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Preventive Misconception and Adolescents' Knowledge about HIV Vaccine Trials

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Abstract

Objective—Adolescents have had very limited access to research on biomedical prevention interventions despite high rates of HIV acquisition. One concern is that adolescents are a vulnerable population, and trials carry a possibility of harm, requiring investigators to take additional precautions. Of particular concern is preventive misconception, or the overestimation of personal protection that is afforded by enrollment in a prevention intervention trial.

Methods—As part of a larger study of preventive misconception in adolescent HIV vaccine trials, we interviewed 33 male and female 16–19 year olds who have sex with men. Participants underwent a simulated HIV vaccine trial consent process, and then completed a semi-structured interview about their understanding and opinions related to enrollment in a HIV vaccine trial. A grounded theory analysis looked for shared concepts, and focused on the content and process of adolescent participants' understanding HIV vaccination and the components of preventive misconception, including experiment, placebo and randomisation.

Results—Across interviews, adolescents demonstrated active processing of information, in which they questioned the interviewer, verbally worked out their answers based upon information provided, and corrected themselves. We observed a wide variety of understanding of research concepts. While most understood experiment and placebo, fewer understood randomisation. All understood the need for safer sex even if they did not understand the more basic concepts.

Conclusions—Education about basic concepts related to clinical trials, time to absorb materials and assessment of understanding may be necessary in future biomedical prevention trials.

Keywords

Preventive Misconception; Adolescent; HIV; Bioethics; Clinical Trial; Vaccine; Qualitative

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INTRODUCTION

Adolescence, a time of increasing HIV risk and delays in HIV diagnosis, is a period of high relevance to HIV biomedical prevention. [1] Among adults, clinical trials of biomedical interventions have demonstrated some efficacy at lowering HIV transmission. Examples include an antiretroviral (ARV)-based vaginal microbicide, post-exposure ARV prophylaxis, pre-exposure ARV prophylaxis and an HIV vaccine (RV 144). [2–6] However, few of these biomedical interventions have been tested in adolescents.

The ethics of research with adolescents is complex. Of particular concern to adolescent participation in a biomedical HIV prevention trial is preventive misconception and the possibility of risk compensation. Preventive misconception is the overestimation of one's level of personal protection that is afforded by being enrolled in a prevention trial. [7] It is composed of two parts: (1) the tendency to overestimate the probability of assignment to the experimental intervention and (2) the assumption that the unproven experimental intervention is efficacious. Preventive misconception raises concerns for risk compensation, in which trial participants increase their sexual risk behaviours under the assumption that they have been assigned to an efficacious intervention. [8] Avoiding preventive misconception requires that adolescents understand the concepts of experiment (the intervention may not work), placebo and random assignment. Avoiding risk compensation requires that adolescents understand and follow recommendations for safer sex behaviours.

Adolescents differ from adults in key areas relevant to HIV prevention, making clinical trials and the complex ethical issues they raise, necessary. [9] Biological and behavioural differences suggest that interventions may behave differently with adolescents, compared to adults. Examples of biologic differences include a longer time period to development of AIDS, [10] different ARV pharmacokinetics, [11] and different immune responses to vaccines. [12] Differences in sexual behaviour may also lead to different intervention effects. Adolescent relationships and sexual behaviours differ from adults in relationship length, partner characteristics and sexual practices. [13–15]

Legal and regulatory issues also differ for minors. Minor adolescents who cannot legally consent to clinical care in their state must have parental permission in addition to adolescent assent to participate in research. Although local institutional review boards (IRBs) may waive parental permission and allow the adolescent to provide consent to research, [1, 16] parental permission cannot be waived in FDA-regulated (ie, experimental drugs) research. [17] In HIV prevention research, these regulatory requirements raise legal and ethical issues around confidentiality and disclosure of sexual behaviour and sexual orientation. [18]

There are concerns that these differences might put adolescents in an HIV vaccine trial at a higher risk for preventive misconception and risk compensation. [19–23] However, little empiric data exist on preventive misconception and risk compensation among adolescents. US focus groups explored adolescent understanding of HIV prevention research concepts, and found that many participants held views consistent with preventive misconception. [24] Similarly, two surveys of South African adolescents' knowledge of HIV vaccine trials describe participant difficulty with elements of preventive misconception, in particular, the concept of placebo. [25 26]

¹In the U.S., minors under 18 years of age can be permitted to give their own consent, not just assent, to research in specific circumstances relevant to HIV prevention. One reason is that the U.S. federal regulations 45CFR46 do not define children by age; Instead, regulations define children as those that cannot consent to their own clinical care in that jurisdiction.[16] While this is generally less than 18 years of age, minor adolescents in the U.S. can provide their own consent for STD-related clinical care in all 50 states, and therefore can provide their own consent for STD-related research.

