Should we consider anal cancer screening in women living with HIV? Results from the EVVA study on anal intraepithelial neoplasia prevalence and acceptability of screening

E. Kaufman[1], A. de Pokomandy[1,2], C. de Castro[2], M. Munoz[1,2,3], B. Lessard[1,2,4], M.-H. Mayrand[5], L. Charest[3], M. Auger[6], V. Marcus[6], A. Burchell[7], M. Klein[2], F. Coutlée[2,8]

[1]McGill University, Faculty of Medicine, Family Medicine Department, Montreal, Canada; [2]McGill University Health Centre (MUHC), Chronic Viral Illness Service, Montreal, Canada; [3]Clinique Médicale l'Actuel, Montreal, Canada; [4]Clinique Médicale du Quartier Latin, Montreal, Canada; [5]Centre Hospitalier de l'Université de Montréal (CHUM), Department of Obstetrics & Gynecology, Montreal, Canada; [6]McGill University Health Centre (MUHC), Pathology Department, Montreal, Canada; [7]Ontario HIV Treatment Network, Toronto, Canada; [8]Centre Hospitalier de l'Université de Montréal (CHUM), Department of Microbiology & Infectious Diseases, Montreal, Canada

Aim

- To measure the prevalence of precancerous anal lesions and assess the acceptability of screening for anal cancer in women living with HIV (WLHIV)

Background

- The incidence of anal cancer in WLHIV is 24 times greater than in the general population[1]
- Parallels between cervical and anal cancer include:
  - **Human papillomavirus (HPV)** causes both cancers
  - We can detect precancerous lesions, i.e. "**anal or cervical intraepithelial neoplasia" (AIN or CIN)**; grades 2-3 are considered high grade and at higher risk of progressing to invasive cancer
- Potential screening tools to consider for anal cancer:
  - HPV testing & cytology (akin to cervical PAP tests) – patients with abnormal results would be referred for high-resolution anoscopy (HRA)
  - HRA directly, with biopsies – to detect and treat AIN-2,3 before it progresses to invasive cancer
  - Digital Rectal Exam (DRE) – to detect palpable early cancer once already invasive
- Should we consider routine anal cancer screening for WLHIV?
  - A proposal supported by the success of cervical cancer screening
  - The burden of anal cancer is high in this population
  - Uncertainty remains about long-term benefits of screening – other ongoing studies in men who have sex with men (MSM) to follow
  - Acceptability of screening tools in WLHIV must be confirmed[2]

Methods

- The "EVVA" study
  "**E**valuation of HP**V**, HI**V** and **A**IN in women"
  - Ongoing cohort of 150 WLHIV in Montreal (QC, Canada), recruited during routine HIV care
  - 5 study visits: every 6 months for 2 years
  - Cervical & anal cytology with HPV testing at each visit
  - HRA with biopsies and DRE at baseline and 2 years
- Screening procedures compared for acceptability:
  - **Cervical cytology** (pap tests):Cells are collected with a wooden spatula & cytobrush through a speculum
  - **Anal HPV testing and cytology (anal swabs)**: For both tests, cells are collected with a saline-moistened Dacron swab inserted 3-5cm into the anal canal and rotated upon removal
  - **Digital anorectal exams (DRE)**: A gloved finger with gel is inserted into the anus to detect palpable cancer
  - **High-resolution anoscopy (HRA) + biopsies**: Xylocaine gel is applied, the anal canal is visualized via an anoscope, and biopsies are taken of suspicious lesions. If HRA appears normal, 2 targeted biopsies are taken in all participants
- Acceptability questionnaire
  - Administered at final visit or study withdrawal
  - Procedures are compared with yearly cervical pap tests, which are accepted as routine care in WLHIV
- Analyses consist of descriptive statistics

For more information

Elaina Kaufman, MSc. Candidate:
elaina.kaufman@mail.mcgill.ca

Dr. Alexandra de Pokomandy, Principal Investigator:
alexandra.depokomandy@mcgill.ca

Results

Characteristics & AIN/HPV Prevalence

Table 1. Baseline characteristics of EVVA study population compared to acceptability questionnaire respondents

