form of illicit drug use after marijuana (Johnston, O’Malley, Bachman, & Schulenberg, 2010). In particular, 12.5 million Americans reported using prescription painkillers for nonmedical purposes (SAMHSA, 2008). Further, between 1999 and 2007 patients admitted for treatment for prescription opioid abuse quadrupled and opioid-related deaths have more than tripled (SAMHSA, 2009; Warner, Chen, & Makuc, 2009). The most common motives for prescription opioid misuse were to relieve pain, get high, and experiment (McCabe, Cranford, Boyd, & Teter, 2007). The adverse consequences of prescription opioid misuse include addiction, negative hormonal and immune system effects, the development of tolerance, and increased sensitivity to pain (hyperlgesia). Those who misuse prescription opioids also have higher health care costs, disability, and increased rates of surgery (Manchikanti & Singh, 2008).

From a demographic standpoint, females, blacks and those of lower socio-economic status are at higher risk for misuse (Sung, Richter, Vaughan, Johnson, & Thom, 2005). Youth who have favorable attitudes towards illicit substances are also at higher risk. In particular, past work has highlighted how those with detached or unengaged parents/guardians are at greater risk for misuse—providing a strong rationale for the value of family-based programs that increase parental monitoring (Sung et al., 2005). Additionally, peer use is also a risk factor for initiation and misuse—providing a strong rationale for the value of school-based programs that seek to change youth norms and attitudes (Sung et al., 2005). Arguments for using both family- and
school-based efforts to prevent misuse are strengthened by evidence that the primary sources of prescription opioids are friends or parents (McCabe et al., 2007).

The rise of prescription opioid abuse poses a major threat to public health, and many policy makers and community leaders are seeking to better understand what current programs and policies may be available to prevent youth from misusing this specific class of substances. Unfortunately, because of the value of prescription opioids for medical purposes, devising efficient interventions that prevent misuse while not compromising pain management practices is essential (Fischer, Gittens, & Rehm, 2008). This work considers approaches to evaluating the cost-effectiveness of such interventions below.

**Illustrative Study of Propensity Models Within Cost-Effectiveness Analysis**

This dissertation project presents an illustrative example of the process involved in applying the potential outcomes framework and using propensity and marginal structural models to improve causal inference within CEAs of real-world prevention efforts. The development of this approach will fill a crucial methodological gap that previously limited prevention scientists’ capacity to draw causal inferences about the efficiency of real-world prevention efforts. Specifically, by accounting for confounding within CEAs, prevention researchers can begin to parse out the impact of important factors that influence real-world prevention efforts and further contextualize that impact in terms of cost.

Using the method outlined above, I evaluated the cost-effectiveness of programs delivered within the PROSPER trial. This work considers fifteen specific research questions. The first three consider the added value of the SFP program with no distinction between the school programs:
1. What is the incremental cost-effectiveness of delivering just a school program within PROSPER versus no program at all?

2. What is the incremental cost-effectiveness of delivering a school program and the SFP program together within PROSPER versus no program at all?

3. What is the incremental cost-effectiveness of delivering a school program and the SFP program together within PROSPER versus just receiving a school program?

In addition, I examined whether particular school programs are more cost-effective than others as well as whether particular school programs delivered with the SFP program have differential levels of cost-effectiveness. This includes answering the three questions above for each school program delivered within the trial:

4. What is the incremental cost-effectiveness of delivering just the Life Skills Training program within PROSPER versus no program at all?

What is the incremental cost-effectiveness of delivering the Life Skills Training program and the SFP program together within PROSPER versus no program at all?

What is the incremental cost-effectiveness of delivering the Life Skills Training program and the SFP program together within PROSPER versus just receiving the Life Skills Training program?

5. What is the incremental cost-effectiveness of delivering the All Stars program within PROSPER versus no program at all?

What is the incremental cost-effectiveness of delivering the All Stars program and the SFP program together within PROSPER versus no program at all?
What is the incremental cost-effectiveness of delivering the All Stars program and the SFP program together within PROSPER versus just receiving the All Stars program?

6. What is the incremental cost-effectiveness of delivering the Project Alert program within PROSPER versus no program at all?

What is the incremental cost-effectiveness of delivering the Project Alert program and the SFP program together within PROSPER versus no program at all?

What is the incremental cost-effectiveness of delivering the Project Alert program and the SFP program together within PROSPER versus just receiving the Project Alert program?
Chapter 2:

Methods

Participant & Community Recruitment

The PROSPER project recruited 14 communities in Iowa and 14 communities in Pennsylvania based upon four criteria that included (1) school district enrollment between 1,301 and 5,200 students, (2) at least 15% of families eligible for reduced cost lunch, (3) maximum of 50% of the adult population employed or attending a college or university, and (4) the community could not be involved in other university-affiliated, youth-focused prevention initiatives. Participating communities were predominantly rural and had a median household income of $37,070. Communities were matched by geographic location and size; each pair of communities was randomized into intervention and control conditions. Detailed descriptions of community recruitment, selection and randomization are available in previous reports (see Spoth, Redmond, et al., 2007; Spoth et al., 2004).

Procedure

Within the PROSPER dissemination trial, all families in intervention communities were offered a family-based prevention program in the 6th grade (Strengthening Families Program 10-14), but not all families who were offered enrolled in and received the family program. In addition, all youth in the intervention communities received one of three school-based substance abuse programs in the 7th grade (All Stars, Life Skills Training, or Project Alert).

Measures
**Program Receipt.** The school program each youth received was tracked. These programs included All Stars (N=2356), Life Skills Training (N=1422) and Project Alert (N=2334). Family program receipt was tracked using attendance records of whether families had enrolled in and attended the family-based prevention program (N=827).

**Confounders.** A variety of measures are used in the propensity models to account for confounders that influence program receipt.

*Participant-Level Confounders.* Sixteen participant-level (youth and family) measures were used to account for potential differences between groups receiving levels of programming. These included (1) measures of youth demographics (gender, ethnicity, age, enrollment in school lunch programs) and (2) youth functioning (stress management, problem solving, assertiveness, frequency of risk activities, frequency of self-oriented activities, academic achievement, frequency of school absences, attitude towards school, school bonding and achievement, deviant behaviors, antisocial peer behavior); (3) youth proclivity towards alcohol and substance abuse (substance refusal intentions and efficacy, positive expectations, perceptions of and attitudes toward substance abuse, as well as cumulative alcohol and substance initiation and use indices); (4) family environment (parent marital status, youth residence with biological parents, affective quality between parents and youth, parental involvement, parent management of child, family cohesion); and (5) each family’s geographic distance from the program site.

