HPV and the HPV Vaccine in persons living with HIV

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Outline

- Brief review of HPV associated disease
- Brief review of HPV vaccines in general
- Summary of data from HPV vaccine in HIV positive girls and women study conducted across Canada

Diseases caused by Human Papilloma Virus (HPV)

- Cervical cancer
  - 2nd most common cancer in women worldwide
  - HPV biologic prerequisite for disease
  - HPV Causes 99%
- Vulvar cancer
- Vaginal cancer
- Genital warts – HPV causes 100%
- Other less common diseases can be caused by HPV
  - Head and neck cancers – 22-50%
  - Respiratory papillomatosis – 76%
  - Penile cancer– 42%
  - Anal cancer – 60-88%

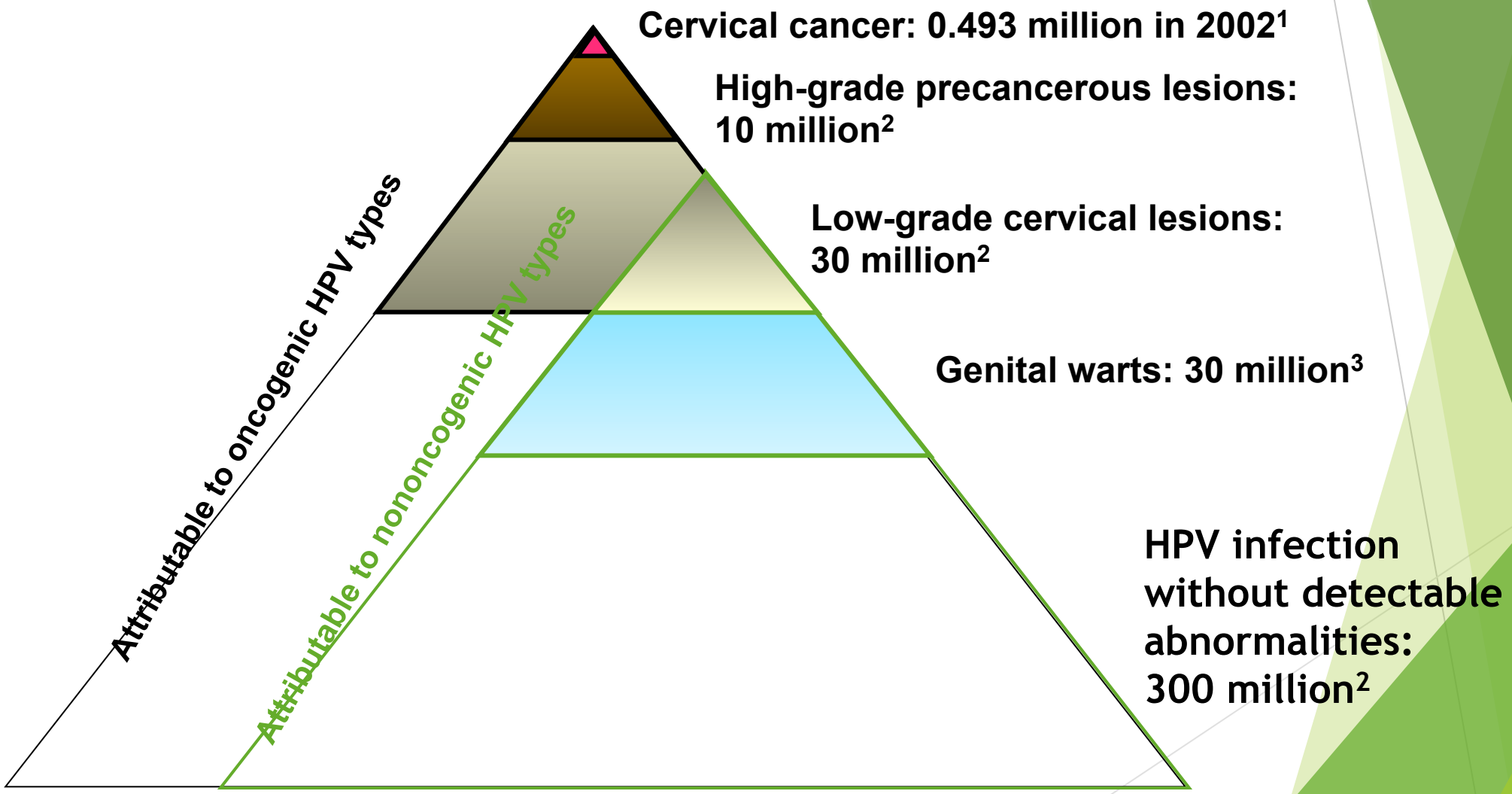
HPV Classification

- 40 types of HPV infect the genital tract
- Classified based on risk of cancer

- **High Risk**:
  - 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82

- **Low Risk**:
  - 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81

World Burden of Cervical Disease and Genital Warts



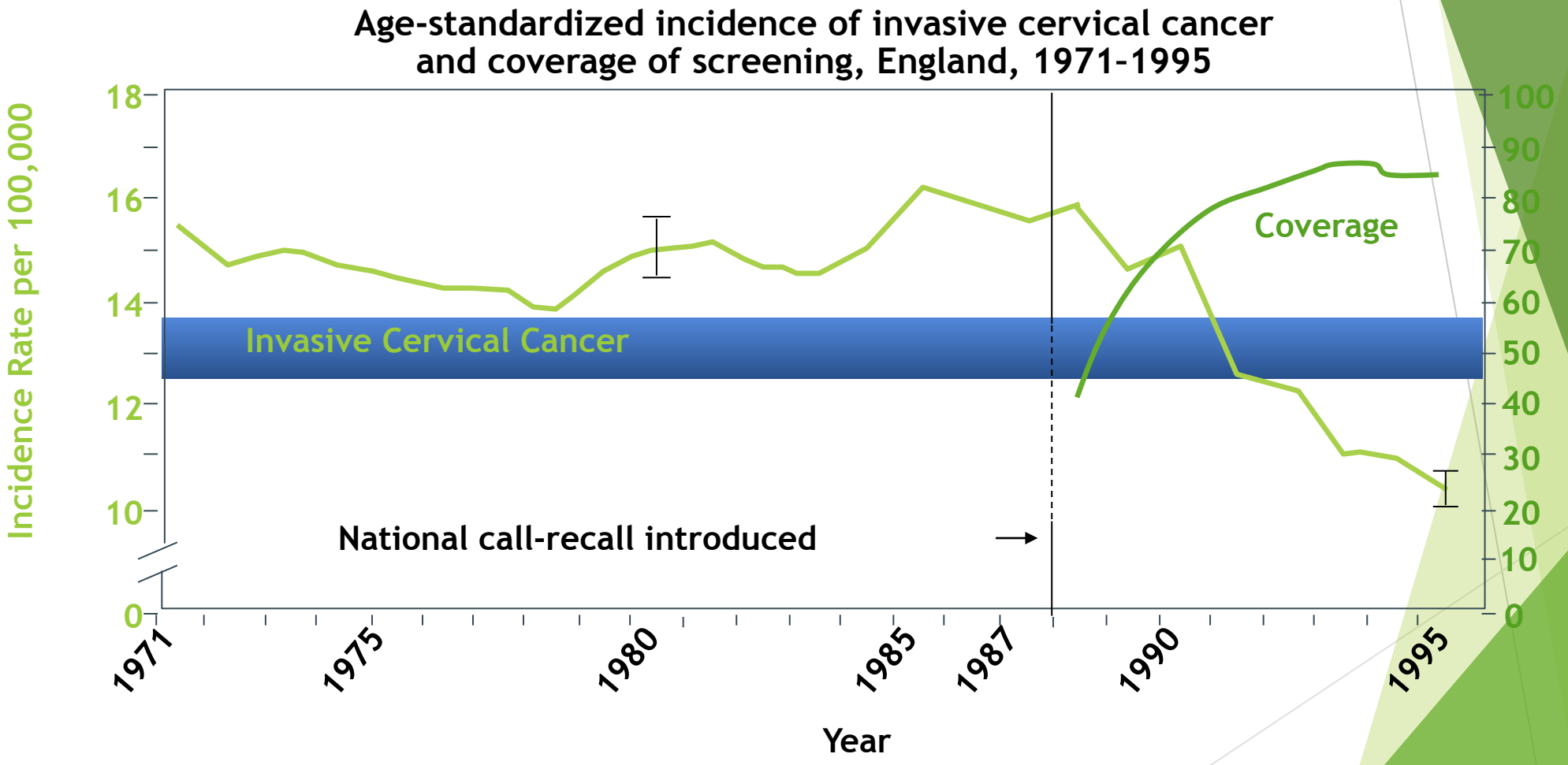
1. Parkin DM, Bray F, Ferlay J, Pisani P. *CA Cancer J Clin*. 2005;55:74–108. 2. World Health Organization. Geneva, Switzerland: World Health Organization; 1999:1–22. 3. World Health Organization. WHO Office of Information. *WHO Features*. 1990;152:1–6.

