HPV Board 2025
Antwerp, Belgium

Anal Cancer Screening Guidelines: Evidence and Practical Implications

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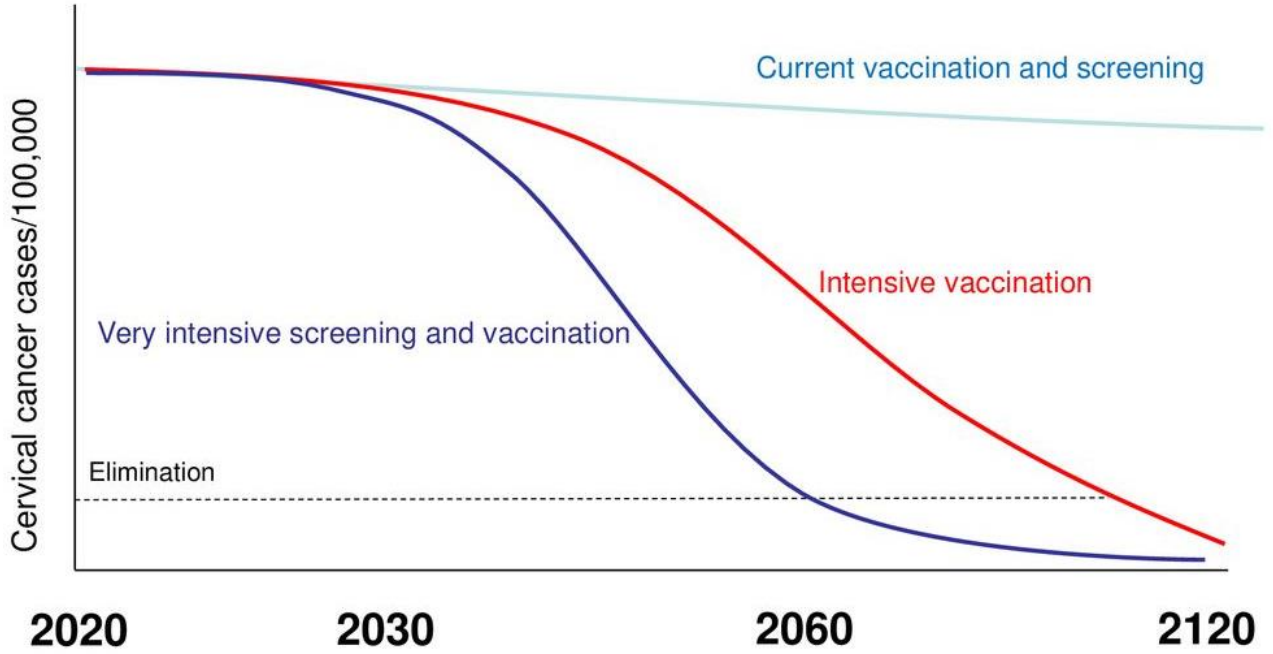
Disclosures

- I have no conflict of interest.

Towards anal cancer prevention: Following the path of cervix?



World Health Organization

Dr Tedros Adhanom Ghebreyesus
Director-General

Cervical Cancer: An NCD We Can Overcome
Intercontinental Hotel, Geneva
19 May 2018

WHO call to action for elimination of cervical cancer by 2100

- It took over 40 years from discovery of the role of HPV in cervical cancer to formulating goals for world-wide cervical cancer elimination
- What can we learn from this process to accelerate anal cancer prevention?

Goal of cancer screening

Performing screening

- In a population at sufficient risk
- That is asymptomatic

To

- Reduce cancer mortality
- Reduce cancer morbidity
- Prevent cancer (ANCHOR)

- DARE
- High resolution anoscopy
- Anal cytology
- Anal HPV testing
- Biomarkers

To identify anal precancers and early cancers for treatment

Critical questions

Who to screen?