*Organizational-Level Confounders.* Twenty-four measures of PROSPER prevention team-leader and team-member functioning were used to account for other potential differences in receipt (i.e., aggregated to a team-level score). These include team-member involvement, team focus on work, members’ perceptions of decision making and influence on team, degree of team
communication, team leadership, tension, culture, unity and willingness to integrate new team members as well as ease of program integration.

Infrastructure-Level Confounders. Eleven school-infrastructure-level measures were used to account for selection effects that may result from confounders within the school programming infrastructure. These included level of the school’s general prevention activities, provision of pro-social activities, use of a structured curriculum, school personnel involvement in program selection, integration of a school program, knowledge and supportiveness of SFP, and collaboration with potential community partners.

Community/School-Level Confounders. Twelve community-level measures are used to account for potential selection effects including indicators of poverty, availability of substances, and extension reputation. School-level measures include school demographics, climate, perceptions of helplessness due to community problems, and indicators of parental involvement.

Prescription Opioid Misuse. To evaluate youth prescription opioid misuse, each participant was asked whether they had ever used prescription opioids for non-medical purposes at pre-test (fall sixth grade) and at the end of each year through 11th grade [Have you ever used Vicodin, Percocet or Oxycontin not prescribed by a doctor?].

Analytic Framework

The ultimate goal of this analysis is to estimate the incremental cost-effectiveness ratios (ICER) for different levels of program receipt. The numerator of an ICER is the difference in costs for two interventions. The denominator of the ICER is the difference in the average effect sizes of the two interventions.
In total twelve ICERs are calculated within this analysis. Four ICERs are calculated to estimate the aggregate (i.e., all school programs combined) and individual (i.e., Project Alert, Life Skills Training, and All Stars separately) school program’s cost effectiveness relative to the control group (school program only). Then four ICERs are calculated to estimate the aggregate and individual school programs’ cost-effectiveness with the additional family program compared to the control group (school and family program). Last, four ICERs are calculated to estimate the aggregate and individual school program cost-effectiveness with the additional family program compared to receiving only the school program (i.e., the incremental impact). Each ICER corresponds to one of the twelve questions outlined above. To calculate the ICER, estimates of the program’s costs and benefits were needed. Then, to provide context for the magnitude of the ICER, a threshold analysis was carried out. A threshold analysis compares the ICERs for each program combination to a societal willingness-to-pay (WTP) threshold (described below). Lastly, sensitivity analyses were used to evaluate the robustness of the ICER.

Estimates of Program Cost. The costs of the evidence-based prevention programs delivered within the PROSPER dissemination trial were estimated in an earlier cost analysis that disaggregated the day of implementation costs and costs of the entire PROSPER delivery and support system (Crowley et al., 2012). These represent the costs generally included in the literature as required for program delivery and are significantly less than the total costs of adopting, implementing and sustaining programming. To develop comparable cost-effectiveness estimates, day of implementation costs are used in the outcome analyses. For the school program, these costs include the expenditures to purchase the program curriculum, train
facilitators (teachers), as well as subsidize school materials and infrastructure. The average cost to provide the school program to a single student was $27. The day of implementation costs for the family-based program include expenditures for purchasing the program curriculum and program supplies, training and paying facilitators, recruiting families, as well as providing child care, family meals and incentives to maintain family attendance. The average cost to provide the family program to a single family was $348.

**Estimates of Program Benefits.** In order to estimate the benefits of receiving the different programs delivered within PROSPER as well as the benefits of receiving multiple programs, a five-step analytic framework is employed (see Coffman et al., 2011). These steps include (1) defining the causal effects, (2) estimation of participant propensity to receive different program levels, (3) calculation and application of inverse probability weights to account for selection effects, (4) evaluation of the balance between program levels, and (5) outcome analyses of the impact of different program levels on ever using prescription opioids for nonmedical purposes. Overall missingness was low, and the average missingness of an item was about 10.0% (SD=9.7%). Multiple imputation was used to account for any missing data (STATA MI mvn; Little & Rubin, 2002; Royston, 2004; Schafer & Graham, 2002). This procedure uses an iterative Markov chain Monte Carlo (MCMC) method to impute missing values using a joint modeling approach under a multivariate normal model. The mvn approach uses estimates from the EM algorithm as starting values for the MCMC procedure. Twenty imputations were obtained and each imputation was drawn after a burn-in period of 100 iterations. The mvn procedure applied to handle missing data allowed for complete data analysis for both the propensity models and the outcome analysis.
Defining Casual Effects. The causal effects are defined using marginal structural models, which are models for potential outcomes (Robins, 2001). For the first three research questions, let \( s \) denote receipt of the school program and \( f \) denote receipt of the family program. The potential outcomes are denoted at \( Y(s, f) \): \( Y(0,0) \) if the youth did not receive either the school or family program, \( Y(1,0) \) if the youth received the school program, but not the family program, \( Y(1,1) \) if the youth received the school and family program. Thus, \( Y(0,1) \) does not exist. The causal effects corresponding to research questions 1-3 are (i) the effect of receiving the school program versus not receiving the school program \( E[Y(1,0) - Y(0,0)] \), (ii) the effect of receiving the school program and receiving the family program versus not receiving either program \( E[Y(1,1) - Y(0,0)] \), and (iii) the effect of receiving the school and family program versus receiving only the school program \( E[Y(1,1) - Y(1,0)] \).

The marginal structural model for the potential outcomes is given as:

\[
E[Y_{ij}(s, f)] = \beta_0 + \beta_1 s + \beta_2 s f
\]

Thus, the marginal structural model specifies that for those who did not receive either program, \( E[Y(0,0)] = \beta_0 \) for those receiving both programs, \( E[Y(1,1)] = \beta_0 + \beta_1 + \beta_2 \), and for those receiving the school program, but not SFP, \( E[Y(1,0)] = \beta_0 + \beta_1 \).

Thus, the causal contrasts given in Equations 1-3 are equal to:

1. \( (\beta_0 + \beta_1) - \beta_0 = \beta_1 \)
2. \( (\beta_0 + \beta_1 + \beta_2) - \beta_0 = \beta_1 + \beta_2 \)
3. \( (\beta_0 + \beta_1 + \beta_2) - (\beta_0 + \beta_1) = \beta_2 \)
Note that by leaving out the main effect for the family program, there is a monotonic function because $E[Y(0,1)] = \beta_0 = E[Y(0,0)]$. In other word, participants could not receive the family program if they did not receive a school program.

