



# HPV testing in Nkhoma CCSP in Malawi

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Central Malawi



Project is based on funding of £399,000 from the Scottish Government International Fund for Development in Malawi, 2013-2016 to **reduce the burden and mortality from cervical cancer in Nkhoma Hospital and 10 associated health centres**





# Extending Scottish Expertise to Malawi:



## Aims:

- **Sensitisation** of healthcare professionals and local population to value of cervical screening
- **Upskilling** VIA
- Providing **treatment by cold coagulation** through Scottish professionals spending time in Nkhoma
  - **Nkhoma Hospital CCSP is a 'see and treat' programme**
- Ensuring **good follow-up** of all non-negative VIA patients
- Increasing **awareness of data collection and analysis** to establish a robust evidence base for appropriate cervical screening
- **Providing HPV testing** for potential triage to VIA
- Developing a **curriculum module based on cervical cancer screening and prevention** for nurses and midwives in conjunction with VSO and Colleges of Nursing



# Creating the environment for a successful 'see and treat' programme of cervical screening - 1

## Stage 1: Create clinic



## Stage 2: Raise awareness amongst staff, communities and patients



Explaining screening to women attending Family



Sensitising in ART clinic in hospital



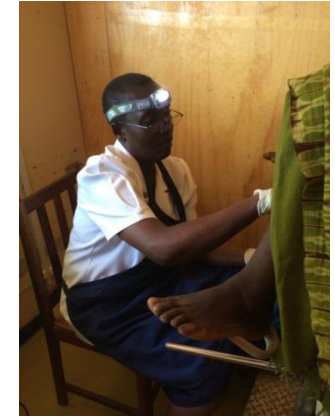
Sensitising in Village  
WAKA



Nkhoma VIA clinic  
Pre-screening talk

# Creating the environment for a successful 'see and treat' programme of cervical screening -2

## Stage 3: VIA & Treatment training



## Stage 4: Outreach to community Health centres



First provide consistent starter pack to every outreach clinic

# Increase in VIA uptake in Nkhoma Hospital

**2012-13**

	Neg	Pos	Sus	Invalid/Blank	Total
2012	365	27	32	7	431
2013 Jan- June	166	14	7	0	187
<b>TOTALS FOR 18 MONTHS</b>	531	41	39	7	<b>618</b>

**2013-14**

Year	Total attendance (Nkhoma)	First attendance	VIA +ve	Cold coagulation given
2013 (Q4)	752	639	55 (8.6%)	39 (70.9%)
2014 (whole year)	4377	3698	229 (6.2%)	197 (86.0%)

# A complete care package for cervical disease prevention

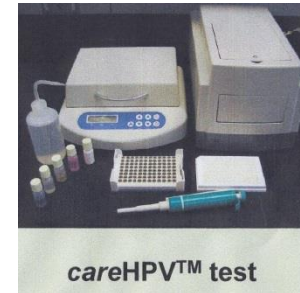
- Screening by VIA and cold coagulation treatment of early lesions
- Follow-up clinics at 3-6m and 12m post treatment
- Out-patient biopsy for 'suspicion of cancer' only, with high risk clinic on first Monday of each month
- Increased surgical skills - radical hysterectomy
- Specific palliative care clinic in VIA setting
- HPV testing.... ..



# HPV as a potential screening test

- **Options**

- Test designed for areas with no electricity or running water eg *careHPV*



**Cartridge-contained molecular test with partial genotyping eg Cepheid Xpert HPV**



- High-throughput automated platform with partial genotyping eg Abbott rtHPV, Roche cobas HPV or Hologic (GenProbe) APTIMA

