

# HPV research in Ghana

## Update on ACCESSING

**Adequate Capacity building, Education and Cervical cancer Screening by new Scientific Instruments in Ghana**

**Andreas M. Kaufmann, Amrei Krings, Kofi Effah**

**Gynäkologische Tumor Immunologie**

**Clinic for Gynecology**

**Charité Campus Benjamin Franklin, Campus Mitte**

*andreas.kaufmann@charite.de*

# **ACCESSING: Adequate Capacity building, Education and Cervical cancer Screening by new Scientific Instruments in Ghana**

## **Vision:**

- **Make cervical cancer screening available for women in Ghana.**

## **Mission:**

- **Build a network, capacity and infrastructure for sustainable HPV testing in the North Tongu District => Ghana.**

## **Aim:**

- **Demonstrate the feasibility of combined usage of self-sampling at the community level and low-cost, low-tech HPV testing in decentralized health structures.**
- **Establish first representative epidemiological data on HPV prevalence in Ghana.**

# ACCESSING\*: Screening by self-sampling and lower cost HPV and Arbor Vita oncoprotein E6 cervical test for detection of dysplasia in rural regions and high risk women



# From Research to Application. Using adequate modern technology?



# DIFFICULTY IN ACCESSING HEALTH CARE (both ways)



# Catholic Hospital Battor / Ghana

CHB/Charité ESTHER clinical partnership



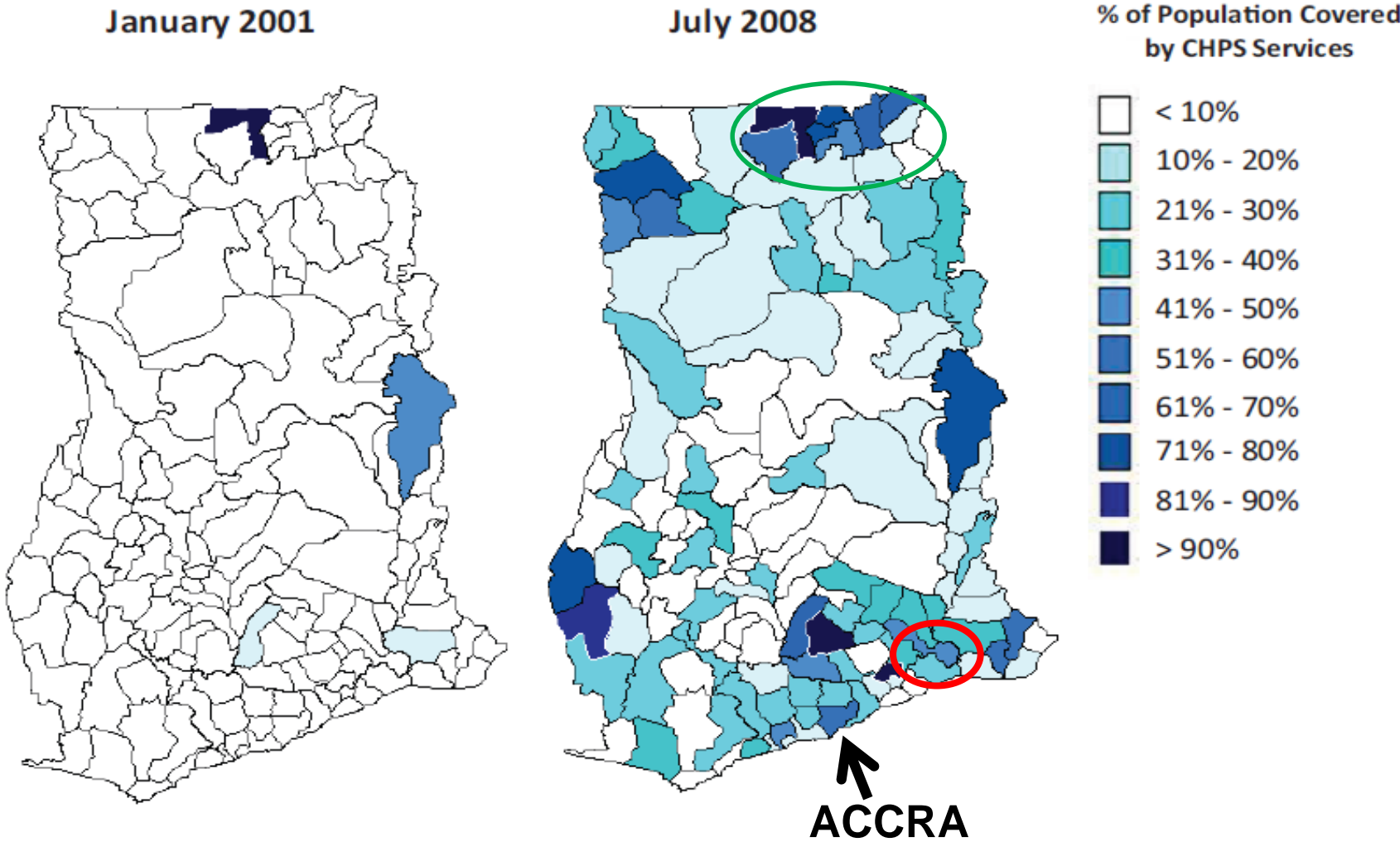


# Ghana, North Tongu District Adidome/Battor



**Dr. Wolfgang Siebert (GRVD),  
Sr Dr. Edgitha Gorges (retired),  
Dr. Kofi Effah (PI; Battor)  
(v.l.)**

# Coverage by Community Health Planning and Services (CHPS) and location (red circle) of the feasibility study center, Battor, North Tongu District, Ghana.





# Building capacity and infrastructure in Ghana

## CHPS System and Community Health Worker



# Initial Project (ESTHER & GIZ funded clinical partnership)

This sampling device offers women, professionals and health authorities the opportunity to increase women's access to user-friendly and effective screening.



*Feasibility:  
Combination of self-  
sampling in villages*

*with low-tech HPV  
detection Kit allows*

*screening of women  
in remote areas*

# Gender

## Cervical cancer screening begins at Battor Catholic Hospital

By Zainabu Issah, BATTOR

**M**ORE than 2,000 women at Battor, a community in the North Tongu District of the Volta Region, are to undergo a cervical cancer screening at the

Battor Catholic Hospital, a cervical cancer screening centre.

