Willingness to Join an Anal Cancer Screening and Prevention Trial

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Introduction

HIV-infected men and women are at elevated risk for developing anal cancer. The AIDS Malignancy Consortium is conducting a five-year randomized, controlled trial to determine whether treatment of anal high-grade squamous intraepithelial lesions (HSIL) can prevent anal cancer. HIV-infected men and women over 35 will be screened and those with anal HSIL will be randomly assigned to have their HSIL removed (intervention arm) or not removed (monitoring arm). Both arms will be monitored for progression to cancer at regular intervals for five years, and cancer incidence in the two arms will be compared. The present study used mixed methods to assess willingness to join the proposed five-year trial among HIV-infected men and women in 20 cities and patients presenting to the UCSF Anal Dysplasia Clinic.

Methods

Qualitative Focus Groups and Interviews

- 30 Focus Groups with HIV+ men and women (n=241) were video-recorded and analyzed using Transana software to explore views on participation in medical research and willingness to join this specific trial ($50 incentive).
- 25 clinicians and case workers were emailed a description of the trial and interviewed by telephone using a structured guide to assess willingness to refer patients to the trial ($100 incentive). All but one were willing to refer patients to the trial.

Quantitative Surveys

- 20 new patients were recruited from the UCSF Anal Dysplasia Clinic for a longitudinal survey about their willingness to participate in the study before and after HSIL diagnosis ($100 incentive for 2 surveys).
- 258 HIV+ Survey Participants recruited from clinics and ASOs in 20 cities completed online survey ($25 incentive).

Focus Groups and Surveys

Surveys only

Demographics

		FG (n=241)		Survey (n=258)	
Variable	Category	N	%	N	%
Sex	Male	202	82.8	201	77.9
	Female	42	17.2	57	22.1
Age	35-39	31	12.7	34	13.2
	40-49	126	51.6	129	50
	50-59	75	30.7	76	29.5
	60-75	12	4.9	19	7.4
Race/ethnicity	White	94	38.5	96	37.2
	African American	100	41	87	33.7
	Hispanic	47	19.3	58	22.5
	Asian/Pacific Islander	0	0	2	0.8
	Native American	0	0	4	1.6
	Mixed race	0	0	11	4.3
Education	11th grade or less	5	2	18	7
	High school/GED	78	32	30	11.6
	Trade school	0	0	15	5.8
	Some college	95	38.9	97	37.6
	College graduate	30	12.3	62	24
	Graduate degree	13	5.3	35	13.6
	Unknown	0	0	1	0.4
Income	Under $10,000	83	34	59	22.9
	$10,000 - $19,999	78	32	86	33.3
	$20,000 - $29,999	30	12.3	32	12.4
	$30,000 - $39,999	13	5.3	27	10.5
	$40,000 - $49,999	7	2.9	17	6.6
	$50,000 or more	13	5.3	29	11.2
	Unknown	17	7	8	3.1
Time HIV+	< 12 months	12	4.9	7	2.7
	1-4 years	46	18.9	40	15.5
	5-9 years	34	13.9	37	14.3
	10-19 years	75	30.7	89	34.5
	20+ years	77	31.6	84	32.6
	Unknown	0	0	1	0.4

HPV Knowledge

9 True/False questions about HPV were only asked of survey participants who had ever heard of HPV. The median score was 7 correct. Items missed the most (indicated in red) normalize HPV infection.

Some types of HPV are related to developing anal cancer.	T	84.4%
HPV can be transmitted in ways that do not involve sexual activity.	T	50.8%
Some types of HPV can cause anal or genital warts.	T	92.0%
HPV is the most common sexually transmitted infection.	T	48.2%
Anal cancer is only a risk for HIV-positive men.	F	93.0%
Anal cancer rates are rising among men who have sex with men.	T	78.4%
There are always visible symptoms when someone has HPV.	F	83.4%
The majority of women have HPV by age 50.	T	38.2%
Anal cancer is only a risk for people who have anal sex.	F	87.4%

"They told me to wait a year and I was a little nervous... This was new to me and I didn't know how common it was and when I heard it I -- it's scary. But when I found out and had more information I was able to calm down. And now I can wait and not worry so much." (Female discussing her dysplasia diagnosis)

How the Trial Was Described

A virus called human Papillomavirus, or HPV, causes some kinds of cancers, including anal cancer and cervical cancer. Anal cancer is a rare disease, occurring in roughly one in 1,000 HIV-infected people per year, although rates of anal cancer in the United States have been steadily increasing in recent years.

Anal cancer can be fatal. If not found early enough, it can sometimes be successfully treated with drugs and radiation therapy, which can cause serious side effects that could last for years. When anal cancer is detected at its earliest stages, there is growing evidence that it can be removed with a simple surgical procedure.

Sometimes HPV can cause abnormal changes in anal tissue. A doctor might insert a finger into the anus and feel for possible larger abnormalities, such as warts or cancers. Another kind of smaller abnormality in anal tissue that might not be felt is, called "high grade squamous intraepithelial lesions," or HSIL for short. HSIL is more likely than not to turn into anal cancer. Nearly half of HIV positive men over the age of 35 have HSIL, and 10% of HIV positive women have HSIL. As HIV-positive people live longer thanks to HIV medications, their risk of developing anal cancer has increased.

