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Positive Social Impacts Related to Participation in an HIV Prevention Trial Involving People Who Inject Drugs

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Abstract

Although attention has focused on whether participants actually derive better medical outcomes in research, the social benefits experienced in research have not been systematically examined. At regular follow-up visits during a phase III randomized trial assessing the safety and efficacy of a long-term versus a short-term drug treatment intervention in decreasing HIV transmission and mortality conducted in China and Thailand, participants identified research-related negative and positive social impacts (PSIs). Open-ended PSI responses were coded using standard qualitative techniques. Among 1025 participants, only 4 reported a negative social impact; however, 77% reported at least one PSI over the 104 week follow-up period. Given the high prevalence of PSIs we observed, future research should embed assessments of negative and positive social impacts experienced by participants in research not only to ensure their well-being, but also to inform policy and conceptual work related to research ethics.

Keywords

social impacts; benefits; HIV prevention; research ethics; injection drug use

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Ethics Approval: The study was approved by the following research ethics committees: Chiang Mai University Research Institute for Health Sciences; Ministry of Public Health Ethical Review Committee for Research in Human Subjects; Guangxi Center for Disease Prevention and Control Institutional Review Board (IRB); Xinxiang Uighur Autonomous Region Bureau of Health Disease Control and Treatment IRB; The Chinese National Center for AIDS/STD Control and Prevention IRB; and Johns Hopkins Medicine IRB.

Trial Registration: clinicaltrials.gov number NCT002702

Introduction

Determining whether research is ethically appropriate necessitates evaluating its risks and benefits. For some HIV-related research, this can be particularly complex due to the nature of the HIV pandemic, which often affects vulnerable people who may be stigmatized due to their sexual or drug use behaviors.

At the outset of a multinational clinical trial involving treatment of injection drug use as a means of preventing HIV-infection, there was understandable concern about the potential social risks to participants. At the trial sites, injection drug use is highly stigmatized and people who inject drugs face a substantial risk of being detained.[1] Accordingly, an array of measures was taken to minimize risks[2] and to regularly assess whether participants had experienced any negative social impacts. Similarly, although participants were expected to derive benefits since the study included drug treatment and counseling, they were also asked about any positive social impacts (PSIs) related to the trial.

In this study we sought to understand the nature of the surprisingly high number of reported PSIs reported and those who reported them.

Methods

Study Population

HPTN 058 (NCT00270257) was a phase III randomized trial assessing the safety and efficacy of a drug treatment intervention in decreasing HIV transmission and mortality among HIV-uninfected people who inject drugs in China (Xinjiang, Nanning and Heng County) and Thailand (Chiang Mai) from 2007–2012. Participants were randomized to a long-term versus short-term use of buprenorphine/naloxone (BUP/NX) and counseling.

The study was approved by the following research ethics committees: Chiang Mai University Research Institute for Health Sciences; Ministry of Public Health Ethical Review Committee for Research in Human Subjects; Guangxi Center for Disease Prevention and Control Institutional Review Board (IRB); Xinxiang Uighur Autonomous Region Bureau of Health Disease Control and Treatment IRB; The Chinese National Center for AIDS/STD Control and Prevention IRB; and Johns Hopkins Medicine IRB.

Outcome Measures

At weeks 26, 52, 78 and 104, participants were asked about research-related negative and positive social impacts. Negative social impacts were queried with closed-ended items including incarceration, financial, health care and employment issues and problems with personal relationships. PSIs were assessed with the open-ended question: “Has your participation in this study had a positive or beneficial impact on your life? Please describe.” Responses were translated into English by trial staff. PSI data were reviewed and coded by two independent coders, using a codebook of common themes developed from the data (percent agreement of 95%). Following initial coding, some codes were combined based on similarity or redundancy.

Identical transcribed responses were noted in 770/778 visits (99.0%) at the Heng County, China site. The uniformity of response to an open-ended question format indicated problems in administering the question at this site, thus data from Heng County were excluded in our analysis.

Statistical Analysis

Participants were categorized as a minority ethnic group if they did not identify with the majority ethnic group (i.e., Han for Chinese participants and Thai for Thai participants). Bivariate analyses were assessed with the chi-square test for categorical and Students t-test for continuous variables. The effect of the study intervention on the number of participants reporting PSIs assessed both study arm and period of active BUP/NX treatment, adjusted for site, using logistic regression with the Generalized Estimating Equation to account for repeated measures. Interaction between arm and period was not statistically significant so models without interaction are reported. SAS software (SAS Institute Inc., Cary, NC, USA) was used for all quantitative analyses.

