

# Management of women with HIV who are HPV positive

Hennie Botha  
Antwerp 2022



# Should we manage it (them) differently?



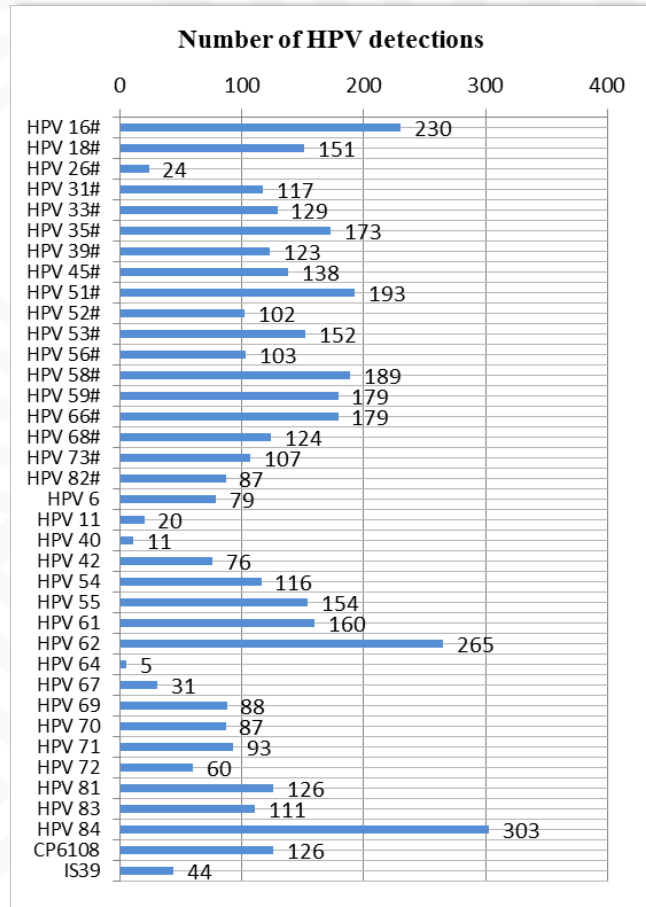
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## Ethics

- Justice
  - Work towards **fully effective** pre-cancer and cancer management in PLWH
- First do no harm (non-maleficence)
  - **Minimize side effects** of ARV's
- Do good (beneficence)
  - **Long term protection** against cancer after precancer treatment (and not give false hope)
  - Equal PFS and OS?
- Autonomy
  - Accurate estimation of risk

# WLWH: Detection of HPV genotypes



Proportion of Women Who Had	Number	%
Any HR risk HPV Type Detected	287	94.3%
Any Low Risk HPV Type Detected	284	94.7%
No HPV Detected	2	0.7%
HPV 16 and/or HPV 18	160	53.3%
HPV 16 and HPV 18	46	15.3%
Only one HR type detected	18	6.0%
High-Risk types- two to four	115	38.3%
High-Risk Types- five to nine	129	43.0%
High-Risk Types -ten or more	25	8.3%

*AIDS 2014, 28:000–000*



# Combination antiretroviral therapy reduces the detection risk of cervical human papilloma virus infection in women living with HIV

Michèle D. Zeier<sup>a</sup>, Matthys H. Botha<sup>b</sup>, Susan Engelbrecht<sup>c,d</sup>, Rhoderick N. Machekano<sup>e</sup>, Graeme B. Jacobs<sup>c</sup>, Shahieda Isaacs<sup>c</sup>, Marije van Schalkwyk<sup>a</sup>, Haynes van der Merwe<sup>b</sup>, Deidre Mason<sup>b</sup> and Jean B. Nachega<sup>a,f,g</sup>



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- cART reduced detection of any HPV by 77% (OR 0.23, 95% CI 0.15–0.37)
- cART reduced the risk of HPV-16 detection (OR 0.50, 95% CI 0.37–0.67)
- Every month on cART reduced the detection of any HPV type by 9% (OR 0.91, 95% CI 0.89–0.94)

*AIDS* 2014, **28**:000–000



# Warts in WLWH are often associated with pre-cancer or cancer



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- 49 participants with large warty lesions
- Mean age 34.2y
- Worst histological diagnosis:
  - C. acuminata in 46.9%
  - VIN1 and VIN2 in 4.1% each
  - VIN3 in 34.7%
  - Squamous cancer in 10.2%
- Histology of warty lesions is essential to diagnose pre-invasive lesions or invasive cancer

Vaccs group: Poster SASMO 2022







## GENERAL GYNECOLOGY

**The economic burden of noncervical human papillomavirus disease in the United States**

Delphine Hu, MD; Sue Goldie, MD

Am J Obstet Gynecol 2008;198:

**CONCLUSION:** The economic burden of noncervical HPV disease is substantial. Analyses that assess the value of investments in HPV prevention and control programs should take into account the costs and morbidity and mortality rates that are associated with these conditions.