For research questions 4-6, again let $s$ denote the school program, but now rather than $s = 1$ or 0, $s$ takes on the following values: $s = 0$ if the youth did not receive any school program, $s = 1$ if the youth received Life Skills, $s = 2$ if the youth received All Stars, $s = 3$ if the youth received Project Alert. As before, $f$ denotes the family program and equals 1 if the youth received SFP and 0 otherwise. Thus, the potential outcomes are $Y(0,0)$ if the youth did not receive any of the three school programs or the family program, $Y(1,0)$ if the youth received Life Skills Training and did not receive the SFP 10-14, $Y(1,1)$ if youth received Life Skills Training and received the SFP 10-14 versus not receiving either program $Y(1,0)$, the effect of receiving the Life Skills Training and receiving the SFP 10-14 versus not receiving either program $E[Y(1,1) - Y(0,0)]$, the effect of receiving the Life Skills Training and SFP 10-14 versus receiving only the school program $E[Y(1,1) - Y(1,0)]$ (Research Question Grouping 4), the effect of receiving the All Stars versus not receiving the school program $E[Y(2,0) - Y(0,0)]$, the effect of receiving All Stars and receiving SFP 10-14 versus not receiving either program $E[Y(2,1) - Y(0,0)]$, the effect of receiving All Stars and SFP 10-14 versus receiving only the school program $E[Y(2,1) - Y(2,0)]$ (Research Question Grouping
5), (6) the effect of receiving Project Alert versus not receiving the school program \( E[Y(3,0) - Y(0,0)] \), the effect of receiving Project Alert and receiving SFP 10-14 versus not receiving either program \( E[Y(3,1) - Y(0,0)] \), the effect of receiving Project Alert and SFP 10-14 versus receiving only the school program \( E[Y(3,1) - Y(3,0)] \) (Research Question Grouping 6). The marginal structural model for the potential outcomes is given as:

\[
E[Y_{ij}(s, f)] = \beta_0 + \beta_1 l + \beta_2 a + \beta_3 p + \beta_4 lf + \beta_5 af + \beta_6 p
\]

Where \( l, a, \text{and } p \) are dummy variables and \( l = 1 \) if the youth received Life Skills and 0 otherwise, \( a = 1 \) if the youth received All Stars and 0 otherwise, and \( p = 1 \) if the youth received Project Alert and 0 otherwise. Thus, the causal effect given in Equations 4-12 are equal to:

4. \((\beta_0 + \beta_1) - \beta_0 = \beta_1\)
5. \((\beta_0 + \beta_1 + \beta_4) - \beta_0 = \beta_1 + \beta_4\)
6. \((\beta_0 + \beta_1 + \beta_4) - (\beta_0 + \beta_1) = \beta_4\)
7. \((\beta_0 + \beta_2) - \beta_0 = \beta_2\)
8. \((\beta_0 + \beta_2 + \beta_5) - \beta_0 = \beta_2 + \beta_5\)
9. \((\beta_0 + \beta_2 + \beta_5) - (\beta_0 + \beta_2) = \beta_5\)
10. \((\beta_0 + \beta_3) - \beta_0 = \beta_3\)
11. \((\beta_0 + \beta_3 + \beta_6) - \beta_0 = \beta_3 + \beta_6\)
12. \((\beta_0 + \beta_3 + \beta_6) - (\beta_0 + \beta_3) = \beta_6\)

Because marginal structural models are models for the potential outcomes and not all the potential outcomes are observed, they cannot be estimated without further assumptions. Specifically, to estimate these models the assumption is made that there are no unaccounted for
confounders influencing receipt of either the school or family programs, and thus, the causal
effects are estimated using inverse probability weighted models for the observed outcomes.

**Propensity Score Estimation Process.** Within this project, two sets of propensity scores
are estimated. Using multinomial logistic models, the propensity a person receives—(1) no
program, (2) the school program, and (3) the school and family program together, is estimated
using a multinomial logistic regression. Because communities voluntarily picked one of the three
offered school programs, a second set of propensity scores is then estimated for receipt of the
different school-based programs also using a multinomial regression (Tchernis, Horvitz-Lennon,
& Normand, 2005). Both of these analyses were carried out using the GLIMMIX procedure in
SAS 9.1 (Littell, 2006) that allows for specification of a link function, which for multinomial
logistic and count data estimated here is log. This procedure also estimates error terms for non-
normally distributed dependent variables. The propensity models to estimate these scores employ
confounders across participant, organizational, infrastructure and community levels to predict
program receipt and meet the stable unit treatment value assumption (SUTVA; described above).
In order to test whether the logit link was appropriate, the Hinkley test was employed (Hinkley,
1985). This test includes the logit propensity score squared as a covariate in the propensity
model to test whether it is significantly related to the treatment condition in the presence of the
other confounders.

**Inverse Probability of Treatment Weight Calculation.** Next the inverse probability
weights for the combination of school program (IPW_s) and family programming (IPW_f) actually
received by each participant are calculated. The IPWs are similar to survey weights and allow us
to make adjustments to the sample data to account for selection effects affecting both school and
family program receipt by up-weighting those who are underrepresented and down weighting
those who are over represented (Hirano & Imbens, 2005). When modeling multiple variables—such as the two types of program receipt considered here—the product of the variables’ weights is used (Robins et al., 2000).

Let \( \hat{\pi}_{s0} \) be the estimated propensity to be in the control (i.e., no school program), and let \( \hat{\pi}_{s1} \) be the estimated propensity to be in any school program, then for youth in the control, \( w_{ts} = \frac{1}{\hat{\pi}_{s0}} \) and if the youth is in any school program then \( w_{ts} = \frac{1}{\hat{\pi}_{s1}} \). Next, let \( \hat{\pi}_{f0} \) be the estimated propensity to not receive the family program and \( \hat{\pi}_{f1} \) be the estimated propensity to receive the family program. For youth who receive the family program, \( w_{tf} = \frac{1}{\hat{\pi}_{f1}} \) and for youth who do not receive it, \( w_{tf} = \frac{1}{\hat{\pi}_{f0}} \). The product, \( w_{ts} \ast w_{tf} \), of the weights for school and family program receipt are used for addressing research questions 1-3, The same weights for family program receipt are used to address research question 4-6, but the weights for program receipt of the school program are different. Let \( \hat{\pi}_{l} \) be the estimated propensity of receiving Life Skills Training, \( \hat{\pi}_{a} \) the estimated propensity of receiving All Stars, and \( \hat{\pi}_{p} \) the estimated propensity of receiving Project Alert. For youth who receive Life Skills, \( w_{tl} = \frac{1}{\hat{\pi}_{l}} \). For youth who receive All Stars, \( w_{ta} = \frac{1}{\hat{\pi}_{a}} \). For youth who receive Life Skills, \( w_{tp} = \frac{1}{\hat{\pi}_{p}} \). The product, \( w_{ts} \ast w_{tf} \) is the weight used for addressing research questions 4-6.

