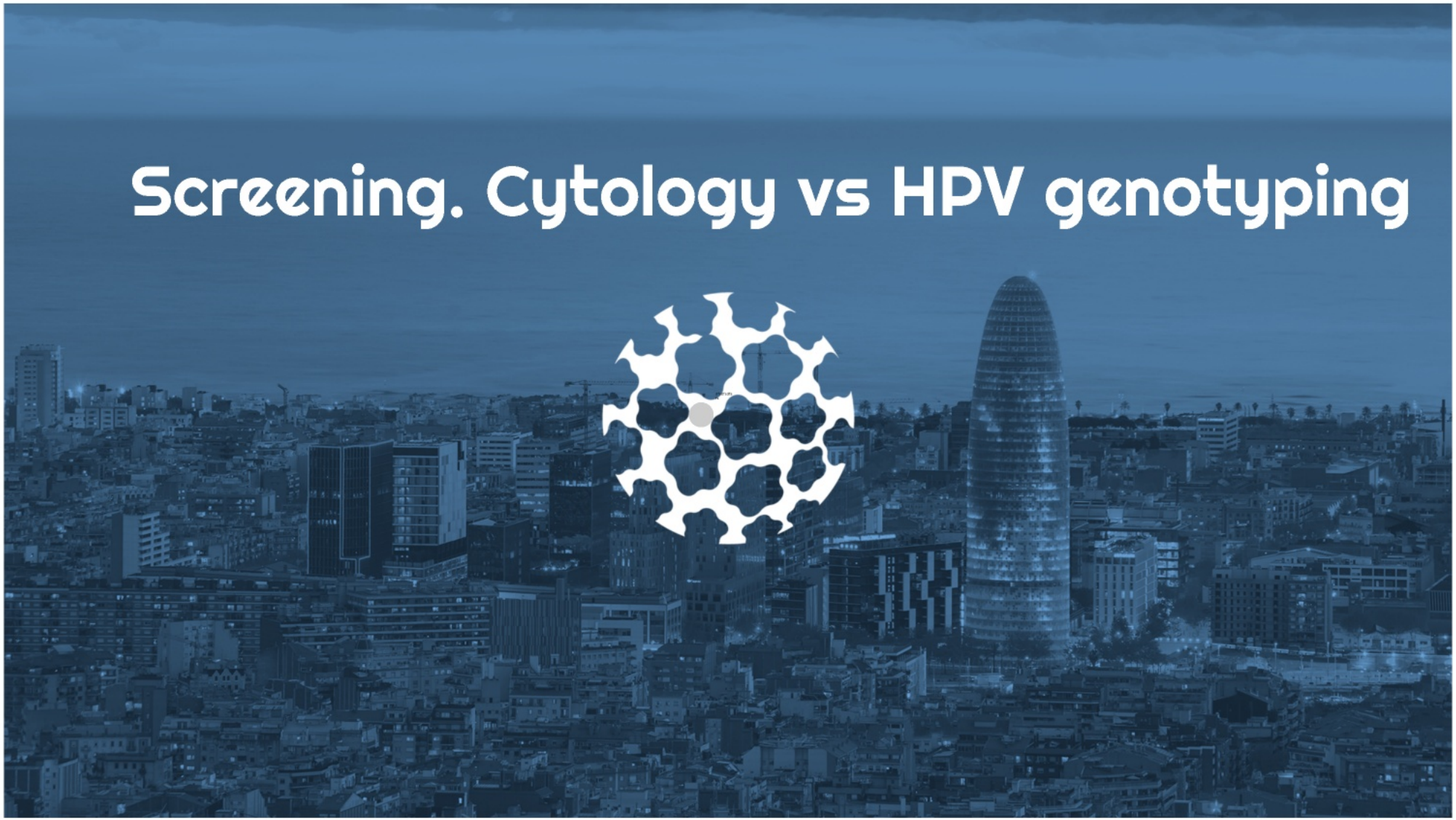
Screening. Cytology vs HPV genotyping



University Hospital Virgen del Rocio, Seville
Infectious Diseases Unit

CÉSAR SOTOMAYOR
SALUD SEXUAL

Several **screening approaches**, including **cytology** and **hrHPV testing** have been **evaluated** for anal cancer screening in different populations.

Currently, there are not enough data on **comparative effectiveness** or evaluating the **harms and benefits** of these strategies to recommend a **preferred option**.

WHY ?

Several **screening approaches**, including **cytology** and **hrHPV testing** have been **evaluated** for anal cancer screening in different populations.

Currently, there are not enough data on **comparative effectiveness** or evaluating the **harms and benefits** of these strategies to recommend a **preferred option**.

WHY ?

- Most **anal cancer screening** studies have been **cross-sectional**.
- Few **prospective studies** were limited to **2–3 years follow-up**.
- Studies vary in **design and cohorts**.
- Further, longitudinal studies evaluating different screening approaches are lacking.

Lifetime Risk of HPV Infection

A significant proportion of the population is affected by HPV, with many individuals encountering it by mid-life.

Heterosexual Risk: **84%**. Approximately 80% of men and women will be infected by **age 45**.

Certain demographics, such as men who have sex with men, exhibit even higher transmission rates.

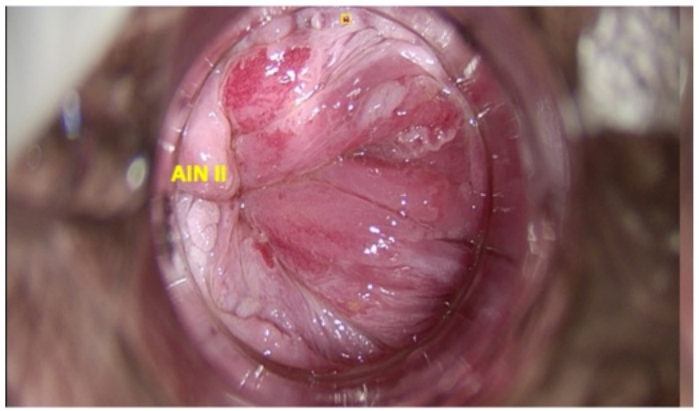
Based on an **80-90% prevalence** of anal infection in some groups.

This contributes to the rise in HPV-related cancers, highlighting the need for effective screening and prevention strategies.

Chesson HW, et al. Sex Trans Inf. 2014.
Burgos J, et al. AIDS 2017.
Viens LJ, et al. MMWR 2016.
Cheng L, et al. J. Clin. Onc. 2022.
Parkin DM, et al. CA 2005.