## RESEARCH ARTICLE

## Open Access

**The quality of life of patients with genital warts: a qualitative study**Gitte Lee Mortensen<sup>1\*</sup>, Helle K Larsen<sup>2</sup>

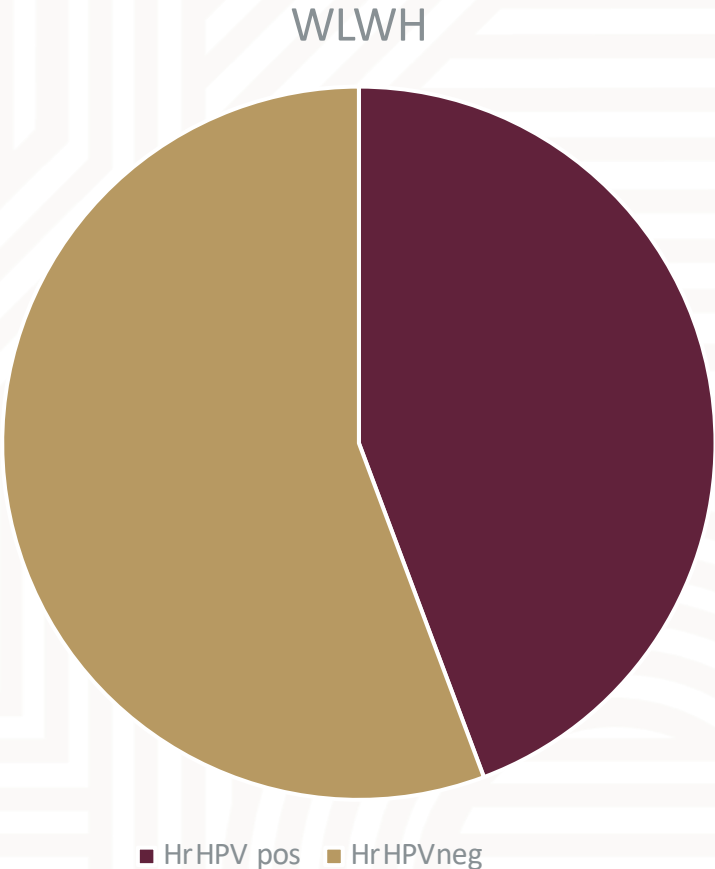
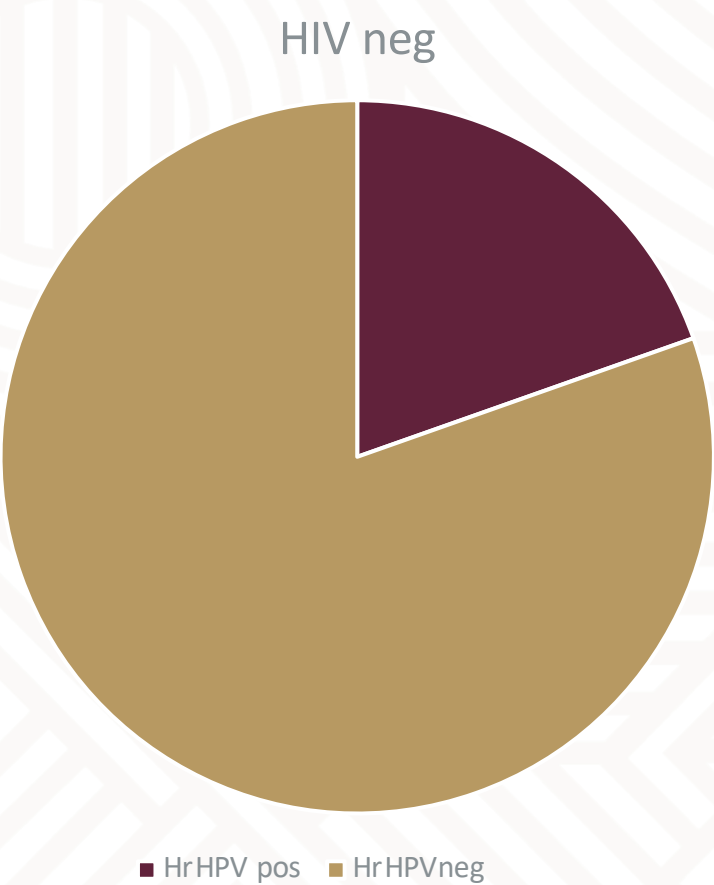
BMC Public Health 2010, 10:113

