HPV Infection in gay men and vaccine acceptance:

Findings from the ManCount Survey

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A Multi-Agency Collaboration

Study Team

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HPV (Self-collection) Component

- Dr. Chen Zhou, Dr. Dirk van Niekerk, Dr. Kathy Seballos, Jane Lo, Dr. Gina Ogilvie, Darlene Taylor, Wendy Mei, Dr. Alberto Severini, Dr. Natasha Press

Community Advisory Committee

- Robert Hong (VCH), Paul Harris (BCCFE), Shimpei Chihara (ASIA), Elgin Lim (BCPWA), Richard O'Donnell (VCH), Chris Buchner (Qmunity), Robin Parry (Qmunity), Matthew Taylor (PEERS), Hywel Tuscano (YouthCO), Jesse Brown (YouthCO), Devon MacFarlane (VCH), Jody Jollimore (HIM)

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Community Partners

- Celebrities
- Fountainhead
- Numbers
- Odyssey
- Pumpjack
- Little Sisters
- Rhizome Café
- F212
- Boys 'R Us
- Club 40/50
- GAB Youth
- Gay Warriors
- Metro Vancouver Kink
- Primetimers
- AIDS Walk
- Davie Days
- Fuck Off and Dance
- Gay Men's Health Summit
- Koodo
- Oddball
- Out on Screen
- Pride Society
- Red 8
- Vick Vancouver Party
- Spectrum Health
- AIDS Vancouver
- Pender Community Health Centre
- Three Bridges Community Health Centre
- Pine Street Clinic
- BCCDC STI Clinic / Bute Street Clinic

Outline for presentation

- To present the findings from:
  - A sub-study of ManCount survey which used self-collected rectal swabs to measure the prevalence of HPV infection and other conditions (Study 1)
  - An analysis of survey data related to acceptance of HPV vaccine among survey participants (Study 2)

Background

ManCount

Human Papillomavirus (HPV)

- One of the most common STIs (most common viral STI)
  - Approximately 40 HPV types transmitted sexually
  - Transmitted through genital sex, oral sex, manual to genital sex
  - Condoms help reduce the risk but are not fully protective
- Associated with genital warts and various cancer types (cervical, anal, penile, oropharyngeal)
  - Approximately 90% of anal cancer is due to HPV
  - Genital warts: HPV 6, 11; Cancers: HPV 16, 18
- Difficult to monitor HPV trends
  - Not reportable
  - Often undiagnosed/clinically diagnosed
  - Typically requires special studies to measure incidence, prevalence

HPV infection in MSM

- MSM are at increased risk of HPV infection, particularly HIV positive men
- Greater incidence of anal cancer (rates per 100,000 men)
    - HIV negative MSM 13 to 37
    - HIV positive MSM 75 to 137
    - All males 2

Piketty, AIDS 2008; 22:1203-11. Frisch, J Natl Cancer Inst 2000; 92:1500-10.

Johnson, Cancer 2004; 101:281-8.

HPV Vaccine

- Quadrivalent HPV vaccine (Gardasil^{TM}) approved in Canada for males aged 9-26 years (Feb 2010), for:
  - Prevention of infection with HPV 6, 11, 16, 18
  - Prevention of genital warts caused by HPV 6, 11
- High vaccine efficacy:
  - 90.4% for HPV 6/11/16/18-related external genital warts in males
  - 77.5% for anal intraepithelial neoplasia in MSM
- NACI currently reviewing the evidence to consider recommendations for use in males or MSM
- One option for protection of MSM is a targeted vaccine program delivered by health care providers (HCP)

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Giuliano et al, IPV, 2009. Palefsky et al, IPV, 2010

Anal cytology screening ("anal pap")

- Analogous to cervical cancer cytology screening / pap test
- Results indicate whether there is any cellular dysplasia, that could be a precursor for anal cancer and would require further testing
- No recommendations for use in MSM
  - Lack of trial data demonstrating that screening programs have an impact on anal cancer rates or mortality
- Limited use world-wide, often focused on HIV positive MSM
- One anal dysplasia clinic in BC (St. Paul's Hospital)

M-Track Survey

- M-Track is an enhanced HIV surveillance system, coordinated by PHAC (behavioural and biological)
  - Monitors trends in HIV, viral hepatitis, other STI
  - Monitors trends in sexual and testing behaviours
  - Direct population sampling
  - Cross-sectional surveys at regular intervals

