

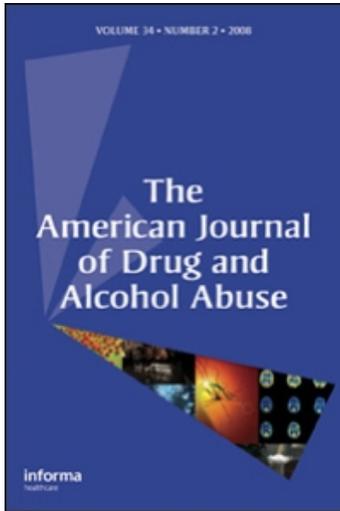
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W. Scott Comulada^a; Robert E. Weiss^a; William Cumberland^a; Mary Jane Rotheram-Borus^a

^a Semel Institute for Neuroscience and Human Behavior and the AIDS Institute, University of California, Los Angeles, California, USA

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Reductions in Drug Use Among Young People Living with HIV

W. Scott Comulada, Dr.P.H., Robert E. Weiss, Ph.D.,

William Cumberland, Ph.D., and Mary Jane Rotheram-Borus, Ph.D.

Semel Institute for Neuroscience and Human Behavior and the AIDS Institute,
University of California, Los Angeles, California, USA

Abstract: ZIP models were used to detect reductions in drug abuse among young people living with HIV (YPLH) over 15 months when most young people abstain from use. YPLH ($n = 171$) aged 16 to 29 years were randomly assigned to an 18 session intervention or a delayed-intervention condition. The ZIP models showed significant reductions in abuse of multiple substances over time in the non-delayed intervention. Previous analyses did not find significant reductions. Intervention efficacy often cannot be detected if there are highly skewed distributions of outcomes, such as drug abuse. ZIP modeling offers an opportunity to more reliably detect behavioral changes.

Keywords: Adolescents, health behaviors, HIV, substance abuse transmission acts

INTRODUCTION

Prevention for HIV+ persons is a top priority for the Centers for Disease Control and Prevention (1). We previously demonstrated that when young people living with HIV (YPLH) attended a three-module intervention delivered in small groups (Teens Linked to Care [TLC]) (2, 3) or in individual sessions (Choosing Life, Empowerment, Action, and Results [CLEAR]) (4), the YPLH reduced their unprotected sexual acts. Drug abuse was an entry criterion for this study. Therefore, all participants were active users at the time of recruitment. When using logistic regression analyses that examined only reductions in use (4), we

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Address correspondence to W. Scott Comulada, Dr.P.H., 10920 Wilshire Blvd., Suite 350, Los Angeles, CA 90024, USA. E-mail: scomulad@ucla.edu

Table 1. Number of times using each substance over the past three months

	0 counts		1–100 counts		>100 counts	
	%	n	%	n	%	n
Cocaine	79	135	20	35	<1	1
Crack	89	152	8	13	4	6
Heroin	94	161	5	8	1	2
Inhalants ^a	87	148	12	20	1	2
Marijuana	33	57	42	72	25	42
Methamphetamines	73	124	16	28	11	19
Stimulants	85	146	12	21	2	4

^a1 missing observation excluded from table.

did not find significant reductions in drug use as a function of the intervention. The current analysis evaluates a different, more powerful analytic strategy that allows the simultaneous examination of both elimination of use of a specific drug (a yes-no event) and reductions in use over time. In this article we re-examine the effects of the intervention on drug abuse, considering the impact of the highly skewed distributions in the reports of drug use by young people.

YPLH use a broad range of drugs: e.g., marijuana, cocaine, methamphetamine, heroin, and ketamine (2, 5). In a typical sample of substance-using young people, most young people do not use each drug. Thus, if we analyze the impact of reducing drug use from *use* to *non-use*, a very high proportion of participants will be non-users. Table 1 demonstrates that there is zero-inflation in the reports of drug use at baseline among YPLH in the CLEAR intervention (5). The usage distribution is very skewed.