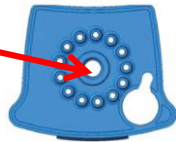




# Cepheid Xpert HPV



1 ml



Liquid  
Cervical  
sample



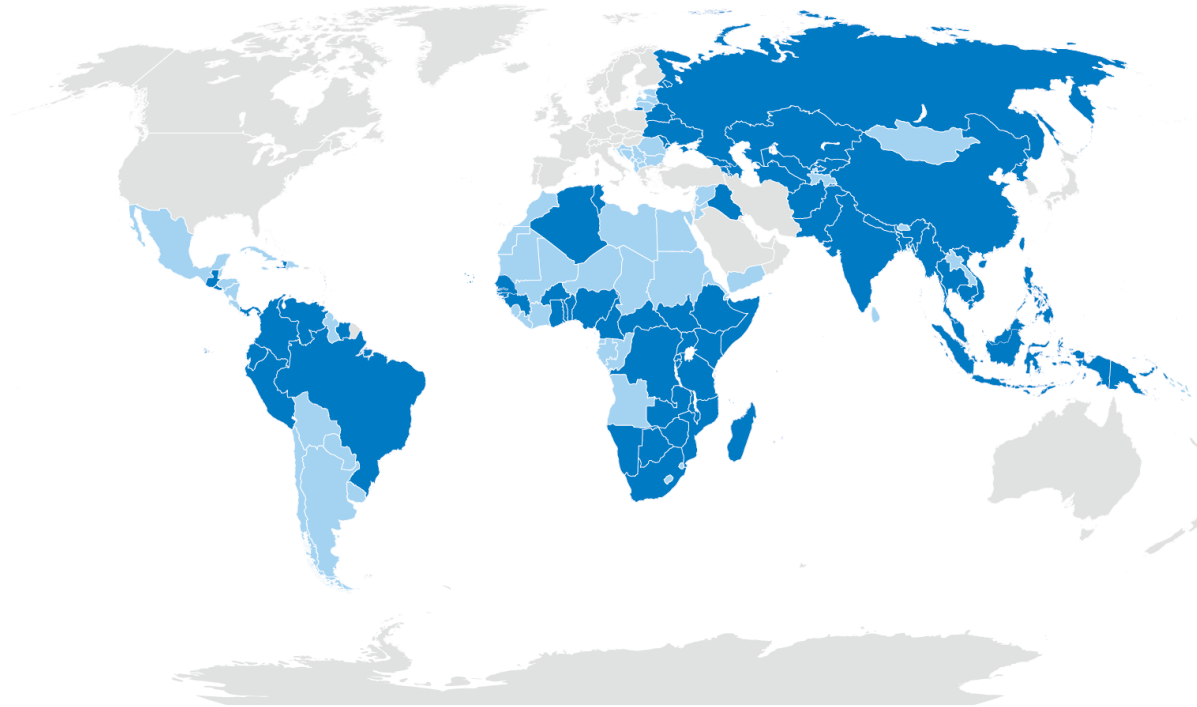
Results in ~60mins



GeneXpert® IV

- Qualitative test for detection of E6/E7 region of HR-HPV
- Xpert HPV specifically identifies **HPV16** and **HPV 18/45** in two separate detection channels
- and reports **11 other high risk types** (31, 33, 35, 51, 52) + (51, 59) + (39, 56, 66, 68) in a pooled result [31+; 51/59; 39+]
- Uses cervical cells collected in PreservCyt®
- <2 hrs TRT between sample taken and results back to clinic

# Xpert instruments are widely used, especially for TB detection & identification



20 countries with more than 30 GXs installed (represent 81% of the total base)

South Africa still the largest installed base (34% of the world total VS 37% end of 2013)

*(Information from Cepheid)*

# GenXpert HPV Performance

Specificity and sensitivity in pre-clinical study\*

For $\geq$ CIN2	Xpert® HPV	NAAT 1	NAAT 2
Sensitivity	<b>90.8%</b> (84.7-95.0%)	<b>90.8%</b> (84.7-95.0%)	81.6% (74.2-87.6%)
Specificity	42.6% (38.5-46.9%)	39.6% (35.5-43.8%)	47.7% (43.4-51.9%)

For $\geq$ CIN3	Xpert® HPV	NAAT 1	NAAT 2
Sensitivity	<b>92.3%</b> (84.8-96.9%)	<b>92.3%</b> (84.8-96.9%)	<b>80.2%</b> (70.6-87.8%)
Specificity	<b>40.0%</b> (36.1-44.0%)	<b>37.2%</b> (33.3-41.2%)	<b>45.0%</b> (40.9-49.0%)

## Xpert HPV References

\*Einstein MH, Smith KM, Davis TE, Schmeler KM, Ferris DG, Savage AH, Gray JE, Stoler MH, Wright TC Jr, Ferenczy A, Castle PE. **Clinical evaluation of the cartridge-based GeneXpert human papillomavirus assay in women referred for colposcopy.** J.Clin. Microbiol. 2014; 52(6):2089-95. <http://jcm.asm.org/content/early/2014/04/03/JCM.00176-14.full.pdf>

Castle PE, Smith KM, Davis TE, Schmeler KM, Ferris DG, Savage AH, Gray JE, Stoler MH, Wright TC Jr, Ferenczy A, Einstein MH. **Reliability of the Xpert HPV assay to detect high-risk human papillomavirus DNA in a colposcopy referral population.** Am J Clin Pathol. 2015; 143(1):126-33.