ManCount

- A sexual health survey for gay, bisexual and other men who have sex with men in Vancouver
- <u>Vision</u>: To collect relevant data to inform collective action to prevent the transmission of HIV and improve sexual health
- <u>Objectives</u>:
  - To measure the prevalence of HIV, Hepatitis C, syphilis
  - To track trends in testing and sexual behaviours

ManCount Survey

- Vancouver site of the M-Track surveillance system
- Recruitment at gay community venues, groups, events
- Questionnaire and collection of dried blood spots (DBS) for testing for HIV and other sexually transmitted infections
- Eligible if identified as a man who has sex with men, age 19 years or older
- Survey ran from August 2008 to February 2009
- 1169 men participated
- 1139 (97.4%) contributed a dried blood spot

Study 1:
Self-collected rectal swabs (prevalence, feasibility)

Self-collection of rectal swabs

- Can be tested for Human Papillomavirus (HPV), *Chlamydia*, gonorrhea, and abnormal anal cells (anal dysplasia)
- High prevalence among gay men and other MSM, particularly HIV positive men
- In general, considered equivalent to specimens collected by health care providers
- Methodology developed and validated in the Vanguard study (BCCFE)

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Lampinen et al. STD 2006; 33(6):386-388.

Objective

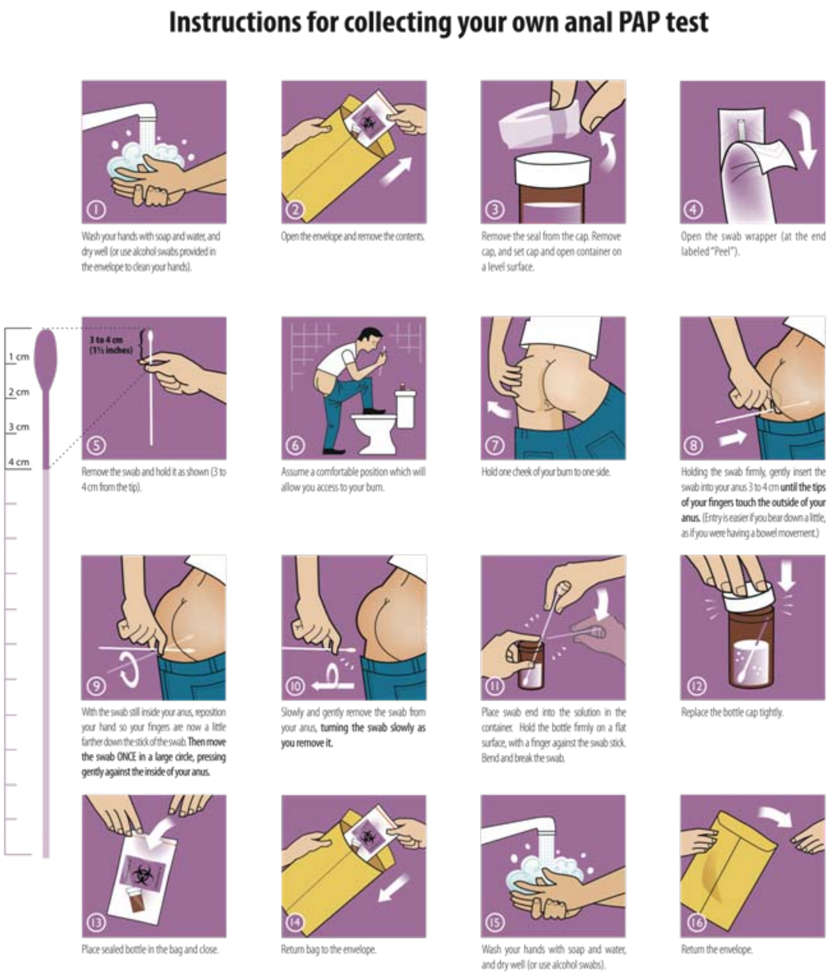
- To use self-collected rectal swabs to measure the prevalence of HPV, *Chlamydia,* gonorrhea, and abnormal anal cytology among gay, bisexual and other MSM in Vancouver
- Why include with ManCount?
  - Can include questionnaire and DBS data (e.g., risk behaviours, HIV status) along with swab results
  - May be feasible way to measure prevalence by "tagging onto" an existing venue-based HIV surveillance system