Research on preventive misconception and risk compensation among adults shows mixed results. In a study of informed consent for a shingles vaccine, one-third of participants demonstrated at least one element of preventive misconception, through an overestimation of the vaccine's effectiveness or an underestimation of assignment to placebo. [7] Most, but not all, adult HIV biomedical prevention trials did not find evidence of risk compensation. Examples of trials showing no evidence of risk compensation included male circumcision, [27] postexposure prophylaxis, [28] and HIV vaccine trials. [29 30]

The purpose of our study was to examine adolescents' understanding of key aspects of a hypothetical HIV vaccine clinical trial, including preventive misconception, after an informed consent process. We specifically examine adolescents' understanding of the purpose of the prevention trial, the concepts of placebo, experiment and randomisation and the need to practice safer sex. We used qualitative methods because they are particularly useful when little is known about a topic, or when existing data show conflicting results.

MATERIALS AND METHODS

Participants

Semistructured qualitative interviews were conducted as part of a larger hypothetical HIV vaccine study at four Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) sites in the USA. Sites were located in California, New York, Maryland and Louisiana. If an actual US-based adolescent HIV vaccine trial were to become available, it would likely be conducted through the ATN. Inclusion criteria included HIV-negative women and men, ages 16–19 years, who reported sex with men, and indicated a possible willingness to participate in a HIV vaccine trial. Sites recruited from community agencies, youth programmes, clinics and a gay pride event. Each site recruited 6–9 participants using a purposive sampling approach, [31] with study staff identifying adolescents representative of those seen at their site in terms of age, ethnicity, gender and behavioural experience.

Procedures

IRB approval was obtained at each site, and adolescents provided written informed consent. Parental permission was waived. All participants received a standard HIV vaccine trial consent form adapted from adult HIV vaccine trials, and underwent a standard informed consent process that included a review of the consent form. For the purposes of this simulated HIV vaccine trial, we assumed a waiver of parental permission and had adolescents provide their own consent (rather than assent).

All participants, additionally, received supplemental explanatory pamphlets that addressed the concepts relevant to clinical trial participation and preventive misconception, including experiment, placebo and randomisation. Two-thirds viewed the pamphlets at the time of the simulated HIV vaccine consent, and the remaining qualitative participants viewed the pamphlets at the time of the qualitative interview. Qualitative interviews took place after completion of surveys and procedures for the larger study.

Interviews

Semistructured one-on-one interviews were conducted by trained ATN research staff and lasted 30–60 minutes. An inductive approach to interviewing was used to avoid making assumptions about adolescents' attitudes towards, and understanding of, an HIV vaccine trial. Interviews were audio-recorded, and the first 3–4 audio recordings at each site were closely reviewed near the time of the interview by the first two authors for content and technique; subsequent audio recordings were reviewed in real time if needed. All audio-recordings and field notes are included in the analysis.

The interview guide started with broad questions, “Tell me what you read about the HIV vaccine?”, “Tell me what happens if you would sign up for the trial?” and “What are the benefits (drawbacks) of participating in the trial?” More specific questions were used to explore concepts related to preventive misconception, including, “How do they decide who gets the vaccine?”, “Do you think that you would be one of the people in the vaccine group? Why or why not?” and, “What are your responsibilities in order to be able to stay in the trial?”

Analysis

Interviews were transcribed by a professional medical transcription service, checked by the individual interviewer, and then analysed by two authors (MO and AA), using a grounded theory-based approach. [32] First, a set of initial codes was developed from the literature on preventive misconception and risk compensation, and applied to the data. Examples include ‘understanding of vaccines’, ‘placebo’, ‘experiment’, ‘randomisation’ and ‘sexual risk behaviours.’ We then selected and read each of these initial codes, identifying key concepts within each, such as, ‘poor understanding of probability’, as well as cross-cutting concepts, such as ‘active processing.’ For each of these key concepts, we developed a list of its properties and dimensions. Key concepts were tested against subsequently collected data. Similar concepts were collapsed and differences were resolved by discussion. A core, or overarching, concept was identified from the data (for the following data, it was ‘active processing’), and a conceptual model was created around this core concept.