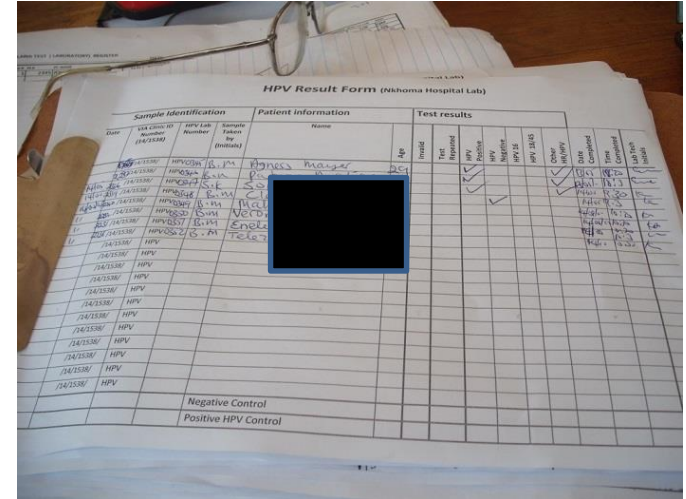
Cuzick J, Cuschieri K, Denton K, Hopkins M, Thorat M, Wright C, Cubie H, Moore C, Kleeman M, Austin J, Ashdown-Barr L, Hunt K, Cadman L. **Performance of the Xpert HPV Assay in a Screening Population.** Papillomavirus Research (PVR) 2015; (submitted)

# Technology & Training Adaptability

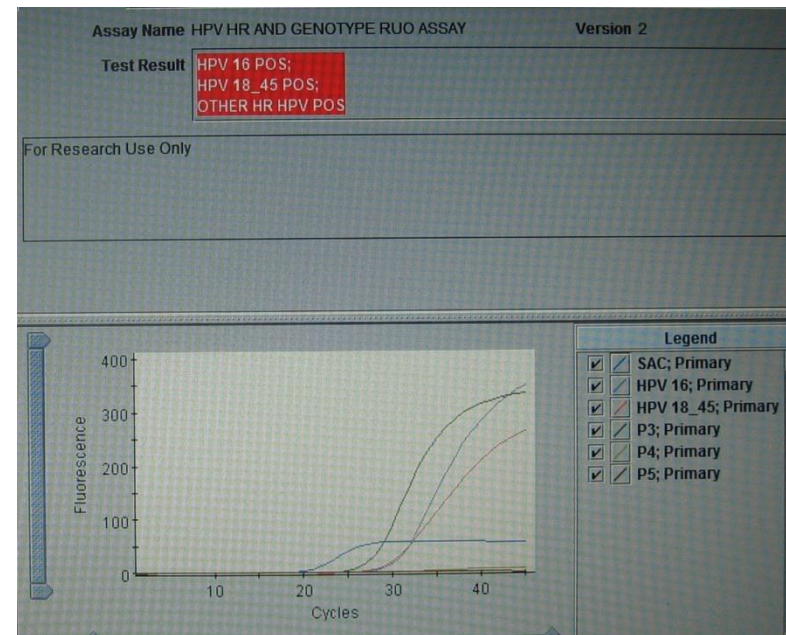
- Temperature stability
  - Kits stored 2-28°C
  - Sample Transport & Storage: 2-30°C for ≤ 6 months after collection
- Reliability
  - SAC to detect single copy human gene monitors for sample cellularity
  - Probe Check control verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability
- Technical support
  - RemoteXpert with wireless connectivity potential provides a data collection, monitoring & Epidemiology Tool, as well as service and support
- Training
  - Cascade training following Cepheid training for lab technologist
  - Potentially suitable for near patient testing in clinic –*trial starts next month*



# First HPV results coming through in Nkhoma



Sample: HPV0018 →  
 Result: Triple positive: HPV 16,  
 HPV18/45 & HPV Other HR



# Alternative transport media for LIMC:

- Near patient use of saline for sample collection in Malawi
- Non-volatile stable transport matrix under evaluation (Natrol)– where delay in reaching lab; aim is to support 30°C storage over several weeks

Date	No of valid results	HPV neg	HPV pos	HPV 16	HPV 18/45	HPV 31	HPV 59/51	HPV 39	Multiple infections
<b>Oct-13</b>	45 (saline)	35	10	3	2	4	2	2	2
<b>Jan-14</b>	51 (saline)	39	12	3	3	4	0	2	0
	51 (PreservCyt)	39	10	3	2	4	0	1	0
<b>Apr-May14</b>	95 (Natrol)	78	17	1	2	10	1	3	1
	95 (PC)	75	20	2	4	10	1	5	2