Methods

- Subset of ManCount participants (September '08 to February '09)
- At completion of DBS and questionnaire, asked to participate in self-collection component
- Informed consent obtained
- On-site (Option 1) or at follow-up site (Option 2)
- Given self-collection kit
- $10 honorarium
- Ethics approval obtained

Self-collection kits

- Instructions
- Alcohol wipes
- Swab
- Thinprep container
- Requisition
- Specimen transport bag



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Laboratory methods

- PreservCyt™ ThinPrep specimen sent to PHSA Lab
- HPV testing:
  - 3 mL to NML for PCR amplification and Linear Array HPV Genotyping Test (Roche Diagnostics)
  - 37 HPV types, β-globin gene
- *Chlamydia*, gonorrhea testing:
  - 1 mL to PHSA Laboratory for GenProbe APTIMA Combo2 Assay
- Anal cytology:
  - Remainder processed by routine methods at PHSA Laboratory
  - Cytology slides reviewed at BC Cancer Agency
  - If adequate, classified according to Bethesda criteria

Analysis

- Comparison of participants and non-participants
  - Multivariate logistic regression model, backward selection
- Estimation of prevalence:
  - 95% confidence intervals
  - HPV: restricted to β-globin positive specimens
  - Anal cytology: restricted to adequate specimens
  - CT, GC: no restriction

Results - Participation

766 approached

268 (35.0%) consented

247 (92.2%) on-site
(Option 1)

21 (7.8%) follow-up
(Option 2)

247 (100%)
specimens collected

5 (23%)
specimens collected

In total, 252 specimens collected

239 (94.8%) specimens of sufficient quality for testing

Reasons for non-participation

*convenience sample of 132 non-participants

Reason	Number	Percent
Uncomfortable with self-collection method	78	59.1%
Not enough time / process would take too long	23	17.4%
Onsite washroom or follow-up site inaccessible	16	12.1%
Not comfortable with self-collection at the venue	15	11.4%
Other reason	16	12.1%

Participation by venue type

Venue	Number	Percent
Bathhouse	31/44	70.5%
Community organizations	21/37	56.8%
Bookstore	53/118	44.9%
Bars or pubs	155/527	29.4%
Community event	8.40	20.0%

Factors associated with participation

Variable	Adjusted OR [95% CI]
Greater than high school education	0.57 [0.34, 0.97]
Income < $20,000	1.95 [1.19, 3.20]
One casual sex partner (vs none)	0.34 [0.15, 0.77]
Recruited in bathhouse (vs bar)	3.86 [1.50, 9.91]
Recruited at event (vs bar)	0.18 [0.05, 0.66]
On-site specimen collection available	3.83 [2.06, 7.15]

Additional variables significant on bivariate analysis: bisexual identity (vs gay or homosexual); received money, drugs or goods in exchange for sex; poppers; HIV positive on DBS; smoking; ever having heard of HPV; previous anal pap test.

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Results – Anal Cytology

Specimen adequacy	Number	Percent
Adequate for analysis	149 / 239	62%
Inadequate for analysis	90 / 239	38%
Inadequate for analysis (Vanguard study, same protocol)		*17%*

Reasons for specimen inadequacy:
Mainly anucleated squamous cells (60%)
Obscured by debris (30%)
Scanty or too few cells for interpretation (10%)
Poor cell preservation (9%)

Lampinen et al. STD 2006; 33(6):386-388.

Results – Anal cytology

*Adequate specimens only

Category	Total (n=149)	HIV+ (n=42)	HIV- (n=107)	Sig
Normal cytology	58% [50-66%]	36% [21-50%] *29-76%*	66% [57-75%] *68-100%*	*
High grade squamous intra-epithelial lesion (HSIL)	11% [6-17%]	31% [17-45%] *5-22%*	4% [0-7%] *3-5%*	*
Low grade squamous intra-epithelial lesion (LSIL)	19% [13%-25%]	26% [13-40%] *19-49%*	16% [9-23%] *7-5%*	
Atypical results (ASCUS, ASC-H)	12% [7-17%]	7% [0-15%] *7-26%*	14% [7-21%] *5%*	

Prevalence estimates from other studies in pink font (setting, populations may vary).