Age of acquisition of HPV infection

60% of girls will have acquired genital HPV at 48 months from first intercourse (Collins et al. BJOG 2002;109(1):96-98)

- Prevalence decreases with age from a peak of 23% at 20-24 yrs to a low of 4% at 45-59 yrs
- Age of first intercourse in Canada – mean of 15.7 years
- Typically 2 years prior with genital contact

Success of pap smear screening



1. Quinn M, Babb P, Jones J, Allen E. *BMJ*. 1999;318:904–908.
Adapted with permission from the BMJ Publishing Group.

Cervical cancer among Aboriginal women in Canada

Alain A. Demers PhD, Erich V. Kliewer PhD, Olivia Remes BSc, Jay Onysko BA MA, Katherine Dinner MSc, Tom Wong MD MPH, Gayatri C. Jayaraman MPH PhD

CMAJ 2012. DOI:10.1503 /cmaj.110523

- Aboriginal women in Canada 1.7– 3.5 times higher incidence of cervical cancer than among other groups of Canadian women.
- Deaths associated with cervical cancer has been up to four times higher among Aboriginal women than among non-Aboriginal women.
- Poor rates of pap screening are improving but remains to be seen if this will change outcomes.

Why the need for a vaccine?

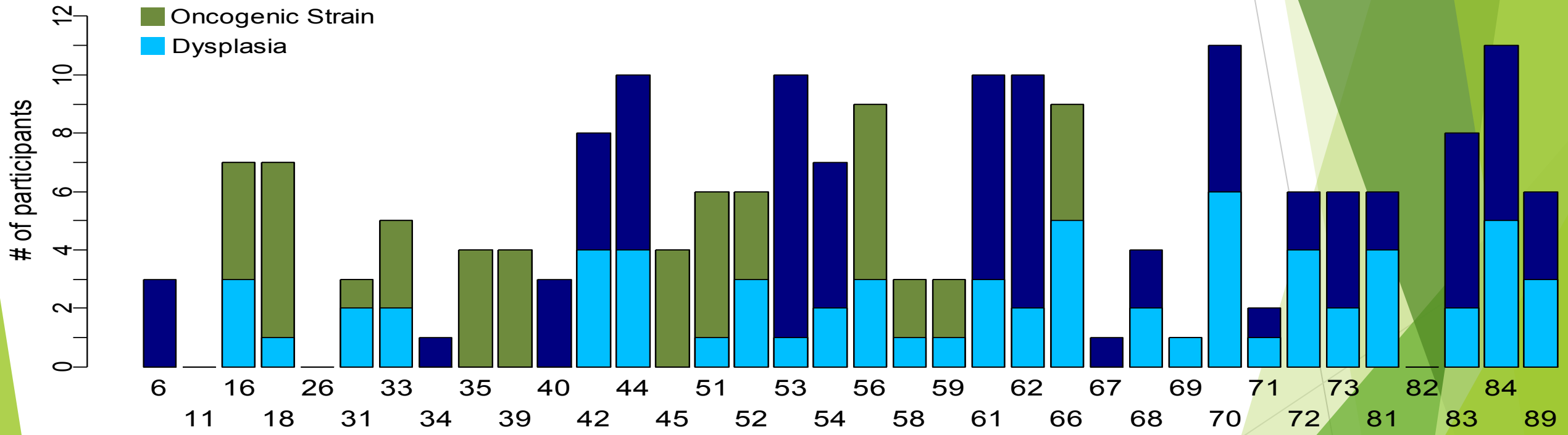
- Vaccine prevents the infection that causes the disease
- Most vulnerable populations can't or don't access pap screening
  - In Canada – immigrants, northern, aboriginal persons have higher rates of cervical cancer
- MSM – high rates of anal cancer – no adequate screening
- Head and neck cancers – no screening options
- HIV positive persons – at highest risk for HPV infection and disease