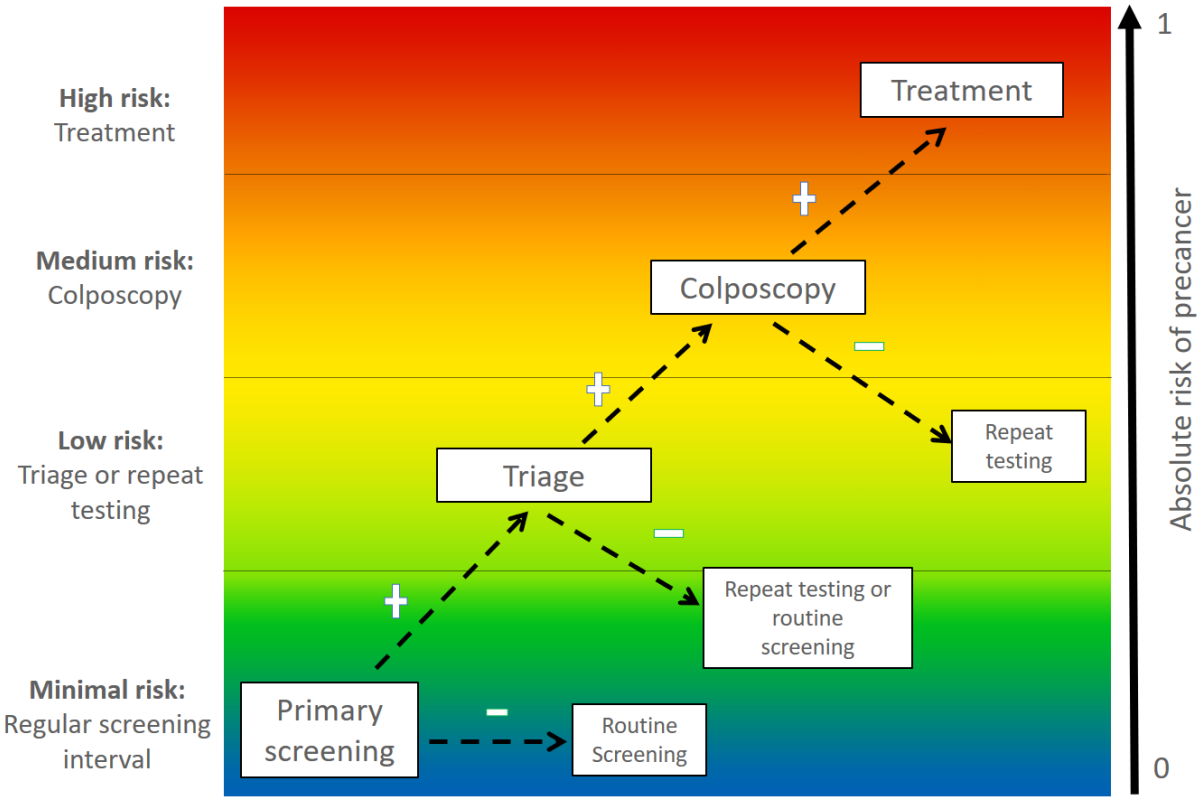
When to screen?

Screening with what test?

What management (including treatment)?

Risk based screening and management

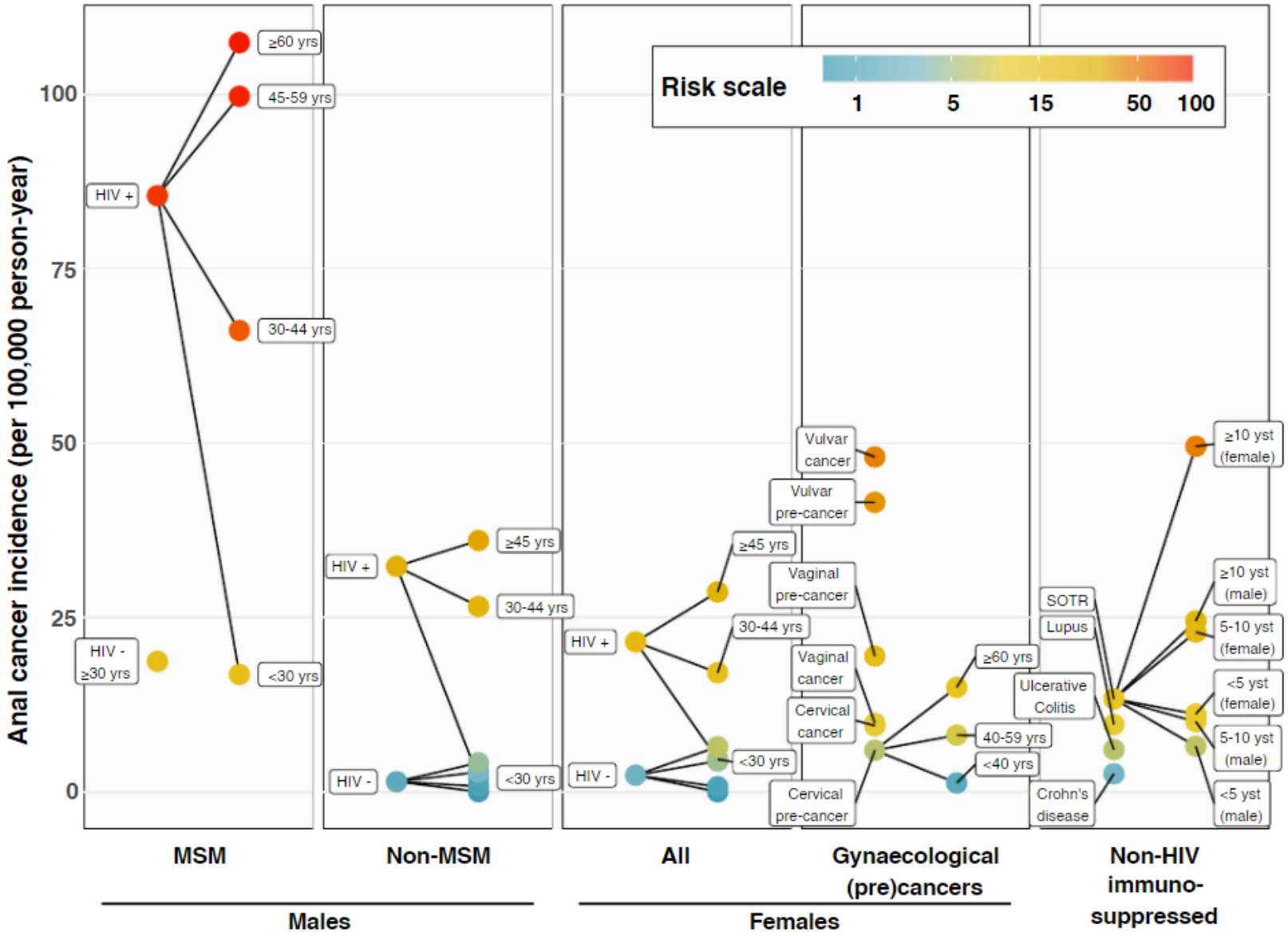
Risk-based management in cervical cancer screening



