HPV versus cytology screening in South-Africa: the way forward

Dr. Suzette M Jordaan

South Africa

- 9 provinces managed autonomously; diverse population – 55 million plus about 5m legal/illegal immigrants and migrant workers
- 11 official languages; rural/suburban and urban areas – mountainous areas as well as desert.
- Rural areas - 43% of population
- Long distances to travel to health care facilities.
- Rural health care facilities have a shortage of basic equipment, e.g. light sources; swabs; specula

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Cervical cancer

- Cervical cancer remains the second most common cancer diagnosed in women in South Africa with an estimated 7.735 new cases in 2012, with 4.248 women dying from the disease.

- Like the rest of Africa, the country has a chronic shortage of health care workers

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Shortage of medical staff

- More than 70% of South Africa's medical staff works in private health care facilities. South Africa has one doctor for every 3 707 to 4 918 of their citizens. This ratio in the developed countries is an average of one doctor for every 242 to 539 of its inhabitants.
- Patients in rural areas suffer due to these shortages as South Africa struggles to attract and retain enough medical staff to provide health services not only in the urban areas, but particularly in remote locations. In South Africa, 43.6% of the population lives in rural areas, but only about 12% of the country's doctor's work in rural healthcare facilities.

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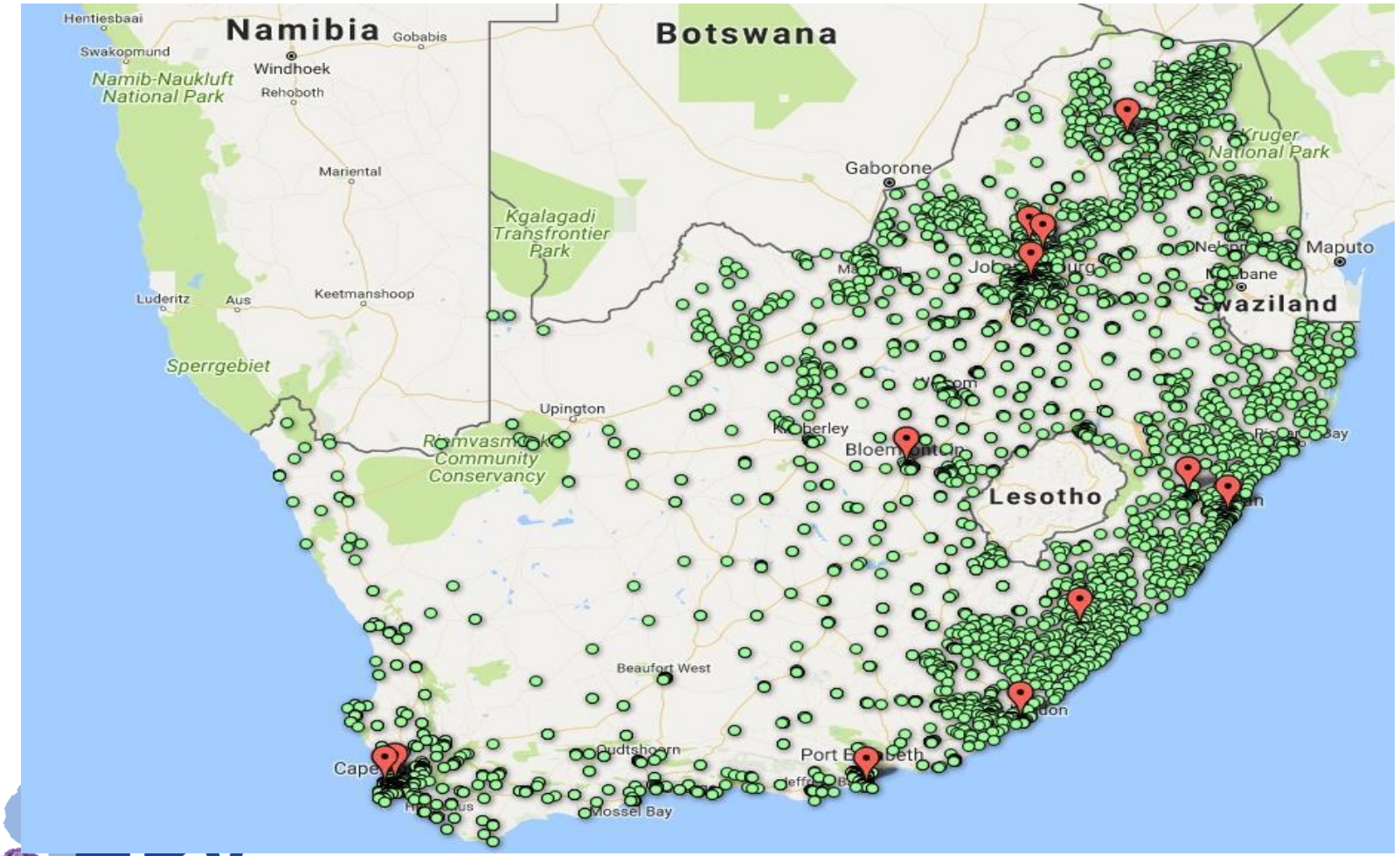
Health care facilities and laboratories