Results – HPV infection

Betaglobin (marker of adequacy)	Number	Percent
β-globin positive	159 / 239	67% [62-72%]
β-globin negative	80 / 239	33% [28-38%]

Kappa statistic for agreement between β-globin results and adequacy for anal cytology: 0.31 (fair agreement). Concordance in 68.2% of specimens. Of 76 discordant specimens, 33 did not have detectable β-globin yet were adequate for cytology.

Results – HPV infection

*β-globin positive specimens only

Category	Total (n=159)	HIV+ (n=42)	HIV- (n=116)	Sig
HPV Negative	38% [30-45%] *17-35%*	21% [9-33%] *6-65%*	43% [34-52%] *8-60%*	*
Low Risk HPV type	37% [30-44%] *36-59%*	62% [47-77%] *7-52%*	28% [20-37%] *8-67%*	*
High Risk HPV type	47% [39-55%] *29-41%*	71% [57-85%] *25-84%*	39% [30-48%] *22-33%*	*

<u>Low Risk HPV</u>: 6,11,40,42,43,44,54,61,70,72,81

<u>High Risk HPV</u>: 16,18,26,31,33,35,39,45,51,52,53,56,58,59,66,68,73,82

Prevalence estimates from other studies in pink font (setting, populations, HPV classification may vary). Classification from: Munoz, NEJM 2003; 348:518-527.

Results – HPV infection, vaccine-preventable

*β-globin positive specimens only

Category	Total (n=159)	HIV+ (n=42)	HIV- (n=116)	Sig
HPV 16 or 18	23% [17-31%]	41% [26-57%]	17% [11-25%]	*
HPV 6, 11, 16 or 18	38% [31-46%]	55% [39-70%]	33% [24-42%]	*

Prevalence estimates from other studies in pink font (setting, populations, HPV classification may vary). Classification from: Munoz, NEJM 2003; 348:518-527.

Results – *Chlamydia*, Gonorrhea infection

Infection	Total (n=239)	HIV+ (n=60)	HIV- (n=178)	Sig
Chlamydia	5.4% [2.6-8.3%] *4-9%*	3.3% [0-7.9%]	6.2% [2.6-9.7%]	
Gonorrhea	2.1% [0.3-3.9%] *0-3%*	1.7% [0-4.9%]	2.3% [0.1-4.4%]	

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Prevalence estimates from other studies in pink font (setting, populations may vary).

Conclusions

- Can include self-collected swabs in HIV surveillance systems for MSM (such as M-Track)
- Allows for stratification by HIV status, other characteristics
- Method for monitoring the effects of interventions such as HPV vaccine or anal cytology screening programs
- Prevalence results are similar to what has been reported for MSM in community surveys elsewhere
- Differences between participants and non-participants explained by: incentive, venue type, on-site collection

Limitations

- High proportion of inadequate specimens for cytology or without detectable β-globin
  - Greater than in clinic-based surveys
  - 68% concordance
- Explanation?
  - Limited insertion of swabs into anal canal
  - Varying environmental conditions for on-site collection
  - Interference from recent douching* or lubricant use
  - Study fatigue
  - Intoxication

* 33% of all ManCount survey participants reported douching before anal sex in the past 6 months.

Recommendations

- Only offer on-site specimen collection
- Use venues which have suitable on-site bathroom facility (sanitation, lighting, privacy, counter space)
- Could consider alternative options (e.g., trailer)
- Need sufficient sample size due to poorer overall specimen adequacy
  - Introduce self-collection at multiple sites?

Study 2:
Vaccine acceptance

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Study objectives

- To assess the willingness of ManCount participants to receive HPV vaccine (and associated factors)
- To assess the age at sexual debut in comparison to age at disclosure of sexual orientation to a HCP

Methods

HPV vaccine acceptance

- Proportion of participants who were *willing* or *extremely willing* to receive HPV vaccine

Key survey variables

- Demographics (age, education, ethnicity, income)
- Risk factors (unprotected anal sex with casual partner, concurrent sexual partner, used recreational drugs before/during sex, received money/goods in exchange for sex, previous STI diagnosis)
- Potential confounders (previous diagnosis with genital warts, ever heard of HPV, vaccinated for Hepatitis A or B)

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Methods

Age group

- Based on vaccine approval: ≤ 26 years (eligible), >26 years (not eligible)

Disclosure to HCP

- Proportion who reported ever having told a HCP they had male sexual partners
- Years from sexual debut to disclosure to HCP