HPV-Related Cancer: U.S. Trends

- Cervical Cancer Rates Continue to Decline
    - 9.5% decrease per year in the post-vaccination era



- Anal Cancer Increasing:

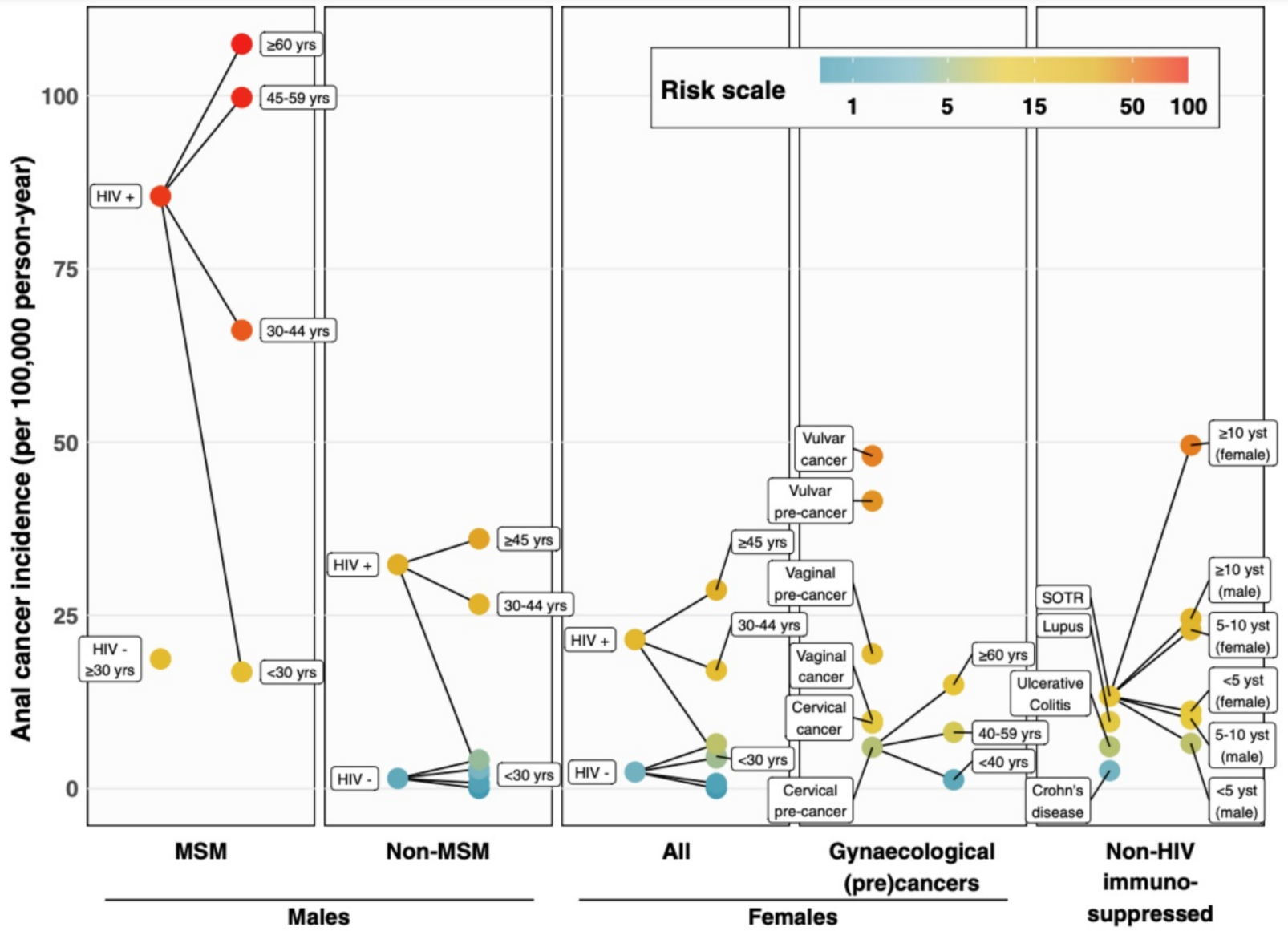
1.8% increase per year among men in the general population.

2.3% increase per year among women.

Still relatively rare in the general population.

Cheng, CL, et al. JAMA Open Net. 2023.
Palefsky, et al. 2022.
Hirsch B, Fine SM, et al. Screening for Anal Dysplasia and Cancer in Adults With HIV Baltimore (MD): Johns Hopkins University; 2022 Aug. Available from: PMID: 32369310.

Anal Cancer Risk Scale



Clifford GM, et.all. Int.J.Cancer, 2021

HIV Infection and HPV-related Malignancy

independent risk factor for anal HSILs and progression to anal cancer among MSM and women

HIV increases risk of **HPV-related malignancy**

Cancer Increased Risk vs General Population

- **Cervical 6x**
- **Anal 19x** (up to 39x in MSM with HIV)
- **OPC** 2-3x

Cervical/anal cancer risk among persons with HIV also associated with:

RISK FACTORS

LIFETIME SEX PARTNERS

PRIOR HISTORY OF AIDS

HISTORY OF LOW CD4 NADIR

SMOKING STATUS

Stelzel, et al. Lancet Global Health. 2021.
Colon-Lopez, V. et al. J Clin Oncology, 2019.
Chiao, et al. 2008

Cervical/anal cancer risk among persons with HIV also associated with:

RISK FACTORS

LIFETIME SEX PARTNERS

PRIOR HISTORY OF AIDS

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SMOKING STATUS

Reasons for screening

ANCHOR study showed that treatment of **HSILs** significantly reduced anal cancer risk among **people with HIV**.

Screening and close follow-up of PLWHIV and HSILs can detect preneoplastic lesions and cancers early

Screening is safe.
Anal cytology testing is both safe and well-tolerated.
HRA and biopsy are safe but may be less well-tolerated

Early detection significantly improves survival rates. 5-year survival rates for early-stage vs disseminated disease (81.9% vs. 34.5%)

Nearly half of those who developed anal cancer were asymptomatic

Palefsky, et al. 2022
NCI SEER 2017
Berry, et al. 2014
Revollo, et al. 2020
Cajas-Monson, et al. 2018

There is no doubt that we need to screen....

Advantages and disadvantages of cytology and HPV genotyping as screening methods.

to screen....

Advantages and disadvantages of cytology and HPV genotyping as screening methods.