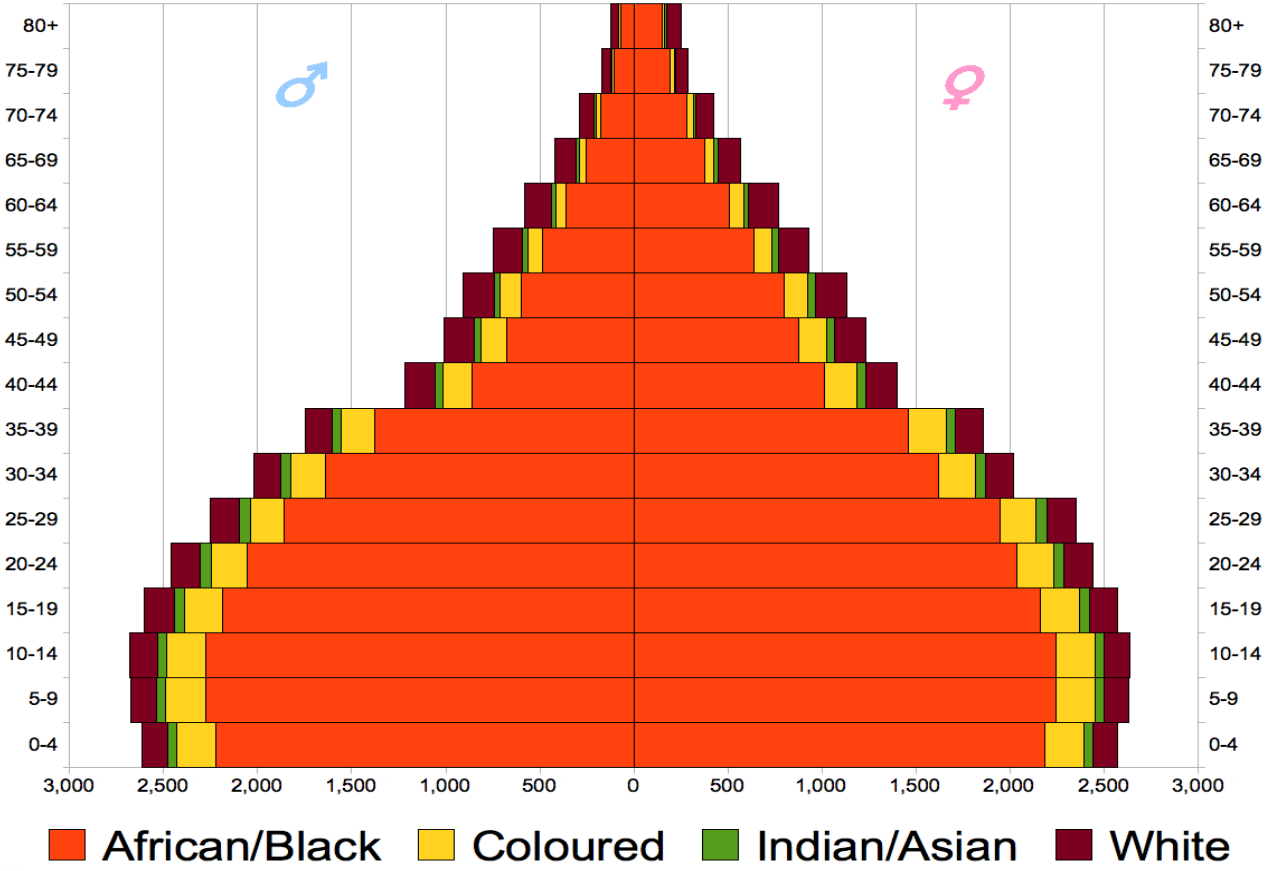


Health care facilities per province

In South Africa 4 526 health facilities

- Gauteng -538
- KwaZulu Natal -739
- Eastern Cape -1101
- Limpopo -612
- Mpumalanga -381
- Northwest -304
- Free State -331
- Northern Cape -231
- Western Cape -476 feed into 12 cytology laboratories

Population groups



HIV

- South Africa has the largest expanding HIV burden in the world and it is estimated that 6.3 million South Africans are currently living with HIV/AIDS, of whom 60% are women
- HIV significantly increases the risk of persistent HPV infections
- the development of cervical cancer is faster in HIV-positive women.

Effect of HIV on cytology diagnosis

abnormal Cytology results per age group - HIV-/HIV+								
Age group	ASC-US %		LSIL %		HSIL plus ASC-H %		Malignant %	
	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+
20-25	1.8	3.8	1.8	5.2	0.4	2.2	0.0	0.1
26-30	2.2	6.0	1.8	8.7	1.1	6.3	0.2	0.8
31-35	2.0	6.4	1.8	8.7	1.6	8.8	0.4	2.0
36-40	1.6	5.5	1.3	7.3	1.3	8.7	0.6	3.5
41-45	1.6	3.9	1.2	4.4	1.2	5.8	0.7	3.0
46-50	1.4	2.7	0.8	2.5	1.0	3.7	1.4	2.7
51-55	1.0	1.5	0.4	1.2	0.9	1.9	2.8	2.7
56-60	0.7	0.8	0.3	0.5	0.5	1.0	2.8	1.4
61+	1.6	1.2	0.6	1.0	1.2	1.5	4.1	2.1

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HIV and HPV

- HIV significantly increases the risk of persistent HPV infections
- HIV-infected women have greater rates of pre-invasive and invasive cervical cancer rates whereas HPV infection promotes the acquisition of HIV
- the development of cervical cancer is faster in HIV-positive women.

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Prevention strategies

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Prevention strategies - Primary

- To prevent women from acquiring HPV infection
- Change sexual practices , e.g. condoms, monogamy
- HPV vaccination – school-based program
- April 2014 – 17 807 public schools
- March-April and September-October 2014 - 419.589 (93.2%) and 329.665 (73.3%) girls were vaccinated respectively
- in 2015, 356.228 (79%) received the first vaccine dose while 283.453 (63%) received both doses.

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Secondary prevention

- Secondary prevention is to prevent precursor lesions from becoming invasive carcinoma

Modalities include:

-Cervical cytology – 12 NHLS Cytology laboratories

- LBC currently implemented in public sector
- HPV screening available at Private laboratories
- VIA – currently not encouraged at primary care facilities