- Risk-based framework independent of the test used
- Principle: “Similar management of similar risk”
- Established clinical action thresholds for cervix (not universal, actions may differ between settings)
- Risk data are universally applicable since biology is the same across settings
- Risk thresholds are not established for anal cancer screening
- HRA capacity is limited in many settings
- Treatment is more complex for anal region compared to cervix

Wentzensen JCV 2015

Who and when to screen?
Anal cancer incidence in different populations

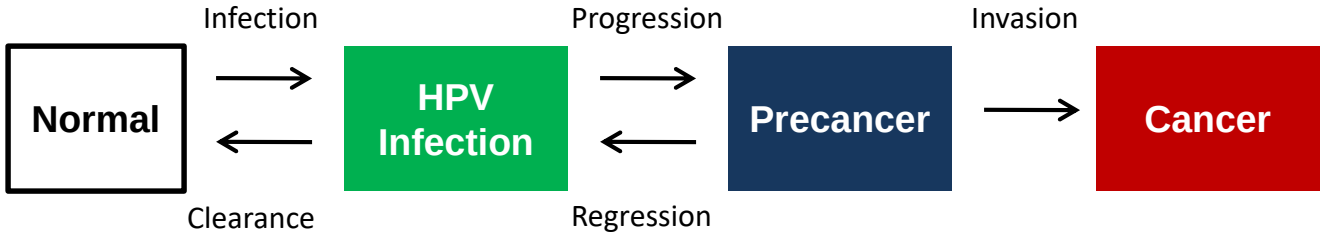


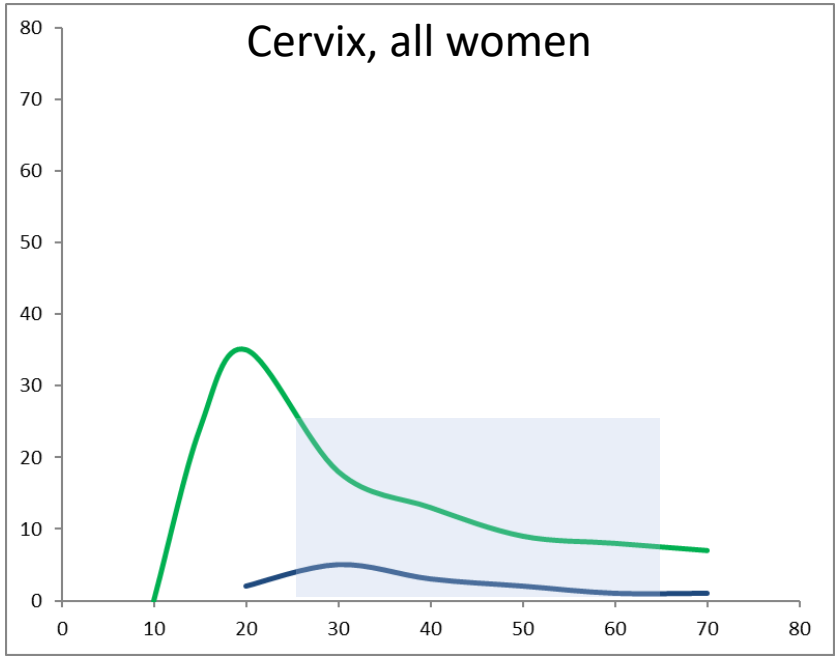
At least 16 different populations, defined by:

