Published in final edited form as:

Prev Med. 2014 May ; 62: 71–77. doi:10.1016/j.ypmed.2014.01.029.

Can We Build an Efficient Response to the Prescription Drug Abuse Epidemic? Assessing the Cost Effectiveness of Universal Prevention in the PROSPER Trial

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Abstract

Purpose—Prescription drug abuse has reached epidemic proportions. Nonmedical prescription opioid use carries increasingly high costs. Despite the need to cultivate efforts that are both effective and fiscally responsible, the cost-effectiveness of universal evidence-based-preventive-interventions (EBPIs) is rarely evaluated. This study explores the performance of these programs to reduce nonmedical prescription opioid use.

Methods—Sixth graders from twenty-eight rural public school districts in Iowa and Pennsylvania were blocked by size and geographic location and then randomly assigned to experimental or control conditions (2002-2010). Within the intervention communities, prevention teams selected a universal family and school program from a menu of EBPIs. All families were offered a family-based program in the 6th grade and received one of three school-based programs in 7th-grade. The effectiveness and cost-effectiveness of each school program by itself and with an additional family-based program was assessed using propensity and marginal structural models.

Results—This work demonstrates that universal school-based EBPIs can efficiently reduce nonmedical prescription opioid use. Further, findings illustrate that family-based programs may be used to enhance the cost-effectiveness of school-based programs.

Conclusions—Universal EBPIs can effectively and efficiently reduce nonmedical prescription opioid use should be further considered when developing comprehensive responses to this growing national crisis.

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Prescription drug abuse has reached epidemic proportions in the United States with youth populations being especially vulnerable to abuse and addiction (CDC, 2011; Fischer et al., 2008; Havens, 2011; Hernandez and Nelson, 2010; Manchikanti and Singh, 2008; Maxwell, 2011; *ONDCP*, 2011;). At the center of this growing crisis are prescription opioids, with over 12 million Americans having used this pharmaceutical class for nonmedical purposes. Adolescent populations are particularly vulnerable to opioid misuse and abuse, with early initiation increasing the likelihood of future addiction (Compton and Volkow, 2006; McCabe, 2012, 2011, 2009; Meier, 2012). In turn, these nonmedical user are estimated to cost society over \$53 billion each year through their greater burden on health and service systems as well as increased rates of disability (Birnbaum et al., 2011; Coben et al., 2010; Hansen et al., 2011a; Johnston et al., 2010; SAMHSA, 2009).

The rise in nonmedical prescription opioid use poses a major threat to public health and many policy makers are seeking to craft practical responses (*ONDCP*, 2011). Unfortunately, devising cost-effective initiatives that do not compromise pain management practices remains difficult (FDA, 2013; Fischer et al., 2008; Katz et al., 2007). Despite development of approaches for reducing misusers' access to prescription opioids (e.g., prescription-monitoring-systems, interdiction efforts), supply side methods are often resource intensive and may be difficult to effectively deploy during times of budgetary uncertainty. Instead policymakers may wish to engage more efficient solutions (Spath, 2011a). For instance, demand reduction approaches that prevent nonmedical use, especially in at-risk populations, may offer a more fiscally responsible option (Catalano, 2009; Currie, 2005; O'Connell et al., 2009; Spath, 2011b).

One such approach is the use of universal school and family evidence-based-preventive-interventions (EBPIs). Universal prevention programs¹ target a whole population group (e.g., school) that has not been identified based upon individual risk (e.g., prenatal care, childhood immunization; (Greenberg et al., 2001). For instance, universal school programs are offered to all students in a school and universal family programs can be offered to all families in community with no prior screening. These programs differ from other demand reduction approaches (e.g., public education and awareness campaigns) through their focus on reducing substance abuse risk (pro-abuse norms and expectations of use) and cultivating protective factors (refusal skills, social bonding, parental monitoring; (Hawkins et al., 1992; Kumpfer and Alvarado, 2003). Universal EBPIs are increasingly delivered within the context of formal prevention delivery and support systems that facilitate implementation and sustainability of prevention efforts (e.g., *PROSPER*, *Weed & Seed*, *Communities-that-Care*, *SPF-SIG*, *Getting-to-Outcomes*; (Crowley et al., 2012; Hawkins, 1992, 2009; Spath et al., 2004; Wandersman, 2000). Large demonstration trials, including the PROSPER study, have illustrated that EBPIs, delivered within these systems, represent a promising strategy for reducing nonmedical prescription opioid use (Aos et al., 2011, 2004; Guyll et al., 2011; Spath et al., 2007a, Under Review; Spath, 2006), but relatively little work has sought to evaluate these programs' capacity to efficiently reduce nonmedical prescription opioid use in everyday contexts (Spath et al., 2008). This lack of evaluation has contributed to

