

## Developmentally inspired drug prevention: middle school outcomes in a school-based randomized prevention trial

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### Abstract

Prior investigations have linked behavioral competencies in primary school to a reduced risk of later drug involvement. In this randomized prevention trial, we sought to quantify the potential early impact of two developmentally inspired universal preventive interventions on the risk of early-onset alcohol, inhalant, tobacco, and illegal drug use through early adolescence. Participants were recruited as they entered first grade within nine schools of an urban public school system. Approximately, 80% of the sample was followed from first to eighth grades. Two theory-based preventive interventions, (1) a family–school partnership (FSP) intervention and (2) a classroom-centered (CC) intervention, were developed to improve early risk behaviors in primary school. Generalized estimating equations (GEE) multivariate response profile regressions were used to estimate the relative profiles of drug involvement for intervention youths versus controls, i.e. youth in the standard educational setting. Relative to control youths, intervention youths were less likely to use tobacco, with modestly stronger evidence of protection associated with the CC intervention (RR = 0.5;  $P = 0.008$ ) as compared to protection associated with the FSP intervention (RR = 0.6;  $P = 0.042$ ). Intervention status was not associated with risk of starting alcohol, inhalants, or marijuana use, but assignment to the CC intervention was associated with reduced risk of starting to use other illegal drugs by early adolescence, i.e. heroin, crack, and cocaine powder (RR = 0.32,  $P = 0.042$ ). This study adds new evidence on intervention-associated reduced risk of starting illegal drug use. In the context of ‘gateway’ models, the null evidence on marijuana is intriguing and merits attention in future investigations.

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### 1. Introduction

This report builds from prior work of the Prevention Research Center at Johns Hopkins University Bloomberg School of Public Health, presenting new evidence from an epidemiologically-based randomized prevention trial of two developmental interventions for primary school students. The aim is to estimate a possibly protective intervention influence with respect to risk of early-onset use of tobacco, marijuana, and other drugs (to mean age 13 years).

Prior reports on the evaluation have described the two interventions, which were put into place in 1993, and have presented evidence of their beneficial impact with respect to early target responses. In brief, there were a classroom-centered (CC) intervention and a family–school partnership intervention (FSP), both implemented by the regular classroom teachers in Grade 1. The CC intervention involved an augmentation of the primary school classroom curriculum, with concurrent refinement of the same classroom teacher’s approach to management of unruly and maladaptive classroom behavior. The FSP intervention augmented the usual and customary teacher approach by adding an emphasis on parent–school communication and partnership building. Additional weekly home–school learning, communication activities, and periodic parenting

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workshops were also included in an effort to demonstrate the benefits of greater parent involvement and collaborative work with teachers to optimize target behaviors and school performance. Early published evidence on the CC and FSP interventions was positive, with intervention-associated improvements in proximal targets of school performance and social adaptation, and with reduced risk of early-onset tobacco smoking to mean age 12 years (Ialongo et al., 1999; Storr et al., 2002).

The participating children have been followed through middle school and the current investigation estimates the hypothesized persistence of an effect on tobacco smoking and a possibly protective intervention effect on a multivariate response profile of other drug use targets. This profile encompasses data on early-onset starting to use alcohol, inhalant drugs, marijuana, and other illegal drugs (e.g. cocaine, heroin), as well as tobacco smoking, with newly gathered data through the middle school years.

The underlying logic, theory, and conceptual models to support early developmental preventive interventions directed toward youthful drug involvement have been evolving for several decades (e.g. see Kellam et al., 1975, 1983, 1994a,b; Cicchetti and Schneider-Rosen, 1984; Kellam and Rebok, 1992; O'Donnell et al., 1995; Ialongo et al., 1999). Despite advancements in developmental research, most school-based drug prevention programs offer drug-specific content to promote resistance skills against peer pressure to use drugs, or to raise levels of awareness about drug hazards and perceived harmfulness of drug use (e.g. Pentz et al., 1989; Prinz et al., 2000). In contrast, this prevention program is inspired by a more general theory of child development in which a youth's characteristics, conditions, and processes observed at one stage in life might be modified in order to achieve a more health-promoting set of behaviors later in life. For this reason, this type of program is referred to as 'developmentally-inspired' prevention. Gottfredson and Wilson (2003) have summarized evidence from several early developmental interventions directed toward youthful drug involvement and have substantiated the potential public health significance of these approaches.