Statistical analyses

- Bivariate analysis
- Multivariate logistic regression to determine significant independent predictors of vaccine acceptance

Results – HPV vaccine acceptance

Willingness to receive HPV vaccine	Number	Percent (n=1041)
Extremely willing	312	30.0%
Willing	385	37.0%
Neutral	214	20.6%
Unwilling	35	3.4%
Extremely unwilling	95	9.1%

- Overall, HPV vaccine acceptance was 67.0% (95% CI: 64.1% - 69.8%)

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Results – HPV vaccine acceptance by age

Age group	Willing to vaccinate	Percent	*p* value
< 25 years	115/189	60.8%	0.009
25 – 34 years	228/347	65.7%	
35 – 44 years	179/258	69.4%	
45 – 54 years	111/165	67.3%	
≥ 55 years	60/76	78.9%	

- No significant difference in vaccine acceptance among men ≤ 26 years vs men aged >26 years (63.7% vs 68.2%, respectively; p=0.174)

Results – Multivariate analysis

Survey variable	Willing to vaccinate	Percent	AOR (95% CI)
Income < $20,000	161/277	58.1%	
Income ≥ $20,000	523/746	70.1%	1.49 (1.07 – 2.08)
Recreational drugs	156/256	60.9%	
No recreational drugs	541/785	68.9%	1.41 (1.01 – 1.96)
History of genital warts	137/181	75.7%	1.73 (1.14 – 2.64)
No history of genital warts	560/860	65.1%	
Vaccinated for HBV or HAV	543/775	70.1%	1.44 (1.02 – 2.04)
Not vaccinated	140/243	57.6%	
Disclosed to HCP	565/806	70.1%	1.57 (1.07 – 2.30)
Had not disclosed to HCP	116/208	55.8%	

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Results – Disclosure to HCP

	Disclosed (%)	Median age at disclosure (IQR)	Median years from sexual debut to disclosure (IQR)
Total (n=1121)	882 (78.7%)	21 (18 – 25)	4 (1 – 8)
Age ≤ 26 (n=303)	218 (72.0%)	19 (17 – 21)	2 (1 – 4)
Age 27 – 34 (n=277)	214 (77.3%)	21 (18 – 24)	2 (0 – 5)
Age 35 – 44 (n=277)	231 (83.4%)	22 (19 – 28)	6 (2 – 11)
Age ≥ 45 (n= 257)	213 (82.9%)	25 (20 – 30)	8 (4 – 14)

- Overall, median age at sexual debut was 17 years (IQR: 14 – 20 years)
- Among men ≤ 26 years of age who had not disclosed, 67% reported two or more lifetime sex partners

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Conclusions

- High proportion (67%) of MSM accepting of HPV vaccine
  - Increased with age, not significantly different by eligibility
- In multivariate analysis, vaccine acceptance was more likely if:
  - Income >= $20,000/year
  - No recreational drug use before or during sex
  - Previous diagnosis of genital warts
  - Receipt of Hepatitis A or B vaccine
  - Had disclosed to HCP that had male sex partners

Conclusions

- Overall, 79% of men had communicated with a HCP about having male sexual partners
  - Median 4 yrs after sexual debut
- Among men eligible for HPV vaccine, 72% had disclosed to a HCP
  - Median 2 yrs after sexual debut
- Time from sexual debut to disclosure, and risk for HPV infection during this period, may limit the effectiveness of targeted HPV vaccine programs for MSM
  - Possible that men may disclose to HCP when wouldn't otherwise in order to access the vaccine?

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Limitations

- Venue-based recruiting may have captured a sample of MSM more likely to communicate with HCP
- Other factors potentially associated with disclosure to HCP and vaccine acceptability were not assessed (access to health care, out-of-pocket vaccine cost)

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Summary

Key Findings

- HPV infection and abnormal anal cytology is prevalent among MSM in Vancouver
  - Particularly HIV+ men, similar to other jurisdictions
- Feasible to use M-Track or other HIV surveillance systems for MSM to measure these outcomes
  - Can be used to monitor impacts of prevention programs
  - Specimen adequacy may be issue in community-based samples
- Most MSM in Vancouver would be willing to use HPV vaccine if it were available

Implications for HPV Vaccination programs

- Two models for vaccination of males:
  - Vaccinate all males in childhood (parallel to female programs)
  - Targeted vaccination programs for MSM
- Our findings suggest the most benefit to MSM would be from a general male vaccination program
- This strategy and impact on MSM needs to be explored within the context of planning activities for HPV vaccine (i.e., cost-effectiveness, modeling)