**Balance Evaluation.** Next the balance of the different groups is evaluated before and after weighting to ascertain whether the adjustment using the IPWs successfully balanced the different groups. Balance was evaluated using standardized mean differences. Group overlap was also evaluated by examining boxplots of the distributions of the logit propensities by school and family program.
**Outcome Analysis.** The fifth step evaluates how receiving different amounts of programming impacts participant outcomes using the IPWs. In this case, prescription opioid misuse is evaluated in terms of receipt of the school and family program as well as by each school program. To evaluate the effect of differential program receipt, I constructed two logistic models to examine differences between program receipt using the IPW estimation method.

Model 1 (Questions 1-3):

\[
\text{logit}[PR(Y)] = \beta_0 + \beta_1 s + \beta_3 sf
\]

Model 2 (Questions 4-6):

\[
\text{logit}[PR(Y)] = \beta_0 + \beta_1 l + \beta_2 a + \beta_3 p + \beta_4 lf + \beta_5 af + \beta_6 pf
\]

For Model 1, \(\beta_1\) is the effect of receiving either no programs vs. the school program, and \(\beta_2\) is the effect of receiving the family program in addition to the school program. For model 2, \(\beta_1\) is the effect of receiving Life Skills Training vs. not, \(\beta_2\) is the effect of receiving All Stars vs. not, \(\beta_3\) is the effect of receiving Project Alert vs. not, \(\beta_4\) is the effect of receiving SFP in addition to Life Skills, \(\beta_5\) is the effect of receiving SFP in addition to All Stars, and \(\beta_6\) is the effect of receiving SFP in addition to Project Alert. Thus the IPWs are employed to meet the assumption that no confounders are unaccounted for in the outcome analysis; these \(\beta\)'s, which correspond to those in the marginal structural models, can be interpreted as causal effects.

The outcome model, which is fit using the PROC GLIMMIX procedure, includes a binary outcome measure of whether youth had ever misused prescription opioids. PROC GLIMMIX allows a weighting function that may be employed to include the IPWs in the model and provides robust standard errors. This procedure allows for the inclusion of the two-level nested design of the model, with individuals nested within communities (Littell, 2006).

**Sensitivity Analysis.** In order to account for sampling error assumed to be present in our analyses and because the ICER inequality is probabilistic, a measure of uncertainty is needed to
evaluate the variability of the estimates. This uncertainty can be gauged with a bootstrapping approach that entails drawing numerous subsamples from the full data to estimate variation in estimates (Briggs, 1999). One advantage of using bootstrapping within CEAs of prevention programs is that error variation—due to sampling—does not rely on any distributional assumption for the outcomes of interest. This project employs STATA’s bootstrapping procedure that samples the full data 1000 times to create confidence intervals around the ICER.

**Threshold Analysis.** In order to provide context for the ICERs, a threshold analysis was carried out. Threshold analyses consider current willingness to pay estimates for a change in a specific outcome and compares a program’s ICER to determine if the cost of changing a specific outcome is above or below that threshold (Briggs, Sculpher, & Buxton, 1994; Drummond, 2005). By doing this, the absolute efficiency may be assessed. Specifically, while calculation of the ICERs allows for relative comparisons of different programs’ productive efficiency, a Willingness to Pay (WTP) threshold provides an absolute metric around which to compare program efficiency. There are a variety of methods for estimating individuals’ willingness to pay. Among these include estimates derived from cost-of-illness analyses (Drummond, 2005). As this analysis is estimating PROSPER’s cost-effectiveness to prevent prescription opioid misuse, recent estimates of the societal costs of prescription opioid misuse were considered and a WTP threshold was calculated.

Recent analyses have placed the cost of prescription misuse at between $53.2 and $55.7 billion annually. An estimated 12.5 million individuals reported using prescription opioids for nonmedical purposes with 13.6% meeting the DSM-IV criteria for abuse or dependence (Birnbaum et al., 2011; R. N. Hansen, Oster, Edelsberg, Woody, & Sullivan, 2011). This translates into an average societal cost of $4,132 per opioid misuser per year. As stated above,
the average course of misuse for this age group (late adolescence and early adulthood) is 2.17 years (Catalano, White, Fleming, & Haggerty, 2011). Based upon this previous work, youth who misuse prescription opioids cost society an estimated $8,900.

This estimate serves as the basis for our Willingness to Pay threshold, where allocating less than the cost of an opioid misuser to preventing this misuse is an economically efficient decision. This is a highly conservative estimate of the cost of a youth misuser, as it is based on a national average that ranges across the lifespan. In particular, the cost of youth misusers account for a disproportion of societal costs as youth health costs (driving, injury), lost productivity (academic underachievement, dropout) and criminal justice costs are generally much greater (Heckman, 2006; Klietz, Borduin, & Schaeffer, 2010; O’Connell et al., 2009). Additionally, this estimate does not include a variety of downstream and intangible costs (estimating only substance abuse treatment, medical complications, productivity loss and criminal justice costs). By using a more conservative estimate, researchers can reduce the likelihood a program will be deemed cost-effective when it is not, which increases confidence in the findings when a program is below this threshold.
Chapter 3:

Results

The results are presented in six sections below. These sections consider the handling of missing data, the estimation of the two propensity models, the impact of inverse probability weighting, the findings from the effectiveness and cost-effectiveness analysis, and the results of the threshold analysis.

Handling Missing Data. Twenty imputed data sets were created to account for missingness in the data using the multiple imputation mvn procedure in STATA. Somewhat higher prevalence rates of prescription opioid misuse (in grades 9-11) were seen in the full imputed data compared to the observed data (Table 1). This may be the result of increased attrition among individuals who were suspended from their school where measurement took place, attending off-sight remedial schooling, vocational preparation, or those students who left the school permanently (Pirie et al., 1989; Siddiqui, Flay, & Hu, 1996).