The current investigation has the advantage of additional follow-up assessments completed through the period of early adolescence, when youths enter the period of highest risk for starting to use illegal drugs (e.g. see Wagner and Anthony, 2002). As such, we are able to probe for a general protective intervention impact on all of the above-listed drugs and drug groups under study, and for evidence of specific intervention impact on some but not all drugs. Because we have multiple targets or response variables under study, our approach is multivariate. In specific, we use a multivariate response profile analysis method based on the generalized estimating equations (GEE), which simultaneously estimates intervention effects on all of these interdependent drug responses. That is, within the framework of a single multivariate response regression model we are able to estimate drug-specific intervention impact (e.g. impact on

risk of starting to smoke tobacco versus impact on risk of starting to drink alcohol without parental permission). Additionally, we have explored potential effect-modification of intervention impact in relation to baseline characteristics, with specific focus on male–female differences.

## 2. Methods

### 2.1. Epidemiologic sample and setting

This work extends our Center's line of prior randomized field trials with first graders recruited in 1985–1986, which tested Good Behavior Game and Mastery Learning interventions (e.g. see Kellam and Anthony, 1998). Recruitment for the current randomized trial occurred in Fall 1993. Nine urban primary schools were designated within a single public school catchment area in one of the mid-Atlantic states of the United States. Within each school, there were three (or more) Grade 1 classrooms, which were assigned at random to intervention/control status.

At the time of entry to each school, first-graders were assigned at random to the three designated classrooms (with balancing for male–female ratios). Within each school, three cooperating Grade 1 teachers also were assigned at random, one per classroom. Across these 27 classrooms, there were 678 children, and we attempted to recruit all of these children and their families for participation in the trial, without exclusions (i.e. all entering first-graders were eligible). Males comprised slightly more than 50% of the sample; 85–90% were of African–American heritage, and almost all of the rest were of Euro-American heritage. At school entry, the age range was from 5.3 to 7.7 years (mean, 6.2 years; S.D., 0.3 years). Three-fifths (62.3%) of the children received free or reduced lunch—a proxy for family income. Written parental consent was obtained for 97% of the 678 eligible children; others failed to respond to consent requests; a small number refused outright. We found no statistically significant consent versus no consent differences in terms of sociodemographic characteristics assessed via school records (ethnicity, age, sex, and free lunch status)—i.e. no  $P < 0.05$ .

The interventions were provided over the first grade year, following a pretest assessment in the early Fall, soon after school entry and consents. At follow-up, 5, 6, and 7 years after randomization (sixth through eighth grades), approximately 84% (566/678) of the sample was available and was re-assessed in early adolescence (mean age 13 years). Attrition across these years was unrelated to intervention status and participants who were lost to follow-up did not differ from participants with complete data with respect to baseline teacher ratings, academic achievement, ethnicity, sex, or free lunch status (i.e. no  $P < 0.05$ ). The majority of the 566 youth involved in the follow-up assessments completed all assessments. Of the 678 youth in the original cohort recruited in 1993, 566 participated in the sixth, seventh or eighth grade assessment. Five hundred and one completed

all outcome assessments and only seven youths completed only the sixth grade assessment, i.e. 99% ( $n = 559$ ) had a seventh or eighth grade assessment. Outcome data reported in this investigation was based on data from all available outcome assessments.

## 2.2. Interventions

Prior research reports by Ialongo et al. (1999) and Storr et al. (2002) provide details on the research design, interventions, and assessment strategies. Here, we offer a concise explanation of the approach.

### 2.2.1. The classroom-centered (CC) intervention

The CC intervention consisted of three components: (1) curricular enhancements; (2) improved classroom behavior management practices; and (3) supplementary strategies for children not performing adequately (Dolan, 1986; Dolan et al., 1993). An interactive read-aloud component was added to increase listening and comprehension skills. Readers' Theater and journal writing were added to increase composition skills, whereas the "Critique of the Week" was added to increase critical thinking skills. The existing mathematics curriculum was replaced with the Mimosa math curriculum, a whole language approach to the development of mathematics skills. The class was divided into three small heterogeneous groups, which provided the underlying structure for the curricular and behavioral components of the intervention. Concurrent behavior management practices of the regular classroom teacher were enhanced by the Good Behavior Game (GBG) (Barrish et al., 1969), which involves a whole class strategy to decrease disruptive behavior and has been successfully employed in a prior trial to reduce early-onset tobacco smoking (Kellam and Anthony, 1998). In the current study, the GBG was refined to include a focus on off-task and inattentive behaviors in line with the results of Rebok et al. (1996). The strategies employed with respect to academic non-responders included individual, or small-group tutoring, and modifications in the curriculum to address individual learning styles (such as making the non-responders team leaders). This approach created an opportunity for more positive attention from teachers and peers.