Targeted programs may be cost-effective

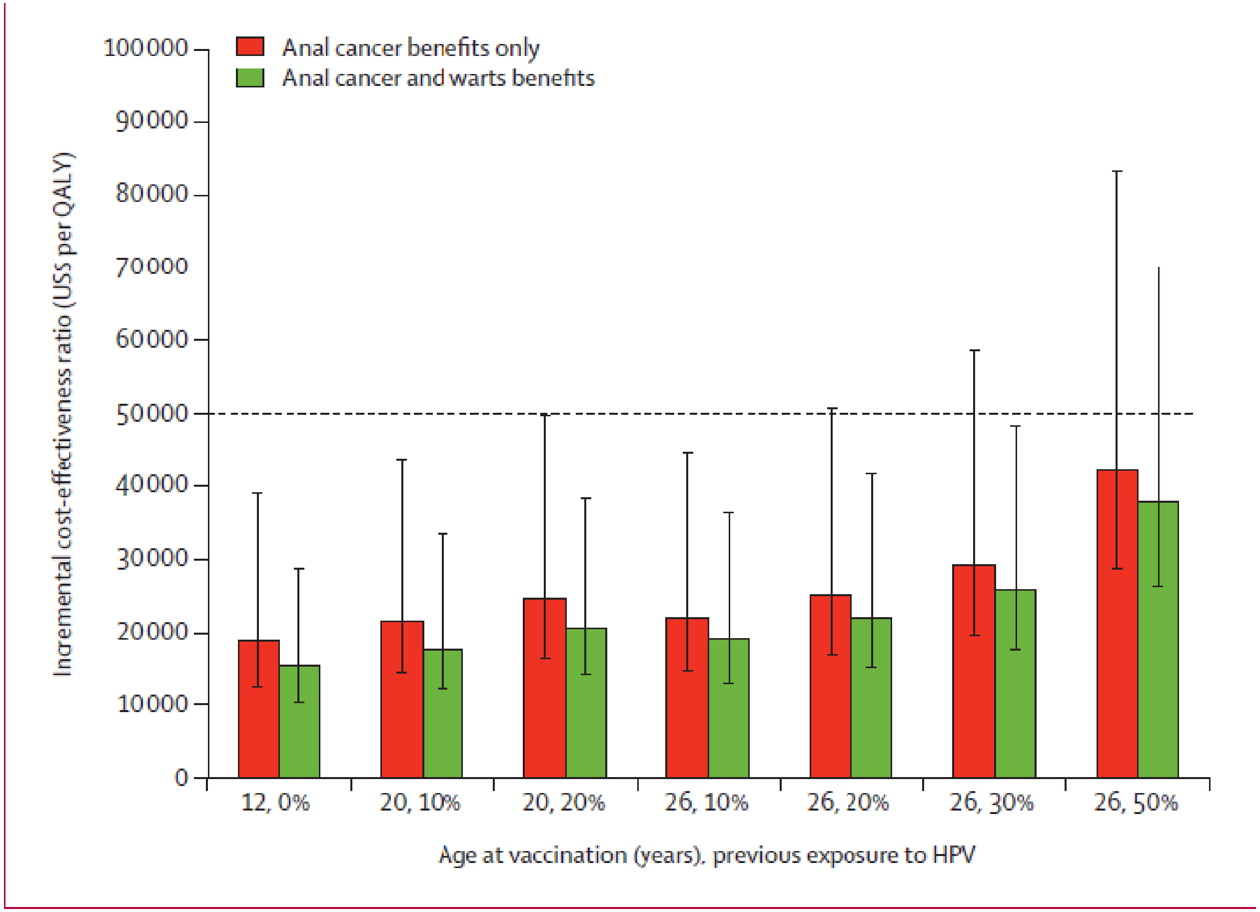

Figure: Effect of age at vaccination and previous exposure to vaccine-targeted HPV types on cost-effectiveness ratios of HPV vaccination of MSM

Kim et al. Lancet Infectious Diseases, 2010.

Thank-you

- Thanks to the Pacific AIDS Network for partnership for this teleconference
- All study findings available at www.mancount.ca
- Contact info: mark.gilbert@bccdc.ca