Given these distributions, standard regression techniques are inadequate for analyzing the outcomes, in this case, the impact of an intervention case management approach on reducing drug abuse. When analyzing drug use, both binomial (*use/non-use*) and count data are combined in these distributions. To more sensitively examine the impact of an intervention on drug use, we utilize longitudinal zero-inflated Poisson (ZIP) models (6, 7) to examine reductions of the frequency of use among drug users.

METHODS

Sample

From 1999 to 2002, 253 YPLH aged 16 to 29 (median age = 23) were voluntarily recruited to participate in a cognitive behavioral HIV

transmission-reduction intervention trial, mostly from medical providers and social service agencies in Los Angeles, San Francisco, and New York. We had an eligibility criterion of using alcohol or illicit drugs at least 5 times in the last 3 months to coincide with the study aim of reducing transmission acts among substance users. Seventy percent of those recruited ($n = 176/253$) were eligible and randomized into one of two immediate intervention conditions (telephone or in-person), or a delayed condition. Analyses were conducted on the 171 YPLH not missing substance use information at baseline. YPLH were interviewed at baseline, 3, 6, 9, 15, and 21 months through a computerized assessment. YPLH in the delayed condition received the in-person intervention after the 15 month interview. Details may be found in previous publications on CLEAR (4, 5).

Most YPLH included in analyses are bisexual or gay males (69%; 9% heterosexual males and 22% females), Black (27%) or Latino (43%), and had no AIDS diagnosis (77%); about half reported experiencing HIV symptoms (56%). At baseline, self-reported substance use rates over the past three months were 21% for cocaine, 11% for crack, 6% for heroin, 14% for inhalants, 67% for marijuana, 27% for methamphetamines, and 15% for stimulants/amphetamines. We exclude heroin use from our analyses due to low rates of use.

Substance Use Measures

YPLH reported the number of days using in the past 3 months and the average number of times used per day for cocaine, crack, heroin, inhalants, marijuana, methamphetamines, and stimulants/amphetamines. Frequency of use was estimated by multiplying the number of days in the past 3 months used by the average number of times used per day. We considered reports of using any substance 5 times a day by 90 days (equaling 450 times) or more to be outliers and Winsorized (8) 28 marijuana outliers and 20 outliers across the remaining drugs by replacing their values with 450.

A validation study to assess over-reporting of use was conducted on 82 of the participants whose reported substance-use frequency exceeded 4 times in the past 3 months at baseline. Urine samples were collected and compared to reported use. Thirty-three percent of those testing positive for cocaine metabolites had reported cocaine or crack use (Kappa = .31); 84% of those testing positive for marijuana had self-reported marijuana use; 83% of those testing positive for amphetamine had reported amphetamine use (Kappa = .76). A Kappa of .31 suggests

poor agreement between self-reported and urine-sample test results for cocaine and crack use.

Statistical Analysis

We conducted intent-to-treat analyses and examined the intervention effect on each substance use frequency measure from baseline to 15 months post randomization. The frequency of use is visibly zero-inflated across all substances. The percentage of zeros is shown in Table 1 for the frequency of use for each drug at baseline. Similar patterns are seen at other time points. At least half of the subjects were reported non-users for each substance across all time points.

Inappropriate statistical models such as standard Poisson regression models, which assume a Poisson distribution for the frequency of use outcome, may lose power to determine an intervention effect. Erroneous statistical assumptions usually inflate the variance, causing reduced power to identify intervention effects. For example, an intervention may impact substance users through two mechanisms: users may be influenced to become non-users, and they may reduce use frequency. An intervention effect may be masked if the intervention only influences participants to become non-users but does not reduce substance use among participants who remain substance users, or vice versa.

The longitudinal Zero-inflated Poisson (ZIP) model (6, 7) allows the two mechanisms of the intervention effect to be explored in the presence of zero-inflated count data. A zero is allowed to come from two processes: one process, with probability p , the zero or “non-user” state, has zeros as the only possibility, and the other process, with probability $1-p$, has Poisson distributed counts which could in turn be zero, e.g. counts from substance users who were not using when the data were collected. The non-user state is modeled via a logistic regression and the Poisson distributed counts are modeled via a Poisson regression conditional on counts not being in the non-user state.