The men and women participating in this study considered their quality of life to be significantly lowered because of genital warts



# Well controlled HIV and HPV detection

900 unscreened women (495 HIV neg and 405 HIV pos)



Unpublished VACCS group

# Cytology in WLWH: Behaviour of LSIL



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- High rate of underlying histologic CIN II/III
- TF, recurrence significantly higher in WLWH
- Higher incomplete excision in HIV
- ARV started *before* LEEP improves outcome
- Higher CD4 count improved excision outcome

## Progression and Persistence of Low-Grade Cervical Squamous Intraepithelial Lesions in Women Living With Human Immunodeficiency Virus

Michèle Desiré Zeier, MD,<sup>1</sup> Matthys Hendrik Botha, MMed, PhD,<sup>2</sup>  
Frederick Haynes van der Merwe, MMed,<sup>2</sup> Ingrid Eshun-Wilson, MD,<sup>1</sup>  
Marije van Schalkwyk, MD,<sup>1</sup> Marina la Grange, BOccTher,<sup>1</sup>  
Deidre Mason, MD,<sup>2</sup> Mercia Louw, MMed,<sup>3</sup> and Jean B. Nachega, MD, PhD<sup>1,4,5</sup>

Zeier. J Low Genit Tract Dis. 2012

## Outcomes after an excisional procedure for cervical intraepithelial neoplasia in HIV-infected women

Laura L. Reimers<sup>a</sup>, Susan Sotardi<sup>a</sup>, David Daniel<sup>b</sup>, Lydia G. Chiu<sup>a</sup>, Anne Van Arsdale<sup>a</sup>, Daryl L. Wieland<sup>c</sup>, Jason M. Leider<sup>c</sup>, Xiaonan Xue<sup>d</sup>, Howard D. Strickler<sup>d</sup>, David J. Garry<sup>c</sup>, Gary L. Goldberg<sup>a,d</sup>, and Mark H. Einstein<sup>a,d,\*</sup>



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- TF in 55% of CIN 2+
- Most recurrent lesions were high grade (>70%)
- TF increased with LEEP compared to cold knife conization (RR=1.76; 95% CI: 1.15–2.64)
- TF associated with **low CD4+ count** ( $p = 0.04$ ) and higher HIV RNA level
- TF associated with **positive margins** (HR = 6.12; 95% CI: 1.90–19.73)
- “**avoid raising expectations of cure** and instead focus on the achievable goal of cancer prevention”