HPV typing I

HPV typing has been used to stratify the risk of cervical cancer and follow-up in women with low-grade cervical disease and post-treatment for high-grade disease.

Its direct applicability to HPV-related anal disease screening and treatment in men and women is still under study.

High-risk HPV infection was associated with anal HSILs in several studies; **however, the high prevalence of HPV among MSM with HIV may limit the usefulness of the test in that population.**

NYSDOH. AIDS Institute guideline: screening for anal dysplasia and cancer in adults with hiv, 2022.

HPV typing II

A meta-analysis from the National Cancer Institute found overall high sensitivity but low specificity of HPV testing for anal cancer screening, especially in studies limited to MSM with HIV.

Overall, the prevalence of AIN2+ was 20% and varied across different populations, ranging from 22% in MSM LWH to 13% and 12% in women and MSM without HIV, respectively.

HHS Public Access
Author manuscript
Int J Cancer. Author manuscript; available in PMC 2023 December 01.

Published in final edited form as:
Int J Cancer. 2022 December 01; 151(11): 1889–1901. doi:10.1002/ijc.34199.

A Systematic Review and Meta-Analysis of Cytology and HPV-related Biomarkers for Anal Cancer Screening Among Different Risk Groups

Megan A. Clarke[1], Ashish A. Deshmukh[2], Ryan Suk[2], Jennifer Roberts[3], Richard Gilson[4], Naomi Jay[5], Elizabeth A. Stier[6], Nicolas Wentzensen[1]

In studies with **HPV genotyping**, the **sensitivity and specificity of HPV16 were 46% and 83%,** respectively; **performance did not seem to improve with the addition of HPV18 in studies evaluating HPV16/18 genotyping, although direct comparisons are needed.**

Category	HPV Positivity	Sensitivity	Specificity	Risk of AIN2+
HPV16 genotyping (n=10 studies)	23% (95% CI, 20-26%, τ 2=0.05)	45.5% (95% CI, 34-57%)	83.4% (95% CI, 79-87%)	HPV16 Positive: 39% (95% CI, 25-56%, τ 2=0.92) HPV16 Negative: 13% (95% CI, 8-20%, τ 2=0.58)
MSM with HIV (n=5 studies)	24% (95% CI, 20-28%, τ 2=0.03)	42.4% (95% CI, 27-59%)	80.4% (95% CI, 74-85%)	HPV16 Positive: 29% (95% CI, 13-54%, τ 2=1.18) HPV16 Negative: 12% 95% CI, 6-25%, τ 2=0.80)
HPV16/18 Genotyping (n=8 studies)	30%	44.1%	77.4%	

Adapted from Clarke and Wentzensen, 2018

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HPV Testing

Absence of high-risk HPV may indicate that there is no concerning dysplasia.

Testing for high-risk HPV may be a useful tool for determining whether HRA is needed in patients with an anal cytology result of ASC-US.

Currently, HPV testing for anal cancer may require laboratory validation.

NYSDOH. AIDS Institute guideline: screening for anal dysplasia and cancer in adults with hiv, 2022.

Anal Cytology I

Anal cytology testing is a well-validated technique. When compared with anal histology, the sensitivity and specificity of anal cytology are similar to those of cervical cytology.

Among patients with HIV, the sensitivity of anal cytology was 90% when CD4 count was ≤400 cells/mm3 and 67% when CD4 count was >400 cells/mm3 (P=.005).

Anal cytology alone is acceptable for anal cancer screening (BII).

Anal cytology shows a moderate sensitivity and low specificity for detecting high-grade lesions.

Hirsch B, Fine SM, et al. Screening for Anal Dysplasia and Cancer in Adults With HIV Baltimore (MD): Johns Hopkins University; 2022 Aug. Available from: PMID: 32369310.
Stier EA, Jay N. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702.
Nathan, et al. 2010.
Darragh and Winkler 2011.

Anal cytology shows a moderate sensitivity and low specificity for detecting high-grade lesions.

70%

SENSITIVITY

Indicating its **ability** to **correctly identify** those with squamous intraepithelial lesions (SILs).
A **cytologic result** of **HSIL** is predictive of HSILs on biopsy

LOW SPECIFICITY

It **struggles** to **accurately predict** the **lesion** = cannot determine that the lesion will not be high grade on biopsy

IMPLICATIONS

Due to low specificity, reliance solely on anal cytology may not effectively determine the grade of lesions in histology.

Anal cytology

Immediate HRA referral is recommended for individuals with cytologic diagnosis of atypical squamous cells of undetermined significance (ASC-US) or worse cytology (ASC-US+)

Repeat cytology screening in 12 months is recommended for individuals with negative for intraepithelial lesions or malignancy (NILM) cytoloy.

In settings with limited HRA capacity, it is acceptable to only refer individuals with high-grade cytology (HSIL) or atypical squamous cells, cannot exclude HSIL (ASC-H) to immediate HRA.

Repeat testing in 12 months recommended for individuals with low-grade cytology (LSIL) or ASC-US, and repeat testing in 12–24 months with NILM results.

Stier EA, Jay N. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702.

Co test

Cytology and hrHPV co-testing is acceptable for anal cancer screening(BII).

Effective Combination:
Combining high-risk HPV testing with anal cytology helps identify patients for whom high-resolution anoscopy (HRA) can be deferred (CII).

High-risk HPV DNA testing significantly increases sensitivity to detect high-grade dysplasia and cancer when used with anal cytology.

NYSDOH. AIDS Institute guideline: screening for anal dysplasia and cancer in adults with hiv, 2022. www.hivguidelines.org.

Gaisa, et al. 2021.

Stier EA, Jay N. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702.