The screening is under a project being funded by GIZ in collaboration with the German Rotary Volunteer Doctors (GRVD).

The screening will be done within a two-year period at the hospital, and some community health officers will visit women in the community who may not be able to go to the hospital to participate in the exercise.

Giving an overview of the North Tongu Cervical Cancer Project at a workshop at Battor to discuss and start the

project, Dr Kofi Effah, a gynaecologist, said the screening would involve a self-sampling method where the women would have the chance to conduct self-examination using a Delphi screener, which, according to him, "is easy to use, culturally acceptable, comfortable to sample, and independent of a gynaecologist visit".

### About Delphi screener

The Delphi screener is a new self-sampling device that is designed to overcome the challenge of limited resources and lack of access to health facilities and qualified staff to undertake sample-taking and analysis.

During the screening, the Delphi screener will be used in combination with the Arbor Vita E6 onco-protein test, a new low-cost on-site test developed to detect E6 onco-proteins of Human Papilloma Virus (HPV) 16 and HPV 18, which together cause most cervical cancers.

The test is designed to overcome the major limitation to implementing cervical cancer screening in countries with limited

resources due to lack of access to infrastructure for more sophisticated tests.

Also, health workers with little training can screen women with the Arbor Vita E6 test, and results will be obtained within three hours.

### Problems of cervical cancer screening in Ghana.

Dr Effah said one of the challenges to cervical cancer screening in the country was the lack of organised national cervical screening programme that would get every woman involved in the exercise.

"What we have is opportunistic screening and this is not good as we will not be able to address the situation effectively," he said.

Also, he said, there was difficulty in getting access to those who needed to be screened to undergo such exercise and possibly recall them when they were diagnosed to be positive.

Dr Effah said it was also difficult for the women at risk of cervical cancer to reach the few centres and most patients came to the hospitals

with advanced cancers.