### 2.2.2. The family-school partnership (FSP) intervention

The family-school partnership intervention (FSP) was designed to improve achievement and reduce early aggression and shy behavior by enhancing parent-school communication and providing parents with effective teaching and child behavior management strategies. The major mechanisms for achieving these aims were (1) training for teachers/school mental health professionals and other relevant school staff in parent-school communication and partnership building, (2) weekly home-school learning and communication activities, and (3) a series of nine workshops for parents led by the first grade teacher and the school psychologist or social worker.

The workshop series for parents began immediately after the pretest assessments in the Fall of first grade and ran for seven consecutive weeks. Two follow-up or booster workshops were held in the Winter and Spring, respectively. The initial parent workshops aimed at establishing an effective and enduring partnership between parents and school staff; they set the stage for parent-school collaboration in facilitating children's learning and behavior. Subsequent workshops focused on improving parents' teaching skills and support for their children's academic achievement. The Parents and Children series, a videotape modeling group discussion program, formed the basis for the positive discipline component of the intervention. A voice mail system was also put in place to maintain parent involvement and provide consultation as needed regarding learning or behavior management difficulties. To augment family-school communication, parents were asked to fill out and return comment sheets to indicate whether and when they completed the assigned weekly home-school learning activities and to report problems encountered during these activities.

### 2.2.3. Control/standard educational setting

For the youths randomly assigned to the control condition, there was no special prevention program. For these youths, the primary school experience was one of the usual and customary curriculum for this public school system. Note that participation in our program did not interfere with special services, such as special education or psychological services deemed customary and routine by the school system. Both intervention and control youth were serviced by the school system under standard protocols and procedures, however, control youth did not receive our interventions, but were monitored and assessed overtime by intervention staff.

## 2.3. Fidelity of interventions

Several steps were taken to establish, monitor, and maintain the integrity of the CC and FSP interventions. First-grade CC and FSP teachers completed 60 h of training and received certification. The training materials were outlined and coded. Information on specific intervention contacts was standardized; both teachers and school social workers or psychologists met with intervention experts on an individual basis as often as needed to effectively implement the intervention. See Ialongo et al. (1999) for more detail on the strategies employed to maintain the fidelity of the interventions, and for a discussion of the difficulty faced when parents did not follow through with the FSP intervention plans.

## 2.4. Overall assessment plan

Baseline assessments were completed at school entry, after consents. These assessments included teacher ratings of the targeted early risk behaviors of attention/concentration problems and aggressive and shy behaviors. Parent reports

of parent disciplinary practices were also obtained at baseline. Follow-up assessments with respect to drug involvement were conducted during the Spring of sixth through eighth grades. For the child self-report assessments, audio computer-assisted self-interview (ACASI) methods were used to administer standardized item sets previously developed and refined by Anthony and colleagues between 1985 and 1992, as described in numerous prior reports, including extended descriptions in full-length doctoral dissertation monographs (e.g. Chilcoat, 1992; Chilcoat et al., 1995; Chilcoat and Anthony, 1996; Crum et al., 1996; Johanson et al., 1996; Kellam and Anthony, 1998; Wilcox, 2003).

## 2.5. Specific measures at baseline

### 2.5.1. Parent management

Structured interview of parent management skills and practices—parent version (SIPMSP; Capaldi and Patterson, 1994). The SIPMSP was designed to assess the major constructs included in Oregon Social Learning Center model of the development of antisocial behavior in children (e.g. see Patterson et al., 1992). SIPMSP subscales assessed (1) parental monitoring and supervision (e.g. “How often is child out after dark without an adult present?”), (2) inconsistent discipline (e.g. “How often can child talk you out of punishing him/her?”), (3) parental reinforcement and involvement (e.g. “How often do you spend time with child in a fun activity?”), and (4) rejection of the child (“How difficult is it to be patient with child?”). Parents were asked to respond to questions regarding their disciplinary practices in forced choice response formats. Parents responded on a “1” (almost always) to “5” (never) frequency scale for the monitoring items used in the current investigation. Previous investigations have shown that parent monitoring and disciplinary practices are strong indicators of parental management and help account for risk of early-onset drug involvement (Chilcoat and Anthony, 1996; Chilcoat et al., 1995; Dishion and McMahon, 1998). See Capaldi and Patterson (1994) and Chilcoat (1992) for details on psychometric characteristics of these measures.