Clinical Infectious Diseases
MAJOR ARTICLE

High-risk Human Papilloma Virus Testing Improves Diagnostic Performance to Predict Moderate- to High-grade Anal Intraepithelial Neoplasia in Human Immunodeficiency Virus–infected Men Who Have Sex With Men in Low-to-Absent Cytological Abnormalities

Pompeyo Viciana,[1] Yanoelkis Milanés-Guisado,[1] María Fontillón,[2] Ana Domínguez-Castaño,[2] Cesar Sotomayor,[1] Nuria Espinosa,[1] Luis F. López-Cortés,[1] and Karin Neukam[1,2]; for the SeVIHanal Study Group

[1]Unidad Clínica de Enfermedades Infecciosas y Medicina Preventiva, Hospital Universitario Virgen del Rocío, [2]Instituto de Biomedicina de Sevilla/CSIC/Universidad de Sevilla, and [3]Servicio de Anatomía Patológica, Hospital Universitario Virgen del Rocío, Sevilla, Spain

Prospective cohort of PLWH

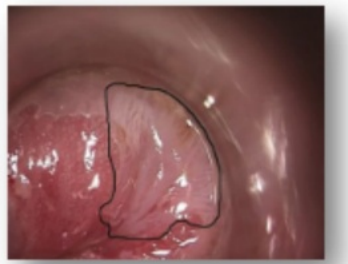
2004

Outpatient HIV Clinic
University Hospital Virgen del Rocio
(Seville)

In 2010, a specialized program for screening and treating anal dysplasia (SCAN) was established for MSM within the Seville Cohort of People Living with HIV at Risk for Anal Cancer (SeVIHanal Cohort, clinicaltrials.gov: NCT03713229

HOSPITAL UNIVERSITARIO Virgen del Rocío

* in those with confirmed histological *High grade Squamous Intraepithelial Lesions*



- Total 705 visits. 426 patients included.
- aLBC alone is suboptimal to identify candidates for HRA-guided bx
- aLBC / HR - HPV showed better performance and a positive interaction and synergistic effect.
- Low prevalence of **histological** HSIL was only observed for the composite aLBC/HR-HPV testing endpoint:
  - *Normal / No HR - HPV* (10%)
  - *LSIL / No HR - HPV* (4%)
- HRA may be spared in the setting of LSIL / no HR HPV following aLBC screening.

SEVIHANAL
Seville Cohort of People Living with HIV at Risk for Anal Cancer

Viciana P, Milanés-Guisado Y. High-risk Human Papilloma Virus Testing Improves Diagnostic Performance to Predict Moderate- to High-grade Anal Intraepithelial Neoplasia in Human Immunodeficiency Virus-infected Men Who Have Sex With Men in Low-to-Absent Cytological Abnormalities. Clin Infect Dis. 2019 Nov 27;69(12):2185-2192.

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l Men Who Have Sex
logical Abnormalities

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ituto de Biomedicina de Sevilla/IBiS/CSIC/Universidad de Sevilla, and [3]Servicio de

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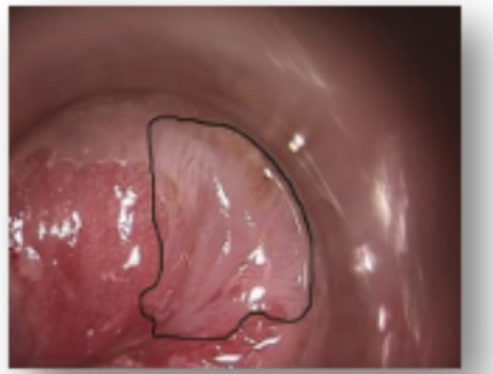

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Co test II

ORIGINAL CONTRIBUTIONS: COLORECTAL CANCER

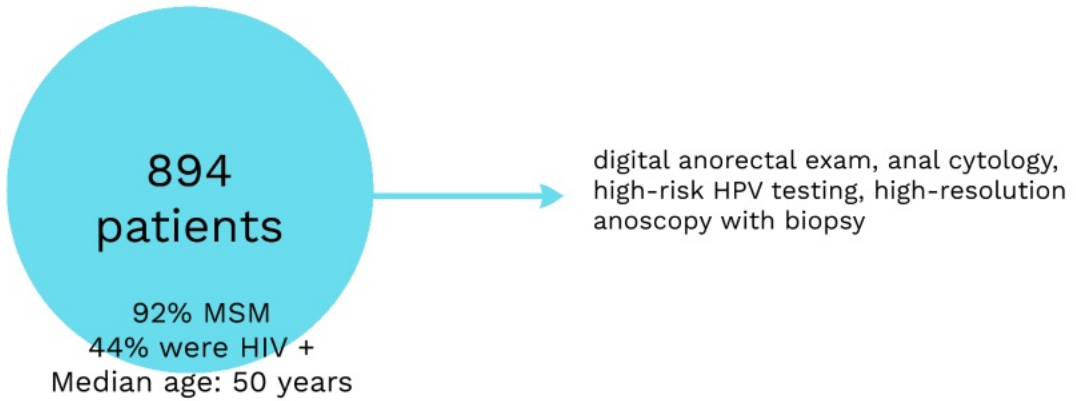
Testing for Human Papillomavirus Strains 16 and 18 Helps Predict the Presence of Anal High-Grade Squamous Intraepithelial Lesions

Sambursky, Jacob A. B.S.[1]; Terlizzi, Joseph P. M.D.[2]; Goldstone, Stephen E. M.D.[2]

Author Information

Diseases of the Colon & Rectum 61(12):p 1364-1371, December 2018. | *DOI:* 10.1097/DCR.0000000000001143

- High-risk HPV testing shows superior sensitivity (96% vs 89%; p = 0.03) and negative predictive value (99% vs 96%; p = 0.008) compared to cytology.
- Testing for HPV 16/18 enhances specificity (48% to 71%; p < 0.0001) and positive predictive value (24% to 37%; p = 0.003) versus all high-risk strains.
- **Patients with benign cytology who test positive for HPV 16/18 experience a 31-fold increased risk of HSILs.**



Found that screening with anal cytology plus high-risk HPV testing significantly improved the sensitivity and negative predictive value beyond cytology alone

Sambursky, et al. 2018.