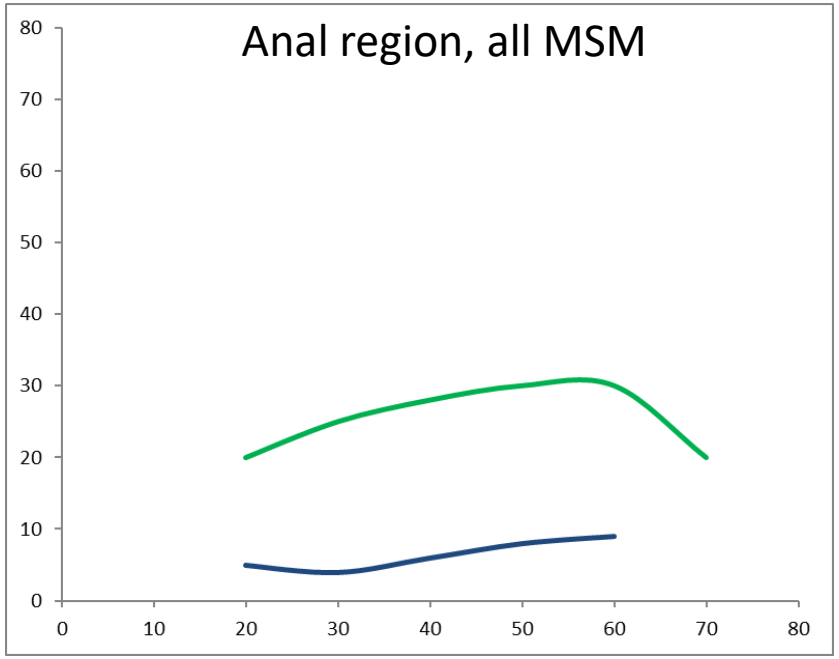
- sex
- sexual behavior,
- HIV status
- other immunosuppressive disorders
- history of anogenital (pre)-cancers

