Concordance of Self- and Clinician-Collected Anorectal Swabs for Human Papillomavirus (HPV) Detection in HIV-Negative Men Who Have Sex with Men (MSM)

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Background

- Anal squamous cell cancer (ASCC) is rare in the United States but incidence is rising
- ASCC screening endorsed by New York State Department of Health and HIV Medicine Association of the Infectious Disease Society of America) for HIV-positive MSM
- No guidelines for ASCC screening for HIV-negative MSM despite higher ASCC incidence (5.1 per 100,000 men) compared to general population of U.S. men (1.8 per 100,000 men)

Background

- Initial ASCC screening method – Anal canal swabs to detect DNA from high-risk HPV (HR-HPV) types
- Self-collected swabs have potential for rapid, easy, cost-effective detection of HR-HPV DNA
- Prior demonstration of comparable detection of HR-HPV DNA for paired self-collected and clinician-collected swabs (Clin Inf Dis 2006;42(2):308-9)
- Details of self-collection process variable among studies with optimal collection method undetermined

Study Aims

1. Determine sensitivity and specificity of self-collected anal swabs for HPV DNA detection assuming clinician-collection as gold standard
2. Determine concordance of self-collected and clinician-collected swabs for HPV DNA detection

Methods – Inclusion and Exclusion Criteria

- Inclusion Criteria:
  - Men age 18 years or older
  - Self-reported prior sexual contact with other men
  - Negative HIV test within 3 months prior to study visit
  - Permitted men with history of anogenital warts or receipt of HPV vaccine
- Exclusion Criteria:
  - Current or prior diagnosis of anal cancer
  - Limited manual dexterity prohibiting utilization of self-collected swab

Methods – Study Workflow

- Cross-sectional study design – All participants attended a single in-person study visit
- Study visit steps:
  1. Informed consent given
  2. Completion of online pre-intervention survey
  3. Self-collection of single anal swab
  4. Clinician-collection of single anal swab
  5. Blood sample collected for type-specific HPV antibody testing
- Following study visit, participants completed an online post-intervention survey assessing their perceptions of the swab self-collection method

Methods – Self-Collection Process

- Self-collection instructions adapted from Lampinen TM, et al. Sex Transm Dis 2006; 33(6)386-8
- Polyester-tipped swab (Puritan Medical Products, Guilford, Maine) inserted 3-4 cm into anal canal
- Swab rotated once for self-collection and then removed and agitated in liquid media transport vial (PreservCyt; Hologic, Inc., Marlborough, MA) for 30 seconds
- Clinician-collected swab was rotated 3-4 times because of use as “gold standard” collection method

Methods – Sample and Data Analysis

- Sample Processing
  - HPV Genotyping: DNA extraction → Polymerase chain reaction → Restriction fragment length polymorphism → Agarose gel electrophoresis
- Statistical Analysis
  - Sensitivity and specificity of self-collection calculated using HPV types detected via clinician-collection to define positive and negative values
  - McNemar's test used to calculate proportion of HPV DNA positive results for self-collected samples compared to clinician-collected samples
  - Kappa statistic used to calculate inter-rater agreement of HPV DNA results detected between paired self-collected and clinician-collected samples

Participant Characteristics

- N = 78 participants with paired anal swab samples
- Mean age of 35 years (Interquartile Range = 26-41 years)
- 83.3% Caucasian race, 91% Non-Hispanic ethnicity
- 92.3% reported 3 or more sexual partners in past year
- Prior anal pap?
  - No – 64.1%
  - Yes – 16.7%
  - Unsure – 19.2%
- HPV vaccine status?
  - At least 1 dose – 34.6%
  - All 3 doses – 5.1%
  - Never received – 52.6%
  - Unsure – 12.8%

Table 1. Pairwise Comparisons of HPV DNA Prevalence For Self- and Clinician-Collected Anorectal Swabs

	Self-Collected, n (%)	Clinician-Collected, n (%)	*p*-value	Sensitivity	Specificity
Any HPV	54 (69.2%)	57 (73.1%)	0.440	84.2%	71.4%
Any HR-HPV*	33 (42.3%)	43 (55.1%)	0.012	69.8%	91.4%
4v HPV†	16 (20.5%)	23 (29.5%)	0.034	60.9%	96.4%
9v HPV‡	25 (32.1%)	33 (42.3%)	0.090	62.5%	89.1%
HPV Type 16	3 (3.8%)	8 (10.3%)	0.024	37.5%	100%
HPV Type 18	3 (3.8%)	5 (6.4%)	0.159	60%	100%

*HR-HPV = High-risk HPV types; Includes types 16, 18, 26, 30, 31, 33, 34, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82, 85, and 97

†4v HPV = 4-valent HPV vaccine types (6, 11, 16, 18)

‡9v HPV = 9-valent HPV vaccine types (6, 11, 16, 18, 31, 33, 45, 52, 58)

Table 2. Agreement of HPV DNA Results Between Self-Collected and Clinician-Collected Sampling Methods Among MSM (N = 78)

	Percent Agreement	κ (95% CI*)
Any HPV	80.8	0.53 (0.42 – 0.65)
HR-HPV**	79.5	0.60 (0.49 – 0.71)
4v HPV Types†	85.9	0.63 (0.52 – 0.74)
9v HPV Types‡	76.9	0.51 (0.40 – 0.62)
HPV Type 16	93.6	0.52 (0.42 – 0.62)
HPV Type 18	97.4	0.74 (0.63 – 0.85)

*CI = confidence interval

** HR-HPV = High-risk HPV types; Includes types 16, 18, 26, 30, 31, 33, 34, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82, 85, and 97

†4v = 4-valent, in reference to the HPV vaccine containing HPV types 6, 11, 16, and 18

‡9v = 9-valent, in reference to the HPV vaccine containing HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58

Conclusions

- Low sensitivity and moderate-to-high specificity for detection of high-risk and vaccine-preventable HPV types with self-collected anal swab method compared to clinician-collected method
- Moderate inter-rater agreement of self-collected and clinician-collected anal swabs
- Higher number of false-negative HPV results seen with self-collection method suggest need for modification of instructional methods
  - Nature of collection being blind as an inherent limitation for sampling HPV DNA present
  - HPV DNA detection may improve with increased number of swab rotations
- Study limitations:
  - Cross-sectional study design – Unknown if and to what degree improvement in detection would occur with repetition of self-collection process
  - Convenience sample of participants drawn from a single metropolitan area
  - Clinical applicability of results impacted by HR-HPV DNA detection remaining an adjunctive marker to cytology for ASCC screening

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