Prevention strategy - Tertiary

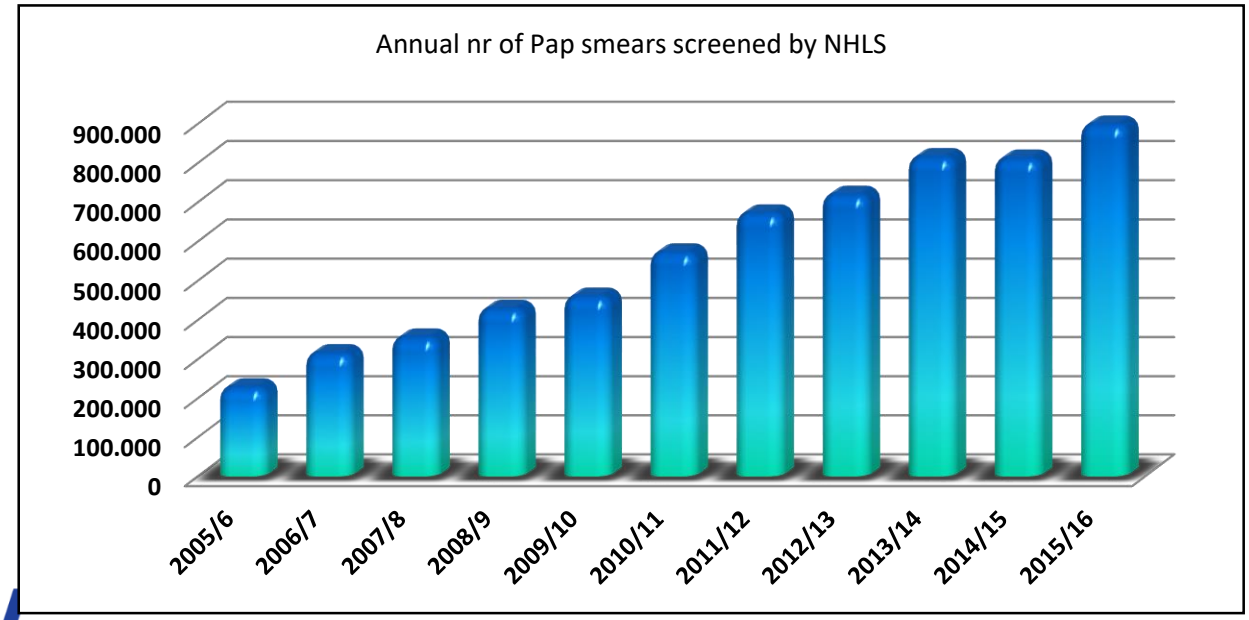
- Shortage of health care workers and much needed equipment
- Long waiting lists at Colposcopy clinics
- Women from rural areas usually arrive for treatment when it is already too late

Challenges and progress of screening policies

- National cancer control program (2000 /2004-till 2017)
- HIV Counseling and Testing (HCT) (2011) CD4 count < 250