HPV in HIV positive persons

- HIV positive women have high rates of HPV infection
  - More multiple infections (J Acquir Immune Defic Syndr, 2013)
  - HIV positive women have higher rates of HPV infection than HIV negative women (48.6 vs 28.7%) *(Blitz et al. JID 2013)*
- Types found in HIV positive are different than HIV negative (J Med Virol 2008)
  - N. York cohort – 56,53,16,58,MM7,MM8, and 33 (JID 2006)
- However in some studies the most prevalent types in HIV positive women are 16 and 18 assoc. with HSIL (Lancet Oncology, 2009)
- HAART is associated with increased regression of pre-cancerous lesions and clearance of oncogenic HPV (*Blitz et al. JID 2013)*

HPV DNA Types by Dysplasia in WHIV

Canadian data from vaccine study



HPV Vaccines

- Preventative HPV vaccines first introduced in 2008 have significantly reduced rates of cervical cancer and HPV infection rates.
- There are 2 currently available vaccines approved for use in women and girls age 9-55 and men and boys age 9-26
  - qHPV – 6,11,16,18
  - bHPV – 16, 18
- 9 Valent (6,11,16,18, 31,33,45,52 and 58) vaccine now FDA and Health Canada approved for use in HIV- women and girls age 9-26

HPV vaccines in HIV negative populations

- **women:**
  - **>90% efficacy against cervical/vulvar and vaginal pre/cancer**

  (NEJM. 2007 May)

  - **86% efficacy against anal infection**

  (Lancet Onc. 2011 Sep)

- **men (including MSM):**
  - **75% efficacy against anal pre-cancer**

  (IAIDS, 2010, Vienna)

HPV vaccines

- Current public health programming varies by province
- Most have school based free vaccine in Grade 6 offering the qHPV vaccine in either 2 or 3 doses
- Only PEI offer vaccine to boys
- No comprehensive program for HIV positive persons
- Update in school based programs has been incomplete and variable across provinces
- Still need pap screening as coverage is very incomplete!

A Study of an HPV VLP Vaccine in a Cohort of HIV+ Girls and Women – CTN 236

Primary objective - to evaluate the sero-responsiveness of HIV positive girls and women to an HPV VLP quadrivalent vaccine.

- Study population: HIV positive women and girls, at 14 Canadian sites
  - Approx 10% aboriginal in the study
- Study launched in November 2008
- Enrollment closed in December 2012: 407
- CIHR, Merck and CTN supported

Vaccine immune response at 7 months by HPV Type

HPV Type	N Seroconverted/ N Eligible	% Seroconverted
6	98/99	99.0%
11	144/148	97.3%
16	103/105	98.1%
18	130/142	91.5%

Comparison of serologic response to age comparable HIV-ve

HIV Negative vs HIV Positive Age 15-26						
Month	HPV Type	HIV Negative GMT *	N	HIV + GMT	95% CL	p value
7	6	543	14	322.7	(180.8-576.1)	0.07
	11	762	18	251.1	(147.9-426.6)	**<0.001**
	16	2294	15	1761.2	(1016.7-3051)	0.32
	18	462	17	128.7	(61.2-270.7)	**<0.01**
24	6	113	8	55.6	(23.9-129.2)	0.09
	11	145	8	49	(21.1-113.8)	**0.02**
	16	460	9	135.7	(66.7-276.2)	**<0.01**
	18	52	9	10.3	(5.9-18.1)	**<0.001**