Propensity Models. Propensity models were estimated for both the probability of participants being in the different school programs and the family program. Forty-one confounders were included in the logistic model of family program receipt and forty-two in the model of school program receipt (41 confounders + whether the participant attended the family session). Both models passed the Hinkley’s test described above and were found to have suitable overlap (Figure 1). Inverse probability weights were calculated and further diagnostics of balance were conducted. Unweighted and weighted standardized mean differences (SMD) between the control and treatment groups were calculated for each confounder in both propensity models. Weighting generally lowered or maintained the SMDs of each confounder and no
confounders had an absolute SMD above .2 when weighted, which is generally considered to be small (Cohen, 1992). Finding a small effect size across the confounders included in the model indicates that the different treatment groups are balanced and increases confidence in causal inferences. This balance is similar to the group equivalence achieved through randomization (Rosenbaum & Rubin, 1983).

**Impact of Inverse Probability Weighting.** Next, assessments of how weighting adjusted the outcome of interest were conducted for each condition. Descriptive analysis of the weighting procedure’s impact on prescription opioid misuse revealed differential changes based on a participant’s treatment group. Overall, weights altered prevalence rates by an absolute average of .38% (SD = .50%) and never more than 2%. The Life Skills Training and Project Alert programs’ prevalence rates changed minimally across time and the All Stars program’s prevalence rates changed by less than 2%. Minimal changes occurred in the school and SFP combined conditions or the control group. Figure 3 illustrates the impact of the inverse probability weighting on the prevalence rates of prescription opioid misuse for each school program delivered alone.

**Effectiveness Analyses.** The effectiveness of the different PROSPER program combinations were evaluated to assess the impact of the school and family program, compared to the control condition. Further, the impact of receiving the school and family programs together was compared to only the school program (Table 2). When aggregating the impact of the school programs (Research Questions 1-3), no significant differences in prescription opioid misuse were observed between the School-only or School and Family conditions compared to the control condition (Control v. Combined School Only: $OR=.986$; Control v. Combined School & SFP: $OR=.958$). Thus, we conducted further effectiveness analyses of the different program combinations, evaluating both the impact of each school program compared to the control group,
the impact of each school program and the SFP family program together compared to the control
group, as well as the incremental impact of each of the School and SFP program combinations
compared to the school program alone.

When the impact of each school program was evaluated individually, a richer picture was
revealed (Research Question Groups 4-6). Specifically, receipt of the Life Skills Training
Program led to a significantly reduced probability of youth having ever misused prescription
opioids by grade 11 compared to the control condition (Control v. Life Skills Alone: \( OR = .957 \)).
No significant differences were observed between the All Stars and Project Alert Programs
compared to the control condition (Control v. All Stars Alone: \( OR = .983 \); Control v. Project
Alert Alone: \( OR = .986 \)).

Receipt of the Life Skills and SFP together as well as receipt of All Stars and SFP
together revealed a significant difference from the control condition (Control v. Life Skills &
SFP Combined: \( OR = .910 \); Control v. All Stars & SFP Combined \( OR = .942 \)). Life Skills
Training in conjunction with SFP 10-14 was the most effective in reducing prescription opioid
misuse. The All Stars and SFP combination was the only school and family combination that was
significantly more effective when delivered together, compared to receiving just the school
program (All Stars alone vs. All Stars and SFP combined: \( OR = .927 \)).

When observing the impact of the different program combinations, it should be noted that
SFP may not simply provide an additive reduction in the likelihood of misuse, but instead may
interact differently with each school program. For instance, while the incremental reduction in
the odds ratios when SFP is added to All Stars and Life Skills training is about .04, the odds ratio
for Project Alert increases—although not significantly—with the addition of SFP. Similarly,
when the school and family programs are delivered together and then compared to receiving the same school program alone, the reduction in the likelihood of misuse is not consistent. Specifically, while those who receive SFP and All Stars together experience over a 7% decrease in their likelihood of misuse compared to those who only receive All Stars, those who received Life Skills Training and SFP receive less than a 5% reduction in their likelihood of misuse compared to those who only received Life Skills Training.

**Cost-Effectiveness Analysis.** ICERs were estimated and 95% confidence intervals were calculated using 1000 bootstrap replications to assess the variability of the estimate. Table 3 provides these ICERs (i.e., the difference of the average of the predicted probabilities for the treatment and comparison groups). The Life Skills Training program alone compared to the control group had the lowest ICER and thus is the program option with the greatest relative productive efficiency (ICER = $613). This may be interpreted as follows: it costs $613 (95% CI: $548-693) to prevent one youth from misusing prescription opioids before 12th grade who would otherwise have misused if they had not received the program.

Further analyses evaluated the cost-effectiveness of the school and family combinations to the school only condition (instead of the control condition). By changing the comparison group, the incremental cost-effectiveness of SFP in the context of each school program was evaluated (as opposed to the combined cost-effectiveness of the school and family programs versus the control). In other words, what is being tested is what is gained by receiving the SFP program in addition to a school program. In this context, we observe that while the Life Skills and SFP combination is the most cost effective compared to the control condition, this is not the case when comparing the combined school and family conditions to the school-only conditions. Instead, the lowest ICER when considering the added impact of the family program on those
already receiving the school program was the All Stars and SFP 10-14 combination ($6,299; 95% CI: $5,368-7,452).

**Threshold Analysis.** The threshold analysis allowed for the assessment of the absolute efficiency of the different program combinations. To illustrate this, the ICERs for each program are plotted against a WTP threshold of $7,700. This threshold represents the societal WTP estimate described in the methods section above ($8,900) discounted across five years at a standard rate of 3% (Russell et al., 1996). Thus this threshold approximates a societal WTP to prevent a future case of youth prescription opioid misuse. In other words, if the ICER is less than this societal WTP, then it is more efficient to allocate the resources to program delivery versus doing nothing and allowing the case of opioid misuse to take its course.

