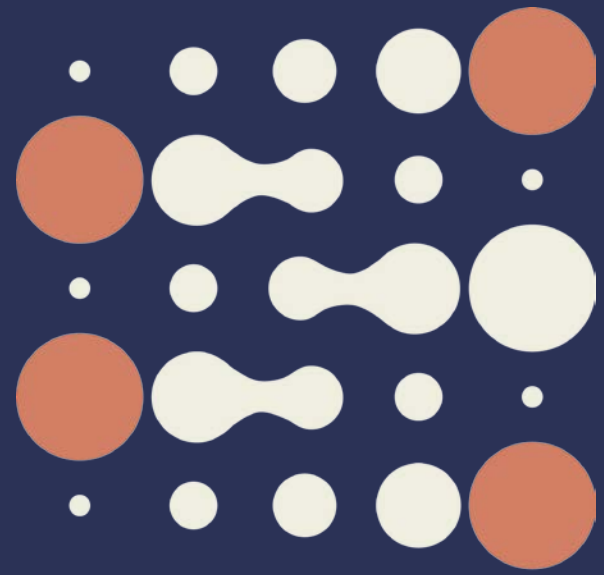
Final outcomes of the RCT comparing thermal ablation, cryotherapy and LLETZ in a screen and treat setting in Zambia stratified by HIV status

Richard Muwonge[1], Mulindi H Mwanahamuntu[2], Namakau Nyambe[3], Leeya F Pinder[4,5], Eric Lucas[1], Emmanuel Muzumbwe[3], Rengaswamy Sankaranarayanan[6], Walter Prendiville[1], Groesbeck P Parham[5,7], Partha Basu[1]

[1] Early Detection, Prevention & Infection Branch, International Agency for Research on Cancer, World Health Organization, Lyon, France
[2] Department of Obstetrics and Gynecology, Women and Newborn Hospital, University of Zambia, Lusaka, Zambia
[3] UNC Global Project–Zambia, Lusaka, Zambia
[4] Department of Obstetrics and Gynecology, University of Washington, Seattle, WA, USA
[5] Department of Obstetrics and Gynecology, University of Zambia, Lusaka, Zambia
[6] Karkinos Healthcare, Kerala Operations, Ernakulam, India
[7] Department of Obstetrics and Gynecology, University of North Carolina, Chapel Hill, NC, USA

Muwonger@iarc.who.int
(Presenter)

International Agency for Research on Cancer
World Health Organization



Introduction/Background/Motivation

- **Even with highly efficacious HPV vaccines, screening will still play a big part in the cervical cancer elimination initiative**
- **Challenges of cervical cancer control in most LMICs**
  - **High burden of both CIN and high-risk HPV infections**
  - **High prevalence of HIV, especially in sub-Saharan Africa**
  - **Poorly developed health systems, low health care budgets, and competing priorities**
  - **Low HPV vaccine uptake, low screening participation rates and high non-compliance rates to further investigation and/or treatment**
- **Screen and immediate treatment (ablative or excision) of women without visible invasive cancers**
  - Cure CIN, prevent future HPV infections and CIN/cancer
- **However, is treatment effectiveness similar among HIV-infected and HIV-uninfected women**
  - **If not, what factors explain the differences?**

