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Exploring evidence for behavioral risk compensation among participants in an HIV vaccine clinical trial

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ABSTRACT

Background: HIV vaccine trial participants may engage in behavioral risk compensation due to a false sense of protection. We conducted an ancillary study of an HIV Vaccine Trials Network (HVTN) vaccine efficacy trial to explore risk compensation among trial participants compared to persons who were willing to participate but ineligible based on previous exposure to the Ad5 virus (Ad5+) across three timepoints.

Methods: Participants were drawn from the Atlanta, GA site of the HVTN 505 vaccine trial. From 2011–2013, all persons who met prescreening criteria for the clinical trial and presented for Ad5 antibody testing were invited to participate in the ancillary study. Data were collected from vaccine trial participants (n = 51) and Ad5+ participants (n = 60) via online surveys across three timepoints: baseline, T2 (after trial participants received 2/4 injections) and T3 (after trial participants received 4/4 injections). Data analyses assessed demographic, psychosocial, and behavioral differences at baseline and changes at each timepoint.

Results: At baseline, Ad5+ participants were less likely to have some college education ($p = 0.024$) or health insurance ($p = 0.008$), and were more likely to want to participate in the vaccine trial "to feel safer having unprotected sex" ($p = 0.005$). Among vaccine trial participants, unprotected anal sex with a casual partner ($p = 0.05$), HIV transmission worry ($p = 0.033$), and perceived chance of getting HIV ($p = 0.027$), decreased across timepoints.

Conclusions: Study findings suggest that persons with previous exposure to Ad5 may be systematically different from their Ad5-negative peers. Unprotected anal sex with a casual partner significantly decreased among HIV vaccine trial participants, as did HIV worry and perceived chance of getting HIV. Findings did not support evidence of risk compensation among HIV vaccine trial participants compared to Ad5+ participants.

1. Introduction

Since the HIV epidemic began, approximately 35 million people have died of AIDS-related causes [1]. Despite challenges in vaccine development [2,3], the introduction of a safe, effective HIV vaccine remains a public health priority [4]. However, the ultimate benefits of HIV vaccination may be reduced by risk compensation [5]. Risk compensation can be conceptualized as an increase in risky behavior due to a decrease in perceived risk of HIV, based on beliefs about the protective effect of the candidate vaccine [5]. It has been hypothesized that high levels of risk compensation in recipients of a vaccine with low efficacy could result in increased HIV incidence [6–9].

HIV vaccine trial participants may be particularly prone to risk compensation [10]. Although trial participants undergo a rigorous consent process and are provided with explicit behavioral risk-reduction counseling throughout the trial, they may nonetheless engage in risk compensatory behavior due to a false sense of

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protection. Recent studies of HIV vaccine trial participants have not shown support for risk compensation, possibly due to effective risk-reduction counseling [11–15]. Similarly, studies assessing risk behavior among participants in clinical trials for pre-exposure prophylaxis (PrEP), another critical biomedical HIV prevention method, have also not shown evidence of risk compensation [16–19]. However, counseling may not effectively impact all participants [20]. Conducting social and behavioral studies alongside clinical trials remains critical [21].

The largest recent vaccine efficacy trial completed in the United States was the HIV Vaccine Trials Network (HVTN) 505 clinical trial [22]. Enrollment began in 2009 and was halted in 2013 due to lack of efficacy. The vaccine regimen used in this trial was a DNA prime–recombinant adenovirus type 5 boost (DNA/rAd5) HIV-1 vaccine [22]. The goal of the HVTN 505 trial was not to develop a vaccine for FDA licensure; rather, to produce a safe and reliable vector platform. Due to previous evidence supporting its safety and outcomes, Ad5, the same non-enveloped DNA virus vector utilized in the U.S.-based Step study, was utilized in the HVTN 505 study. However, follow-up analyses from the Step study found that participants with previous Ad5 exposure (Ad5+) were more likely to contract HIV than participants without previous exposure [23]; thus, Ad5+ persons were ineligible to participate in the HVTN 505 study. Prevalence estimates for Ad5, transmitted via both fecal and respiratory secretions, range from 30–60% in the United States, and are much higher in international settings [24–26]. High prevalence may pose an issue for Ad5 vectored vaccines, as pre-existing Ad5 immunity has the potential to attenuate the immunogenicity of Ad5-vectored vaccines [27–29].

To learn more about Ad5+ persons and address the potential health threat posed by risk compensation associated with participation in an HIV vaccine clinical trial, we conducted a small, hypothesis-generating ancillary study of the HVTN 505 study. The ancillary study assessed sexual risk behaviors and risk perceptions among participants in the HVTN 505 study compared to persons who were willing to participate but ineligible based on Ad5+ status across three timepoints.