¹Not to be confused with universal precautions taken by prescribers to reduce the risk of misuse among patients (Gourlay and Heit, 2009)

universal EBPIs being largely overlooked and underutilized in recent federal and state responses.

Limited work in this area has in part resulted from data limitations and methodological uncertainty around how to model the complex selection effects that lead to individuals receiving preventive interventions in school and family health service settings. In order to better understand the capacity of universal prevention efforts to reduce nonmedical prescription opioid use, we demonstrate a methodological approach to evaluate the cost-effectiveness of receiving multiple preventive interventions within different service settings. Specifically, through the use of propensity and marginal structural models we are able to first model who receives different programs when they are delivered in actual service contexts and then use these models to assess the incremental cost-effectiveness of programs. This differs from previous work that has assessed universal prevention largely within tightly controlled research trials that may overestimate intervention impact when programs are translated to non-research contexts. We first evaluate the cost-effectiveness of three substance abuse school-based EBPIs to prevent nonmedical prescription opioid use (Life Skills Training, All Stars & Project Alert) delivered within the PROSPER delivery and support system. Next, the impact of a combined school and family-based programming approach is assessed for each of the three school programs with a family-based EBPI (SFP: 10-14). This work builds on current understanding of universal prevention programs' effectiveness and provides insight into their cost-effectiveness. Through these analyses we gauge the real-world performance of universal programs in order to identify cost-effective approaches for reducing this growing epidemic.

Methods

In order to evaluate the cost-effectiveness of the four universal EBPIs in actual service settings, propensity and marginal structural models were fitted within a cost-effectiveness analysis of the PROSPER dissemination trial.

Sample

The National Institute of Health funded PROSPER dissemination trial included 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 at or attending a college or university, and (4) the community could not be involved in other university-affiliated, youth-focused prevention initiatives. Communities were matched by geographic location and size; each pair of communities was randomized into intervention and control conditions by the principal investigators (Spoth et al., 2007b, 2004). Approximately half the sample comprised the control condition (N=5,292; Figure 1). Within the intervention communities, local prevention teams led by local cooperative extension agents and school officials selected a universal family and school program from a menu of EBPIs (Spoth et al., 2004). All families in intervention communities were offered the Strengthening Families 10-14 program (SFP:10-14) in the 6th grade, but not all families enrolled (N=827). In addition, all youth in the intervention communities (N=5,026) received

one of three school-based substance abuse programs in the 7th grade (All Stars (N=1,936), Life Skills Training (N=1,166) and Project Alert (N=1,924). Thus while the PROSPER participants were randomized to either intervention or control groups, the type of school intervention they received and whether they attended the family program was not randomized. Additional information about the different EBPIs may be found in Appendix 1. Program adherence was high for both school and family programs ($M = 90\%$; see (Spath et al., 2011). The participating universities' IRBs approved the study procedures before recruitment began.

Measurement

Estimates of Program Cost—The costs of the evidence-based prevention programs delivered within the PROSPER dissemination trial were estimated in an earlier prospective five-year cost analysis (Crowley et al., 2012). Opportunity costs were estimated from budgetary, sustainability, and volunteer-time data that tracked both expenditures from the parent grant and inputs from any outside sources. The cost to provide a school program to a single student was between \$9-\$27 and the average cost to provide the family program to a single family was between \$311-\$405. These costs included expenditures on curriculum and program supplies, facilitator time, family attendance incentives and volunteer/in-kind donation for programming.