Variable		% or median (range) Study population (n=150)	Acceptability questionnaire respondents* to date (n=75)
Age (median, range)		45 (19-67)	46 (32-67)
Place of birth	Canada	22.7%	25.3%
	Africa	44.0%	46.7%
	Caribbean	28.7%	25.3%
	Other	4.7%	2.7%
Cigarette smoking	Current	16.7%	13.3%
	Past	14.7%	17.3%
	Never	68.7%	69.3%
Intravenous drug use	Current	1.4%	2.7%
	Past	8.8%	9.6%
	Never	89.9%	87.7
CD4 count (cells/μL of blood)	<200	6.2%	5.3%
	200-500	35.6%	34.7%
	>500	58.2%	60.0%
HIV viral load <40 copies/mL		78.7%	73.3%
Prevalent anal hrHPV**		51.3%	60.0%
Prevalent cervical hrHPV		30.0%	32.0%
Prevalent AIN 1		42.0%	45.8%
Prevalent AIN 2 or 3		16.8%	15.3%

*73.3% of questionnaire respondents completed all study visits
**High-risk HPV types 16,18,31,33,35,39,45,51,52,56,58,59,66,68

Pain

0=No pain at all; 10=Worst pain ever felt

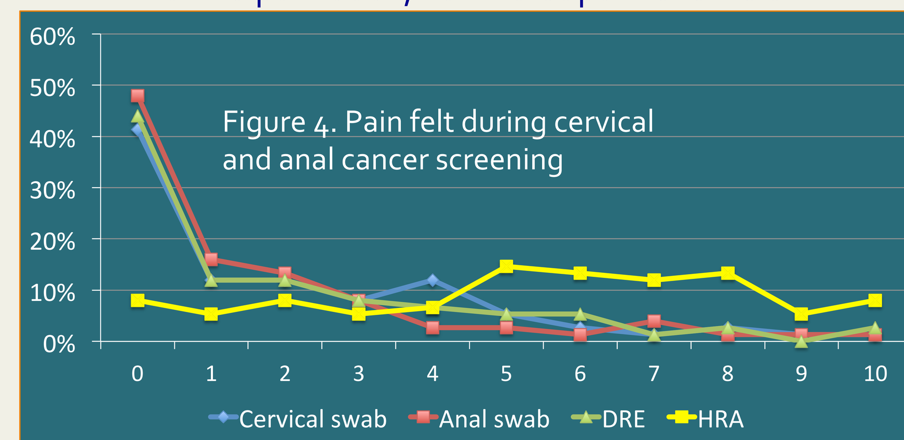

Figure 4. Pain felt during cervical and anal cancer screening

Cervical/Anal swab & DRE: median = 1/10
HRA: median = 6/10

Table 2. Respondents' perceptions of pain felt during anal screening procedures *relative to cervical paps* (n=75)

Procedure	Pain compared to cervical pap tests: Less	Equal	More
Anal swab	28%	49%	23%
Digital Rectal Exam (DRE)	32%	33%	35%
High-Resolution Anoscopy (HRA)	4%	13%	83%

Acceptability of anal screening compared to cervical paps*

0=Not acceptable (Don't want to do it ever again);
10=Very acceptable (So easy I could do it even more often)
***Yearly cervical paps were considered "very acceptable"(10/10) by 80%(95%CI:71-89) of respondents**

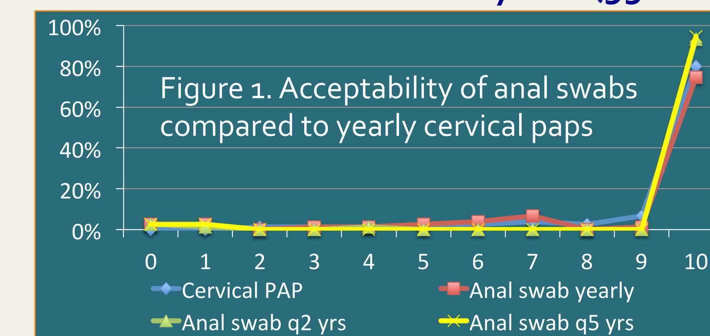

Figure 1. Acceptability of anal swabs compared to yearly cervical paps

What would be a "very acceptable" frequency of screening with anal swabs?

75% (95%CI:65-85) said "yearly"
93% (95%CI:88-99) said "every 2 years"
95% (95%CI:89-100) said "every 5 years"

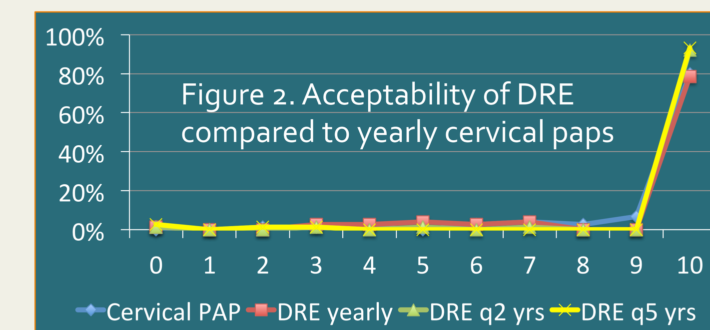

Figure 2. Acceptability of DRE compared to yearly cervical paps

What would be a "very acceptable" frequency of screening with DRE?