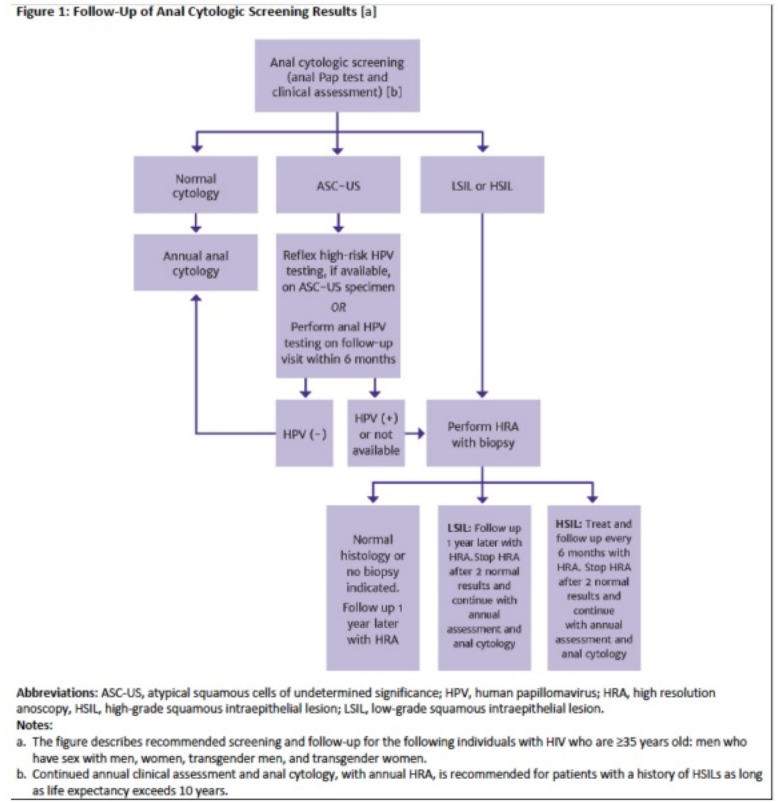
Co test [III]

HRA referral is recommended for individuals with ASC-US or LSIL who test positive for hrHPV, and those with ASC-H or HSIL cytology results regardlessof HPV results.

Repeat screening in 12 months is recommended for individuals with ASC-US who test hrHPV negative (and in 12–24 months for those with NILM cytology testinghrHPV negative).

Management of NILM, LSIL with hrHPV negative test results is at the discretion of the provider—either HRA referral or repeat screening in 12 months are acceptable options.

Stier EA, Jay N. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702.



Hirsch B, Fine SM, et al. Screening for Anal Dysplasia and Cancer in Adults With HIV Baltimore (MD): Johns Hopkins University; 2022 Aug. Available from: PMID: 32369310.

Co test III

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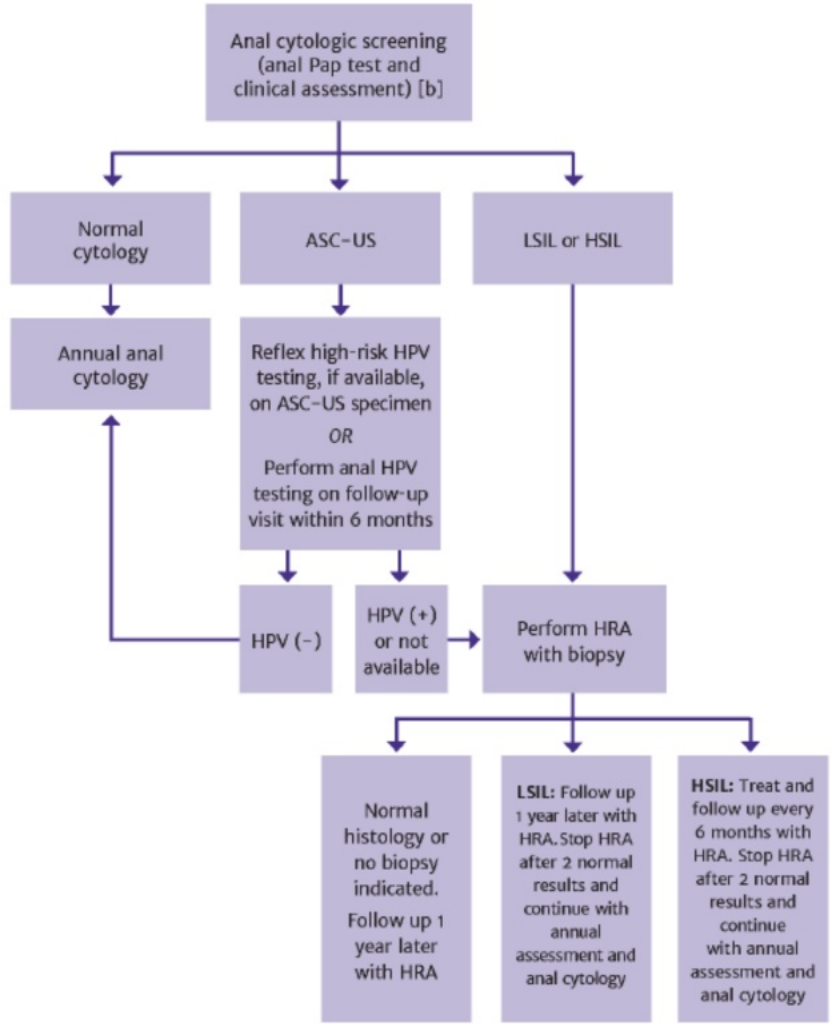
Figure 1: Follow-Up of Anal Cytologic Screening Results [a]



Abbreviations: ASC-US, atypical squamous cells of undetermined significance; HPV, human papillomavirus; HRA, high resolution anoscopy, HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion.

Notes:

a. The figure describes recommended screening and follow-up for the following individuals with HIV who are ≥35 years old: men who have sex with men, women, transgender men, and transgender women.

b. Continued annual clinical assessment and anal cytology, with annual HRA, is recommended for patients with a history of HSILs as long as life expectancy exceeds 10 years.

Hirsch B, Fine SM, et al. Screening for Anal Dysplasia and Cancer in Adults With HIV Baltimore (MD): Johns Hopkins University; 2022 Aug. Available from: PMID: 32369310.

Our clinical guidelines are about to make their grand entrance in one week.....

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Retos y oportunidades en el abordaje de las ITS

MINISTERIO DE SANIDAD

GEITS seimc

21 de octubre de 2024
16.30 h - 20 h
Casa de la Ciencia, Delegación CSIC - Valencia