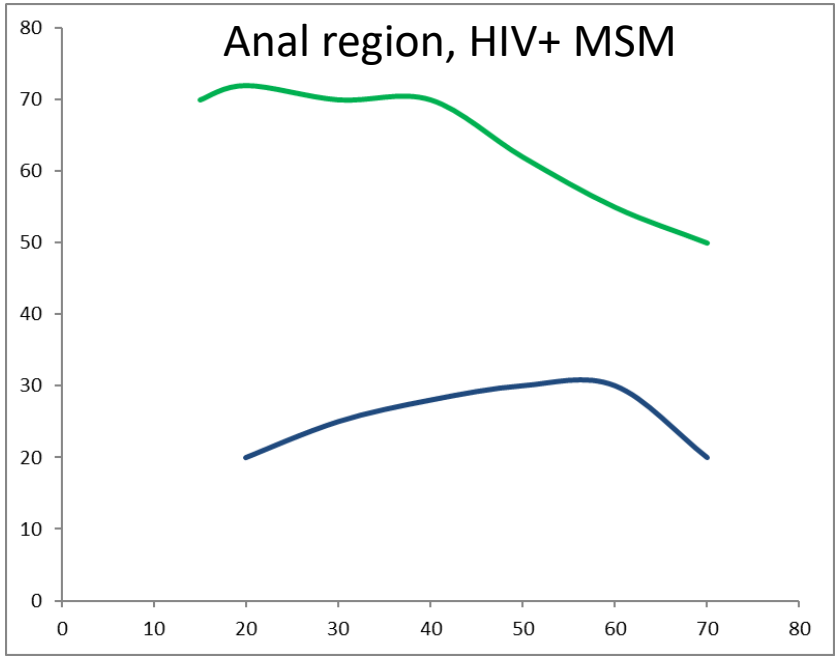
Clifford 2020 IJC

Age distribution of HPV infection and precancer









HPV-based screening

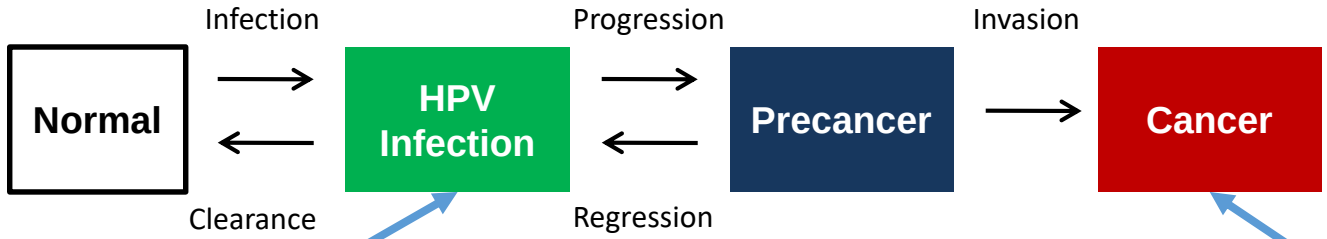
- Important role of specific biomarkers for identifying precancers

Clarke and Wentzensen 2018 Cancer Cytopathology

Comparing cervical and anal carcinogenesis

Prevalence of precancer among HPV-positives is much higher for anal vs. cervical region

Risk of invasion is lower for anal HSIL compared to cervical HSIL



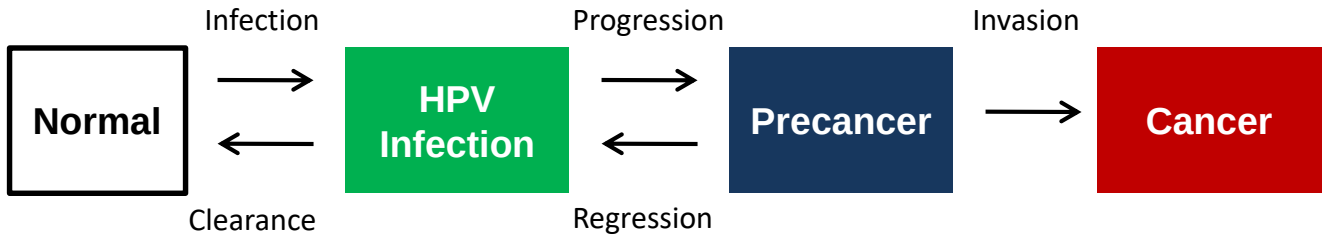
Anal HPV prevalence is high, even in low-risk populations

Population-wide anal cancer incidence is much lower than cervical cancer incidence

Age distribution of anal HPV infection is more even compared to cervix

Small subgroups with very high anal cancer incidence, but low proportion of cases

Screening with what test?
Biomarker summary, systematic review of screening tests



Host changes Viral changes

HPV, HPV genotype

HPV methylation

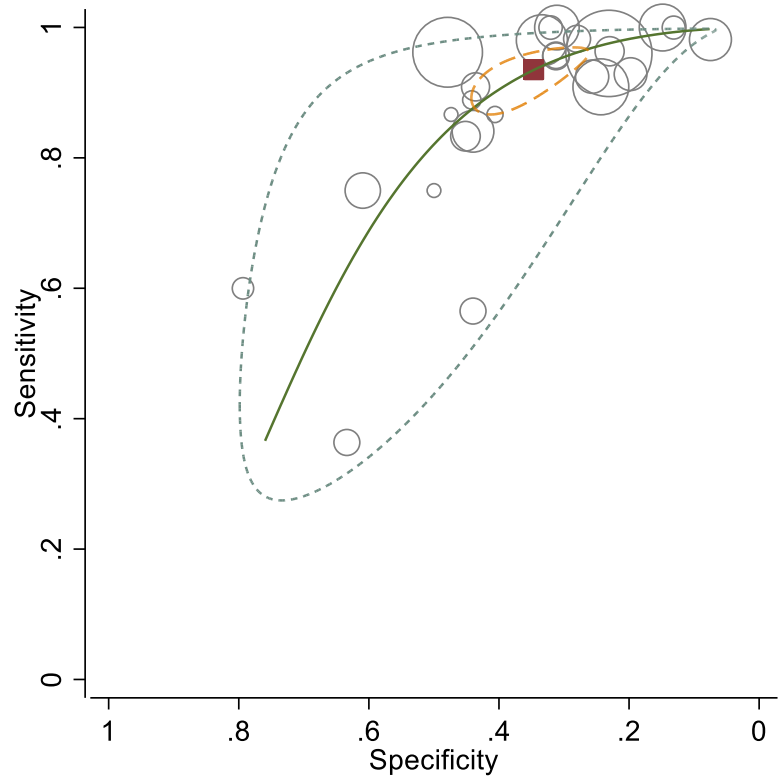
p16/Ki-67 dual stain

HPV integration

Somatic mutations

Host gene methylation

Cytologic abnormalities



Clarke IJC 2022

Screening with what test?