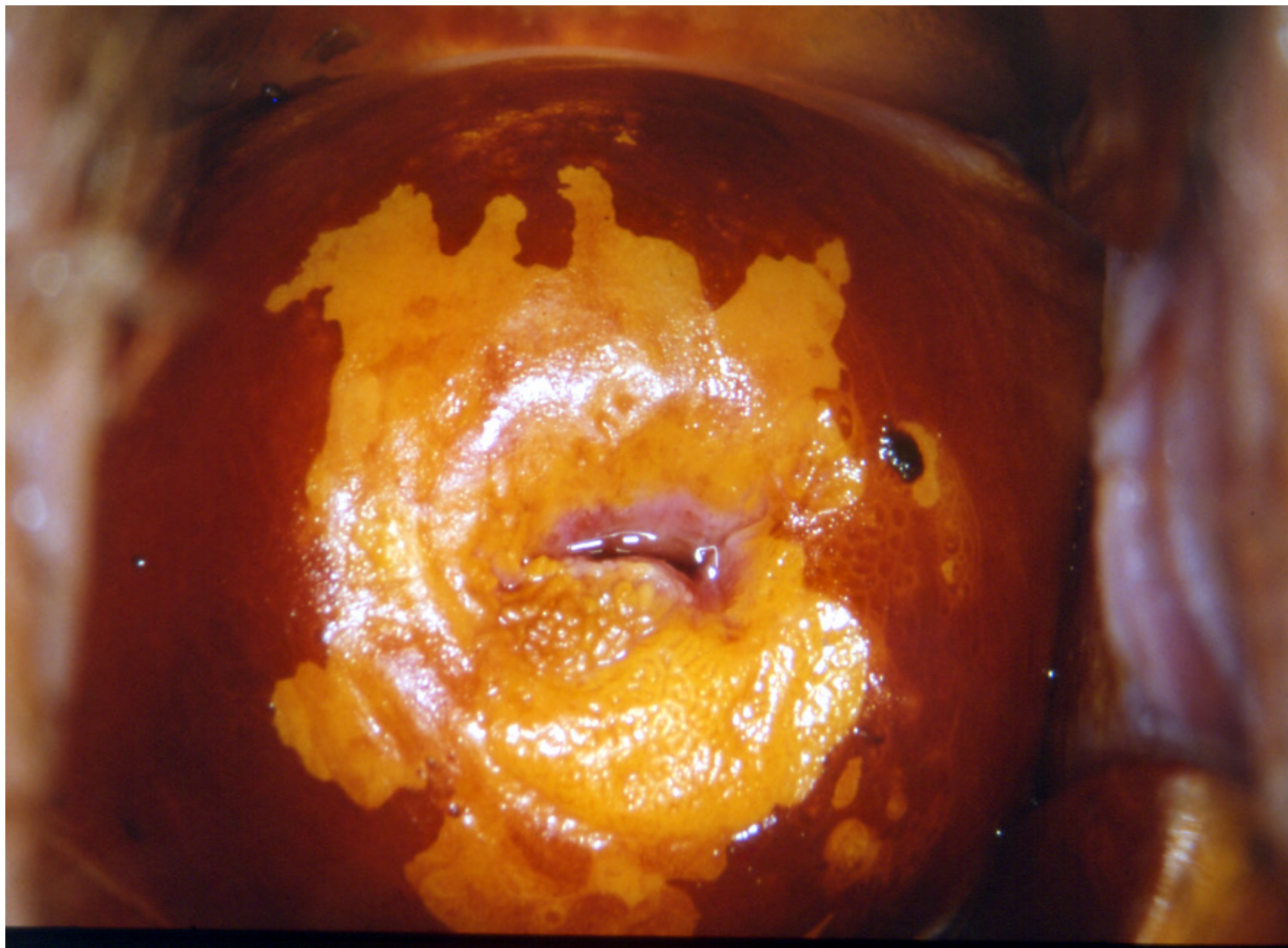
*Gynecol Oncol.* 2010 October ; 119



# Residual or Recurrent Precancerous Lesions After Treatment of Cervical Lesions in Human Immunodeficiency Virus–infected Women: A Systematic Review and Meta-analysis of Treatment Failure

Pierre Debeaudrap,<sup>1</sup> Joelle Sobngwi,<sup>2</sup> Pierre-Marie Tebeu,<sup>3,4,5</sup> and Gary M. Clifford<sup>6</sup>

- Strong evidence for high risk of treatment failure in WLWH (OR 2.7, 95% CI 2.0–3.5)
- Predictor of TF was positive margin status (OR 3.4, 95% CI 1.5–7.7).
- Further data is needed on long-term outcomes after ablative treatment in WLWH



## The use of thermal ablation in diverse cervical cancer “screen-and-treat” service platforms in Zambia

Mulindi Mwanahamuntu<sup>1</sup> | Sharon Kapambwe<sup>2</sup> | Leeya F. Pinder<sup>1,3</sup> | Jane Matambo<sup>4</sup> | Susan Chirwa<sup>4</sup> | Samson Chisele<sup>1</sup> | Partha Basu<sup>5</sup> | Walter Prendiville<sup>5</sup> | Rengaswamy Sankaranarayanan<sup>5</sup> | Groesbeck P. Parham<sup>1,6</sup>

- 2123 women treated with about 16% HIV positive
- Mild cramping most common adverse effect
- Providers overwhelming preference for TA over cryotherapy
- TA was **feasible, safe, and acceptable** in diverse clinical contexts
- Is it effective in the long term?