16.30 h - 17 h	**Abordaje integral de las ITS – enfoque nacional desde la perspectiva institucional.** **Dra. Julia del Amo Valero,** directora de la División de Control del VIH, ITS, hepatitis virales y tuberculosis, Dirección General de Salud Pública y Equidad en salud, Ministerio de Sanidad.
17 h - 18 h	**Presentación de la actualización de la Guía de manejo de ITS.** **Dra. Mar Vera,** Centro Sanitario Sandoval. IdISSC. Hospital Clínico San Carlos. Madrid, **Dr. César Sotomayor, Unidad** de Enfermedades Infecciosas - Microbiología y Parasitología del Hospital Universitario Virgen del Rocío, Sevilla y **Dr. Javier Gómez Castellá,** Jefe de Área Asistencial y de Investigación, División de Control del VIH, ITS, hepatitis virales y tuberculosis, Dirección General de Salud Pública y Equidad en salud, Ministerio de Sanidad. **Dinamizadores: Dr. Juan Carlos Galán,** Jefe sección Hospital Ramón y Cajal. IRYCIS. CIBERESP y **Dra. Maider Arando,** Unidad de Infecciones de Transmisión Sexual Vall d'Hebron-Drassanes. Hospital Vall d'Hebron. Barcelona
18 h - 19.30 h	**Modelos de cribado de ITS en diferentes Comunidades Autónomas.** **País Vasco** - Cribado gestacional de ITS. **Dr. Luis Piñeiro,** Servicio de Microbiología, Hospital Universitario Donostia, San Sebastián y **Dra. Izaskun Lasa,** Servicio Ginecología, Hospital de Bidasoa / **Cataluña** - Programa Drassanes Exprés. **Dr. Yanick Hoyos,** facultativo especialista en microbiologia · Vall d'Hebron Barcelona Hospital Campus / **Comunidad de Madrid** - Unidad móvil de búsqueda activa y atención rápida de ITS en población vulnerable. **Dr. Jorge Valencia,** médico adjunto del Servicio de Enfermedades Infecciosas y Tropicales, Hospital Infanta Leonor / **Andalucía** - Manejo de casos y estudio de contactos desde Epidemiología. **Dr. Eduardo Briones,** Unidad de Salud Pública. Distrito Sevilla. Servicio Andaluz de Salud. **Moderador: Jordi Casabona,** Director Científico del Centro de Estudios Epidemiológicos del VIH y las ITS de Cataluña

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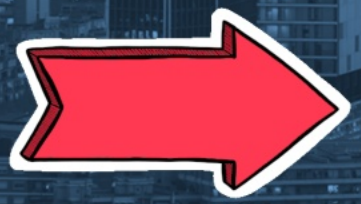

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DOCUMENTO
DE CONSENSO

DIAGNÓSTICO Y TRATAMIENTO DE LAS INFECCIONES DE TRANSMISIÓN SEXUAL EN ADULTOS, NIÑOS Y ADOLESCENTES

GOBIERNO DE ESPAÑA
MINISTERIO DE SANIDAD
SECRETARÍA DE ESTADO DE SANIDAD
DIRECCIÓN GENERAL DE SALUD PÚBLICA Y EQUIDAD EN SALUD
DIVISIÓN DE CONTROL DEVIH, ITS, HEPATITIS VIRALES Y TUBERCULOSIS

GEITS
GRUPO DE ESTUDIO EN INFECCIONES DE TRANSMISIÓN SEXUAL

GeSIDA
GRUPO DE ESTUDIO DEL SIDA

GEHEP
Grupo de Estudio de Hepatitis Víricas

eimc

What has been decided by the expert panel regarding anal dysplasia screening in our national Sexually Transmitted infections guidelines 2024?

ATTENTION

Population	Screening Age	Anal Cancer Incidence (Cases/100,000 persons-year)
Risk Category A (incidence ≥ 10 times compared to the general population)		
GBMSM and trans women with HIV	35	>70/100,000
Women with HIV	45	>25/100,000
Men who have sex with women	45	>40/100,000
GBMSM and trans women without HIV	45	>18/100,000
History of vulvar HSIL or cancer	Within 1 year of diagnosis	>40/100,000
Solid organ transplant recipient	10 years after transplant	>25/100,000
Risk Category B (incidence up to 10 times higher than the general population)		
Cervical/vaginal cancer	Shared decision-making starting at age 45	9/100,000
Cervical/vaginal HSIL	Shared decision-making starting at age 45	8/100,000
Perianal warts (male or female)	Shared decision-making starting at age 45	Unknown
Persistent cervical HPV 16 (>1 year)	Shared decision-making starting at age 45	Unknown
Other immunosuppression (e.g., rheumatoid arthritis, lupus, Crohn's disease, ulcerative colitis, systemic steroid therapy)	Shared decision-making starting at age 45	6/100,000

Adapted from: Stier EA, Clarke MA, et al. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702.

Translated from "Documento de consenso sobre diagnóstico y tratamiento de las infecciones de transmisión sexual en adultos, niños y adolescentes. SEIMC-GEITS, 2024. Pending publication.

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Women with HIV	45	>25/100,000
Men who have sex with women	45	>40/100,000
GBMSM and trans women without HIV	45	>18/100,000
History of vulvar HSIL or cancer	Within 1 year of diagnosis	>40/100,000
Solid organ transplant recipient	10 years after transplant	>25/100,000
Risk Category B (incidence up to 10 times higher than the general population)		
Cervical/vaginal cancer	Shared decision-making starting at age 45	9/100,000
Cervical/vaginal HSIL	Shared decision-making starting at age 45	8/100,000
Perianal warts (male or female)	Shared decision-making starting at age 45	Unknown
Persistent cervical HPV 16 (>1 year)	Shared decision-making starting at age 45	Unknown
Other immunosuppression (e.g., rheumatoid arthritis, lupus, Crohn's disease, ulcerative colitis, systemic steroid therapy)	Shared decision-making starting at age 45	6/100,000

Adapted from: Stier EA, Clarke MA, et al. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. Int J Cancer. 2024 May 15;154(10):1694-1702.

Translated from "Documento de consenso sobre diagnóstico y tratamiento de las infecciones de transmisión sexual en adultos, niños y adolescentes. SEIMC-GEITS, 2024. Pending publication.

Screening test	Triage test	Test results	Management	Low HRA capacity*
Cytology	None	NILM	Repeat screening 12 months	Repeat screening 12-24 months
		ASC-US or +	HRA referral	ASC-US/LSIL – Repeat screening 12 months HSIL and ASC-H. HRA referral
	hrHPV testing of ASC-US or +	ASC-US / hrHPV negative LSIL/ hrHPV negative	Repeat screening 12 months Shared decision between the physician and the patient: referral to HRA or repeat screening	Repeat screening 24 months Repeat screening 12 months
		ASC-US or LSIL + hrHPV positive	HRA referral	ASC-US/LSIL + hrHPV (not 16 positive), repeat in 12 months. HPV 16 positive (regardless of cytology, refer to HRA
		ASC-H/HSIL (regardless of HPV)	HRA referral	HRA referral

Abbreviations: ASC-H, atypical squamous cells cannot exclude high-grade; ASC-US, atypical squamous cells of undetermined significance; hr, high risk; HRA, high-resolution anoscopy; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; NILM, negative for intraepithelial lesion or malignancy.