Screening recommendations for cervical and anal cancer

- Cervical screening guidelines
  - HPV-based screening age 30-65
  - Triage with cytology, dual stain, extended genotyping, methylation
- Focused on general population, different guidelines for immunocompromised individuals

- Anal screening guidelines
  - CDC guidelines
  - **Recently published IANS recommendations**
- Strong focus on immunocompromised populations

Perkins JAMA 2023, Stier IJC 2024

The IANS GUIDELINES

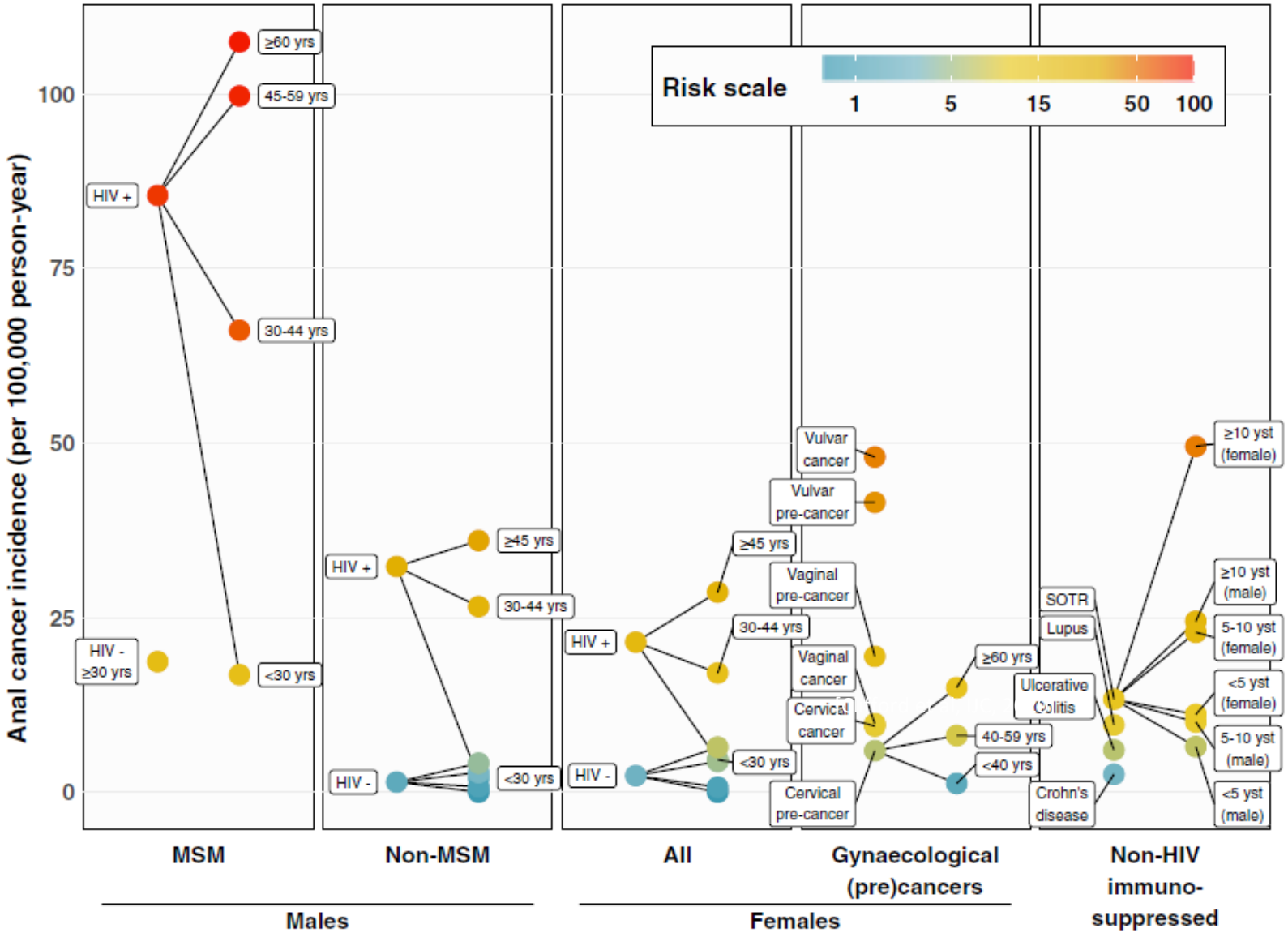
International Anal Neoplasia Society's consensus guidelines for anal cancer screening