Nonmedical Prescription Opioid Use—To evaluate youth nonmedical prescription opioid use, each participant was asked whether they had ever used prescription opioids for nonmedical purposes at the 6th grade pre-test (2002-2010) and at the end of each year through 12th grade [*Have you ever used Vicodin®, Codeine, Percocet or OxyContin® not prescribed by a doctor?*].

Analytic Approach

As described above, PROSPER participants were randomized at the community level to treatment groups. However, which school-based EBPI they received was chosen by each community's team and families chose whether to attend the evening family program. Thus, in order to estimate the benefits of receiving the different school programs as well as the benefits of receiving the school and family programs together, a multi-step analytic framework was employed. This included (1) estimation of participants' propensity to receive different programs, (2) fitting marginal structural models to estimate the impact of receiving different programs on ever using prescription opioids for non-medical purposes, (3) calculation of incremental cost-effectiveness ratios, and (4) threshold analyses to assess whether a program represents an efficient societal investment.

Propensity & Marginal Structural Models—Propensity and marginal structural models are well-established analytic tools used to improve causal inference when using observational data (Robins et al., 2000; Rosenbaum and Rubin, 1983). Propensity models were employed here to estimate the probability that an individual will receive each of the programs based upon a variety of prespecified covariates (See Appendix 1). Within this evaluation, we estimated individuals' probabilities of receiving seven possible outcomes (i.e., participants' propensity to receive either no program, one of the three school programs,

or one of the three school programs and the family program). These probabilities were then transformed into inverse probability weights—which may be used similarly to survey weights—to balance the different possible forms of treatment receipt on the confounders included in the propensity model. These weights were used to adjust marginal structural models, to estimate the effectiveness of the programs to reduce nonmedical prescription opioid use. PROC GLIMMIX was implemented to fit multi-level logistic models that accounted for the nested structure of the trial (i.e., participant nested within school, (Littell, 2006) Further description of the covariates that were included in the propensity models and how the propensity and marginal structural models were implemented may be accessed in Appendix 1 & 2.

Incremental Cost-Effectiveness Analysis—Next, the incremental cost-effectiveness ratios (ICERs) for different levels of program receipt were estimated (Figure 1). The numerator of an ICER is the difference in costs for treatment outcomes (e.g., school program versus control). The denominator of the ICER is the difference in the average effect sizes of the two interventions. ICERs were calculated for each program combination that significantly reduced nonmedical use compared to the control condition (at the $p < .05$ level). Statistical bootstrap techniques were employed to construct 95% confidence intervals around each ICER (using 1000 replications; (Briggs et al., 1997)

Threshold Analysis—Each ICER was considered relative to the societal cost of allowing youth to engage in nonmedical prescription opioid use (i.e., Willingness-to-Pay). Recent analyses have placed the cost of nonmedical prescription opioid use at between \$53.2 and \$55.7 billion annually. An estimated 12.5 million individuals reported using prescription opioids for non-medical purposes (Birnbaum et al., 2011; Hansen et al., 2011b). This translates into an approximate average societal cost of \$4,132 per nonmedical opioid user per year. The average course of nonmedical use for this age group (late adolescence and early adulthood) is 2.17 years (Catalano et al., 2011). Based upon this previous work, it can be estimated that youth who engage in nonmedical prescription opioid use cost society approximately \$8,966 per year. When discounted across the six years of program follow-up within the PROSPER trial, at a standard rate of 3%, this figure rounds to \$7,500 (Russell et al., 1996). This estimate serves as the basis for a Willingness-to-Pay (WTP) threshold, where allocating less than \$7,500 (i.e., the estimated societal cost of an adolescent or young adult nonmedical opioid user) to preventing a single case of nonmedical use is an economically efficient decision. In other words, if the 95% confidence interval of this ICER falls below this societal WTP, one could make a case that it is more efficient to allocate the resources toward prevention services versus doing nothing and allowing the case of nonmedical opioid use to take its course.