### The way forward

To improve access to cervical cancer treatment in the country, Dr Effah said there was the need for treatment of the disease to be captured under the National Health Insurance Scheme (NHIS) and called for the extension of the screening exercise to other parts of the country.

### Health Director's remarks

The Volta Regional Director of Health Services, Dr Joseph Teye Nuerty, called for a concerted effort by all health professionals in the region to intensify their health education at the out-patient units and other centres to create awareness about cervical cancer.

He also appealed to all health workers in the North Tongu and South Tongu districts to take advantage of the services at the Battor Catholic Hospital to encourage others to go through the test and also show a high level of professionalism to their clients.

### Fact Sheet

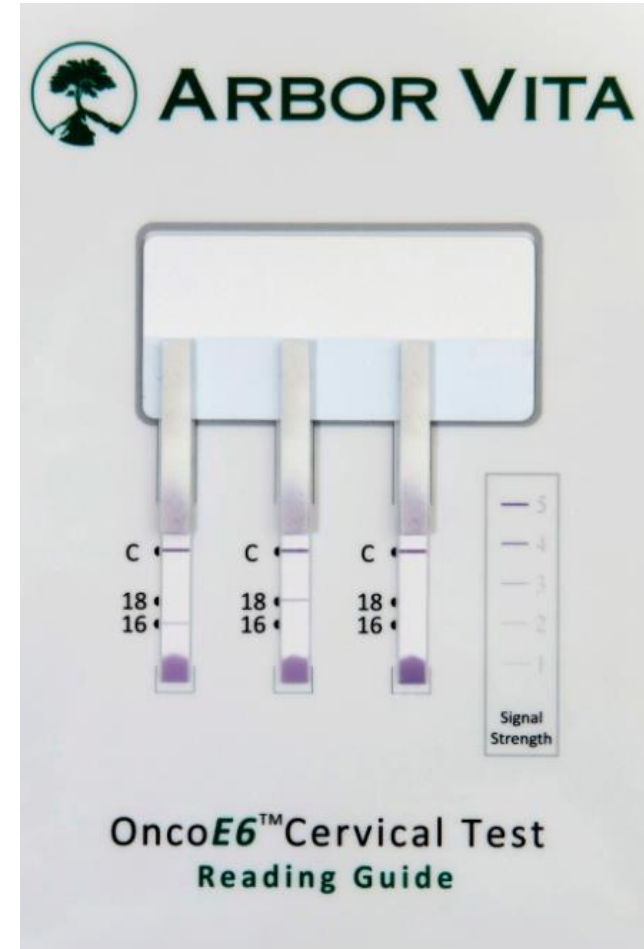
Globally, there are **493,000** new cases of cervical cancer each year.

**274,000** women die of the disease annually with about **85 per cent** occurring in developing countries.

# Oncoprotein E6 Cervical Test (Biomarker for disease)

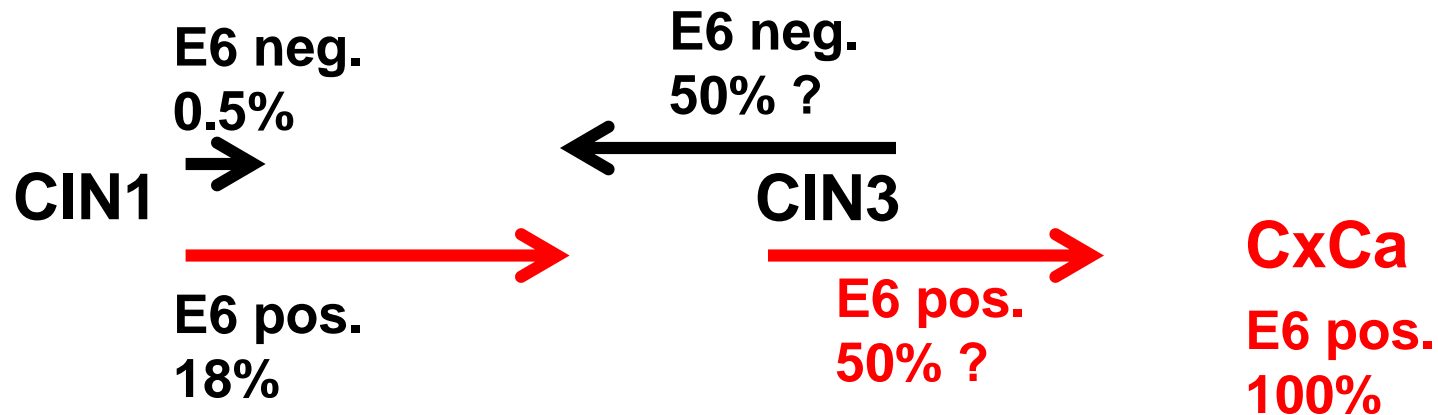
- Lateral flow Immunoassay Test
- Detection of HPV16 and 18 (typing)
- 9 samples in <3 h (hands on time appx. 2 h)
  