Contents lists available at ScienceDirect

## Preventive Medicine

journal homepage: [www.elsevier.com/locate/ypmed](http://www.elsevier.com/locate/ypmed)



### Review Article

# Worthy of further consideration: An updated meta-analysis to address the feasibility, acceptability, safety and efficacy of thermal ablation in the treatment of cervical cancer precursor lesions



Thomas C. Randall<sup>a,\*</sup>, Catherine Sauvaget<sup>b</sup>, Richard Muwonge<sup>b</sup>, Edward L. Trimble<sup>c</sup>, Jose Jeronimo<sup>d</sup>

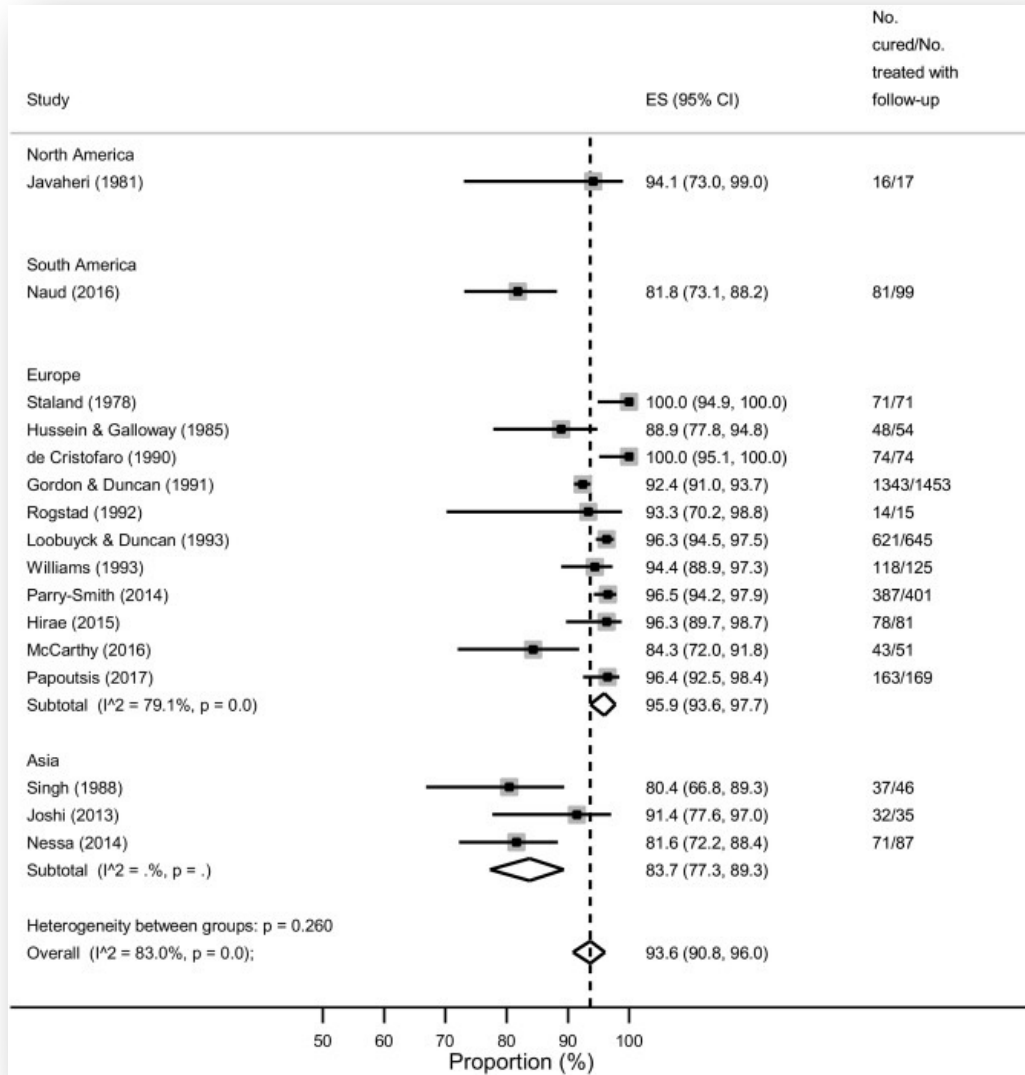
<sup>a</sup> Gynecologic Oncology, The Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