### 2.5.2. Social adaptational status (SAS)

Teacher observation of classroom adaptation—revised (TOCA-R; Werthamer-Larsson et al., 1991). The TOCA-R is designed to assess each child’s adequacy of performance on the core tasks in the classroom as rated by the teacher. It involves a structured interview administered by a trained member of the assessment staff. The interviewer follows a script precisely and responds in a standardized way to issues the teacher initiates. The interviewer records the teacher’s ratings of the adequacy of each child’s performance on three basic tasks: accepting authority (the maladaptive form being aggressive behavior); social participation (or shy behavior); and concentration and being ready for work (the maladaptive form being concentration problems). Teachers rate the child’s adaptation on a frequency scale from 1 to

6 (1: not at all, 6: always). The scale to measure authority acceptance and aggressive behavior includes items on breaking classroom rules, damaging property, and starting fights. The scale to assess social participation and shy or socially withdrawn behavior includes items about playing with classmates and initiating social interaction. The attention/concentration construct is tapped by items on paying attention, staying on task, and getting distracted. Werthamer-Larsson et al. (1991) found sound psychometric characteristics of the TOCA-R. Cronbach’s coefficient alpha for the TOCA-R total scale was 0.96.

## 2.6. Specific measures at follow-up (springtime weeks of sixth through eighth grades)

### 2.6.1. Drug use

During middle school, the students were trained to use ACASI assessment methods. Each student sat with individualized headphones and a response keyboard connected to a laptop computer, which had been pre-programmed to present each standardized item in sequence, using both visual and audio format, along with standardized answer choices. The assessment was self-paced, and the students marked their responses under private conditions that were maintained by a member of the assessment staff, who took care not to observe the responding and to prevent observation by others in the vicinity.

Standardized items on drug involvement were from the prior Center research by Anthony and colleagues, described above, and also included item sets from the ACASI assessments developed for the National Household Survey on Drug Abuse (SAMHSA, 2000). Here, as in the prior work of Chilcoat et al. (1995) and Chilcoat and Anthony (1996), our focus is upon early-onset drug initiation—that is, whether the youth reported starting to use one or more of the following drugs or drug groups by the time of the final assessment in Grade 8 (or at the last available outcome assessment which for the majority of youth was eighth grade): tobacco, alcoholic beverages, inhalants (e.g. glue, gases), marijuana, or other illegal drugs such as cocaine and heroin. Here, ‘early-onset’ refers to onset of drug use prior to mid-adolescence.

The ACASI methods were used to promote greater completeness and accuracy of response, and to protect privacy. Additional steps were taken as well: (1) a federal certificate of confidentiality was secured; its protections were explained during the youth assent process; (2) youths were encouraged to stop the interview at any time and to ask for a change to a new location if they felt the confidentiality of their responses might be compromised by the location originally chosen for the interview; and (3) the assessors were young adults, many with African-American heritage (in balance with the youth sample), which we believe may promote development of trust and rapport, with resulting increases in completeness and accuracy of response. Whereas bioassays for drug detection have value once recent drug use

has become sufficiently prevalent to cross detection thresholds, the self-report method is required for assessments of age at first drug self-administration and early-onset drug use, as noted in a recent review by Anthony (2000).

## 2.7. Approach to statistical analysis

### 2.7.1. Demographic characteristics and variance estimation

Our approach is that of an ‘intent to treat’ analysis, wherein baseline assignment to CC, FSP, and control status governed intervention values for the analysis. For example, there was no re-assignment to control status when parents failed to implement the FSP intervention plans. Children randomly assigned to FSP intervention status have been counted as being in that group without respect to the parent’s actual participation and involvement.

### 2.7.2. Regression models and generalized estimating equations (GEE)

Estimation procedures via cross-classification and regression models required statistical analysis procedures that account for clustering of youths within classrooms. Hence, in general, the Taylor series linearization approach and the generalized estimating equations approach have been used for variance estimation via STATA software (StataCorp, 1990). The GEE-based multivariate response profile approach is an analogue to repeated measures analysis of variance (repeated measures ANOVA and MANOVA) and multivariate analysis of covariance (MANCOVA). But these more conventional longitudinal approaches require (a) Gaussian response variables with a compound symmetry assumption and (b) deletion of respondents with missing data values. In contrast, the GEE approach is well-suited for skewed binary response variables (e.g. via a logarithmic link) and permits inclusion of all participants for whom there is at least one response variable. The original GEE approach is described by Zeger and Liang (1986) and in later applications (e.g. see Chilcoat and Breslau, 1997; Furr-Holden and Anthony, 2003). A brief description of the GEE application in the current investigation follows.

The analysis sequence began with initial cross-classifications and logistic regression estimates of intervention impact. Thereafter, a GEE multivariate response profile analysis model (logistic link) was used to express the cumulative occurrence of drug use through middle school as a function of intervention status and covariates, with the five following response variables in the multivariate response vector, all coded as 1 when the youth had used the listed drug by the time of the final assessment, and 0 when the youth had not used the listed drug: tobacco (0/1), alcohol without parental permission (0/1), inhalants (0/1), marijuana (0/1), and other illegal drug use (0/1).