- **Sensitivity** for CIN3+ 53.5%  
for CervixCa 91.7%
- **Specificity** for CIN3+ 98.9%
- **PPV** for CIN3+ 40.8%
- **NPV** for CIN3+ 99.37%

- ⇒ High specificity for disease
- ⇒ Simple, robust technology
- ⇒ Low resource settings



# Biomarker for high grade and progressive disease

AVE6 positivity



**Need for a conclusive and verified biomarker for progressing disease!**

# *Simplicity of Oncoprotein E6 Cervical Test (Workstation Setup)*



# HPV genotyping Testing „HPV Easy“ (AID/GenID)

**Multiplex PCR**  
**E1 gene**  
**18 HR-HPV**  
**11 LR-HPV**  
**GAPDH**



•	••••	••••	••••
Ko	spez	GapDH	HPV16
••••	••••	••••	••••
HPV18	HPV26	HPV31	HPV33
••••	••••	••••	••••
HPV35	HPV39	HPV45	HPV51
••••	••••	••••	••••
HPV52	HPV53	HPV56	HPV58
••••	••••	••••	••••
HPV59	HPV66	HPV67	HPV68
••••	••••	••••	••••
HPV69	HPV70	HPV73	HPV82
••••	••••	••••	••••
HPV85	HPV97	HPV06	HPV11
••••	••••	••••	••••
HPV40	HPV42	HPV44	HPV54