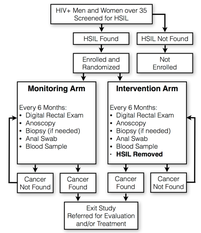
One way to detect HSIL is to insert a swab an inch or two into the anus, swirl it around to collect cells, and test them for any abnormalities. This is called an "anal Pap smear," which is similar to a cervical Pap smear used to screen for and prevent cervical cancer in women. An anal Pap smear can sometimes miss detecting HSIL, however, so even people with normal anal Pap smear results are usually recommended to have them repeated again every year. People with abnormal Pap smear results are recommended to have their anal tissue examined with a procedure using a microscope. This procedure is known as "high resolution anoscopy," or HRA for short.

Before the HRA procedure, a small clear plastic tube called an "anoscope" is inserted into the anus, and the clinician uses a small magnifying lens called a "colposcope" to look for any abnormal areas. If the clinician sees areas that might be HSIL, he or she will take a small tissue sample (called a biopsy). The tissue is tested to confirm whether or not HSIL is actually present.

Screening women with cervical Pap smears, followed by treatment of high-grade lesions, is the standard procedure of medical care for women. This method has been proven to prevent most cases of cervical cancer. Unlike cervical Pap smears, however, there are no national guidelines recommending anal Pap smears to screen for and help prevent anal cancer.

Although many experts believe that removing HSIL prevents anal cancer, it has not yet been proven in a scientific study. The University of California San Francisco is planning a medical study to determine if routine screening and treatment of anal lesions will prevent anal cancer among HIV positive men and women. If proven, anal Pap smear screening of high-risk men and women would become a standard procedure of care.

The study would include thousands of participants who have HSIL, which could, but will not necessarily progress to anal cancer if left untreated. Only participants with HSIL would be part of the study. All participants would be randomly assigned to one of two groups: an intervention group or a monitoring group. Like flipping a coin, you would have a 50/50 chance of being assigned to either group.

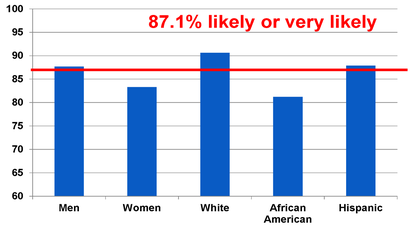


If you were randomly assigned to the intervention group, you would have your HSIL removed with one of two methods, depending on the size, number and location of HSIL areas. One way is to apply an acid at 3-4 visits every 2-3 weeks. Another method of treatment is infrared coagulation (IRC), in which a probe is applied to HSIL seen and heat energy is used to destroy the area. IRC may also need to be performed several times, usually at four-month intervals. Both of these methods cause some bleeding and discomfort, but overall are usually well tolerated.

If you were randomly assigned to the monitoring group, you would not have your HSIL areas removed, but they would be closely examined. Both groups would be carefully monitored every four months and immediately referred for treatment if they developed anal cancer. If the study researchers find that the group who has their HSIL removed (the intervention group) has significantly fewer cases of cancer after five years, the study would help establish new screening and treatment guidelines for all HIV positive patients. If the group who does not have their HSIL removed (the monitoring group) has the same or fewer cases of cancer after five years, the study would show that removing HSIL does not reduce rates of anal cancer. At this point, we don't know which half of the study participants will have fewer cases of cancer at the end of the five years.

Willingness to Participate

Assuming you had HSIL (high grade anal abnormalities that could progress to anal cancer), what is the likelihood that you would enroll in the study that has been described?



"If you think of it, we're sitting here today because someone took those experimental drugs, and somebody didn't. And, because of those efforts, I can sit here now and take my one pill, and I knock it out ... somebody has to do it." (Male)

Enthusiasm for participating in the trial was high across all genders and ethnic groups, with 51.5% of participants expressing equipoise about randomization. Of those with a preference, 71.8% preferred the intervention arm.

"I would like to be in the group with the tissue removed if I had a choice… because to remove a suspicious cancer cell I think is better than leaving it in your body to see if it develops further...Nip it in the bud type thing." (Female)

"I think a little bit of a disadvantage if you're just being monitored, but you know, but that's what the study is. You flip a coin and wherever group you end up in…" (Male)

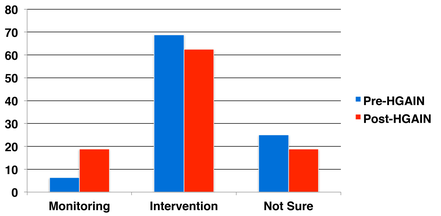
69% of survey participants said they were likely or very likely to remain in the study if randomized to the monitoring arm.

"I feel fortunate that I'm constantly being screened and cleared. It's like, okay good, I don't have it. And - if something were to start to jump off, how bad can it get within three months before it's caught?" (Male)

"I've been going to see my HIV doctor every three months for ten, eleven years…because I think it's my job for my health to do that." (Male)

Preference for Study Arm Pre- and Post-HSIL Diagnosis

We surveyed 20 new UCSF clinic patients (19 male) at two points: time 1 was after initial exam but before HSIL diagnosis, and time 2 was after receiving HSIL diagnosis. Among this population who expected treatment, when asked which arm they would choose if they had a choice, there was a strong preference for the intervention arm.



Despite this, 70% reported that they would be "likely" or "very likely" to join the trial and potentially be randomized to the monitoring arm. Diagnosis with anal HSIL did not affect willingness to enroll in the proposed anal cancer prevention trial, but a few more participants expressed a preference for the monitoring arm post diagnosis.

Conclusions

- HIV+ men and women reported a desire to join the trial with only slight variations by race/ethnicity.
- Main motivation cited was a sense of gratitude to previous HIV research cohorts and altruism towards the HIV community.
- Even patients diagnosed with HSIL at UCSF clinic were overwhelmingly willing to join study.
- Combined with community-based outreach and education about the high incidence of anal HSIL among HIV-infected men and women, recruitment to the RCT should prove feasible.

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