In keeping with the ‘gateway’ progression, most users of illegal drugs in this sample had previously tried either tobacco and alcohol; when illegal drugs such as cocaine or

heroin had been used, there almost always was a prior history of marijuana use. Whereas a multivariate analysis of variance approach might be useful for estimation with interdependent Gaussian response variables, the GEE approach with a logistic link accommodates the discrete character of these binomial early-onset drug use response variables, allows statistical adjustment for covariates, and provides relative risk estimates with a widely appreciated information value: when the estimate for intervention status is lower than the null value of 1.0, the estimate is consistent with a protective influence of the intervention (i.e. intervention-associated reduced occurrence of drug involvement). This GEE multivariate response profile analysis model first yields a summary estimate in the form of a single relative risk estimate, borrowing information across all five response variables, under the parsimonious assumption that the responses are interchangeable, and a single slope is sufficient to characterize the intervention impact. Then, the GEE model is elaborated to challenge this parsimonious ‘single slope’ assumption and to allow each response variable to have its own slope estimate of intervention impact. Our focus is upon point and interval estimation of the intervention impact, with confidence intervals as a gauge of uncertainty in the estimates, and with *P*-values used as an aid to interpretation about the strength of the evidence.

To explore possible subgroup variation in the estimates (i.e. effect-modification), we introduced baseline covariates as well as product-terms (e.g. male  $\times$  CC and male  $\times$  FSP). However, the exploration of effect-modification yielded no remarkable findings (all *P* > 0.10).

## 3. Results

Among the 566 youths who completed follow-up assessments from sixth through eighth grades, 220 had started to smoke tobacco (39%), 190 had started to drink alcoholic beverages without parental permission (34%), 116 had started to use marijuana (20%), 73 had tried inhalant drugs (13%), and 29 had tried cocaine powder, crack, or heroin (5%). Presented in Table 1, these estimates provide initial evidence of intervention-associated reduced risk of early-onset tobacco use and early-onset use of illegal drugs other than marijuana, but little evidence of impact on early-onset alcohol use, inhalants use, or marijuana use. Table 1, Footnote e, provides details from basic chi-square analysis and exact tests.

Table 1 also displays a selection of other baseline characteristics, and presents drug-specific estimated cumulative incidence proportions for the discrete covariates. Some of these baseline covariates had distributions that were modestly imbalanced across the intervention and control groups of the design, despite randomization. This imbalance motivated the use of regression models with covariate adjustment to re-estimate the possible intervention impact. A term for teacher-rated problems, as observed at baseline soon after school entry, also was included as a baseline covariate in

Table 1

Estimated cumulative incidence of early-onset drug use in relation to randomized intervention status and other key covariates

Baseline values of covariates under study	Number of subjects, <i>n</i>	Tobacco smoking		Alcohol use without parents <sup>a</sup>		Marijuana smoking		Inhalants use		Other illegal drug use <sup>b</sup>	
		Number of users	CI <sup>c</sup>	Number of users	CI	Number of users	CI	Number of users	CI	Number of users	CI
All participants at follow-up	566	220	0.39	190	0.34	116	0.20	73	0.13	29	0.05
Intervention assignment											
Control: standard educational setting <sup>d</sup>	178	83	0.47	52	0.33	34	0.19	25	0.14	13	0.07
Classroom-centered intervention	192	66	0.34 <sup>e</sup>	65	0.34	40	0.21	23	0.12	5	0.03 <sup>e</sup>
Family–school partnership intervention	196	71	0.36 <sup>e</sup>	73	0.37	42	0.21	25	0.13	11	0.06
Sex											
Male <sup>d</sup>	306	124	0.41	115	0.38	72	0.24	46	0.15	23	0.08
Female	260	96	0.37	81	0.31	44	0.17	27	0.10	6	0.02
Family type											
Mother alone <sup>d</sup>	141	58	0.41	60	0.43	30	0.21	18	0.13	10	0.07
Other	353	133	0.38	108	0.31	68	0.19	48	0.14	17	0.05
Alcohol use affected family											
Not at all	468	179	0.38	159	0.34	91	0.19	63	0.13	26	0.06
Little to a lot <sup>d</sup>	26	12	0.46	9	0.35	7	0.27	3	0.12	1	0.04
Tobacco use affected family											
Not at all	468	177	0.38	157	0.34	91	0.19	61	0.13	25	0.05
Little to a lot <sup>d</sup>	25	13	0.52	10	0.40	6	0.24	5	0.20	2	0.08
Drug use affected family											
Not at all	393	140	0.36	125	0.32	77	0.20	46	0.12	19	0.05
Little to a lot <sup>d</sup>	101	51	0.50	43	0.43	21	0.21	20	0.20	8	0.08

<sup>a</sup> Alcohol use without parental permission.