- HIV Counseling and Testing HCT (2014) CD4 count < 500
- Universal Test and Treat (2016) regardless of CD4 count

National cancer control program 2000

- Cervical cancer screening program – 2000 re-launched in 2004
- Screen 70% of asymptomatic women 30 y and older
- Target – 6.866.222 – 686.622 per annum (10 y)



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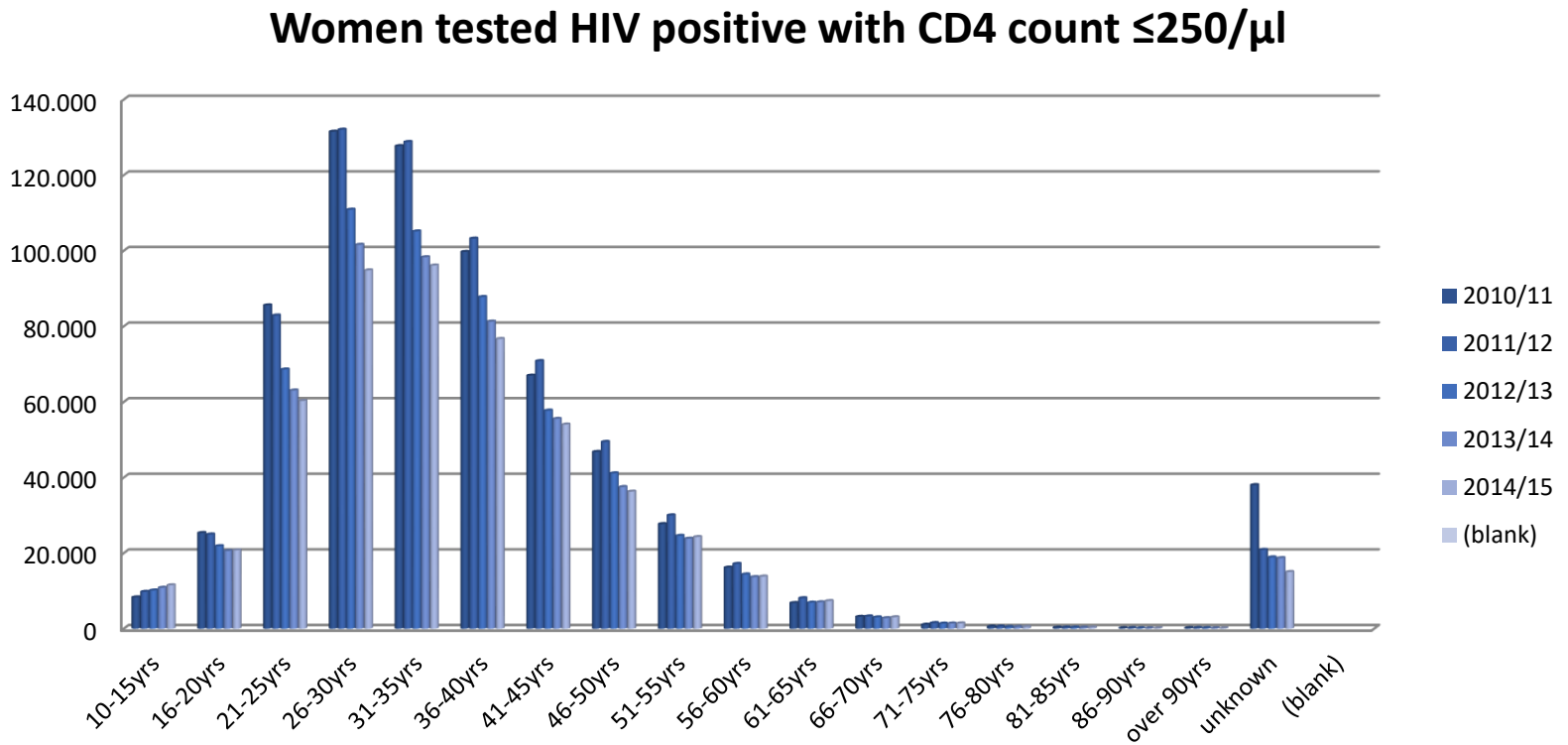
HIV Counseling and Treatment screening program (HCT)