Main objectives

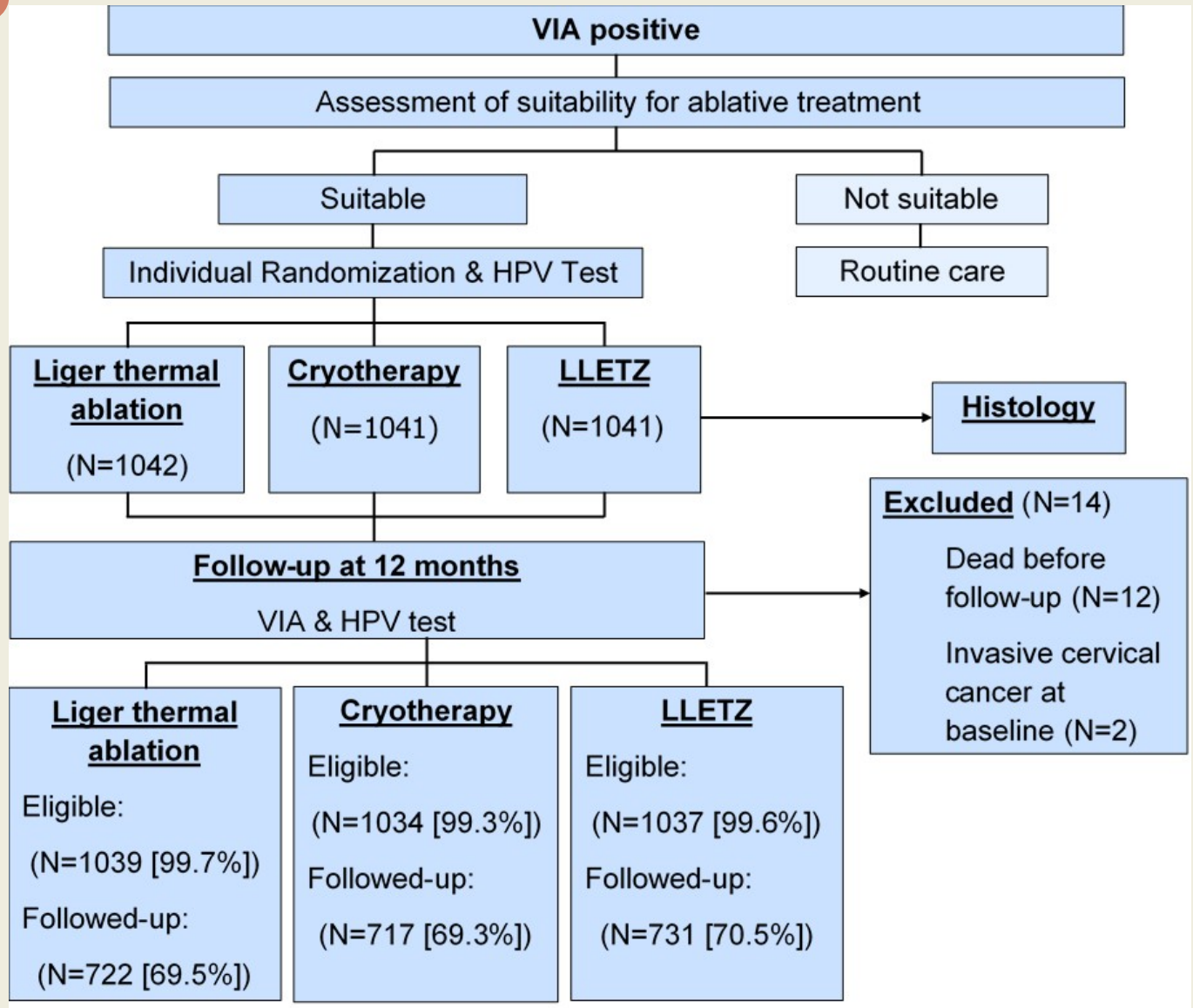
- Compare efficacy of treating cervical lesions between HIV-infected and HIV-uninfected women.
- Assess efficacy of the new handheld, battery operated thermal ablator compared to that of cryotherapy in treating women with cervical lesions, stratified by HIV status

Strategy

- Used data from an RCT comparing treatment success between thermal ablation, cryotherapy and LLETZ in a screen and treat setting in Lusaka, Zambia