Two threshold analyses were carried out, one that compared the ICERs of the program combinations to the control condition and one analysis that compared the combined school and family conditions to the school-only conditions. Figure 4 plots the ICERs of the school-only and combined school and family conditions compared to the control conditions. Figure 5 plots the ICERs of the combined school and family program conditions compared to the School-only condition. The mean ICERs are plotted with the program cost along the y-axis and the program’s incremental effectiveness along the x-axis. These two pieces of information allow for the estimation of the mean ICER, but do not describe the uncertainty inherent in this estimate. The bootstrapping procedure described above provides a 95% confidence interval to estimate this uncertainty and is also included in the threshold analyses. To be considered cost effective from a societal perspective, the ICERs confidence interval cannot cross the threshold. If the 95% confidence interval of a program combination does not cross the WTP threshold, then it is likely
that it would be more efficient to allocate societal resources to that programming option than to allow those individuals to misuse prescription opioids.

Looking at Figure 4, the mean of each of the school-based programs alone were below the WTP threshold for prescription opioid misuse and none of the school-only ICER confidence intervals crossed the threshold. Despite not crossing the WTP threshold, Life Skills was the only school program that when delivered alone significantly reduced misuse compared to the control group. Thus, the Life Skills Training program would be considered a cost effective approach for reducing prescription opioid misuse. Further, when compared to the control group, individuals who received SFP as well as either All Stars or Life Skills Training were both below the WTP threshold. In the context of the effectiveness analysis where both Life Skills and All Stars significantly reduce misuse, both of these would be cost-effective allocations of societal resources. In the context of the above cost-effectiveness analysis, where the Life Skills and SFP combination has a lower ICER than the All Stars and SFP combination, we can infer that the most efficient allocation of societal money would be to invest in the combined delivery of the Life Skills and SFP programs.

Looking at Figure 5, the mean ICER for both the combined Life Skills and SFP condition compared to Life Skills-only condition and the All Stars and SFP condition compared to receiving only All Stars are below the WTP threshold. Of the two conditions, only the confidence interval of the All Stars and SFP condition did not cross the WTP threshold. In the context of the effectiveness analysis, adding SFP to the All Stars program instead of delivering the All Stars program alone led to the greatest reduction in the likelihood of misuse compared to adding SFP to either of the other school programs. Similarly, driven by the larger incremental gain attained by SFP’s addition to All Stars over the other programs, the ICER for the All Stars
and SFP condition was the lowest compared to the incremental gain from adding SFP to Life Skills or Project Alert. In this context, it can be inferred that it is a more efficient use of societal resources to deliver All Stars and SFP together then to deliver the All Stars program by itself.
Chapter 4:

Discussion

The objective of this project was to increase the capacity of prevention scientists to examine the efficiency of evidence-based prevention programs delivered in real-world contexts. This work applied the potential outcomes framework and employed marginal structural models to estimate program effectiveness, and it employed CEA and threshold analyses to estimate the relative and absolute cost effectiveness of EBPI combinations delivered within the PROSPER trial. This section discusses the value of propensity and marginal structural models for evaluating real-world prevention as well as the results from the effectiveness, cost-effectiveness and threshold analyses. Additionally, I explore how these results may be used to inform decision making around EBPI delivery, providing three possible scenarios below.

As discussed above, evaluating the effectiveness and efficiency of EBPIs within real-world settings is hindered by the need to both draw strong causal inferences about program impact and maintain study generalizability. In this particular context, a community’s choice to adopt and a participant’s decision to receive EBPIs are important factors that influence the success of real-world prevention efforts. Methods for strengthening causal inference about intervention impact, such as randomization, mask these factors and obscure our understanding of how programs will actually function when used by local communities. This work illustrates how propensity and marginal structural models can allow researchers to run dissemination trials that mimic real-world delivery while still drawing causal inferences about program impact. Further, as many community prevention efforts offer multiple intervention components or programs, marginal structural models also allow researchers to assess the numerous confounders that lead
to differential receipt of services. Thus, this approach allows researchers to better understand how to increase the efficiency of prevention efforts. In particular, prevention systems—such as PROSPER, Communities that Care, or Getting to Outcomes—support local prevention efforts to deliver multiple EBPIs (Hawkins, 1992; Spoth et al., 2004; Wandersman, 2000). As such this approach could be used to explore the impact of different program combinations delivered within these systems.

**Effectiveness and Relative Efficiency.** The results of the effectiveness analysis illustrate the capacity of evidence-based programs to reduce prescription opioid misuse. Additionally, these results indicate the potential for family-based prevention programs to provide an added benefit to school-based programs, but this effect can vary depending on the school program. For instance, only one school program when used alone within the PROSPER trial—Life Skills Training—significantly reduced the likelihood that a youth will misuse prescription opioids. While All Stars alone did not significantly reduce misuse, together with SFP the programs significantly reduced misuse. In contrast, the interaction of Project Alert and SFP did not significantly change the likelihood of opioid misuse.

When assessing the cost-effectiveness of the different program combinations, the estimates reveal that the Life Skills Training program alone is the most cost-effective relative to the other program combinations. Further, of the six possible intervention options (i.e., each school program with or without SFP), Life Skills was the most cost-effective. This finding replicates previous evaluations illustrating the effectiveness of the Life Skills Training program to reduce prescription drug misuse more generally (Spoth, Trudeau, Shin, & Redmond, 2008). These results provide evidence that the Life Skills Program, with or without SFP, is the most productively efficient of all the PROSPER program combinations for preventing prescription
opioid misuse. It is possible that for other outcomes such as binge drinking or tobacco use, different program combinations may be more efficient. CEA allows for targeted evaluations of program combinations’ impact on specific outcomes, which represents both a strength and weakness of this approach.

**Threshold Analysis and Absolute Efficiency.** Threshold analyses of each program combination’s ICER can provide an estimate of the absolute cost-effectiveness of the PROSPER programs. Each program-combination found significant in the effectiveness analysis was below the WTP threshold. Based upon these analyses, and as depicted in Figures 4 and 5, when the school programs in the PROSPER trial were delivered alone and compared to the control group they were all below the WTP threshold—although Life Skills is the only school program that when delivered alone is below the threshold and significantly reduces misuse. Similarly, both the All Stars & SFP as well as the Life Skills & SFP combinations were each efficient investments compared to the control condition. Compared to the school programs alone, only those that were delivering All Stars would significantly increase the efficiency of their prevention effort by investing in the delivery of SFP; although those delivering Life Skills also would increase their effectiveness by adding implementation of SFP.