We fit longitudinal ZIP models to each substance use frequency measure over time, from baseline to 15 months, to estimate intervention effects. Covariates in the logistic and Poisson regressions include an intercept, intervention condition indicators (Telephone and In-person), months from baseline interview (Time), and time by intervention indicator interactions to assess the change in slope between intervention conditions over time. Demographic covariates for gender and ethnicity included in the original analyses are included in the Poisson regression, as well as a random effect for each person. Analyses are conducted in a Bayesian framework using WinBUGS version 1.4.1 software (9).

Posterior means (M) and standard deviations (SD) of model parameters are reported and equivalent to parameter estimates and standard errors from a frequentist analysis. Ninety-five percent posterior intervals (95% PI) are also reported for key significant results and range from the 2.5th to the 97.5th percentiles of the posterior densities they are covering.

We plot estimated mean substance use counts over time from the ZIP model results. The ZIP model assumes that a substance use count outcome is the product of a Bernoulli random variable modeled with a logit link and a Poisson modeled with a logarithmic link. As given by Lambert (6), the mean count outcome c_{ij} is estimated as $c_{ij} = \exp(\beta_{ij}) / (1 + \exp(\alpha_{ij}))$, where “exp” is the base e exponential transformation, α_{ij} is the linear predictor from the logistic regression, and β_{ij} is the linear predictors from the Poisson regression for person i at time point j . Random effects are drawn from the predictive posterior density and incorporated into β_{ij} using a parametric version of the smearing estimate (10). An estimate at time point j of the mean substance usage is the median of the c_{ij} calculated for each person and set of draws from the joint posterior of the parameter estimates and random effects.

RESULTS

Parameter estimates from the ZIP model are given in Table 2 and 95% PI are reported for significant intervention by time parameters from the Poisson part of the model. The intervention did not significantly impact conversion to substance non-use, as indicated by the logistic results, but did impact usage among users, i.e., participants not in the zero state, as indicated by the Poisson results. Among users, reductions over time in the in-person and telephone conditions compared to the delayed condition were seen in the frequency of use for crack (95% PI = $-.33$ to $-.09$ and $-.86$ to $-.54$, respectively), marijuana (95% PI = $-.11$ to $-.02$ and $-.19$ to $-.08$, respectively), and methamphetamines (95% PI = $-.60$ to $-.34$ and $-.59$ to $-.39$, respectively). Reductions were also seen for stimulants (95% PI = -1.20 to $-.46$) in the telephone condition and for inhalants (95% PI = -2.14 to -1.32) in the in-person condition compared to the delayed condition. Among users, increases were seen in the frequency of cocaine use in the in-person (95% PI = 2.41 to 2.97) and telephone (95% PI = 1.28 to 1.93) conditions compared to the delayed condition.

Estimated counts during the past three months for each of the seven substances are plotted in Figure 1. The trajectories for cocaine use in the in-person and telephone conditions are fairly flat, showing the positive

Table 2. Posterior means (M) and standard deviations (SD) of parameters estimated from longitudinal ZIP model fit to frequency of substance use measures. Poisson part of model adjusts for gender and ethnicity. Logistic regression models probability of being in zero state (non-user)

Covariate	Cocaine		Crack		Inhalants		Marijuana		Meth		Stimulants	
	M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Logistic												
Telephone	.46	.51	.30	.68	-.25	.54	-.68	.53	.38	.54	1.15	.62
In-person	.51	.52	1.61	.73*	-.15	.59	-.36	.47	1.15	.53*	.56	.63
Time (years)	-.47	.66	.26	.67	-.24	.47	.93	.41*	.27	.54	1.13	.59*
Tel* time	.10	.80	-.24	.87	.21	.70	.20	.62	.68	.71	-.71	.81
In-per* time	.72	.79	-1.20	.86	-.34	.78	-.14	.57	-.02	.71	-.31	.87
Poisson												
Telephone	.56	.81	-.17	.82	-.24	.74	.45	.67	-.17	.77	1.18	1.06
In-person	-.26	.79	2.23	1.65	-.52	.64	1.27	.52*	-1.31	.70*	-1.40	.99
Time (years)	-2.18	.12*	-.14	.04*	.23	.19	.08	.02*	-.15	.03*	.14	.06*
Tel* time	1.61	.16*	-.70	.08*	-.27	.21	-.14	.03*	-.49	.05*	-.83	.19*
In-per* time	2.68	.14*	-.21	.06*	-1.73	.21*	-.07	.02*	-.47	.06*	-.22	.15
R.E. variance	11.68	2.39*	27.22	9.63*	9.12	2.30*	9.85	1.36*	19.85	3.80*	18.41	5.68*