- HCT screening program announced April 2011
- All women tested positive for HIV (CD4 < 250) must have a Pap smear taken

	HIV+ women with CD4 count ≤250/µl			
Year	2011/12	2012/13	2013/14	2014/15
Total	683,913	573,275	536,921	516,287

Women tested HIV positive with CD4 count ≤250/µl



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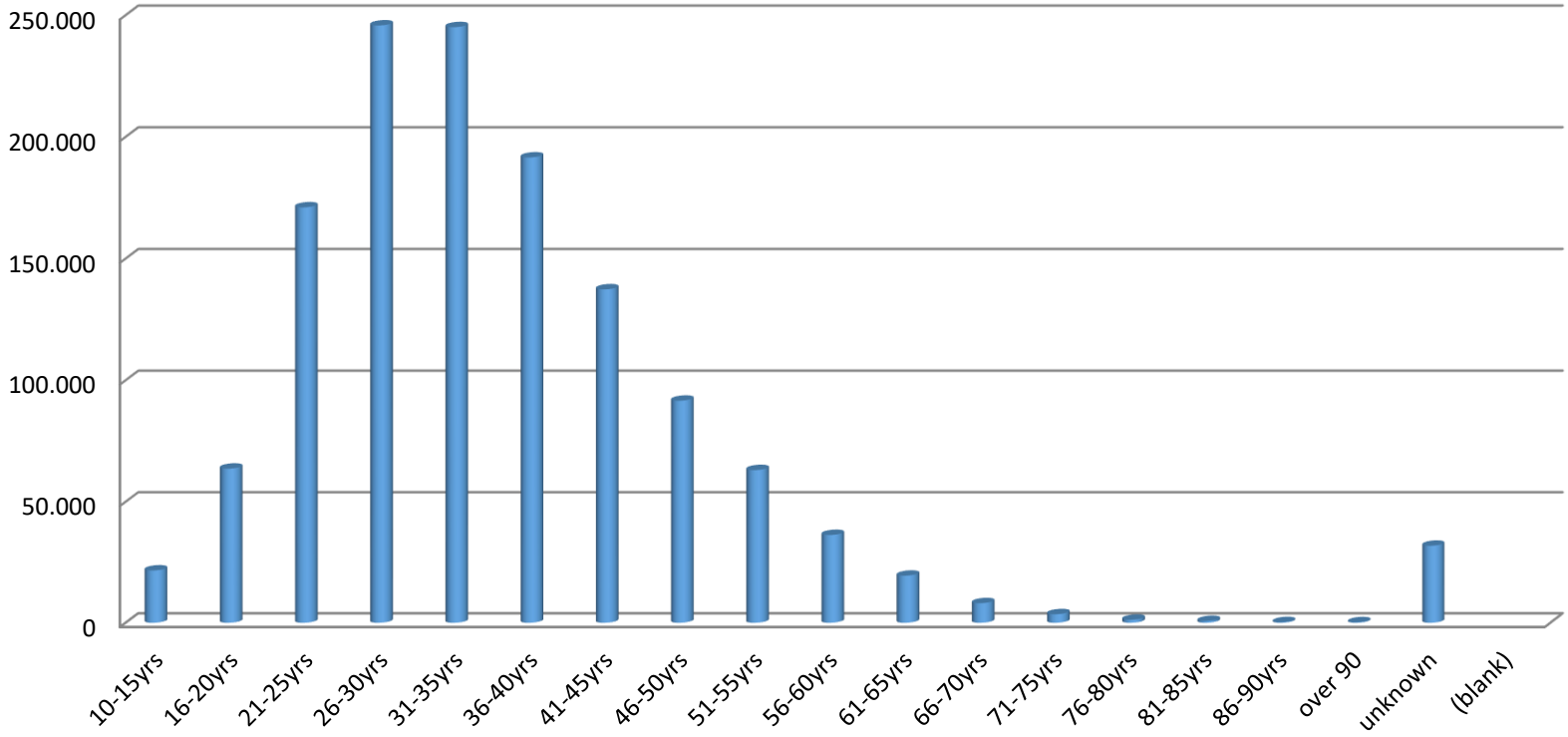
HIV Counsel and Treat program (HCT) and Universal Test and Treat program (UTT)