**Read out by ELISA type staining**

**ELISpot reader**

**96 samples, high throughput**

**Automatic objective reading, evaluation and reporting in 10 min**

**Simple handling**

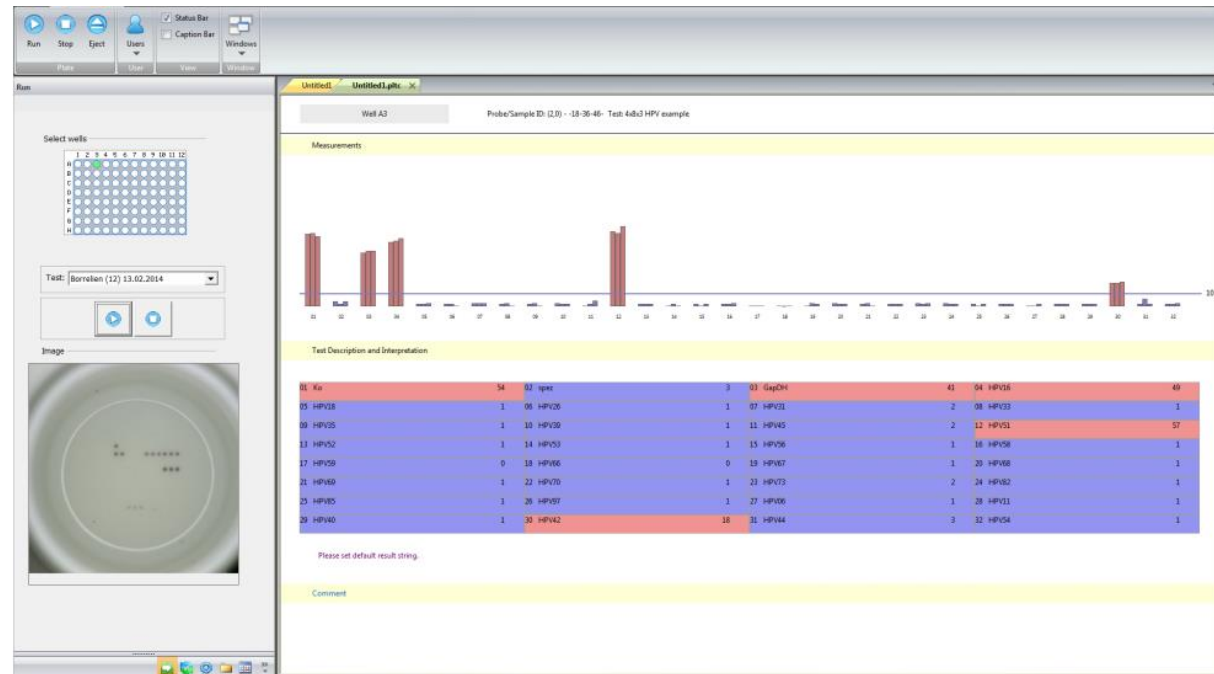
**Simple PCR/reader equipment**

# EliSpot Reader and AiDot analysis software used for HPV Easy readout



Available in many african countries for CD4 characterization in HIV+

10 min readout for 96 well plate  
Evaluation of HPV types  
Related to DNA content  
GAPDH internal control





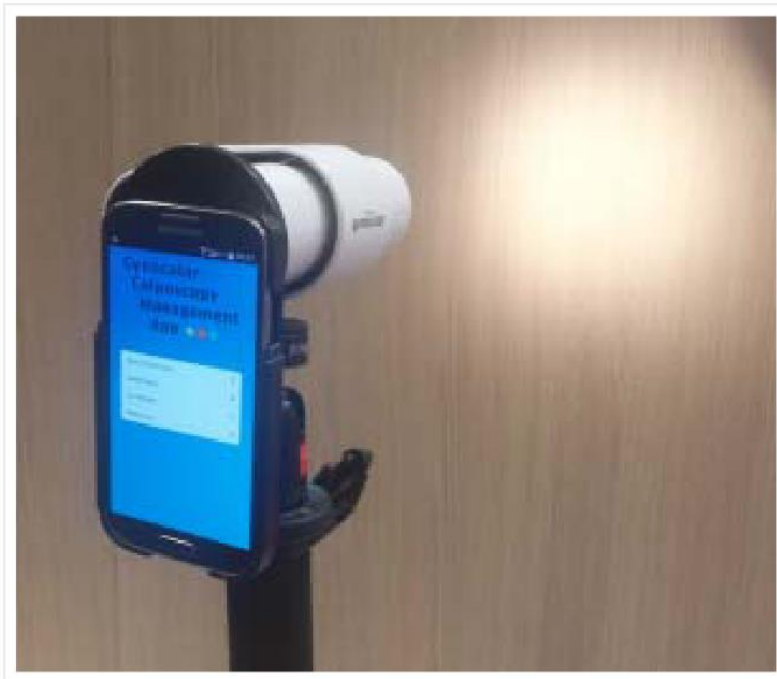
# Gynocular

Portable colposcope

Green/red light  
stand

Smart phone adaptable (cloud)

FDA/CE approved



# Nurse trained to do colposcopy (physician back-up)



# Pilot study in Battor, Methodology

- **250 high-risk women** (100 HIV+, 150 High-Risk HPV detection or lesion) were recruited at Catholic Hospital Battor, Volta Region, Ghana.
- **Vaginal lavage** (from Delphi Screener), **swab** and **cytobrush** samples were collected.
- Vaginal lavage and swab samples **tested with OncoE6 cervical test**.
- Full **HPV genotyping** was done on lavage and brush samples by GP5+/6+ PCR followed by Luminex-MPG readout at the Charité Universitätsmedizin, Berlin.
- **OncoE6 cervical test** positive and/or high-risk HPV+ underwent **colposcopy/biopsy, treatment where indicated**.
- **Pap smears** taken before colposcopy.