*Waiting time of more than 6 m for referral to HRA

Translated from "Documento de consenso sobre diagnóstico y tratamiento de las infecciones de transmisión sexual en adultos, niños y adolescentes. SEIMC-GEITS, 2024. Pending publication.

Cytology + hrHPV co-testing (HPV genotyping)	**None**	**NILM + hrHPV negative**	**Repeat screening 12-24 months**	**Repeat screening 24 months**
		ASC-US+ hrHPV negative	**Repeat screening 12 months**	**ASCUS+ hrHPV negative: Repeat screening 24 months**
		NILM + hrHPV positive (16 negative)	**Shared decision between the physician and the patient: referral to HRA or repeat screening 12 months**	**Repeat screening 12 months**
		LSIL+ hrHPV negative	**Shared decision between the physician and the patient: referral to HRA or repeat screening 12 months**	**Repeat screening 12-24 months**
		ASC-US or LSIL + hrHPV positive **HSIL, ASC-H (regardless of HPV)**	**HRA referral**	**ASC-US/LSIL+ hrHPV (not 16): Repeat screening 12 months** **regardless of HPV, HRA referral**

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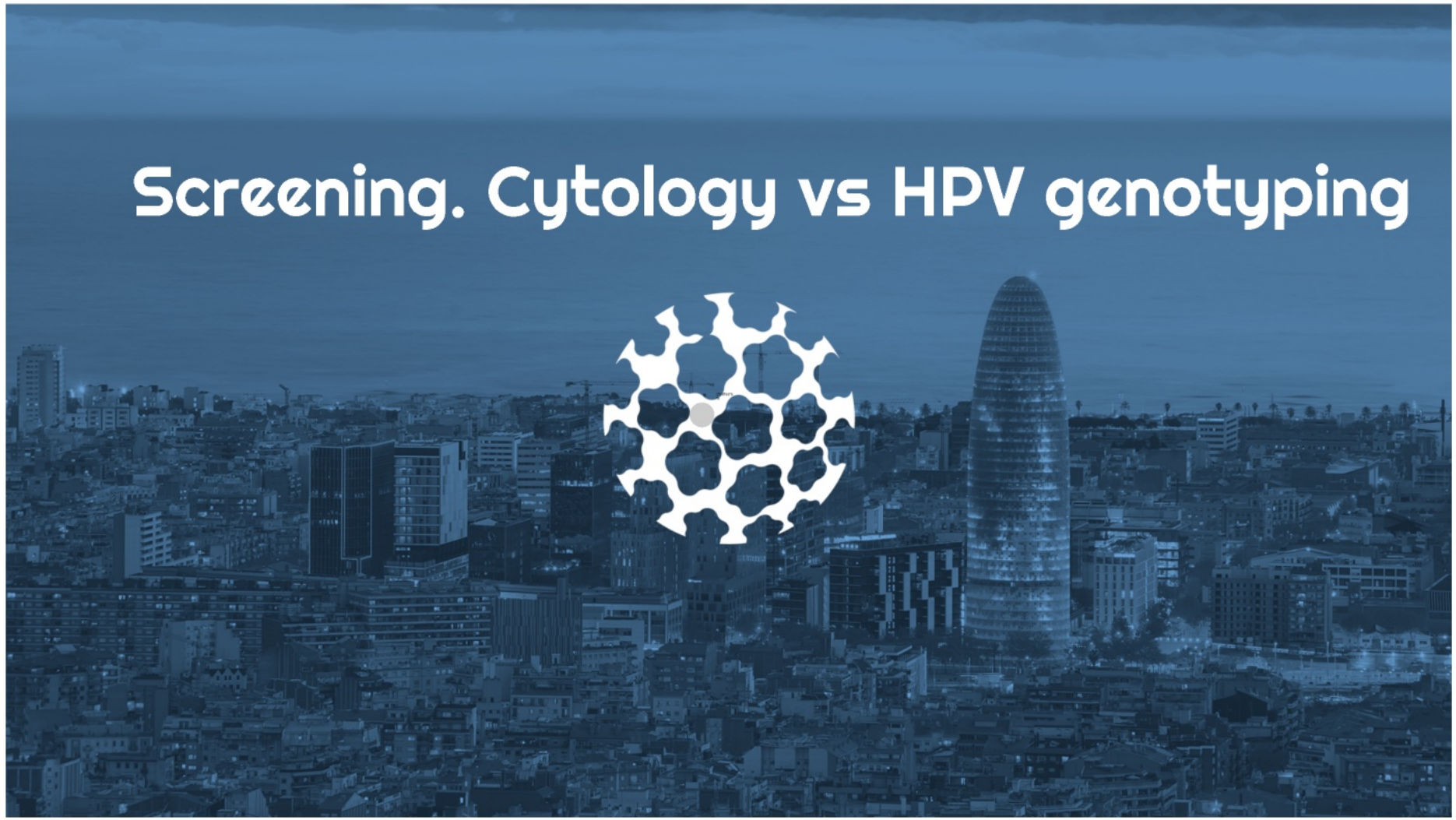
Screening. Cytology vs HPV genotyping



University Hospital Virgen del Rocio, Seville
Infectious Diseases Unit

CÉSAR SOTOMAYOR
SALUD SEXUAL

Key points

- HPV infection is **common**, particularly among certain populations.
- Individuals with HIV experience **higher rates** of cervical, anal, and **oropharyngeal cancers** compared to the **general population**.
- Various methods for anal cancer screening, including **cytology** and **high-risk HPV (hrHPV) testing**, have been evaluated across different populations. However, there is currently **insufficient data** on their **comparative effectiveness**.
- Screening is considered **safe and effective** in **detecting preneoplastic lesions** and cancers early, ultimately **improving survival rates**.
- **Anal cytology testing** is both safe and **well-tolerated**. In contrast, **high-resolution anoscopy (HRA)** and **biopsy** are also safe but may be **less tolerated** by some patients.
- The high prevalence of HPV among men who have sex with men (MSM) living with HIV may limit the effectiveness of HPV typing as a screening tool in this population.
- Anal cytology is a well-validated technique with sensitivity and specificity comparable to cervical cytology (approximately 70%).
- Cytology combined with hrHPV co-testing is an acceptable strategy for anal cancer screening. The combination of hrHPV testing with anal cytology significantly increases sensitivity for detecting high-grade dysplasia and spare HRA in selected patients.

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Thanks for your attention

AND

Don't ask too much !