- HCT program – 2014 – CD4 count <500µl
- UTT program announced September 2016 – all women tested positive for HIV must have a Pap smear taken regardless of CD4 count

Women tested HIV Viral load positive at the NHLS laboratory						
Year	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16
Total	462.339	838.461	851.991	918.560	895.749	1.012.053

Women tested HIV positive with CD4 count ≤500/µl



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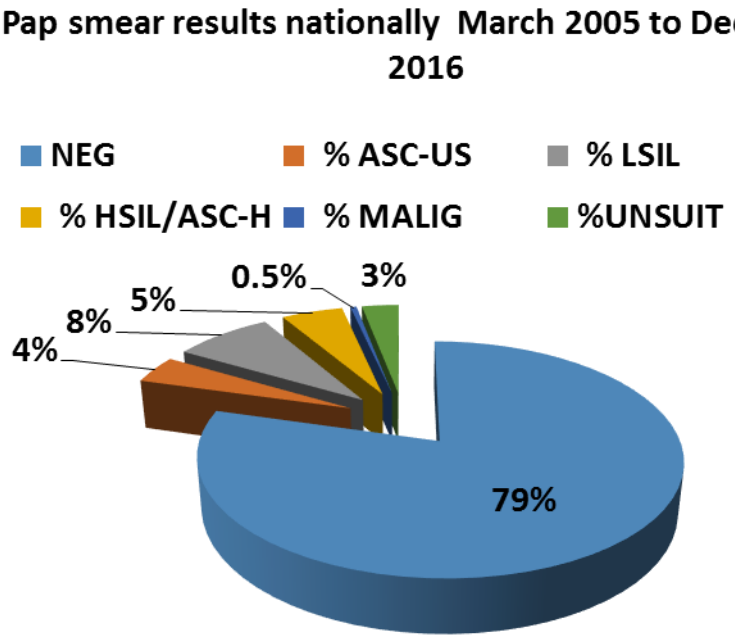
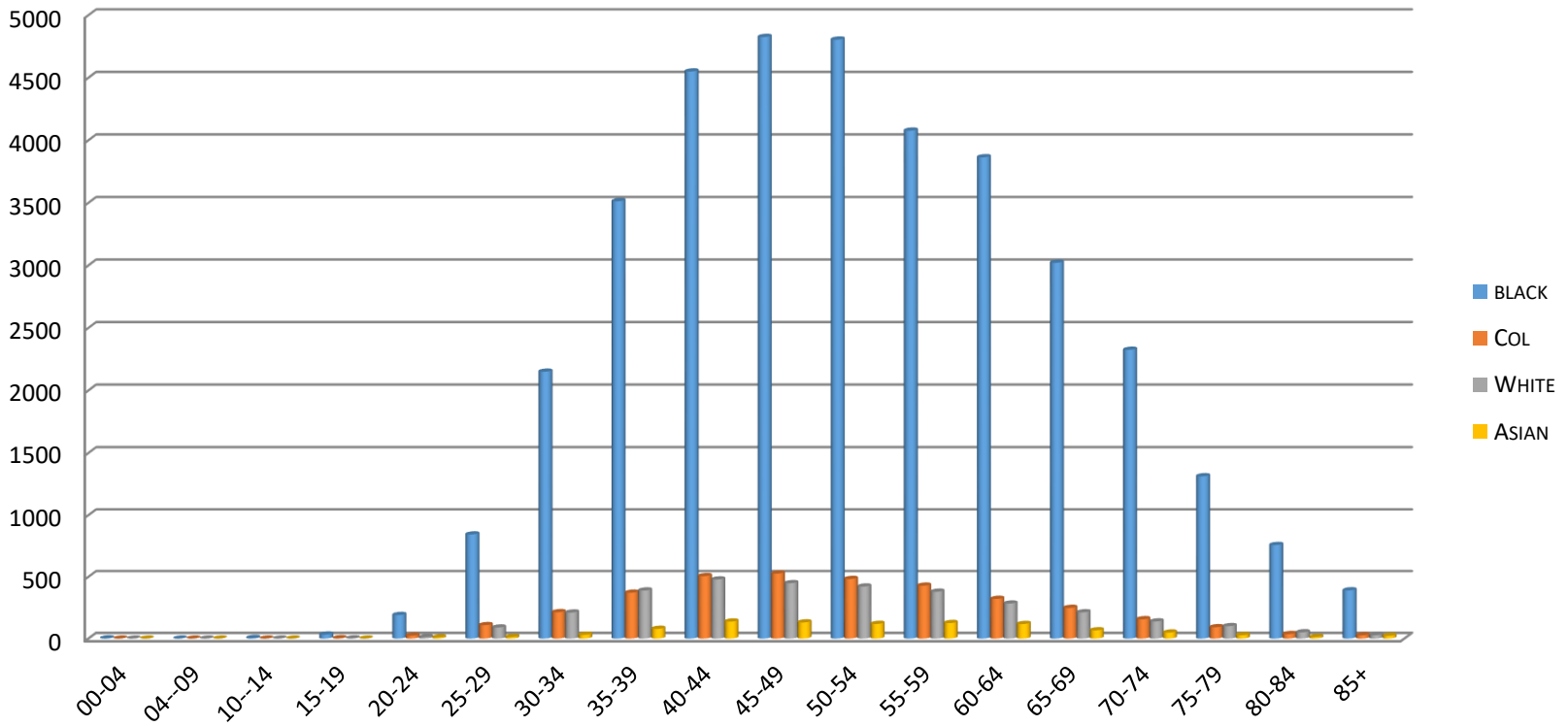
National South African data

- According to the 2011 Census data there are 16.613.832 women over the age of 20 and 11.417.301 women over the age of 30 eligible for Pap smears in South Africa



Age specific incidence of Cervical carcinoma



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Provincial statistics

Province	Females Aged 30+.	Pap smears screened	Pap smear coverage % women aged 20+	Pap smear coverage % women aged 30+	% ASC-US	% LSIL	% HSIL	% MAL	% Unsuit
Western Cape	1.412769	1.102.953	55%	78%	3.7	8.8	4.1	0.2	2
Free State	625.353	383.959	43%	61%	3.8	8.2	3.2	0.9	7
North West	742.755	446.616	42%	60%	2.3	5.8	3.4	0.4	4
Gauteng	2.786.427	1.585.108	38%	57%	4.4	15.8	8.2	0.3	2
Limpopo	1.157.190	636.610	38%	55%	3.0	5.3	3.1	0.1	1
Mpumalanga	822.735	428.645	35%	52%	3.6	4.4	7.0	0.5	1
Northern Cape	257.361	126.095	35%	49%	2.6	5.5	2.1	0.7	6
KwaZulu-Natal	2.133.438	967.907	30%	45%	3.5	9.8	5.8	0.4	3
Eastern Cape	1.479.258	599.879	29%	41%	4.8	6.3	5.0	1.1	2