<sup>b</sup> Screening Group, Early Detection and Prevention Section, International Agency for Research on Cancer, Lyon, France

<sup>c</sup> Global HPV and Cervical Cancer Research and Control, National Cancer Institute, Rockville, MD, USA

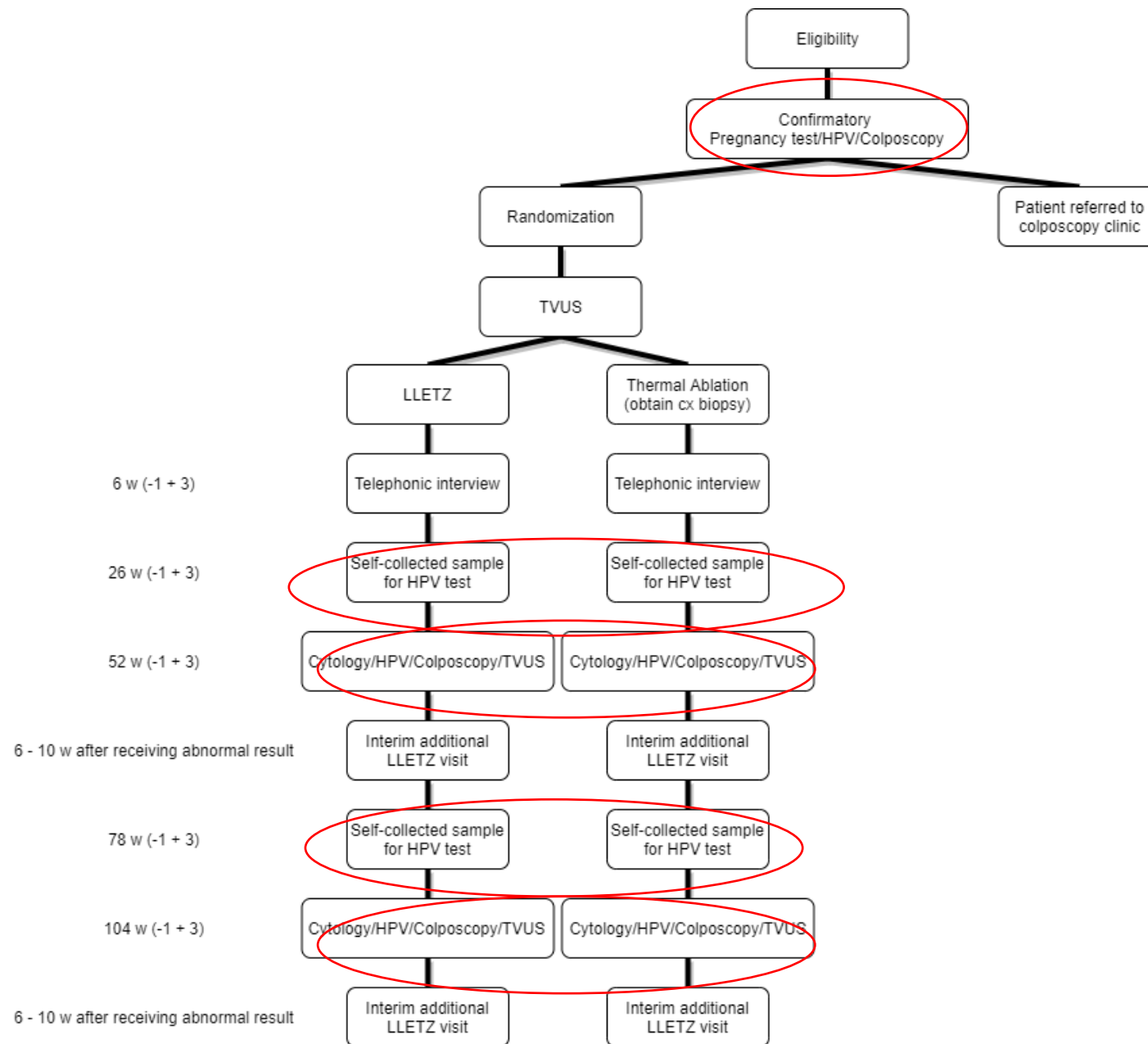
<sup>d</sup> Global Coalition Against Cervical Cancer, Seattle, WA, USA

# Treatment outcomes of TA



- Overall cure rate was 93.8% in 16 studies in women were treated for CIN2 or worse lesions
- Investigators reported a variety of follow up methods to assess cure, including the use of cytology only, cytology with colposcopy and biopsy

Biopsy or **cytology confirmed cure rates** after treatment with thermal ablation among women diagnosed with biopsy confirmed CIN 2+ lesions.