# Results

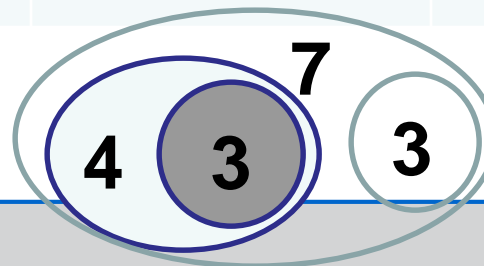
- **91% (228/250) self-sampled.**
- **85% found this easy/very easy and comfortable/very comfortable.**
- **72% of the HIV+ and 30% of formerly HR-HPV+ women were high-risk HPV positive, respectively.**
- **14% of HIV+ patients were CIN2+, compared to 3% of the HR patients.**
- **Of the 9 CIN3+, 4 (44%) tested AVE6 positive from the lavage sample and 3 (33%) from the swab sample.**
- **Of the 19 CIN2+, 7 (37%) tested AVE6 positive from the lavage sample and 4 (21%) from the swab sample.**

# HPV Prevalence

	HIV+ (n=100)	HR group (n=150)
CIN2+	14% (14)	3% (5)
HPV+	80% (80)	38% (57)
hrHPV	72% (72)	30% (45)
Multi hrHPV	<b>47% (47)</b>	17% (25)
Top 10 HPV types	16 (34%)	52 (12%)
	52 (17%)	16 (11%)
	31 (14%)	59 (10%)
	35, 39, 82 (10%)	51 (7%)
	18 (9%)	39 (6%)
	53, 70 (8%)	66 (5%)
	45,73 (7%)	45, 53 (4%)
		35, 53, 58, 70 (3%)

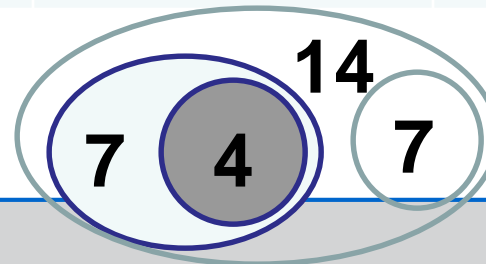
# Self-sampled Lavage detects more 16/18+ CIN3+ by OncoE6™ Cervical Test

	All CIN3+ (n = 9)	HPV 16 or 18 CIN3+ (n = 7)	HPV 16/18 negative CIN3+ (n = 2)
Swab AVE6 Positive	3 (33%)	3 (43%)	0 (0%)
Lavage AVE6 Positive	4 (44%)	4 (57%)	0 (0%)



# Self-sampled Lavage detects more 16/18+ CIN2+ by AVE6

	All CIN 2+ (n = 19)	HPV 16 or 18 CIN 2+ (n = 14)	HPV 16/18 negative CIN 2+ (n = 5)
Swab AVE6 Positive	4 (21%)	4 (29%)	0 (0%)
Lavage AVE6 Positive	7 (37%)	7 (50%)	0 (0%)



# Detection of invasive cancer only by AVE6 oncoprotein test, while cytology failed

No	Lavage AVE6	Swab AVE6	Genotyping Lavage	Genotyping Brush	Cytology	Colposcopy	Histopathology
P123	Pos (16)	Pos (16)	16,51, 52,53, 58	16,51, 52,70	<b>NILM</b>	In/Inv	<b>Cancer IA2</b>

**=> Cone Biopsy, simple Hysterectomy, LN free**



# Conclusion pilot (Delphi Screener)

- **Self-sampling well accepted and not inferior** in detecting dysplasia than swab sampling.
- **Self-sampling in conjunction with OncoE6 cervical test** can be used in communities to detect and triage women with highest risk for severe dysplasia or cervical cancer.
- This allows **secondary cancer prevention** ‘on the doorstep’ **in remote locations**.