<sup>b</sup> Here, 'other illegal drug use' refers to use of cocaine powder or crack or heroin, at least one time by the end of middle school.

<sup>c</sup> The cumulative incidence proportion, CI, is estimated as the proportion of participants who had started to use the drug by the date of assessment. Here, it is the simple ratio of the number of drug users in the subgroup divided by the total number of follow-up participants in that subgroup, given that the follow-up interval from first grade recruitment to the time of middle school follow-up is roughly equal for all participants.

<sup>d</sup> It designates the 'reference group' for a covariate—that is, the subgroup for which the regression term,  $X_i$ , is coded 0 within the context of multiple logistic regression.

<sup>e</sup> Under the null hypothesis of equal cumulative incidence of tobacco use for control versus CC participants, two-sided Fisher's exact test yields  $P$ -value equal to 0.015. Under the null hypothesis of equal cumulative incidence of tobacco use for control versus FSP participants, two-sided Fisher's exact test yields  $P$ -value equal to 0.046. Under the null hypothesis of equal cumulative incidence of 'other illegal drug use' for control versus CC participants, two-sided Fisher's exact test yields  $P$ -value equal to 0.051.

these models to constrain any residual confounding associated with failure to achieve complete balance with respect to important proximal intervention targets that were observable early in first grade. The sample mean for teacher-rated total problems was an estimated 2.29 (S.D. = 0.90). The only appreciable departure from this estimate was detected for initiators of illicit drugs other than marijuana. Users of these drugs were observed to have modestly higher ratings of total problem behaviors as compared to non-users (estimated mean of 2.55 (S.D. = 1.03) for users versus an estimated mean of 2.27 (S.D. = 0.89) for non-users).

Estimates from the regression models, before and after statistical adjustment for covariates, are displayed in Table 2. These estimates tend to confirm the initial impressions about intervention impact. For early-onset tobacco use, there is evidence consistent with a protective effect of both the CC and the FSP interventions. With occurrence of tobacco smoking

among youths in the control classrooms taken as a reference value, the youths in the CC intervention classrooms were less likely to have initiated tobacco use (estimated relative risk,  $RR_u = 0.60$  unadjusted; RR with covariate adjustment,  $RR_a = 0.55$ ; 95% confidence interval for  $RR_a$ , CI = 0.34, 0.88;  $P = 0.013$ ). An apparent protective effect of similar magnitude was observed for youths in the FSP intervention classrooms, again with the control youths providing reference values ( $RR_u = 0.65$ ;  $RR_a = 0.62$ ; CI = 0.39, 0.98;  $P = 0.041$ ).

Corresponding CC and FSP estimates with respect to cumulative incidence of alcohol, inhalants, and marijuana use were null (i.e. evidence supports neither a protective nor a harmful effect of the interventions), as shown in Table 2. However, there is evidence consistent with a protective CC intervention effect in relation to cumulative incidence of illegal drug use other than marijuana use. As

Table 2

Estimated effect of classroom-centered and family–school partnership interventions on drug use: estimates from five separate univariate response regression models for each drug or drug group<sup>a</sup>

	Classroom centered ( <i>n</i> = 192)			Family–school partnership ( <i>n</i> = 196)		
	Estimated relative risk <sup>b</sup>	95% confidence interval	<i>P</i> -value	Estimated relative risk <sup>b</sup>	95% confidence interval	<i>P</i> -value
<b>Tobacco</b>						
No covariates	0.60	0.39, 0.91	0.017	0.65	0.43, 0.98	0.042
Adjusted for covariates <sup>c</sup>	0.55	0.34, 0.88	0.013	0.62	0.39, 0.98	0.041
<b>Alcohol without permission</b>						
No covariates	1.06	0.69, 1.63	0.796	1.23	0.80, 1.88	0.346
Adjusted for covariates <sup>c</sup>	0.95	0.58, 1.54	0.825	1.07	0.67, 1.71	0.777
<b>Marijuana</b>						
No covariates	1.11	0.67, 1.86	0.677	1.16	0.70, 1.92	0.577
Adjusted for covariates <sup>c</sup>	0.94	0.53, 1.68	0.846	1.04	0.60, 1.83	0.876
<b>Inhalants</b>						
No covariates	0.83	0.45, 1.52	0.555	0.89	0.49, 1.62	0.714
Adjusted for covariates <sup>c</sup>	0.79	0.40, 1.54	0.484	0.90	0.48, 1.68	0.730
<b>Other illegal drug use<sup>d</sup></b>						
No covariates	0.34	0.12, 0.97	0.044	0.75	0.33, 1.73	0.506
Adjusted for covariates <sup>c</sup>	0.29	0.10, 0.87	0.028	0.61	0.25, 1.49	0.274

<sup>a</sup> Results based on nested models with classroom cluster.