Results

A total of 1250 participants were enrolled in the clinical trial. Among the three sites included in this analysis, data were available for a total of 789 participants. Only 4 of these participants reported a negative social impact; however, 608 (77%) reported a PSI at least once. Participants reporting a PSI had fewer years of education (7 vs. 9, $p<0.001$), were less likely to be of a majority ethnicity (45% vs. 63%, $p<0.001$), were more likely to have first injected drugs at an older age ($p=0.004$), and reported significantly fewer years since their first injection (8 vs. 10, $p<0.001$) (Table 1).

For drug related PSIs, reduction in drug use was reported at 45% of LT-MAT visits and 36% of ST-MAT visits, and reduction in cravings and withdrawal at 3% of LT-MAT visits and 7% of ST-MAT visits (Table 2). The most frequently reported non-drug-related PSIs among participants in the LT-MAT arm were improved health (11%) and life improvement (11%). Among participants in the ST-MAT arm, gained knowledge (10%) and improved health (10%) were the most frequently reported PSIs.

Participants were significantly more likely to report any PSI in Year 1 of the intervention compared to Year 2 (OR=2.45, CI: 2.45, 3.62), including both drug-related (OR=1.45, CI: 1.21, 1.74) and non-drug-related PSIs (OR=1.85, CI: 1.53, 2.23). Participation in the LT-MAT arm resulted in 22% higher odds of reporting a drug-related PSI (OR =1.22, CI: 1.01, 1.48) and 24% higher odds of reporting a non-drug related PSI (OR =1.24, CI: 1.01, 1.52) when compared to participants in the ST-MAT arm (Table 3).

Discussion

While at the outset of the trial, concern rightly focused on research risks, the number of reported negative social impacts was extremely rare. In striking contrast, participants reported a high number of PSIs. Those receiving financial support from a spouse, family, or friends were less likely to report a PSI, suggesting that they may already benefit from social

supports external to the study. Those who were employed were also more likely to report a PSI, which may suggest that the trial was effective at facilitating participants' ability to find work, which is not surprising given the comprehensive counseling sessions received by all participants. More research is needed, however, to further explore the impact that these and other socio-demographic characteristics may have on participants' likelihood of experiencing PSIs.

Research related benefits have been categorized as "direct", "collateral" (or "indirect"), or "aspirational".[3] Direct benefits relate to the experimental intervention itself, such as a drug curing a disease. Collateral benefits result simply from being enrolled, such as receiving medical care. Aspirational benefits relate to the findings of the study in enhancing scientific knowledge and perhaps improving health. More recently, the term "inclusion benefit" has been used to describe more broadly the benefits which accrue simply as a result of being enrolled.[4]

While prior to enrollment it may be difficult to predict accurately what if any benefits will result, the hope for some or all of these types of benefit may be important for potential participants. In addition, investigators, sponsors, communities, and those charged with the ethical oversight of research should have a sense of the nature, magnitude, and likelihood of associated benefits. Even though benefits and risks related to research may be incommensurable,[5] benefits may offset the burdens and potential risks of participation. Although attention has focused on whether research participants actually derive better medical outcomes,[6] the social benefits experienced in research have not been systematically described. Our data begin this task.

Of course, our results should be interpreted with some limitations in mind. First, the reports of PSIs emanate from a single trial involving vulnerable participants who had engaged in a stigmatized behavior. Accordingly, the nature and prevalence of PSIs might differ in other settings and in other types of research. In addition, the PSIs we describe are based only on self-reports of participants. Further, as questions about social impacts were asked by trial staff, the data may have been susceptible to a social response bias, in which participants may have been inclined to report positive benefits to trial staff in order to maintain good relationships with them. Finally, participants who did not experience PSIs may have dropped out of the study.

While this trial was unable to demonstrate a positive effect in terms of HIV prevention and mortality,[7] documenting the extent of PSIs is helpful in better understanding participants' experiences. The high degree of reported PSIs is conceivably due to the reduction of drug use in settings where it is highly stigmatized. Other factors might include being treated with respect and dignity at study sites or participating in an endeavor directed at decreasing HIV transmission.