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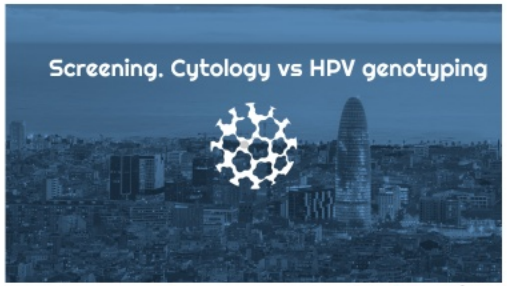
sotomayor_cesar



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Several **screening approaches**, including **cytology** and **hrHPV testing** have been **evaluated** for anal cancer screening in different populations.

Currently, there are not enough data on **comparative effectiveness** or evaluating the **harms and benefits** of these strategies to recommend a **preferred option**.

WHY ?

- Most **anal cancer screening** studies have been **cross-sectional**.
- Few **prospective studies** were limited to **2–3 years follow-up**.
- Studies vary in **design and cohorts**.
- Further, longitudinal studies evaluating different screening approaches are lacking.

Lifetime Risk of HPV Infection

A significant proportion of the population is affected by HPV, with many individuals encountering it by mid-life.

Heterosexual Risk: 84%
Assessed lifetime risk of men and women will be infected by **age 45**.

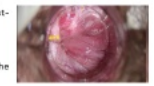
Certain demographics, such as men who have sex with men, exhibit even higher transmission rates.

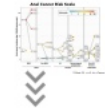
Based on an **80–90% prevalence** of anal infection in some groups.

This contributes to the rise in HPV-related cancers, highlighting the need for effective screening and prevention strategies.

HPV-Related Cancer: U.S. Trends

- Cervical Cancer Rates Continue to Decline
  - 9.5% decrease per year in the post-vaccination era
- Anal Cancer Increasing:
  1.8% increase per year among men in the general population.
  2.3% increase per year among women.
  Still relatively rare in the general population.

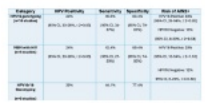




HPV typing :

A meta-analysis from the National Cancer Institute found overall high sensitivity but low specificity of HPV testing for anal cancer screening, especially in studies limited to MSM with HIV.

Overall, the prevalence of AIN2+ was 20% and varied across different populations, ranging from 25% in MSM +WH to 13% and 17% in women and MSM without HIV, respectively.



Adapted from Clarke and Chaturvedi, 2012

Anal Cytology :

Anal cytology testing is a well-validated technique. When compared with anal histology, the sensitivity and specificity of anal cytology are similar to those of cervical cytology.

Among patients with HIV, the sensitivity of anal cytology was 80% when CD4 count was ≤400 cells/mm3 and 67% when CD4 count was >400 cells/mm3 (P=.005).

Anal cytology alone is acceptable for anal cancer screening (BII).

Anal cytology :

Immediate HRA referral is recommended for individuals with cytologic diagnosis of atypical squamous cells of undetermined significance (ASC-US) or worse cytology (ASC-US+)

Repeat cytology screening in 12 months is recommended for individuals with negative for intraepithelial lesions or malignancy (NILM) cytotes.

In settings with limited HRA capacity, it is acceptable to only refer individuals with high-grade cytology (HSIL) or atypical squamous cells, cannot exclude HSIL (ASC-H) to immediate HRA.
Repeat testing in 12 months recommended for individuals with low-grade cytology (LSIL) or ASC-US, and repeat testing in 12–24 months with NILM results.

HPV typing :

HPV typing has been used to stratify the risk of cervical cancer and follow-up in women with low-grade cervical disease and post-treatment for high-grade disease.

Its direct applicability to HPV-related anal disease screening and treatment in men and women is still under study.

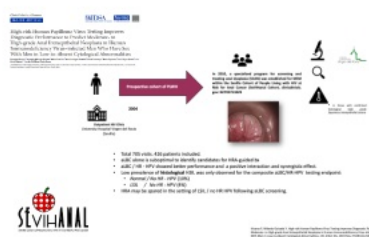
High-risk HPV infection was associated with anal HSILs in several studies; **however, the high prevalence of HPV among MSM with HIV may limit the usefulness of the test in that population.**

HPV Testing :

Absence of high-risk HPV may indicate that there is no concerning dysplasia.

Testing for high-risk HPV may be a useful tool for determining whether HRA is needed in patients with an anal cytology result of ASC-US.

Currently, HPV testing for anal cancer may require laboratory validation.



Reasons for screening

ANCHOR study showed that treatment of **HSILs** significantly reduced anal cancer risk among **people with HIV**.

Screening and close follow-up of PLWHIV and HSILs can detect preneoplastic lesions and cancers early

Early detection significantly improves survival rates. 5-year survival rates for early-stage vs disseminated disease (81.9% vs. 34.5%)

Nearly half of those who developed anal cancer were asymptomatic

HIV Infection and HPV-related Malignancy

independent risk factor for anal HSILs and progression to anal cancer among MSM and women

HIV increases risk of **HPV-related malignancy**

Cancer Increased Risk vs General Population

- **Cervical 6x**
- **Anal 19x** (up to 38x in MSM with HIV)
- **OPC** 2–3x

Co test :

Cytology and hrHPV co-testing is acceptable for anal cancer screening(BII).

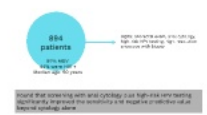
Effective Combination:
Combining high-risk HPV testing with anal cytology helps identify patients for whom high-resolution anoscopy (HRA) can be deferred (CII).

High-risk HPV DNA testing significantly increases sensitivity to detect high-grade dysplasia and cancer when used with anal cytology.

Co test :

Testing for Human Papillomavirus Strains 16 and 18 Helps Predict the Presence of Anal High-Grade Squamous Intraepithelial Lesions

- high-risk –HPV testing shows superior sensitivity (90% vs 69%; p = 0.01) and negative predictive value (98% vs 96%; p = 0.048) compared to cytology.
- Testing for HPV 16/18 enhances specificity (84% to 91%; p < 0.0001) and positive predictive value (14% to 37%; p = 0.003) versus all high-risk strains.
- **Patients with benign cytology who test positive for HPV 16/18 experience a 31-fold increased risk of HSILs.**



Found that screening with anal cytology plus high-risk HPV testing significantly improved the sensitivity and negative predictive value beyond cytology alone

Sanlorenzo, et al. 2015.

Co test :