*not for dissemination; manuscript in preparation*

# Further breakdown of HPV-other Positive results (Paired samples: saline & PreservCyt, Jan 2014)

VIA NUMBER	HPV NUMBER	NAME	HPV RESULT	TYPE OF PROBE SHOWING POSITIVE ON THE GRAPH
31	HPV 0023		Positive	P 3
31	HPV0024		Positive	P 3
274	HPV 0024		Positive	P 3
274	HPV0025		Positive	P 3
21	HPV 0029		Positive	P 3
21	HPV0030		Positive	P 3
32	HPV 0045		Positive	P 3
32	HPV0046		Positive	p3
50	HPV 0069		Positive	P 5
50	HPV0070		Positive	P 5
66	HPV 0099		Positive	P 5
66	HPV00100		Positive	P 5

*not for dissemination; manuscript in preparation*

# HPV in PreservCyt<sup>®</sup> samples, 2014

Date	No of results	HPV neg	HPV pos	Invalid results	HPV 16	HPV 18/45	HPV HR-other	HPV 31+	HPV 59/51	HPV 39+	Multiple infections
Jan-14	51	41	10	0	3	2	5	4	0	1	0
Apr-14	92	72	20	0	2	4	16	10	1	5	2
May-14	126	94	30	2	9	6	19	11	5	4	5
Jun-14	132	112	18	2	4	6	11	9	3	2	2
Jul-14	17	15	2	0	1	0	1	1	0	0	0
Aug-14	20	14	6	0	1	2	4	4	0	0	1
Sep-14	4	3	1	0	0	1	0	0	0	0	0
Oct-14	20	16	2	2	0	0	3	2	0	1	1
Nov-14	75	58	17	0	3	2	10	10	3	6	5
Dec-14	77	60	16	1	8	4	6	2	3	1	2
Total	614	485	122	7	31	27	75	53	15	20	18
Per cent % of positives		79.0%	19.9%	1.1%	5.1%	4.4%	12.2%	8.6%	2.4%	3.3%	
					25.4%	22.1%	61.5%	43.4%	12.3%	16.4%	

*not for dissemination; manuscript in preparation*



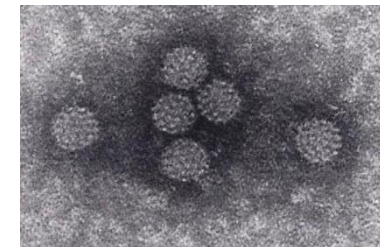
# Preliminary data: HPV positivity and prevalence relative to HIV status

HIV status	Number	HPV neg	HPV pos
Known positive	22	15	7 (31.8%)
Neg /Unknown (codes 3/4)	161	125	36 (22.3 %)

- Known HIV prevalence in women screened was 5.5% (but 46.5% did not know current status)
- HIV prevalence of antenatal women at Nkhoma Hospital is only 1.8% (3,339 mothers tested in 2014)
- The national seroprevalence rate is 10-14%.

***not for dissemination; manuscript in preparation***

# Strengths & Weaknesses of HPV clinical testing in Africa



## Weaknesses

- Procurement and transport
  - Delay in receiving LBC pots, as well as limited number of Xpert HPV tests in early months
- Use of plastics
- Disposal of cartridges, and PreservCyt in pots
- Appropriate temperature of clinic, transport to lab and storage
  - Use cool boxes for clinic to lab
- Cost constraints
  - All HPV tests still too expensive for routine use



## Strengths

- Ease of use of Xpert HPV
  - Several staff carry out tests
- Partial genotyping is a bonus
  - Valuable for epidemiology
- Cheaper alternative collection media look possible
  - ?Even saline
- Rapid turnaround
  - Turn-around of 2 hours from clinic and back to clinic achieved in hospital setting
- Reproducibility of QC results
  - Positive & Negative IQC introduced after every 20 specimens

# Conclusions

- Cepheid Xpert® HPV is a simple and easy to use molecular platform for a hospital laboratory environment
- Nkhoma Hospital Laboratory has achieved rapid turnaround, good reproducibility and identified potentially cheaper collection medium for near patient testing
- *Despite these achievements, we are not yet using HPV testing for triage to VIA. To prevent a woman having to be examined twice in her single visit – once for HPV sample and once for VIA, self sampling will be essential.*

# This project would not have been possible without huge effort from many people, in particular:

- **Nkhoma Hospital**
- **Senior CCSP team**
  - Reynier ter Haar
  - David Morton
  - Savel Kafwafwa
  - Beatrice Kabota
  - Belito Mdetsa
  - Harriet Chauwa
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  - Mike Mautanga,
  - Rose Nkhoma,
  - Ipyana Mwenitete



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