**Approaches for Estimating the Efficiency of Evidence-Based Programming.** This work demonstrates the utility of employing propensity and marginal structural models within cost-effectiveness analyses for estimating the real-world impact of prevention efforts. Specifically, this analysis illustrates the feasibility of applying the potential outcomes framework in estimating inverse probability weights capable of balancing the different program combinations. Further, the results illustrate the capacity to employ these weights within a CEA of large-scale, multi-program dissemination trials.
Analytic Assumptions. To apply this work to future implementations of programs within the PROSPER prevention system, multiple assumptions must be met. First, the program must be delivered with a similar level of implementation quality as measured by program fidelity and participant engagement. It is reasonable to assume such quality can be obtained within PROSPER and sustained over time, as demonstrated by previous studies of PROSPER evaluating these two constructs across a six-year period (Spoth, Guyll, et al., 2011). A second assumption is that, when implemented in a new setting, adopters should not have any novel predisposition to adopt one program over another that was not included in the propensity models of the current study. Specifically, while the PROSPER team members’ and school administrators’ interest in and knowledge about the programs was included in the propensity models, if some new factor changes this knowledge or awareness substantially, it could result in a new programming environment with different dynamics (e.g., adopters learn a program is no longer considered evidence-based). This assumption is reasonable for the All Stars and Life Skills Training programs, although it may not continue to be true for the Project Alert program in light of recent findings of low effectiveness (e.g., Ringwalt, Clark, Hanley, Shamblen, & Flewelling, 2009; St. Pierre, Osgood, Mincemoyer, Kaltreider, & Kauh, 2005).

The Three Decision Makers. This work provided multiple pieces of information that could be useful for individuals seeking to implement prevention efforts focusing specifically on prescription opioid misuse. Consider the perspectives of a funder, a researcher, and a local prevention team interested in prevention of youth prescription opioid misuse.

The Funder: A funder may be interested in getting the most “bang for her buck” and wishes to know what is the least amount of money she can pay to prevent a case of prescription opioid misuse in youth. Based upon these results, the Life Skills Training program alone has the
smallest incremental cost to prevent a case of opioid misuse (ICER = $613). This option would be most attractive to a funder looking for the most efficient program, but the combined Life Skills & SFP program option would be most attractive to a funder seeking to have the greatest reduction in prescription opioid misuse.

The Researcher: Alternatively, a researcher may wish to identify the most effective program combination delivered in the PROSPER trial that can prevent opioid misuse and then may wish to know this option’s incremental cost to prevent a single case. Based on these findings, the Life Skills Training and SFP programs together are the most effective combination. Specifically, the incremental cost to prevent a case of prescription opioid misuse for this program option ranges between $3,525- $4,393.

The Local Prevention Team: Finally, a local prevention team may already be delivering a school-based prevention program and wish to know whether it would be cost-effective to offer SFP in addition to the school program. Based on these analyses, the team would have a better understanding of the cost-effectiveness of different program combinations. If the prevention team was already delivering the All Stars program, it would be cost-effective to offer SFP 10-14. If the team was delivering Life Skill Training or Project Alert, they may not wish to offer SFP 10-14 if their goal is to reduce prescription opioid misuse in a cost-effective manner. This is because the marginal gain of delivering SFP would not be an efficient use of their resources. Instead, assuming they already possessed the capacity, a better investment would be to increase their delivery of Life Skills Training. It is important to note that if the team was interested in only what would be the most effective method of preventing misuse and they were already delivering Life Skills Training the results suggest that they begin delivery of SFP—as this was
the most effective combination. Further, if they were not delivering any prevention programs, the most efficient decision would be to deliver both Life Skills Training and SFP together.

Ultimately, the main conclusion is that Life Skills and SFP delivered together is the most effective and cost-effective option when compared to delivering no program, but in very specific cases where Life Skills Training is already being delivered, the marginal gain in effectiveness may not be worth the substantial costs of providing the family program—when expanding delivery of Life Skills Training is an option. Specifically, if we compare the differences in the prevalence rates in 11th grade prescription opioid misuse for the control (20.42%), Life Skills-only (16.46%), and Life Skills and with SFP program combinations (11.19%), we see that the Life Skills program delivered alone reduced the prevalence rate of misuse by 3.96%. The Life Skills Training and SFP program together reduced the prevalence rate by 9.23% compared to the control group, but when compared to the Life Skills-only group, the marginal reduction in misuse from the Life Skills & SFP group is 5.27%. (Figure 6). The average cost to prevent a case of opioid misuse with only Life Skills Training is $613, but because of the relatively high cost of the SFP, the average cost to prevent a case with the combined Life Skills Training and SFP conditions is $3,959. Even though the incremental reduction in prevalence is greater for the Life Skills & SFP condition compared to the Life Skills-only condition (5.27% v. 3.96% respectively), this greater cost drives up the ICER and leads to the ICER being greater than the societal WTP threshold. A simple way of thinking about this dynamic is that maybe it costs less to achieve that first 4% prevalence reduction (possibly this reduction represents a subset of youth that are more receptive to the school program), and that the next 5.27% prevalence reduction consists of less receptive youth that require more comprehensive services. While this is most
likely an oversimplification, it may be useful for understanding the difference between what makes an effective versus an efficient prevention effort.

The fact that Life Skills does not gain as much from the combined delivery with SFP compared to All Stars appears to be largely due to the greater effectiveness of Life Skills to prevent prescription opioid misuse on its own (as compared to the All Stars program). As noted in previous work by Spoth et al., (2008), none of these programs have content in their curricula that specifically address prescription medication misuse, and the effectiveness of the programs is probably driven by targeting more general risk and protective factors. One such factor is parental monitoring and awareness of youth. Parent monitoring appears to be especially important for prescription opioid misuse both because parents are often the source of the opioids and low engagement itself has been linked to greater misuse. While all three school programs include increasing parental involvement within their logic models, it is unclear whether the potency of each programs’ strategies to engage parents is comparable. Perhaps the Life Skills program employs a more effective approach than the others. Another possibility is that Life Skills is more effective because more sessions are delivered than in the other two curricula (Life Skills = 18 v. Project Alert = 11 and All Stars = 13 sessions).

**Limitations.** CEAs provide a useful analytic technique for assessing the productive efficiency of EBPIs. In particular, they are ideal for evaluations of a single outcome of interest but are limited in their ability to assess the total impact of a prevention effort. To accomplish this, all program effects must be included in the analysis and the value of those effects must be assessed with a common metric (e.g., monetary value, health utilities). While this demonstration could be used to inform only those interested in cost-effective prescription opioid prevention programs, it is unlikely that those building comprehensive substance abuse prevention efforts
would find a single-outcome CEA adequate. Thus, it is suggested that multiple outcomes be assessed within CEAs of real-world prevention efforts.