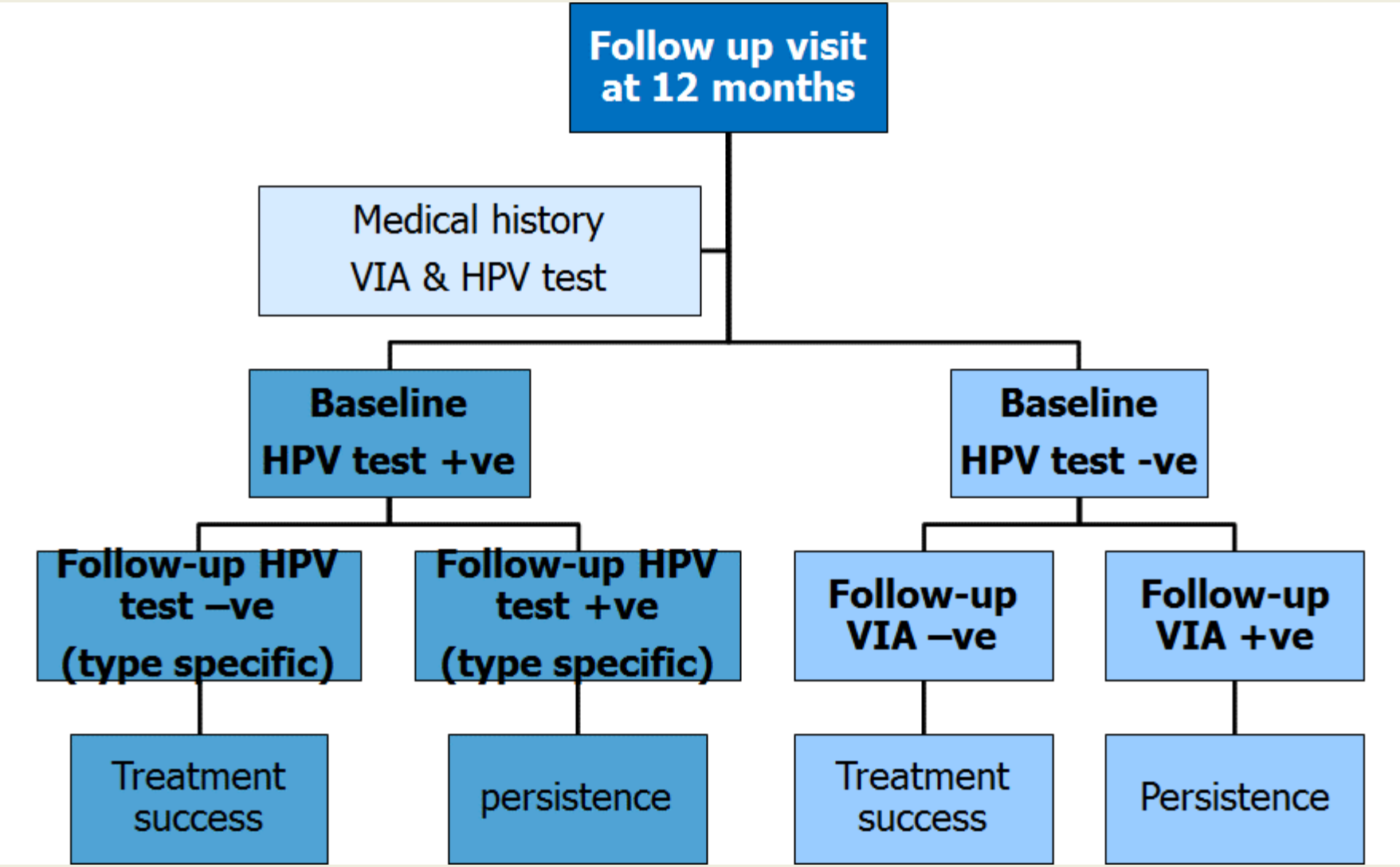
IARC technically supported the development of a new handheld, battery operated thermal ablator

Design - RCT to report safety, acceptability and efficacy of new thermal ablator used in a VIA- Screen & treat program, Lusaka Zambia