2. Methods

2.1. Study participants and sampling

Participants were drawn from the Emory University Hope Clinic (Atlanta, GA) site of the HVTN 505 vaccine trial. From October 2011–April 2013, all participants who met prescreening criteria for the HVTN 505 study and presented for Ad5 antibody testing were invited to participate in the ancillary study. Prescreening criteria for the HVTN 505 study included: (1) MSM or transgender women between the ages of 18–50, (2) fully circumcised, and (3) history of unprotected anal intercourse with one or more male or male-to-female transgender partners or anal intercourse with two or more male or male-to-female transgender partners in the 6 months prior to randomization (full criteria available at clinicaltrials.gov identifier # NCT00865566). Everyone who met prescreening criteria was eligible for an HVTN 505 "1st screen" visit, where Ad5 antibody testing was conducted. Persons with previous exposure to the Ad5 virus (Ad5+) were ineligible to participate in the HVTN 505 study; however, they were eligible to participate in the ancillary study. The rationale for comparing HVTN 505 participants to Ad5+ participants in the ancillary study was that Ad5+ participants were expected to be similar to HVTN 505 participants, with the exception of previous Ad5 exposure. Thus, this group provided a reasonable comparison population to explore the question of whether participation in an HIV vaccine clinical trial impacted risk behavior.

2.2. Recruitment and data collection procedures

Participants were recruited from the pool of persons completing their 1st screening visit for the HVTN 505 study. Upon completion of the screen, recruiters explained the ancillary study and obtained informed consent. Of 195 people approached about the study, 193 provided consent to participate, and 111 enrolled in the study (defined as completing a baseline survey). Reasons for not completing a baseline survey after providing consent were not collected. All participants of the ancillary study completed online surveys, via SurveyGizmo, at three timepoints: (1) Baseline (immediately for Ad5+ participants; prior to enrollment in the HVTN 505 study for vaccine trial participants), (2) Month 2 (after enrolled HVTN 505 participants received two injections of the four-dose series) and (3) Month 7 (after HVTN 505 participants received all four injections). All participants received risk-reduction counseling at baseline; only HVTN 505 participants received risk-reduction counseling throughout the trial, when they returned to the clinic for study visits. Ad5+ participants did not return to the clinic after their 1st screening visit. Electronic gift cards to Target ($10.00) were e-mailed to participants after survey completion at each timepoint. All protocols were approved by NIAID and the Fred Hutchinson Cancer Research Center IRB.

2.3. Measures

Background factors included demographic variables and substance use in the past two months (including: alcohol, marijuana, poppers, cocaine, crack, amphetamines, tranquilizers, hallucinogens, Ecstasy, or Special K).

Sexual behaviors in the past two months included: unprotected anal sex with a main partner, a casual partner, multiple partners, or a partner whose HIV status was positive or unknown; and whether participants always disclosed their own or asked about their partner's HIV status.

HIV prevention behaviors in the past two months included: abstained from sex, had oral sex only, always used a condom, only had sex with HIV negative partners, was always a top (e.g., always engaged in insertive anal sex), used pre-exposure prophylaxis (PrEP), or none.

Psychosocial variables included: sensation seeking (8 items, alpha = 0.915) and impulsivity (6 items, alpha = 0.772) [30]; sexual adventurism (10 items, alpha = 0.821) [31]; positive future orientation (4 items, alpha = 0.846) [32]; self-efficacy for sex communication (4 items, alpha = 0.85) [33]; and self-efficacy for condom negotiation (3 items, alpha = 0.916) [34]. (Table 1). (Detailed information about psychosocial scale variables are available in Supplementary Table 1).

HIV risk-perception beliefs included**:** HIV transmission worry (4 items, alpha = 0.806) [35]; and perceived chance of getting HIV (2 items, alpha = 0.832).

Perceived HIV vaccine advantages included benefits for HIV prevention (3 items; alpha = 0.856); and risk compensation (8 items; alpha = 0.876).

Perceived HIV vaccine disadvantages included costs for sexual health (6 items; alpha = 0.811); stigma (3 items; alpha = 0.927); and financial costs (1 item).

HIV Vaccine trial questions included: Why do you want to participate in the HVTN 505 study?; Do you believe that the experimental HIV vaccine is at least 50% effective at preventing HIV?; Do you believe that the experimental HIV vaccine is at least 90% effective at preventing HIV?; On a scale of 0% to 100%, where 0% means NO protection from HIV, and 100% means COMPLETE protection from HIV: How effective do you believe the experimental vaccine is at preventing HIV?; On a scale of 0% to 100%, where 0% means NO protection from HIV, and 100% means COMPLETE protection from HIV:

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