<sup>b</sup> Relative to the standard educational setting (*n* = 178).

<sup>c</sup> Covariates included age, sex, family type, teacher-rated total problems, parent management, and family history of drug, alcohol, or tobacco use.

<sup>d</sup> Includes heroin, crack, or cocaine.

compared to control youths, those who had been assigned randomly to the CC intervention classrooms at the time of entry to first grade were less likely to have started use of cocaine powder, crack, or heroin by the end of Grade 8 (RRu = 0.34; RRa = 0.29; CI = 0.10, 0.87; *P* = 0.028, from Table 2, first columns of estimates). In contrast, the evidence about FSP impact on illegal drug use is

essentially non-supportive and null: (RRu = 0.75; RRa = 0.61; CI = 0.25, 1.49; *P* = 0.274, from Table 2, second set of columns of estimates). Readers will appreciate the preliminary character of these estimates, given the small number of illegal drug users in the numerators of the cumulative incidence proportions for each intervention/control stratum.

Table 3

Estimated effect of classroom-centered and family–school partnership interventions on drug use: estimates from multivariate regression model with generalized estimating equations<sup>a</sup>

	Classroom centered			Family–school partnership		
	Estimated relative risk <sup>b</sup>	95% confidence interval	<i>P</i> -value	Estimated relative risk <sup>b</sup>	95% confidence interval	<i>P</i> -value
<b>Tobacco</b>						
No covariates	0.60	0.39, 0.91	0.017	0.65	0.43, 0.98	0.042
Adjusted for covariates <sup>c</sup>	0.53	0.33, 0.85	0.008	0.62	0.40, 0.98	0.042
<b>Marijuana</b>						
No covariates	0.83	0.45, 1.53	0.555	0.89	0.49, 1.62	0.715
Adjusted for covariates <sup>c</sup>	0.68	0.34, 1.33	0.257	0.88	0.47, 1.64	0.678
<b>Inhalants</b>						
No covariates	1.11	0.67, 1.86	0.678	1.16	0.70, 1.92	0.577
Adjusted for covariates <sup>c</sup>	1.00	0.57, 1.75	0.99	1.07	0.62, 1.85	0.814
<b>Other illegal drug use<sup>d</sup></b>						
No covariates	0.34	0.12, 1.16	0.044	0.75	0.33, 1.73	0.507
Adjusted for covariates <sup>c</sup>	0.32	0.11, 0.96	0.042	0.63	0.27, 1.51	0.301

<sup>a</sup> Results based on nested models with classroom cluster.

<sup>b</sup> Relative to the standard educational setting (*n* = 178).

<sup>c</sup> Covariates included age, sex, family type, teacher-rated total problems, parent management, and family history of drug, alcohol, or tobacco use.

<sup>d</sup> Includes heroin, crack, or cocaine.

Re-estimation of these relationships within the framework of the GEE multivariate response profile analysis model yields essentially the same conclusions, as shown in Table 3, and provided strong evidence that a single ‘common slope’ model would not provide an adequate summary of the intervention impact on individual drugs. The multivariate model to estimate drug-specific intervention impact yields slightly smaller but not appreciably different point estimates, confidence intervals, and P-values. Because this multivariate response procedure takes response interdependencies into account, it may address concerns about multiple significance tests in this study report.

#### 4. Discussion

The main evidence from this study is consistent with a protective effect of the classroom-centered intervention and the family–school partnership intervention with respect to early-onset tobacco smoking. This evidence complements the estimates previously reported by *Storr et al. (2002)*. What is new about this evidence is the additional follow-up to ascertain tobacco smoking onsets 1–2 years beyond the initial assessments described in the prior report. That is, the apparent protective CC and FSP tobacco impact seems to have persisted through the middle school years. In addition, this report offers new preliminary evidence that the CC intervention (but not the FSP intervention) might be providing protection against early-onset use of illegal drugs like cocaine and heroin (but not marijuana).

Before detailed discussion of the evidence, we would like to mention what we believe to be the most serious limitation with respect to our study estimates. Of primary concern to us is sample attrition, which must be understood in context: by the end of middle school, the children had dispersed to over 100 schools and 18 states. We were able to obtain follow-up assessments on 84% of the original sample of participants. Nonetheless, it is possible that these estimates might change with more complete success in future waves of follow-up, which we hope to achieve in the years to come.