79% (95%CI:69-88) said "yearly"
92% (95%CI:86-98) said "every 2 years"
93% (95%CI:88-99) said "every 5 years"

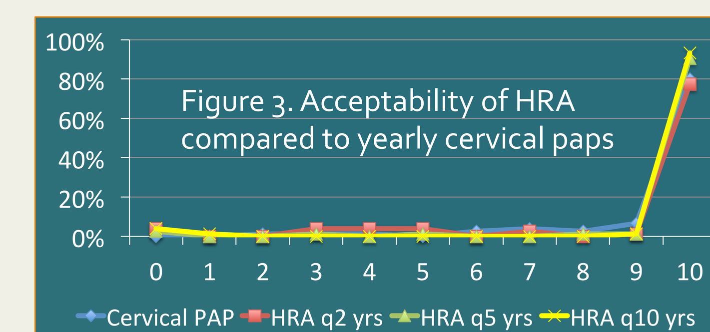

Figure 3. Acceptability of HRA compared to yearly cervical paps

What would be a "very acceptable" frequency of screening with HRA?

77% (95%CI:68-87) said "every 2 years"
91% (95%CI:84-97) said "every 5 years"
93% (95%CI:88-99 said "every 10 years"

...For 4% (95%CI:0-9) screening with HRA is unacceptable even every 10 years!

Reasons for low acceptability (<5/10)

- For yearly anal swabs: "*too painful*" (2), "*too embarrassing*" (1) or "*not necessary that often*" (3)
- For yearly DRE: "*too painful*" (3), "*too long*" (1)
- For HRA every 2-5 years: "*too painful*" (6), "*too long*" (2), "*too far & parking*" (1), "*not necessary that often*" (1)
- For HRA every 10 years: "*too painful*" (2)

Worry about anal cancer

- 25% (95%CI:15-35) were not worried at all;
- 43% (95%CI: 31-54) were extremely worried

Perceived necessity of anal cancer screening

- 73% (95%CI: 63-84) thought it is an absolute necessity
- Only 1% (95%CI: 0-4) were against routine screening

Additional comments from participants

- "*Great for other women, but was too painful for me, as if a nerve was touched*"
- "*I have enough problems, I'm not looking for more*"
- "*Very good screening to ensure everything is good*"

Conclusions

- AIN-2,3 and anal HPV are highly prevalent among WLHIV. To our knowledge, this is the first longitudinal study combining biannual cervical / anal cytology, HPV genotyping, and HRA with systematic biopsies in all participants
- The majority of acceptability questionnaire respondents to date consider **anal cancer screening absolutely necessary** and **very acceptable**
- As expected, acceptability increases as proposed frequency of screening decreases
- Potential adverse psychological effects of screening should be explored
- Pain is the primary reason for low acceptability in our cohort
  - Pain felt during HRA varies widely and is greater than the pain felt during the other procedures (median: 6/10)
  - Nonetheless, acceptability of HRA remains high and pain management can be improved to further increase acceptability
- Both the high prevalence of AIN-2,3 and the high acceptability of screening support proposals for routine anal cancer screening in WLHIV

Acknowledgments

We gratefully acknowledge the women living with HIV who have participated and continue to participate in the EVVA study; the Principal Investigator, Study Coordinator, referring physicians, nurses, clinic staff, and other collaborators; the Research Institute of the McGill University Health Centre (RI-MUHC); the Canadian Institutes of Health Research (CIHR) and the infectious diseases/AIDS network of the Fonds de Recherche du Québec - Santé (FRQS)

Works cited

1. Shiels MS, Cole SR, Kirk GD, Poole C. A meta-analysis of the incidence of non-AIDS cancers in HIV-infected individuals. Journal of Acquired Immune Deficiency Syndromes: JAIDS. 2009;52(5):611-22
2. WHO. Screening for Various Cancers: World Health Organization; 2015 [cited 2015 April 24, 2015]. Available from: http://www.who.int/cancer/detection/variouscancer/en/
3. Ong J, Chen M, Temple-Smith M, Walker S, Hoy J, Woolley I, et al. The inside story. Physicians' views on digital ano-rectal examination for anal cancer screening of HIV positive men who have sex with men. J Med Screen. 2013; 20(4):188-91.