*Significant result indicates 95% posterior interval does not include 0.

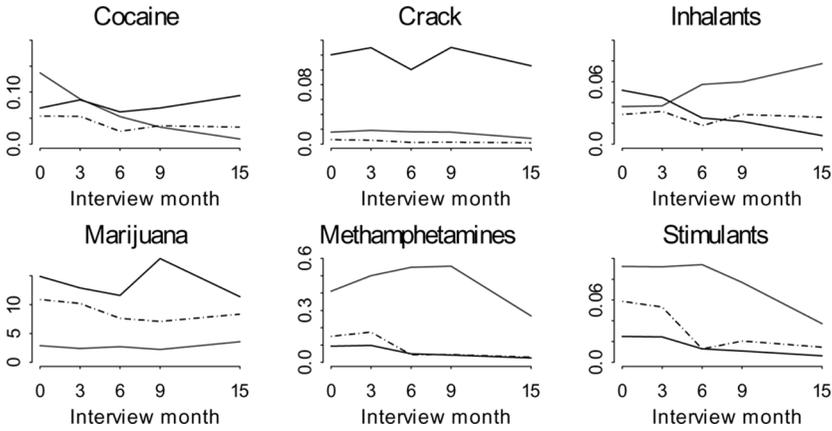


Figure 1. Estimated substance use counts during the past three months at each time point in the delayed (gray lines), in-person (solid black lines), and telephone (dashed black lines) conditions.

time by intervention slope coefficient is due more to a decrease over time in the trajectory of the delayed condition. The fairly large baseline differences in substance use counts relative to trajectories over time are consistent with earlier findings (4), which found the delayed condition to be more sexually risky at baseline compared to the in-person and telephone conditions.

DISCUSSION

Outcome analyses examining the impact of a prevention case management intervention for YPLH demonstrated very different results when a two-step analytic procedure was implemented. In contrast to the findings with random linear regression models, we were able to examine the impact of the intervention of seven specific classes of drugs (cocaine, crack, heroin, inhalants, marijuana, methamphetamine, and stimulants). The binomial outcomes of *use/non-use* were not significantly reduced in the intervention condition: there were significant increases over time in the use of marijuana, methamphetamine, and stimulants over the course of the study (regardless of intervention status) and a significant increase in the in-person case management intervention of crack use. These findings are consistent with developmental patterns in substance abuse for young adults, particularly those with a history of drug abuse. Rates of substance abuse increase until the early 20s (11, 12).

When we examined the impact of intervention condition on the frequency of use among users, we found significant relationships between reductions in use and the intervention condition. Both the telephone and the in-person condition significantly reduced crack, marijuana, and methamphetamines compared to the delayed condition. Reductions were also seen for heroin and stimulants in the telephone condition and for inhalants in the in-person condition compared to the delayed condition. However, cocaine use was significantly lower among young people in the delayed control condition compared to the intervention condition. These findings favor the intervention condition for five of seven drugs. There is no clear explanation for the increase in cocaine use among those in the intervention condition compared to the delayed condition. Future research will have to examine this unexpected outcome.

The methodology for reanalyzing these results has the potential to redirect analyses of substance abuse outcomes for many intervention trials. The zero-inflation problem in the distribution of substance abuse is common. Changing from a user to a non-user is different from reducing frequency of use. ZIP analyses are common in biomedical research (7, 13–15). While they have been used in substance abuse research (16, 17), they are underutilized. We encourage experimentation by other researchers in the future.

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