RESULTS

Participants

Thirty-three interviews were available for analysis. Participants were fairly evenly split by age, gender, ATN site and recruitment venue (see table 1).

Overview of five key cognitive tasks

Five key cognitive tasks were identified as necessary to understand a vaccine clinical trial: understanding vaccines and how they work, understandings of the concepts of experiment, placebo and randomisation, and an acknowledgement of the need to maintain safer sex behaviours (figure 1). We did not observe any clear pattern of differences by age, gender, ethnicity, site of recruitment or timing of receipt of supplemental materials. Therefore, we present data for all participants together.

Active processing of information

Despite undergoing a consent process modeled after adult HIV vaccine trials, adolescent participants in our study demonstrated a dynamic and evolving understanding of research concepts across their interviews, with active processing of the information provided to them. For example, when clinical trials concepts were not clear to participants, many questioned the interviewer. We observed the following processing strategies: (1) expressing uncertainty about their answers and checking in with the interviewer to see if they were answering the questions correctly; (2) giving one answer early in the interview, with later corrections; (3) using information provided and logical reasoning to arrive at an answer and (4) turning the tables on the interviewer and asking the interviewer questions (table 2, quotes 1–3). These processing strategies resulted in adolescents coming to conclusions about the concepts under discussion. For example, one young woman initially was very confident in her answers. However, when the interviewer asked her to elaborate, she realized that she did not fully understand the concepts as well as she initially thought. It was then that she turned the interview back on the interviewer by asking him questions instead of answering them.

Understanding of vaccine

Most adolescents understood that a HIV vaccine was an injectable product that prevents HIV, that it would be useful in preventing, not treating, HIV infection, and would be for uninfected individuals. One participant explained, *“Not the ones who are already infected with HIV, already. It won’t help them but will help people that don’t have HIV, protect them from getting the virus (Female, 18, Site 3).”* Many participants even understood fairly sophisticated topics related to vaccines, such as different vaccine constituents, antibodies and the effect that a vaccine has on routine antibody testing for HIV (See table 2, quotes 4–6).

However, a subset did not completely understand that this vaccine was designed to prevent, rather than treat HIV infection. Two participants expressed the belief that the vaccine could both prevent and cure HIV, and four participants said either that the vaccine could be used only in persons infected with HIV or it could be used both with HIV-infected and HIV-uninfected persons. This was an area where we observed active processing of information, with participants verbally reasoning out their responses, frequently questioning the interviewer, or correcting themselves later in the interview (table 2, quote 1)

An additional subset had trouble understanding vaccine effectiveness. In particular, several had difficulty understanding the concept of a vaccine that is less than 100% effective (table 2, quote 7).

Understanding of experiment

Participants generally understood that the vaccine was experimental and might not work. In order to avoid leading questions, the interviewer only generally asked about what adolescents read about the vaccine, and their understanding of whether the vaccine would work. Even with this more general approach to questions, 14 participants verbalised that the HIV vaccine researchers did not know for sure whether the vaccine would work, and that the study would test whether it would work. For several, the concept that experimental interventions might not work, and that this was a test of efficacy, was obvious: *“Because it’s experimental. I mean, you don’t know. If it worked, then we would all be using it. So we wouldn’t have this experimental study.”* (table 2, quotes 8–9).

However, there were several who did not understand the uncertainty about efficacy, including participants who either said the vaccine would definitely work or not work. Again, this was an area where we observed active processing of information, with participants identifying the different possibilities, verbally reasoning through, and choosing an answer. One participant went back and forth, ultimately concluding that the vaccine would not protect a person from acquiring HIV (table 2, quote 2).

Understanding of placebo

The concept of placebo was generally well understood, with few exceptions. We observed an overall understanding that: (1) the placebo was an injection that contained salt water; (2) one group would get the vaccine and one would get the placebo; (3) participants could not tell the difference between the vaccine and the placebo and (4) participants could experience side effects with the placebo (table 2, quotes 10–13).