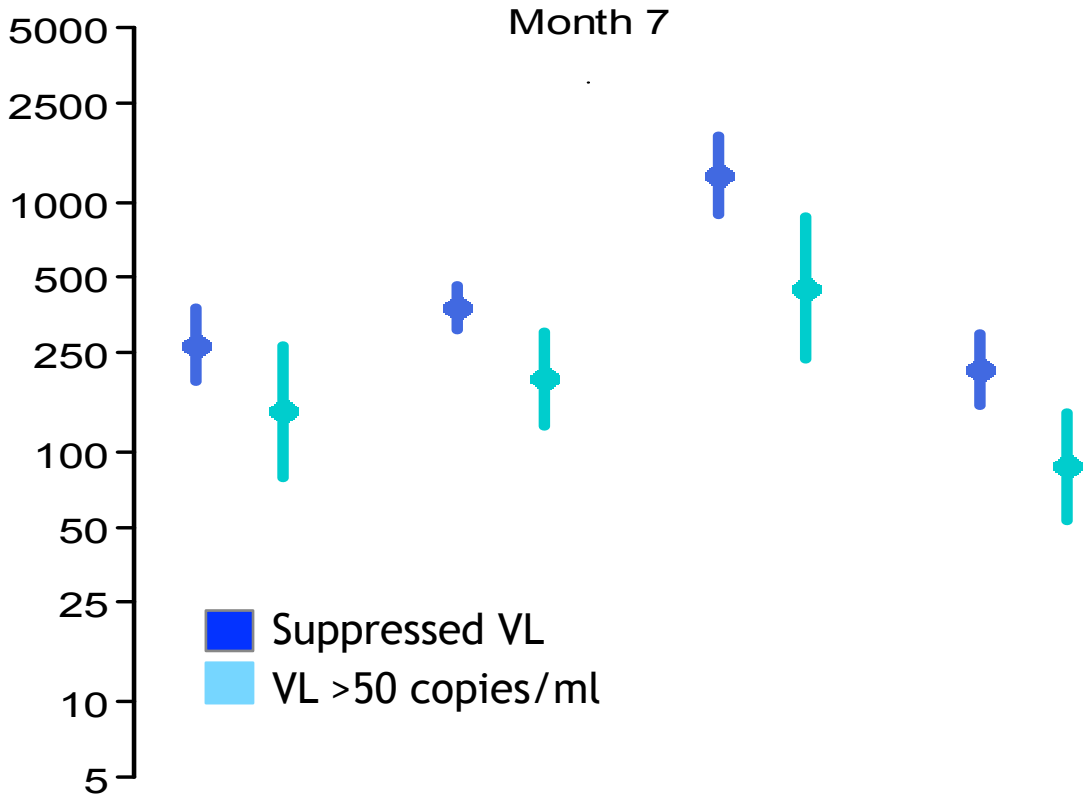
*Joura et al. Vaccine (2008); 26: 6844-6851