## Thermal Ablation vs LLETZ Excision (TALL)

- 872 evaluable participants, aged 30 – 60y
- Colposcopy Clinic
- Test-of-cure: HPV, cytology, colposcopy with images and cervical anatomy
- 2y follow-up



# Management conclusions: pre-cancer



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## Key targets:

- Adequate ARV for HIV viral suppression and immune maintenance
- Proper assessment of **lesion size** and appropriate (wide) excision: aim to **avoid positive** excision margins
- Ablation therapies TF long term?
- Careful follow-up after treatment
- ?Explore **adjuvants** to standard treatment to stimulate immune response
  - Prophylactic vaccines at time of treatment
  - Therapeutic vaccines?

## Elevated Cancer-Specific Mortality Among HIV-Infected Patients in the United States

*Anna E. Coghill, Meredith S. Shiels, Gita Suneja, and Eric A. Engels*

- Cancer-specific **mortality significantly elevated** in PLWH for many cancers
- The elevation in mortality may be .... as a direct relationship between immunosuppression and tumour progression



# HIV Status and Acute Hematologic Toxicity Among Patients With Cervix Cancer Undergoing Radical Chemoradiation

*Hannah M. Simonds, MBChB, MRCP, FRCR,\* Alfred I. Neugut, MD, PhD,†‡§  
and Judith S. Jacobson, DrPH, MBA†‡*



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- Grade 3/4 toxicity (38.9% vs 26.6%), grade 3/4 leucopenia (30.6% vs 10.2%,  $P = 0.003$ )
- WLWH but were less likely to complete chemotherapy: radiation alone (38.9% vs 24.29%,  $P = 0.01$ )



*International Journal of Gynecological Cancer* • Volume 25, Number 5, June 2015



# HIV Infection and Survival Among Women With Cervical Cancer

*Scott Dryden-Peterson, Memory Bvochora-Nsingo, Gita Suneja, Jason A. Efsthathiou, Surbhi Grover, Sebatu Chiyapo, Doreen Ramogola-Masire, Malebogo Kebabonye-Pusoentsi, Rebecca Clayman, Abigail C. Mapes, Neo Tapela, Aida Asmelash, Heluf Medhin, Akila N. Viswanathan, Anthony H. Russell, Lilie L. Lin, Mukendi K.A. Kayembe, Mompoti Mmalane, Thomas C. Randall, Bruce Chabner, and Shahin Lockman*



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- WLWH significantly **increased risk for death** (hazard ratio, 1.95; 95% CI, 1.20 to 3.17) even in those that received curative treatment
- Effect on survival was greater for **women with a lower CD4 count** ( $P = .036$ )
- In the context of good access to ARV in Botswana, HIV (still) **decreases cervical cancer survival**



*J Clin Oncol 34:3749-3757.*

# Outcomes of cervical cancer among HIV-infected and uninfected women treated at the Brazilian National Institute of Cancer (2001–2013)

Mariana P. Ferreira<sup>1,\*</sup>, Anna E. Coghill<sup>2,\*</sup>, Claudia B. Chaves<sup>3,4</sup>, Anke Bergmann<sup>4,5</sup>, Luiz C. Thuler<sup>5</sup>, Esmeralda A. Soares<sup>1</sup>, Ruth M. Pfeiffer<sup>2</sup>, Eric A. Engels<sup>2,†</sup>, and Marcelo A. Soares<sup>1,†</sup>



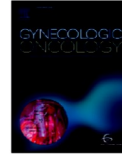
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- HIV not associated with mortality during initial follow-up but was associated more than 1–2 years after diagnosis (overall mortality: HR 2.02, (CI 1.27–3.22); cancer-specific mortality: 4.35, (CI 1.86–10.2)
- WLWH had similar response rates to initial cancer therapy (HR 0.98, 95%CI 0.58–1.66).
- Among women who had a complete response, HIV associated with high risk of subsequent recurrence (HR 3.60, 95%CI 1.86–6.98, adjusted for clinical stage)



*AIDS*. 2017 February 20; 31(4): 523–531.