Results

Here we consider the results of the effectiveness, cost-effectiveness, and threshold analyses in order to ascertain the impact and efficiency of the three school programs with and without the family program compared to those youth in the control group. As presented in Table 1, there is increasing lifetime use of prescription opioids across adolescence with over 25% of seniors ever having used a prescription opioid that was not prescribed by a doctor.

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 (Table 2; incremental effect). Receipt of the Life Skills Training Program led to a significantly reduced probability of youth having ever used prescription opioids for nonmedical purposes by grade 12 compared to the control condition (Control v. Life Skills Alone: 3.9%-4.9% *reduction*). No significant differences were observed between the All Stars and Project Alert Programs compared to the control condition. Receipt of the Life Skills and SFP:10-14 programs together as well as receipt of the All Stars and SFP:10-14 programs together revealed a significant difference from the control condition (Control v. Life Skills & SFP: 10-14 Combined: 5.8%-10.5% *reduction*; Control v. All Stars & SFP:10-14 Combined: 6.8%-8.5% *reduction*). Life Skills Training in conjunction with SFP:10-14 was the most effective in reducing nonmedical prescription opioid use (Figure 2).

Cost-Effectiveness Analysis

Table 2 provides ICERs (i.e., the difference of the average of the predicted probabilities for the treatment and comparison groups) and their standard errors. 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). One may interpret this as a \$613 cost (95% CI: \$548-693) to prevent one youth from misusing prescription opioids before 12th grade who would otherwise have engaged in nonmedical use if they had not received the program.

Threshold Analysis

The Life Skills Training program was the only school program that when delivered alone significantly reduced nonmedical use compared to the control group. Thus, the Life Skills Training program alone would be considered a cost-effective approach for reducing nonmedical prescription opioid use. Further, when compared to the control group, individuals who received SFP:10-14 as well as either All Stars or Life Skills Training were both below the WTP threshold. Thus both Life Skills and All Stars when delivered with SFP:10-14 significantly reduce nonmedical use and would be cost-effective allocation of societal resources. When compared to each other, where the Life Skills and SFP:10-14 combination has a lower ICER than the All Stars and SFP:10-14 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:10-14 programs.

Discussion

Policy-makers and community leaders are actively searching for efficient responses to the growing prescription drug epidemic (FDA, 2013; Maxwell, 2011; ONDCP, 2011). In particular, due to prescription opioids' growing popularity among adolescents and young adults, it is vital that any coordinated strategy meets the needs of this vulnerable population. Without an effective approach for curbing nonmedical use, Federal agencies are being forced to restrict access to prescription opioids –at the cost of greater burden on suffering patients (Volkow, 2011). The present study builds on earlier reports universal EBPIs

implemented effectiveness and demonstrates that universal school-based EBPIs are capable of reducing nonmedical prescription opioid use by youth in a cost-effective manner and may supplement costly approaches to monitor and restrict access (Spoth et al., 2008; Spoth et al., 2008). Further, this evaluation reveals the potential of family-based EBPIs during early adolescence to enhance the efficiency of school-based programs. Thus, by employing propensity and marginal structural models we are able to leverage the unique data within the PROSPER trial to compare the impact of the different school programs and family programs.

In light of these findings, decision makers seeking to craft comprehensive responses to prescription drug abuse may wish to consider the potential value of broader evidence-based drug use prevention efforts that nurture healthy cognitions and behaviors by parents and youth. In particular, current estimates illustrate that nonmedical use is continuing to rise despite early efforts to stem the tide of abuse and now may be time to engage new options (ONDCP, 2011). This approach may reduce demand for tertiary approaches which while cost-effective may garner less public support (e.g., soboxone and methadone maintenance; Polsky et al., 2010).