Elizabeth A. Stier[1] | Megan A. Clarke[2] | Ashish A. Deshmukh[3,4] | Nicolas Wentzensen[2] | Yuxin Liu[5] | I. Mary Poynten[6] | Eugenio Nelson Cavallari[7] | Valeria Fink[8] | Luis F. Barroso[9] | Gary M. Clifford[10] | Tamzin Cuming[11] | Stephen E. Goldstone[12] | Richard J. Hillman[6,13] | Isabela Rosa-Cunha[14] | Luciana La Rosa[15,16] | Joel M. Palefsky[17] | Rosalyn Plotzker[18] | Jennifer M. Roberts[19] | Naomi Jay[17]

Task force assembled in 2018 by Naomi Jay and Beth Stier, public comment period in 2023

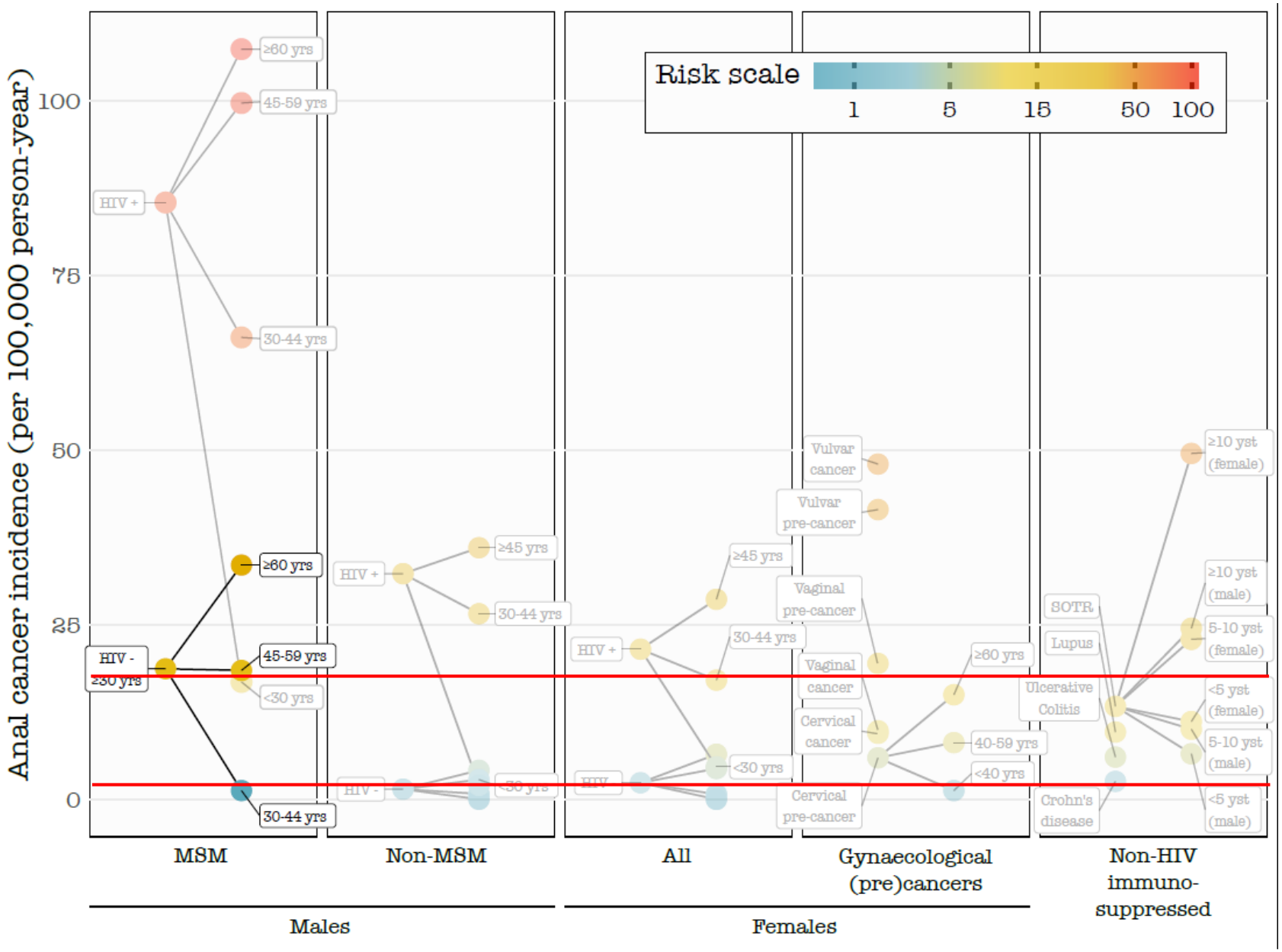
ians International Anal Neoplasia Society

Int J Cancer. 2024 May 15;154(10):1694-1702.