One participant stated that the placebo was another vaccine and we were trying to see which one worked better. A second participant appeared to completely miss the fact that some participants would receive a placebo, saying that everybody gets the vaccine (table 2, quote 14). A third participant struggled with the concept of placebo, confusing it with the ‘placebo effect’ (ie a person believes the placebo to be the real drug and reports an improvement in

symptoms). He actively attempted to make sense of this misunderstanding in the context of what he believed about vaccines and immune mechanisms, leading to the mistaken belief that the placebo could trick your body into making more antibodies.

Even when participants understood that a placebo would be used and only some participants would get the placebo, the logic of using a placebo was not always clear. Several participants questioned why we did not give the vaccine to everyone (table 2, quote 15).

Understanding of randomisation

Participants' understanding of random assignment was more limited. Most were able to repeat back the wording that was used in the consent form and the pamphlets, (eg, that randomisation was like the 'flip of a coin'). However, when asked to explain these answers, responses ranged from adequate understanding to clear misunderstanding. We considered participants to have an adequate understanding of randomisation if they said that: (1) there would be two groups and there was no way to tell which group one might be in; (2) the assignment would be done by some type of random procedure rather than by a personal characteristic or a decision by research staff; (3) their personal chance of getting the vaccine was 50% and/or (4) they could restate phrases from the consent form and supplemental information such as, 'the flip of a coin' into probability statements (eg, a 50% chance).

Even among the 22 participants who expressed an adequate understanding of randomisation, we observed a range of sophistication in their responses. Table 2, quote 16 illustrates a basic understanding of randomisation. Two participants took the phrase, 'flip of a coin' literally, stating that the researchers would flip a coin for each person to decide whether that person would be in the vaccine or placebo group. Others demonstrated a more sophisticated understanding of random assignment, the mechanism of random assignment and the implications of random assignment for their participation in a potential HIV vaccine trial (table 2, quotes 17–8).

Among those making erroneous statements about random assignment, most still understood that there would be two groups, one receiving vaccine and one receiving placebo. However, when they were asked how the researchers decided who would be in the vaccine versus placebo groups, or were asked to explain what they meant by answers such as 'flip of a coin', these participants either made statistically improbable statements, or described non-random approaches to group assignment (table 2, quotes 19–20). One participant repeatedly described his probability of getting the real vaccine as a 'slim chance.' Others felt they would definitely get the vaccine, giving reasons including being able to choose the vaccine group, wanting to be in the vaccine group, being unusually lucky, and having a feeling that they would be placed in the vaccine group.

Acknowledge need for safer sex behaviours

While we observed some misunderstandings consistent with preventive misconception across the concepts of experiment, placebo and randomisation, almost all participants acknowledged the need for safer sexual behaviours, and none of the participants made statements endorsing sexual disinhibition. Most said they should practice safe sex because it was a requirement to stay in the study, because they were not supposed to get pregnant or acquire HIV. An additional six participants explicitly stated they should not have unprotected sex because the vaccine was experimental, with unknown efficacy. These adolescents were actively processing the information provided and linking the information about unknown efficacy to the need to practice safer sex (table 2, quote 3). Another participant recognised the possibility of sexual disinhibition in others who might participate

in an HIV vaccine trial, but clearly acknowledged the need for safer sex behaviours because of the experimental nature of the vaccine (table 2, quote 21).

DISCUSSION

This study extends our understanding of preventive misconception and adolescent capacity to understand and consent to biomedical HIV prevention clinical trials. With some additional education around concepts related to clinical trials and the opportunity to actively process information, most of our adolescent participants understood the key concepts of placebo and experimental design, and approximately two-thirds of participants were able to describe random assignment. These findings suggest that, as with adult populations, 16–19 year old adolescents have the potential to understand enough basic clinical trial concepts to provide informed consent for biomedical HIV prevention trials.

Our findings, particularly that of active processing, are also consistent with literature around adolescents' capacity to consent to clinical research. [33 34] While there is a general consensus that individuals continue to develop decision-making capacity as they move through adolescence into adulthood, [35 36] studies have generally found that by mid-adolescence (approximately 14 years), adolescents have sufficient capacity to consider information and opinions from diverse sources and make their own judgments, [33] and that they have similar capacity to adults in understanding (hypothetical) research procedures, considering alternatives, and making rational decisions. [34]

Consistent with adult [7] and adolescent [24 25] literature, elements of preventive misconceptions did exist. Despite a generally good understanding of the concepts of placebo and experimental design, a small but important subset clearly did not understand these concepts, and another subset needed to actively process the information with the interviewer. Additionally, our study may have had improved understanding of these concepts, because the supplemental pamphlets the participants reviewed addressed the concepts of experiment, placebo and randomisation.