By employing the analytic approach described above we can better understand universal prevention's cost-effectiveness, and these specific analyses reveal the value of intervening across ecological settings when targeting youth populations. Specifically, programs operating in school and family settings may be crucial to successful efforts. These results also emphasize that, like medical treatments, not all evidence-based programs are equivalent and that interventions that have met accepted standards of evidence (e.g., Blueprints) may not be cost-effective. Lastly, this work illustrates that different elements of a multifaceted response are not simply additive and may in fact interact in important ways. For instance, when the Life Skills Training and All Stars programs are delivered with the SFP:10-14 program their performance is enhanced. This is not true for the Project Alert program, which was not significantly better or worse at preventing nonmedical use when delivered with the SFP:10-14 program. Such unique interactions may also extend to efforts that combine prevention with medical treatment, interdiction and enforcement.

This evaluation sought to understand the cost-effectiveness of universal EBPIs specifically on preventing prescription opioid abuse. This is likely a dramatic underestimate of the total societal value from universal programs that are known to not only prevent other forms of substance abuse (e.g., alcohol, tobacco, methamphetamines; Gyll et al., 2011; Spoth et al., 2008b) but a variety of delinquent behaviors linked to long-term criminality and increased use of social service systems (Aos et al., 2011). Nevertheless, compared to approaches that aim to reduce nonmedical use that is already occurring (e.g., treatment), a prevention-oriented approach to nonmedical use may be especially well-suited for society's current needs. For instance, opioid addiction is generally considered a chronic illness and requires costly treatments that quickly overburden community service systems (McLellan, 2000). Consequently, even small reductions in those ever requiring treatment can save substantial public monies. Alternately, because of the important role of prescription opioids in pain management, interdiction and enforcement efforts may harm or stigmatize those with legitimate medical need. Universal prevention efforts that serve entire populations, targeting

risk and protective factors for nonmedical use, can offer society a means of protecting youth populations from nonmedical use while allowing those who are suffering access to the best possible therapies.

Limitations

A substantial body of literature has illustrated that—across settings—adequate capacity is essential for high-quality implementation of evidence-based programs and practices (e.g., hospital, school, clinical). It is increasingly advised that large-scale delivery of such efforts not be attempted without formal capacity building (Samet, 2001; Spoth et al., 2004; Wandersman, 2000). In particular, delivery of universal EBPIs without such support can lead to diminished impact and lower levels of program efficiency (Spoth et al., 2004). In response, substance abuse researchers working with youth populations have developed multiple support systems that can effectively cultivate and maintain such capacity (Dunworth et al., 1999; Hawkins, 1992; Spoth et al., 2004). To maximize the generalizability of these estimates, this study considers program impact when delivered within such a system (i.e., PROSPER; (Spoth et al., 2004). Thus these estimates are not applicable to attempts to deliver universal EBPIs without such support systems as both the costs and effectiveness are likely to differ.

A second limitation of this work pertains to the Willingness-to-Pay threshold based on recent cost-of-illness estimates of prescription opioid nonmedical use. These estimates consider the health and productivity outcomes of individuals misusing prescription opioids, but fail to capture many growing downstream costs (e.g., malpractice litigation, interdiction efforts). Additionally, as little contingent valuation work has sought to estimate Quality Adjusted Life Years (QALYs) for opioid misuse and none have estimated QALYs of nonmedical prescription opioid use within youth populations (Connock et al., 2007; Schackman et al., 2012). Consequently, these estimates most likely undervalue the total societal costs of nonmedical prescription opioid use. This in turn may have resulted in an overly conservative Willingness-to-Pay threshold. This lower threshold is unlikely to have influenced the inferences drawn from this study, as all programming options that significantly reduced nonmedical use were represented by ICERs well below the threshold. Thus this threshold should be updated as revised cost-of-illness estimates become available.

Lastly, it is possible that the control communities also had access to the programs implemented by the intervention communities. This may have led to potentially lower program effectiveness then observed within this evaluation and thus estimates of cost-effectiveness are likely conservative. Further research is needed to explore the cost-effectiveness of combining other substance abuse prevention programs, including those outside family and school settings.