Comparison of serologic response to age compared to HIV-ve

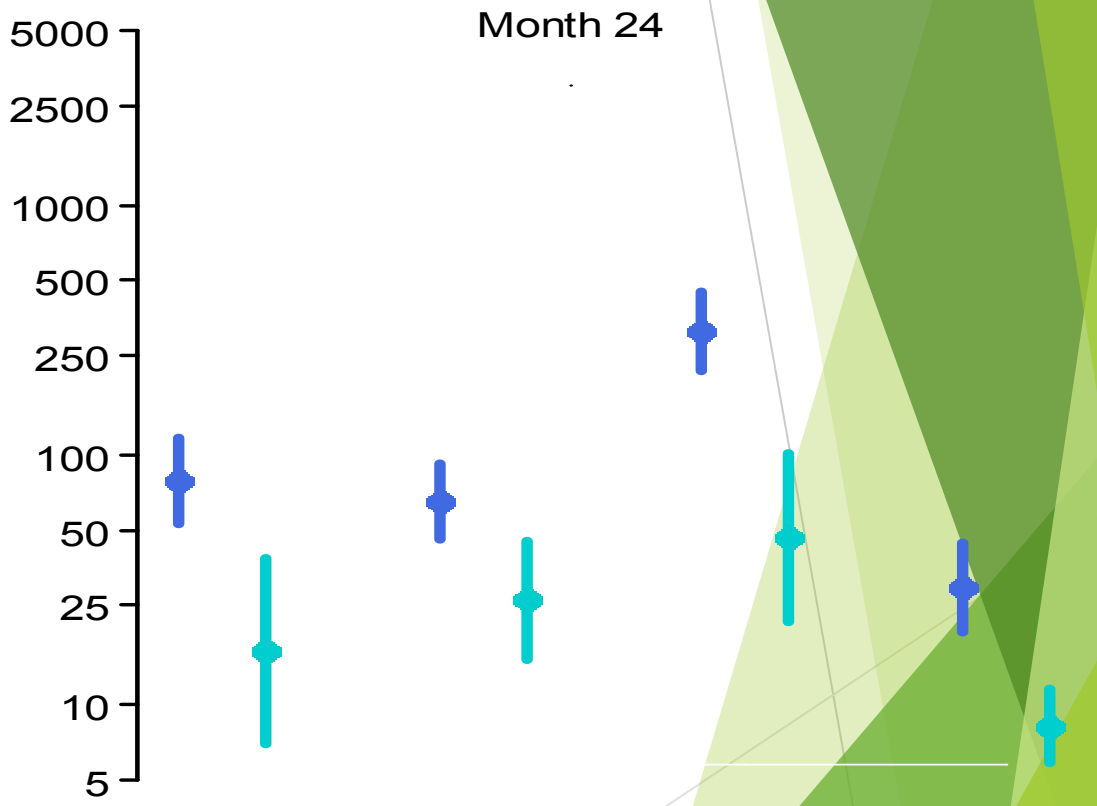
HIV Negative vs HIV Positive Age 24-45						
Month	HPV Type	HIV Negative GMT *	N	HIV + GMT	95% CL	p value
7	6	416	57	209.8	(162.7-270.5)	**<0.0001**
	11	551	92	238.5	(187.2-303.8)	**<0.0001**
	16	2226	61	733.4	(512.3-1049.9)	**<0.0001**
	18	357	90	140.4	(106.0-185.9)	**<0.0001**
24	6	70	37	65	(42.4- 99.4)	0.72
	11	78	53	58.3	(43.7 – 77.8)	**0.05**
	16	278	36	207.2	(138.7- 309.4)	0.15
	18	28	53	27.1	(19.1- 38.1)	0.84

*Castellsague et al. British Journal of Cancer (2011) 105, 28-37.

Seroresponse by VL Status at Baseline



	HPV 6	HPV 11	HPV 16	HPV 18
Ratio of GMTs	1.82	2.19	2.19	2.76
95% CI	1.2-2.8	1.5-3.3	1.3-3.8	1.6-4.6
P-value	<.01	<.001	<.01	<.001



HPV 6	HPV 11	HPV 16	HPV 18
3.80	2.83	2.88	3.11
2.0-7.3	1.6-4.9	1.4-5.8	1.7-5.8
<.001	<.001	<.01	<.001

Conclusions to date from CTN 236

- Although seroconversion rates were higher than anticipated in HIV+ women, peak AB levels were significantly lower than in HIV- women
- Women with a suppressed viral load had a 2-3 fold higher antibody response that was sustained through to 24 month follow up
- Longer follow up is needed to fully understand the rate of decline in AB titers in this population
- Need to consider dosing of HPV in high HIV endemic countries and populations

Summary

- Aboriginal women have higher rates of cervical cancer
- HIV positive women and men have higher rates of HPV infection and of pre-cancer and cancer
- Antiretroviral therapy improves ability to clear HPV and decreases risk for cancer
- HPV vaccines are safe and immunogenic in HIV positive persons BUT work best if given when HIV virus is suppressed
- HPV vaccines should be of benefit to any HIV positive person
- HPV vaccines not fully funded outside of school based programs

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