Selective attrition is a serious methodological problem and we have done our best to keep it to a minimum, within the constraints of human subjects protection procedures that require repeated re-asking of consents and assents to participate each time we re-contact and re-assess the youths. We hope to be able to secure more complete coverage of the baseline sample when the youths have become young adults. Nonetheless, there has been some attrition even in the best of the longitudinal studies of youthful drug involvement, and in our follow-up of the Prevention Research Center participants, we have taken special care to leave open the possibility that a non-participating youth might consent to cooperate in a future round of assessments. For this reason, we cannot employ the same procedures that are used in cross-sectional research to push better interview completion rates toward ever-higher values (e.g. conversion of hard

refusals). These procedures serve well in cross-sectional research and in time-limited prospective studies, but can alienate hesitant participants who might be re-engaged in the future, with passage of time and increased maturity.

Other study limitations such as the modest level of parental non-consent at baseline and the reliance upon self-report assessments of early-onset drug use deserve consideration in relation to the interpretation of our study estimates. In addition, there is some concern regarding our ‘intent to treat’ analysis approach, especially with respect to the FSP intervention, because many FSP-assigned parents did not complete the intervention with fidelity. In response, we note that this randomized trial has been completed under large-sample field conditions suitable for an effectiveness trial; more optimal FSP impact might be found under more constrained and optimized conditions, perhaps with smaller samples and more selective recruitment of enthusiastic parents committed to greater fidelity in relation to the FSP intervention plan, or with an analysis approach other than the ‘intent to treat’ approach. Nevertheless, gauged against potential biases associated with selective attrition, we do not judge these other limitations to be as serious.

Notwithstanding study limitations such as these, some interesting leads have been offered for future investigations. We continue to see evidence consistent with a modest-to-moderate protective effect of both CC and FSP interventions with respect to delay or prevention of early-onset tobacco smoking, and the CC intervention participants showed somewhat lower risk of early-onset use of cocaine powder, crack, and heroin. Observational data suggest that delaying onset of first drug use might yield reduced risk of later more serious drug involvement and risk of drug problems (e.g. *Anthony and Petronis, 1995; Chen and Anthony, 2003*). But here we have some perplexing evidence—in that an apparent delay or reduced risk of early-onset tobacco smoking through the middle school years is not occurring concurrently with a delayed onset or reduced risk of illegal drug use in both intervention groups. In specific, the CC and FSP participants are just as likely as the control participants to have started smoking marijuana; the size of the upper bounds of the 95% confidence intervals for the marijuana effect estimates indicate that we have little hope that the interventions actually were protective against early-onset marijuana use and that we will see emerging evidence of protection in future waves of follow-up assessment, once the incident cases of marijuana use become more numerous. Obvious implications of these experimental results for the ‘gateway’ conceptualization of illegal drug involvement warrant more deliberate investigation. Indeed, this is not the first time that early protections against tobacco smoking or delays in tobacco smoking onset have not been accompanied by concurrent or later reduced risk of marijuana use or other illegal drug involvement (e.g. see *Lynskey et al., 2003; Anthony, 2002*).

We would like to be able to say something definitive about the mediational pathways through which the interventions

might have affected drug involvement by the middle school years. However, when drug involvement binary outcomes are as skewed as in the present study, the study of mediational pathways yields uncertain (less than definitive) conclusions. For this reason, we must delay statements about possible mediation until later in the follow-up interval, after more assessments of drug involvement have been made, at which time we will be able to apply appropriate biostatistical approaches (e.g. structural modeling of the mediational pathways).

Finally, we note that the CC intervention is mounted more readily than the FSP intervention. Whereas teachers in general proved to be conscientious about following the CC intervention plan, many parents were less faithful with respect to the FSP intervention plan. Some FSP-assigned parents failed to attend workshops and other parent–teacher sessions (perhaps because they had hoped to have their children receive the benefit of the CC intervention). This ‘real world’ experience, coupled with the profile of apparent CC intervention benefits, may serve as a guide to other investigators who decide to launch their own lines of drug prevention research within the context of the early developmental intervention paradigm. Special selection processes and accompanying biases continue to constrain inferences about the public health significance of parent-oriented interventions when recruitment or attrition focuses the analysis upon enthusiastic parents or caregivers who will comply fully with specifications of the intervention plan. These constraints on inference may be reduced through continued refinement of modeling-intensive biostatistical approaches when trials face selective recruitment or the ‘broken randomized experiment’ scenario in which there is incomplete intervention compliance by intervention or control participants (e.g. see Barnard et al., 2003).

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