The concept of randomisation appeared more difficult for participants, as approximately one-third did not understand random assignment and demonstrated evidence of preventive misconception in that they overestimated the probability that they would be assigned to the vaccine group. This finding is not surprising, given that US adult populations have poor numeracy and a poor understanding of statistical concepts. [37 38] Future prevention trials with both adolescents and adults may need to provide decision-making support to assure the understanding of random assignment.

Our most important finding was the active processing we observed, which suggests that adolescent participants are generally interested and able, with support, to understand abstract research topics. In our study, the qualitative interview ended up serving as a way for participants to better understand the information they received with a knowledgeable research staff person. For example, many participants asked interviewers to clarify concepts, or were able to work through the logic of the information they received during the interview. This finding suggests that adolescents can be active participants in a consent process, rather than passive recipients of information, and that the consent process should involve a back-and-forth between research staff and potential adolescent participants, with sufficient opportunity to clarify information and ensure understanding.

A central concern regarding preventive misconception is that it could lead to risk compensation. In the contexts of an HIV vaccine trial, risk compensation would take the form of sexual disinhibition, or the practice of unsafe sexual behaviours. Despite our observing elements of preventive misconception, no participants reported that they

personally might engage in risk compensation as a result of participating in this hypothetical trial. This finding, that it is possible for adolescent to demonstrate elements of preventive misconception with little endorsement of risk compensation, suggests that it may be ethically acceptable to tolerate some degree of preventive misconception.

A strength of this study, its qualitative design, also is a limitation. While small samples allow for an opportunity to explore concepts in depth, they may limit generalisability beyond similar groups. A key aim of the ATN is to provide a research infrastructure and access to high-risk HIV-infected and HIV-uninfected youth for HIV treatment and prevention trials. Participants were recruited through ATN sites so that results would be applicable to the adolescents most likely to be enrolled in clinical trials. Also, one limitation is that participants were interviewed after completing quantitative decision-making surveys, and the surveys may have influenced their responses to the qualitative interview. A third limitation is that we interviewed a US-based sample of adolescents. While many developmental processes are universal, differences may exist in family structure, the cultural acceptability of discussing sensitive sexual health issues such as HIV risk and prevention, or adolescents' decision-making roles in society, which could influence findings.

In summary, while adolescent participants displayed a generally adequate understanding of key elements of a hypothetical HIV vaccine clinical trial, a subset demonstrated preventive misconception, particularly in their understanding of randomisation. However, we observed little endorsement of potential risk compensation. The adolescents' engagement in active processing of the key clinical trial concepts was encouraging, and points to potentially effective ways to facilitate adolescents' understanding of, and participation in, biomedical prevention clinical trials.

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Figure 1.

Table 1

Demographic information

Characteristic	n (%)
Age	
16–17 years	18 (54.5%)
18–19 years	15 (45.5%)
Race/Ethnicity	
White, Non-Hispanic	4 (11.1%)
African American, Non-Hispanic	21 (58.3%)
Latino/Hispanic	4 (11.1%)
Other	7 (19.4%)
Gender	
Male	19 (57.6%) – includes 1 transgender M F
Female	14 (42.4%)
ATN Site	
Site 1	9 (27.3%)
Site 2	9 (27.3%)
Site 3	9 (27.3%)
Site 4	6 (18.2%)
Recruitment venue	
Clinic	12(36.4%)
Community organisation	12 (36.4%)
Other venue	9 (27.2%)
Total	33 (100%)