# Pilot 1 (longitudinal)

## PERSISTENCE OF HIGH RISK HPV INFECTIONS AMONG WOMEN IN THE NORTH TONGU DISTRICT OF GHANA

Priscilla Dunyo

Eurogin 2015, Sevilla, Spain



# Methods

- 500 women had been screened and genotyped for HR-HPV in 2010/2011 using nested PCR for E6 (Sotlar et al, 2004).
- 104 patients who were HR-HPV+ but remained untreated were followed up in 2014 and retested for HPV.
  - HPV genotyping was on cytobrush samples by GP5+/6+ PCR followed by Luminex-MPG readout.
  - HPV+ women were recalled for colposcopy and treatment.

# HR-HPV Clearance and Persistence (1)

- 93.3% (97/104) had their original HR-HPV types cleared in ~4 yrs
- 72% (75/104) had no HR-HPV infection after ~4 yrs
- 26% (28/104) were infected with new HR-HPV types after ~4 yrs
- 6.7% (7/104) had 1 or 2 of their original HR-HPV types persisting

- ⇒ **Problem for HPV testing and**
- ⇒ **importance of genotyping HPV test**
- ⇒ **Avoidance of overtreatment!**

## HR-HPV Clearance and Persistence (2)

- Persistent HR-HPV types were 16, 35, 39, 51, 52, 68.
  - Type 52 persisted most frequently (3 patients).
- HPV 16 persistent patient developed microinvasive cervical cancer (case 123). Cytological findings were normal in 2014 but was diagnosed after positive Arbor Vita OncoE6 test result for HPV 16 and genotyping.
- Trend could be seen that rate of new HR-HPV infections increased with age.

# Main study: Screening 2000 in North Tongu

Women representatively selected from census from villages  
Age 18-64, non-pregnant (anamnestic)

- Feasibility (logistics)
- Acceptance; Risk factors questionnaire
- HPV prevalence of individual types
- Disease burden
- Therapy referral and performance rate

Feasibility HPV genotyping by HPV Easy (AID/GenID)

July-October 2015



**Thank you !**

**Rwanda vaccinated 90% eligible girls against HPV!**

# Acknowledgements

## ACCESSING team

Effah, K<sup>1</sup>, Nyarko, K<sup>2</sup>, Krings, A<sup>3</sup>, Gorges, E<sup>1</sup>, Baiden, F<sup>4</sup>, Amuah, J<sup>5</sup>, Borlabi, S<sup>1</sup>,  
Dunyo P<sup>1</sup>, Adaletey R<sup>1</sup>, Schweizer, J<sup>6</sup>, Voll, M<sup>7</sup>, Siebert, W<sup>8</sup>, Kaufmann, AM<sup>3</sup>

- 1) Catholic Hospital Battor, Volta Region, Ghana
- 2) Non Communicable Diseases Control Program, Ghana Health Service, Accra, Ghana.
- 3) Clinic for Gynecology, Charité Universitätsmedizin Berlin, Germany
- 4) Centre for Health Research and Implementation Support, Ghana
- 5) Department of Epidemiology and Community Medicine, University of Ottawa, Canada
- 6) Arbor Vita Corporation, Fremont, CA, U.S.A.
- 7) Delphi Bioscience B.V., Scherpenzeel, The Netherlands
- 8) German Rotary Volunteer Doctors e.V., Dortmund, Germany
- 9) \*ACCESSING (Adequate Cervical cancer Capacity building, Education and Screening by new Scientific INstruments in Ghana): GIZ/ESTHER funded trial



# outputs

- **Screening algorithm**
- **Therapy algorithm**
- **HPV genotype prevalence**
- **HPV genotype persistence (after therapy)**
- **Acceptability**
- **Adequacy of devices**
- **Cost modelling**

## **Capacity Building**

- **Nurses in screening**
- **Physicians in therapy**
- **Lab personnel in techniques, infrastructure**
- **MD/PhD theses**

# Future perspectives

Establish screening in North Tongu district for all women  
(now 10% screened in ACCESSING)

Introduce in other CHPS districts (Upper East; Dr. Awoonor!)

Ghana MoH / Government to make it national policy

**NEED: more Colposcopy/Treatment capacity !??!**  
(Gynoscope, Colposcopists training, treatment units)

PPP: supported by GIZ

Sampler / test producer  
MDS Lancet diagnostic lab



50%

Support by GIZ / BMZ with 50% addl. funding