A second limitation of these analyses is that the use of multiple imputation to account for missing data in this trial most likely increased the uncertainty in the ICER confidence intervals. While it is unlikely that this uncertainty led to any of the program combinations being above the WTP threshold, increased variability may decrease the estimates’ usefulness for planning in health service settings. While this is unfortunate, the choice to use multiple imputation over a FIML approach was made to account for attrition within the sample that may have led to an underestimation of actual prevalence of prescription opioid misuse. Such an underestimation would have most likely been more detrimental to the estimates because it could have decreased the generalizability of the findings to real-world settings—the main impetus for the demonstration of this method.

**Future Directions.** One area of future inquiry includes evaluations that assess whether there is a program component in Life Skills that is redundant with SFP, but that the All Stars program lacks, which leads to this greater potency when SFP is combined with All Stars (but not with Life Skills Training). Such evaluations could be achieved through program optimization techniques such as the Multiphase Optimization Strategy (MOST), which employs fractional factorial designs to evaluate the impact of specific program components (Collins, Murphy, & Strecher, 2007).

In light of the targeted nature of this demonstration, a CEA of multiple outcomes would most likely provide a more complete understanding of programs’ productive efficiency within the PROSPER prevention system. Multiple logistic and analytic issues arise in this work. This
includes the need to develop additional WTP estimates that can be used for threshold analyses of other outcomes. Another challenge is how to interpret multiple related outcomes (e.g., other substance abuse outcomes) that may overlap in their societal impact. In particular, the larger PROSPER trial has demonstrated significant reductions in multiple forms of substance abuse as well as delinquency and criminal activity. While some of the different program combinations may not be cost-effective solutions for reducing prescription opioid misuse, the numerous positive benefits of PROSPER programming is likely to illustrate that the investment in school and family-based EBPIs is an efficient solution to reducing youth substance abuse and violence.

**Conclusion.** The method demonstrated here provides an approach for increasing the relevance of prevention impact analyses by allowing researchers to better contextualize program effectiveness in real-world settings in terms of program costs. Specifically, this analytic approach provides a more refined approach for understanding the impact of combining interventions and may expedite the development of more efficient prevention efforts. Further, analyses such as these can provide important information to not only researchers, but to multiple stakeholders who seek to translate prevention science into practice.
Chapter 5:

References


Figure 1: Overlap of Logit Propensities
Figure 2: Standardized Mean Differences of Confounders Before & After Inverse Probability Weighting. Each line represents one of the confounders included in the propensity model.

- **SFP Attendance**
  - Unweighted vs. Weighted
  - Standardized Mean Differences

- **Life Skills Training**
  - Unweighted vs. Weighted
  - Standardized Mean Differences

- **All Stars**
  - Unweighted vs. Weighted
  - Standardized Mean Differences

- **Project Alert**
  - Unweighted vs. Weighted
  - Standardized Mean Differences
Table 1: Prevalence Rates of Prescription Opioid Misuse in Observed, Imputed and Weighted Data

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<th>Project Alert</th>
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Note: LST = Life Skills Training; SFP = Strengthening Families Program 10-14
Figure 3: Impact of Inverse Probability Weights on Prevalence Rates of Prescription Opioid Misuse by School Program
Table 2: Effectiveness of PROSPER Programs with Inverse Probability Weighting

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Note: LST = Life Skills Training; SFP = Strengthening Families Program 10-14
*p<.05
Table 3: Incremental Effectiveness and Cost-Effectiveness of PROSPER Programs

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<td>$1,619 (1.281,2,152)&lt;sup&gt;T&lt;/sup&gt;</td>
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<td><strong>School &amp; Family Program Versus School Group</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>School + SFP v. School</td>
<td>1.8% (1.3, 2.5%)</td>
<td>$20,498 (15,071, 29,546)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All Stars + SFP v. All Stars</td>
<td>6.0% (2.0, 7.0%)</td>
<td>$6,299 (5,368, 7,452)&lt;sup&gt;T&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life Skills + SFP v. Life Skills</td>
<td>5.1% (4.0, 6.3%)</td>
<td>$7,395 (5,953, 9,359)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Project Alert + SFP v. Project Alert</td>
<td>-3.1% (-4.1, -2.0%)</td>
<td>-$12,274 (-17,203, -7,346)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>A</sup> = The change in predicted probability that a youth would report ever misusing prescription opioids before 11<sup>th</sup> grade

<sup>B</sup> = The incremental cost of preventing a youth from ever misusing prescription opioids before 11<sup>th</sup> grade

<sup>T</sup> = Below WTP threshold for preventing 1 youth from ever misusing prescription opioids before 11<sup>th</sup> grade

Note: LST = Life Skills Training; SFP = Strengthening Families Program 10-14, CI = 95% Confidence Interval
Figure 4: Incremental Cost-Effectiveness of School Programs & SFP 10-14 vs. Control Condition

Note: ICER = Incremental Cost Effectiveness Ratio; WTP = Willingness to Pay Threshold; SFP = Strengthening Families Program
Figure 5: Incremental Cost-Effectiveness of School Programs & SFP 10-14 vs, School Program Alone

Note: ICER = Incremental Cost Effectiveness Ratio; WTP = Willingness to Pay Threshold; SFP = Strengthening Families Program
EDUCATION

**Ph.D**
The Pennsylvania State University, State College, PA (August 2012)
Human Development & Family Studies

**M.S.**
The Pennsylvania State University, State College, PA (May 2010)
Human Development & Family Studies

**B.S.**
James Madison University, Harrisonburg, VA (May, 2008)
Psychology Minor: Sociology (*Magna Cum Laude*)

HONORS AND AWARDS

- **2010-2011** Winner of the Sixth Annual Sloboda & Bukowski SPR Cup Research Competition
- **2010-2012** NIDA Prevention and Methodology Pre-Doctoral Fellowship (T32 DA 0176)
- **2010-2011** Research Society on Alcoholism’s Student Merit Award
- **2007-2008** American Academy of Political & Social Science Junior Fellow

RESEARCH GRANTS AND CONTRACTS

- *NIDA/DESPR Early Career Investigator Travel Awards*. National Institute on Drug Abuse’s Division of Epidemiology, Services and Prevention Research. May, 2011. $1,500

PUBLICATIONS