Anal cancer risk scale : meta-analysis of anal cancer incidence

[Clifford, Int J Cancer, 2021]



Anal cancer risk scale : addition for MSM Uninfected by HIV

[Deshmukh, Clin Infect Dis, 2023]

Risk Category A (Incidence ≥ 10-fold compared to the general population (i.e., 17/100,000))

Population – Risk category	When	Anal cancer incidence per 100,000 p-y
MSM and Transwomen (TW) living with HIV (LWH)	Age 35	>70/100,000 at age 30-44 >100/100,000 age 45+
Women LWH	Age 45	>25/100,00 age 45+
Men (not MSM) LWH	Age 45	>40/100,000 age 45+
MSM and TW not LWH[1]	Age 45	>18/100,000 age 45+ >30/100,000 age 60+
History of vulvar HSIL or cancer	Within 1 year of diagnosis	>40/100,000
Solid Organ Transplant Recipients	10 yrs post-transplant	>25/100,000

Clifford, Int J Ca, 2021; Deshmukh, CID 2023

Risk Category B (Incidence up to 10-fold higher compared to the general population)

Population – Risk category	When	Risk for anal cancer per 100,000 p-y
Cervical/Vaginal Cancer	Shared decision age 45	9/100,000
Cervical/Vaginal HSIL	Shared decision age 45	8/100,000
Perianal warts (male or female)	Shared decision age 45	unknown
Persistent cervical HPV 16 (>1 yr)	Shared decision age 45	unknown
Other immunosuppression (e.g., RA, Lupus, Crohn's, UC, on systemic immunosuppressive therapy)	Shared decision age 45	6/100,000

Clifford, Int J Ca, 2021

Screening for risk category B

Screening should only be offered provided there is sufficient capacity for HRA.

Shared decision making: Process in which a health care provider and patient work together to make a health care decision. The optimal decision considers evidence-based information regarding available options, the provider's knowledge and experience, and the patient's values and preferences.

Screening tools

- Recommendations for different screening tools for detection of anal HSIL were based on evidence generated from systematic review and meta-analysis (Clarke et al. 2022)
- Evidence graded based on strength (A-E) and quality (I-III)
- Data limited on test performance within different risk groups as well as for test combinations
- Data on longitudinal performance (particularly beyond 2-3 years) were scarce
- Recommendations for triage to HRA (i.e., management of abnormal screening results) and surveillance intervals were made primarily based on expert opinion and current practice standards
- Management options for limited HRA capacity using higher test specificity thresholds are provided
  - Limited capacity = HRA wait times of >6 months for individuals with abnormal screening results

Primary Screening Test[1]	Triage test	Evidence[2]
Cytology	None	BII
	HPV (with or without limited genotyping)	CII

[1]All primary screening tests were considered 'acceptable' based on available evidence; limited data to make population-specific recommendations at this time

[2]Grading of Evidence:

Strength: B=Moderate evidence for efficacy or only limited clinical benefit supports recommendation for use

C=Evidence for efficacy is insufficient to support a recommendation for or against use, but recommendations may be made on other grounds

Quality: II=Evidence from at least one clinical trial without randomization, from cohort or case-controlled analytic studies, or from multiple time-series studies, or dramatic results from uncontrolled experiments

Primary Screening Test*	Triage Test	Test Results	Management
Cytology	None	NILM	Repeat screening 12 months
		ASCUS or worse	HRA referral
	hrHPV testing of ASC-US+	NILM, ASC-US/hrHPV-negative	Repeat screening 12 months
		ASC-US or LSIL/hrHPV-positive; ASC-H or HSIL	HRA referral
		LSIL/hrHPV-negative	HRA referral OR repeat screening in 12 months[1]

[1]Modifications for settings with limited HRA capacity provided in recommendations

[2]Provider discretion recommended

Summary and next steps

- Current IANS guidelines are a pragmatic first step to provide evidence based guidance that will be updated as more data become available
- We need a lot more data!
  - Test performance characteristics in different populations (i.e., women LWH, MSM without HIV)
  - Longitudinal studies to determine screening and management intervals
  - Observational data and real-life data are critical complements
  - Performance characteristics for test combinations
  - Novel biomarkers (e.g., extended HPV genotyping, dual stain, methylation)
- Development of clinical action thresholds to inform risk-based decision making is needed, but can be challenging across different populations

Challenges to implementation

- How to reach target populations?
  - Challenges to organized screening
  - Embedding with medical services for underlying conditions
- HRA is critical, how to build capacity?
  - Expand facilities and providers
  - HRA training, certification, and quality control is important (IANS, other organizations)
- Treatment is complex, training is critical
- Regulatory approval of tests for anal cancer screening
  - Wide availability of tests for cervical cancer screening is good
  - Off-label use of tests approved for cervical screening may have implications for access, reimbursement