Table 2

Concepts of Preventive Misconception and Illustrative Quotes

Concept	Illustrative quote
Active processing	
	<p>1 Expressing uncertainty and checking in with interviewer – Purpose of HIV Vaccine</p> <p>“People who have HIV and people who don’t, right? Isn’t it mainly for people who have it, though? Or is it mainly to protect you from getting it. So I guess if you’re concerned with getting HIV, you would most likely get the vaccine.” (Male, 16, Site 4)</p> <p>2 Use of logical reasoning – Unknown effectiveness of experimental vaccine</p> <p>“</p> <p>Adolescent: I read that the vaccine doesn’t prevent you from getting HIV and it doesn’t give you HIV. It’s basically just a vaccine to see how to prevent it from happening.</p> <p>Interviewer: When you say that it doesn’t prevent the HIV disease and it doesn’t give it to you, what do you mean?</p> <p>Adolescent: In the form it said that it doesn’t prevent you from getting HIV in the future, but it doesn’t give you HIV at that time either.” (Male, 16, Site 4)</p> <p>3 Use of logical reasoning - need for safer sex</p> <p>“I read that you can still get HIV, even though you’re taking the vaccine, because ...they don’t know whether it’s preventable or not. ...you still should have protected sex, because it’s [only] a possibility that [the vaccine] is preventing HIV.” (Female, 17 Site 3).</p>
Understanding of vaccine	
	<p>4 Good understanding – vaccine not infectious</p> <p>“No, you can’t get HIV from the vaccine because it’s man-made; it wasn’t made using dead HIV cells or live HIV cells.” (Female 16, Site 1)</p> <p>5 Good understanding –mechanism of action</p> <p>“The vaccine helps boost your antibody, it helps make them stronger and hopefully be able to fight off the virus.” (Male 19, Site 1)</p> <p>6 Good understanding –causes positive HIV test</p> <p>“Because the vaccine would probably cause your body to start making antibodies for the HIV virus, even if it isn’t present, because that’s just your body reacting to the vaccine. So, if you were to go somewhere else and get an antibody test for HIV, it may come back positive.” (Male, 16, Site 3)</p> <p>7 Limited understanding – not 100% effective</p> <p>“You gave us the general information about the side effects that it could possibly have and how [it] doesn’t prevent HIV but it can, it’s gonna prevent it in the long run but it doesn’t stop you from getting it. You still have to protect yourself and stuff like that.” (Male, 16, Site 1)</p>
Understanding of clinical trial concepts	
Experiment	<p>8 Good understanding – concept of experiment</p> <p>“I don’t think it will harm you but I’m not sure if it will protect you just yet. I think that is has a possibility of protecting people if the study goes well.” (Male, 19, Site 4)</p> <p>9 Good understanding –concept of experiment</p> <p>“Well, what I read about it was it’s an experiment to figure out how to prevent it, HIV, and it’s not a for sure thing that it can prevent it or if it does, it’s just like say like an experiment and that’s pretty much it.” (Male, 19, Site 3)</p>
Placebo	<p>10 Good understanding – placebo is injection inactive substance</p>

Concept	Illustrative quote
	<p>“Not everybody in the study would get the vaccine. It would be a mix up of groups...The other two groups, they’ll get something called placebos, which might be salt water or something like that. Only one group really gets the vaccine.” (Male, 16, Site 1)</p>
	<p>11 Good understanding –one group gets placebo, other vaccine</p> <p>“Instead of getting the real vaccine, you would get salt water, but you don’t know this because you’re put into a randomly selected group. Something like that, sugar pills versus real pills.” (Female, 18, Site 2)</p>
	<p>12 Good understanding –can’t tell difference placebo and vaccine</p> <p>“The placebo is just a salt water formula, I guess, that’s got people thinking that it’s the vaccine for the HIV, to prevent HIV, but it’s really not. And you really don’t know if you get it or not, that’s basically it.” (Female, 17, Site 3)</p>
	<p>13 Good understanding – Placebo group can get side effects</p> <p>“Some people might not even get the vaccine. Some people might get the placebo, but there have been known cases where like people will actually get side effects from the placebo as well which is kind of interesting.” (Male, 17, Site 2)</p>
	<p>14 Limited understanding – Everyone gets the vaccine</p> <p>Interviewer: “So who gets the vaccine?”</p> <p>Adolescent: “We do.”</p> <p>Interviewer: “Everybody gets the vaccine?”</p> <p>Adolescent: “No, just the people in the trial that are doing the tests.”</p> <p>Interviewer: “In the trial?”</p> <p>Adolescent: “Mmm hmm [indicates yes].”</p> <p>Interviewer: “Is there another something else that some of the people get?”</p> <p>Adolescent: “Like what, as far as what?”</p> <p>(Female, 18, Site 3)</p>
	<p>15 Limited understanding – Logic of placebo</p> <p>“...Only a small percentage will actually get the real vaccine. That’s where you actually get the real results and you’re just getting [no] results from the guys who got the placebo. It’s in my opinion, I think the placebo thing’s like not helpful at all.” (Male, 17, Site 2)</p>
	<p>16 Basic understanding randomisation</p> <p>Interviewer: “What are the chances that you would be [in the vaccine group]?”</p> <p>Adolescent: “One out of two.”</p> <p>Interviewer: “Do you think you would be in the group that gets the vaccine?”</p> <p>Adolescent: “It’s here nor there. You don’t know.” (Male, 16, Site 1)</p>
	<p>17 More sophisticated understanding randomisation</p> <p>“Well, I don’t know the details on how they do it, but I would assume that they would group everyone by their number, and then assign them a random number in a computer. The computer would pick random numbers and then those participants would get either the placebo or the vaccine.” (Female, 19, Site 2)</p>
	<p>18 More sophisticated understanding randomisation</p> <p>Adolescent: “Well it’s totally random. You wouldn’t know. That’s kind of cool. What that means is from the first group to the second group, no one would know who has the placebo and who actually has the vaccine. That was my understanding of that.”</p>
Randomisation	