- **Baseline samples were taken for HPV testing**
- **Treatment was offered according to randomization arm**
- **Assessment of side-effects and satisfaction immediate post-treatment and 2 weeks later**
- **Follow-up 12 months after treatment**
- **Final findings presented (stratified by baseline HIV status)**

Definition of treatment success at follow-up



- Note: All women recruited in this trial are VIA positive at baseline

Results

- At baseline, 58.6% of the participants were HIV positive (almost all on ARTs)
- Baseline HPV prevalence was higher in HIV infected women

	Participants with follow-up n	Participants with treatment success at follow-up					
		Overall n (%)		Treatment received			
				TA %	Cryo %	LLETZ %	Chi² p-value
All participants	2170	1566	(72.2)	74.0	71.1	71.4	0.406
Baseline HIV status							
Negative	913	783	(85.8)	86.9	83.9	86.5	0.368
Positive	1222	759	(62.1)	62.7	60.9	62.7	
Baseline HIV and HPV status combinations							
HIV negative, HPV negative	629	580	(92.2)	93.8	89.9	92.9	0.732
HIV negative, HPV positive	260	182	(70.0)	71.6	68.5	69.7	0.751
HIV positive, HPV negative	459	417	(90.8)	88.5	90.2	93.8	0.240
HIV positive, HPV positive	732	315	(43.0)	40.8	44.3	43.6	0.223

TA: thermal ablation; Cryo: Cryotherapy; LLETZ: Large loop excision of the transformation zone ; HIV: human immunodeficiency virus; HPV: human papilloma virus; * Treatment success was defined as either a) HPV type-specific clearance at 12 months among women positive for the same HPV type at baseline or b) negative VIA test at follow up, if the baseline HPV test was negative

- TS for the new TA modality was similar to that of cryotherapy and LLETZ, regardless of HIV status
- TS significantly lower among HIV-infected women compared to HIV-negatives (62.1% vs. 85.8%, p-value <0.001)
- TS among women living with HIV was further reduced by co-infection with HPV (43.0%)
- TA is well accepted by providers and participants
- TA is cost-effective, compared to cryotherapy and LLETZ

Discussion and Conclusions

- These final findings will strengthen further the WHO recommendation for use of TA especially in the screen and treat settings of the LMICs
- Unlike cryotherapy that requires refrigerant gas to function, this TA machine is battery driven
- Less treatment time required with TA (30–45 seconds) compared to cryotherapy (11 minutes)
- Investigations are underway to determine the underlying causes of these findings
  - Investigate the association between persistence of HPV and cervical neoplasia and vaginal metabolite levels, vaginal microbiota, HIV viral load, oncogenic HPV types, ARV type and duration among women living with HIV
  - Compare HIV shedding rates at different post-treatment measurement points in the thermal ablation and LLETZ arms to those in the cryosurgery arm among women living with HIV
  - Correlate specific surface morphologic appearances of abnormal acetowhite lesions of the cervix with underlying pathology and to determine to what extent the morphologic appearances of abnormal aceto-white lesions of the cervix accurately predict underlying high-grade precancer in HIV positive and HIV negative women

Related publications/References/Literature cited

Pinder LF, Parham GP, **Basu P**, **Muwonge R**, **Lucas E**, Nyambe N, **Sauvaget C**, Mwanahamuntu MH, **Sankaranarayanan R**, Prendiville W. Thermal ablation versus cryotherapy or loop excision to treat women positive for cervical precancer on visual inspection with acetic acid test: pilot phase of a randomised controlled trial. Lancet Oncol 2020; 21(1): 175-84

Acknowledgements

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Key take-home messages

- **Treatment success using the new handheld battery driven thermal ablator was similar to that of cryotherapy and LLETZ**
- **However, treatment success was significantly lower among HIV-infected women compared to HIV-negatives, regardless of the treatment modality used**
- **With the current WHO initiative for Cervical Cancer Elimination, these findings highlight the challenges in eliminating the disease in women living with HIV.**