Five-year overall survival following chemoradiation among HIV-positive and HIV-negative patients with locally advanced cervical carcinoma in a South African cohort



Hannah M. Simonds<sup>a,\*</sup>, Matthys H. Botha<sup>b</sup>, Alfred I. Neugut<sup>c,d,e</sup>,  
Frederick H. Van Der Merwe<sup>b</sup>, Judith S. Jacobson<sup>c,d</sup>

- Prospective cohort of all locally advanced cervix carcinoma patients referred for RT
- 492 patients commenced treatment with radical intent, including 71 WLWH (14.4%)
- OS was 49.5% vs 35.9% at 5 years ( $p=0.002$ )
- WLWH had poorer survival, however **nearly 40% survived 5 years**, justifying provision of the **best standard of care to WLWH** with cervical carcinoma



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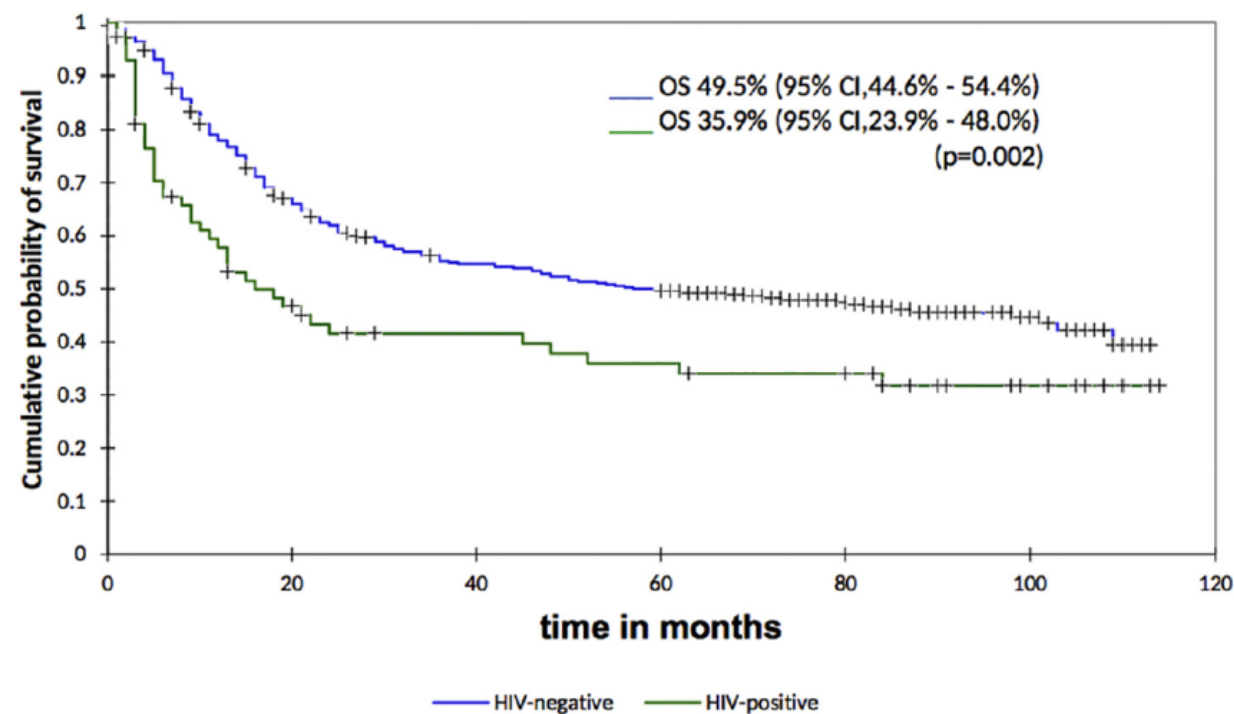


Fig. 1. 5-Year overall survival by HIV status.

# Conclusions

- Treatment of warts, pre-cancer and cancer **more challenging** in PLWH
- Evaluate TF in **thermal ablation** in proper, long term follow-up
- **Toxicity of onco-therapy increased** in PLWH
- Invasive cancers do poorer but still **warrants full treatment** with best standard of care
- Long term cure needs a well functioning immune system



Prevention through vaccination!!!

Thank you