Conclusion

With this work we seek to draw attention to the potential value of universal school- and family-based EBPIs as part of an efficient response to the growing prescription drug epidemic. Given the rapid changes in health care policy and the opportunities provided for prevention and health promotion services in The Affordable Care Act, the use of

community-based prevention services will expand and the evidence here indicates that if effective programs are used it can significantly reduce public and private cost (Koh and Sebelius, 2010). It is vital that future research evaluate the effectiveness and cost-effectiveness of these programs and policies in various US communities in order to truly craft the most efficient response.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This work was supported by grants from the National Institute for Drug Abuse including F32 DA034501 and R01 DA 013709 as well as P50-DA 010075 and T32 DA 17629

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Highlights

- We conducted a RCT of universal evidence-based-preventive-interventions (EBPIs)
- Evaluated the cost-effectiveness of EBPIs to prevent nonmedical prescription opioid use
- Universal school-based EBPIs can efficiently reduce nonmedical use through high school
- Adding a family-based program can enhance prevention cost-effectiveness
- Comprehensive responses to prescription drug misuse should consider universal EBPIs

Figure 1.
Study Participation Summary

Figure 2.
Decision Tree for Cost-Effectiveness Analysis

Figure 3.
Prevalence of nonmedical prescription opioid use among student receiving combined school and family programs

Table 1

Prevalence of Prescription Opioid Misuse Across Programming Options

	Control	All Stars	LST	Project Alert	All Stars + SFP	LST+SFP	10-14	Project Alert + SFP	10-14
6 th	0.5%	0.5%	0.7%	0.7%	1.5%	1.5%	0.8%	0.6%	
7 th	2.1%	2.3%	1.8%	2.0%	2.8%	2.8%	2.7%	3.7%	
8 th	4.2%	5.9%	3.4%	4.5%	4.7%	4.7%	3.1%	8.0%	
9 th	10.0%	10.8%	7.6%	10.2%	7.8%	7.8%	5.6%	14.8%	
10 th	15.0%	15.2%	12.1%	14.4%	11.5%	11.5%	7.7%	18.3%	
11 th	20.9%	21.1%	16.4%	19.4%	16.3%	16.3%	11.5%	22.9%	
12 th	25.9%	26.5%	20.2%	23.3%	19.6%	19.6%	16.3%	26.7%	

LST=Life Skills Training; SFP:10-14 =The Strengthening Families Program 10-14, Trial from 2002-2010

Table 2

Effectiveness and Cost-Effectiveness of Program Conditions Compared to No Universal Program

	Estimate	SE	df	t	p	Incremental Effect ^A	ICER ^B (CI)
School Program Versus Control Condition							
All Stars v. Control	-.010	.0	1	-	.4	1.7% (1.3, 2.1%)	--
		14	1	0.7	75		
			3	2			
Life Skills v. Control	-.053	.0	1	-	.0	-4.4% (-3.9, -4.9%)	\$613 (\$548, 693) ^T
		16	7	3.2	01		
			5	4			
Project Alert v. Control	-.023	0	8	-	.1	1.4% (0.1, 1.9%)	--
		15	2	1.4	46		
			7				
School & Family Program Versus Control Condition							
All Stars + SFP: 10-14 v. Control	-.076	.0	7	-	.0	-7.6% (-6.8, -8.5%)	\$4,923 (\$4,405, 5,552) ^T
		28	4	2.3	20		
			4	4			
Life Skills + SFP: 10-14 v. Control	-.095	.0	2	-	.0	-9.5% (-5.8, -10.5%)	\$3,959 (\$3,525, 4,393) ^T
		37	9	2.5	11		
			2	5			
Project Alert+ SFP: 10-14 v. Control	.016	.0	2	-	.9	-1.6% (-2.6%, -.6)	--
		37	1	0.0	66		
			1	4			

^A The change in predicted probability that a youth would report ever misusing prescription opioids before 12th grade^B The incremental cost of preventing a youth from ever misusing prescription opioids before 12th grade^T Below WTP threshold for preventing 1 youth from ever misusing prescription opioids before 12th grade

CI = 95% Confidence Interval