Regardless, future research should embed assessments of negative *and* positive social impacts experienced by research participants not only to ensure their well-being, but also to inform related policy and conceptual work. To increase efficiency, PSIs might be elicited using closed-ended items, perhaps using codes to develop appropriate instruments based on

the nature of the trial. Further, to minimize the possibility of social response bias, personnel not otherwise working on the trial could assess social impacts. It may also be beneficial to map any changes in local policies outside of the research that may affect the well-being of participants (e.g., new employment programs or changes in enforcement of drug policies). After all, while research rightly focuses on direct benefits, assessing indirect benefits such as PSIs, is also arguably important in helping to ensure the ethical conduct of the research while ensuring the well-being of participants.

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Table 1

Socio-demographic characteristics of participants enrolled at HPTN 058 study sites in Nanning and Xinjiang, China, and Chiang Mai, Thailand

	N (%) or mean (SD)		
	Reported a PSI (N=608)	**Did not report a PSI (N=181)**	**p-value**
Age	36 (7.9)	36 (6.7)	0.86
Male	556 (91%)	161 (89%)	0.89
Married/living with partner	346 (57%)	86 (48%)	0.17
Years of Education	7 (4.7)	9 (3.1)	<0.001
Minority Ethnicity	385 (63%)	82 (45%)	<0.001
Age First Injected Drugs	28 (8.0)	26 (6.5)	0.004
Years since First Injection	8 (6.0)	10 (5.6)	<0.001
Financial Support from:			
Regular Employment	361 (59%)	88 (49%)	0.01
Spouse/family/friends	272 (45%)	97 (54%)	0.04
Other	250 (41%)	82 (46%)	0.32

Table 2

PSIs reported by participants at study sites in Nanning and Xinjiang, China, and Chiang Mai, Thailand

PSI		Week			
	Total visits	**26**	**52**	**78**	**104**
Long Term Medication Assisted Treatment (LT-MAT)					
	N=1173	N=374	N=343	N=254	N=202
Drug-related PSIs					
Reduction in Drug Use	523 (45%)	175 (47%)	151 (44%)	108 (43%)	88 (44%)
Reduce Cravings/Withdrawal	32 (3%)	17 (5%)	10 (3%)	1 (0%)	4 (3%)
Non-drug-related PSIs					
Improved Health	132 (11%)	53 (14%)	33 (10%)	30 (12%)	16 (8%)
Life Improved	131 (11%)	59 (16%)	36 (10%)	24 (9%)	12 (6%)
Gained Knowledge	90 (8%)	27 (7%)	27 (8%)	21 (8%)	15 (7%)
Relationships Improved	84 (7%)	31 (8%)	21 (6%)	19 (7%)	13 (6%)
Program Helpful	70 (6%)	15 (4%)	18 (5%)	20 (8%)	17 (8%)
Economic Improvement	68 (6%)	32 (9%)	15 (4%)	16 (6%)	5 (2%)
Short Term Medication Assisted Treatment (ST-MAT)					
	N=1178	N=369	N=344	N=255	N=210
Drug-related PSIs					
Reduction in Drug Use	425 (36%)	153 (41%)	122 (35%)	97 (38%)	53 (25%)
Reduce Cravings/Withdrawal	83 (7%)	18 (5%)	26 (8%)	17 (7%)	22 (10%)
Non-drug-related PSIs					
Gained Knowledge	117 (10%)	37 (10%)	27 (8%)	26 (10%)	27 (13%)
Improved Health	115 (10%)	50 (14%)	27 (8%)	25 (10%)	13 (6%)
Life Improved	107 (9%)	35 (9%)	38 (11%)	20 (9%)	14 (7%)
Program Helpful	77 (7%)	26 (7%)	19 (6%)	18 (7%)	14 (7%)
Relationships Improved	68 (6%)	24 (7%)	21 (6%)	14 (5%)	9 (4%)
Economic Improvement	29 (3%)	14 (4%)	8 (2%)	5 (2%)	2 (1%)

Table 3

Regression Models of PSIs over Time and Study Arm

	Any PSI		Drug-related PSI		Non-drug-related PSI	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
Time: Year 1 vs. Year 2	2.98 (2.45, 3.62)	<.001	1.45 (1.21, 1.74)	<.001	1.85 (1.53, 2.23)	<.001
Arm: LT-MAT vs. ST-MAT	1.24 (0.96, 1.61)	0.10	1.22 (1.01, 1.48)	0.04	1.24 (1.01, 1.52)	0.04

All models are adjusted by site