Concept	Illustrative quote
	<p>Interviewer: “What do you think your chances would be of getting on the study?”</p> <p>Adolescent: “I’m a pretty logical person, so you wouldn’t know. I take it as a 50/50. I assume that what I was getting it because that’s the whole point. That’s the whole point of placebos, totally think you have it. I’d just be aware that it might not be it. I’d be aware that there is a placebo involved.” (Male, 19, Site 2)</p>
19	<p>Use of language “50/50” but not understanding concept</p> <p>Interviewer: “If you were in the study, do you think that you would be in the vaccine group?”</p> <p>Adolescent: “There’s 50/50 chance.”</p> <p>Interviewer: “So if it was a 50/50 chance would you be in the vaccine group?”</p> <p>Adolescent: “Yeah I believe so yeah.”</p> <p>Interviewer: “Even if it’s a 50/50?”</p> <p>Adolescent: “Yeah.” (Male, 16, Site 1)</p>
20	<p>Non-random approach to group assignment</p> <p>Interviewer: “So would you get the vaccine?”</p> <p>Adolescent: “Yeah.”</p> <p>Interviewer: “If you joined the trial?”</p> <p>Adolescent: Yeah, I would get the vaccine.”</p> <p>Interviewer: “So if you joined the trial, the vaccine trial, you would get the vaccine?”</p> <p>Adolescent: “Right.”</p> <p>Interviewer: You would not get a placebo?”</p> <p>Adolescent: “No.”</p> <p>Interviewer: “ But there’s two different groups you said.”</p> <p>Adolescent: “Mmm hmm [indicates yes], the vaccine and the placebo.”</p> <p>Interviewer: “How do they decide who goes into what group?”</p> <p>Adolescent: “When the tests come back.”</p> <p>Interviewer: “Do you remember how they chose?”</p> <p>Adolescent: “No, I don’t remember.”</p> <p>Interviewer: “And you said you think you would be one of the people in the vaccine group?”</p> <p>Adolescent: “Mmm hmm [indicates yes].” (Female, 17, Site 3).</p>
Acknowledge need for safer sex behaviours	
21	<p>Recognising the possibility of sexual disinhibition, but also the need for safer sex</p> <p>“People hear, ‘oh, well, I’m taking this study and I could have sex all I want with no condoms’ and not knowing if the sexual partner is HIV positive. That may put that in their mind, saying that, ‘okay, well, maybe I should have sex this time, HIV—I mean, I’m protected.’ And who knows? They could get HIV. ... I mean, I just think that that’s just foolish, because you should always protect yourself, no matter or not if you think that you’re protected, you should always, always, always protect yourself against, especially HIV, which can cause AIDS and which can cause death. I think that you should not rely on something that you don’t know if it’s going to work or not. It’s like giving people false hope and with that false hope, it’s like, ‘hey, I got this vaccine, I’m going</p>

Concept	Illustrative quote
	to go have sex, I'm going to have sex with anybody I want and everybody I want, because I'm protected from HIV/AIDS', which is not the case. You should always, always, always protect yourself, use condoms." (Male, 17 Site 3)