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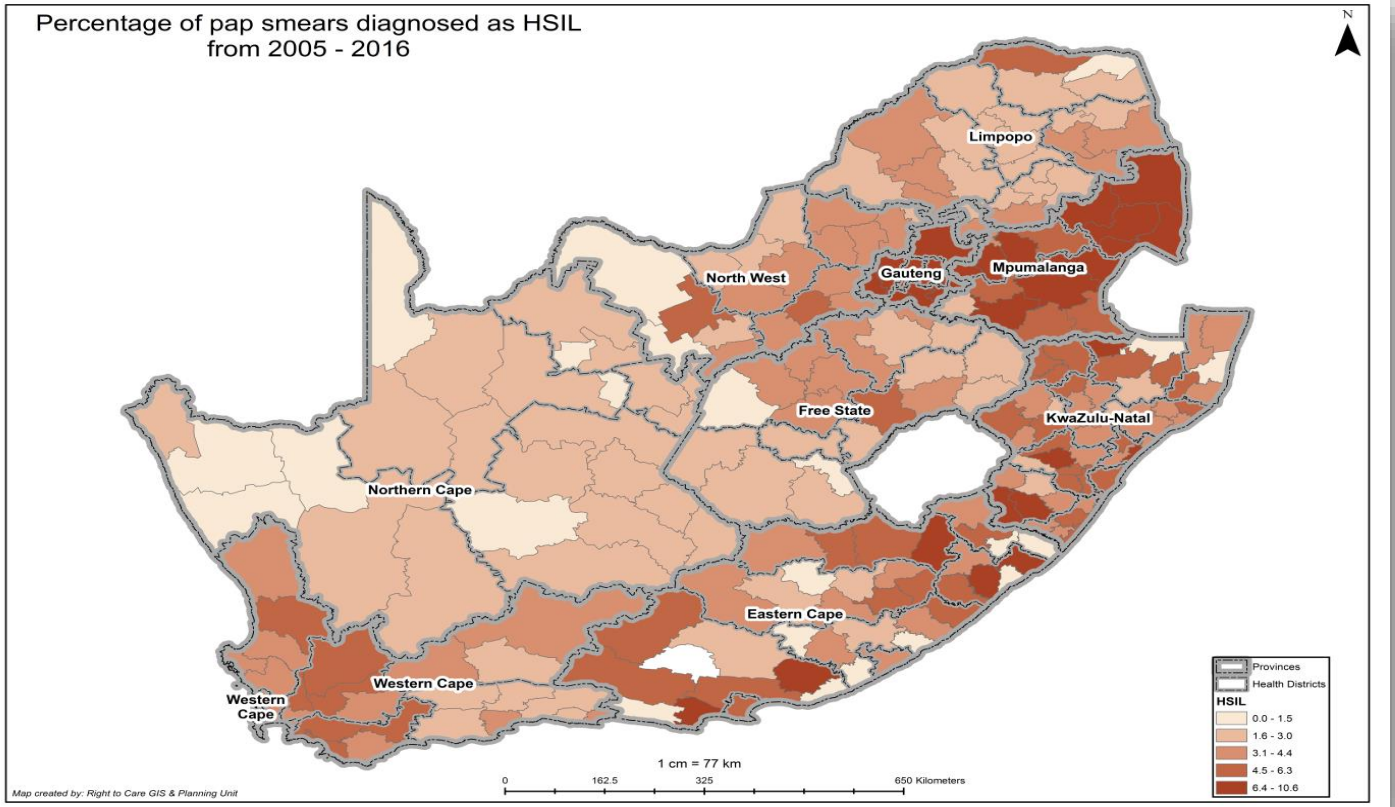
Rural/Suburban/Urban

	Nr of smears	% screened	Adeq	ASC-US	LSIL	HSIL	Malignancy	Unsuitable
Rural	1.341.743	21.4%	55%	3.6%	6.6%	5.0%	0.7%	2%
Suburban	1.070.877	17.1%	68%	3.4%	7.3%	4,5%	0.4%	3%
Urban	3.853.611	61.5%	71%	4.0%	11.0%	6.3%	0.3%	2%
TOTAL	6.266.231							

Choropleth map: Districts and sub-districts HSIL



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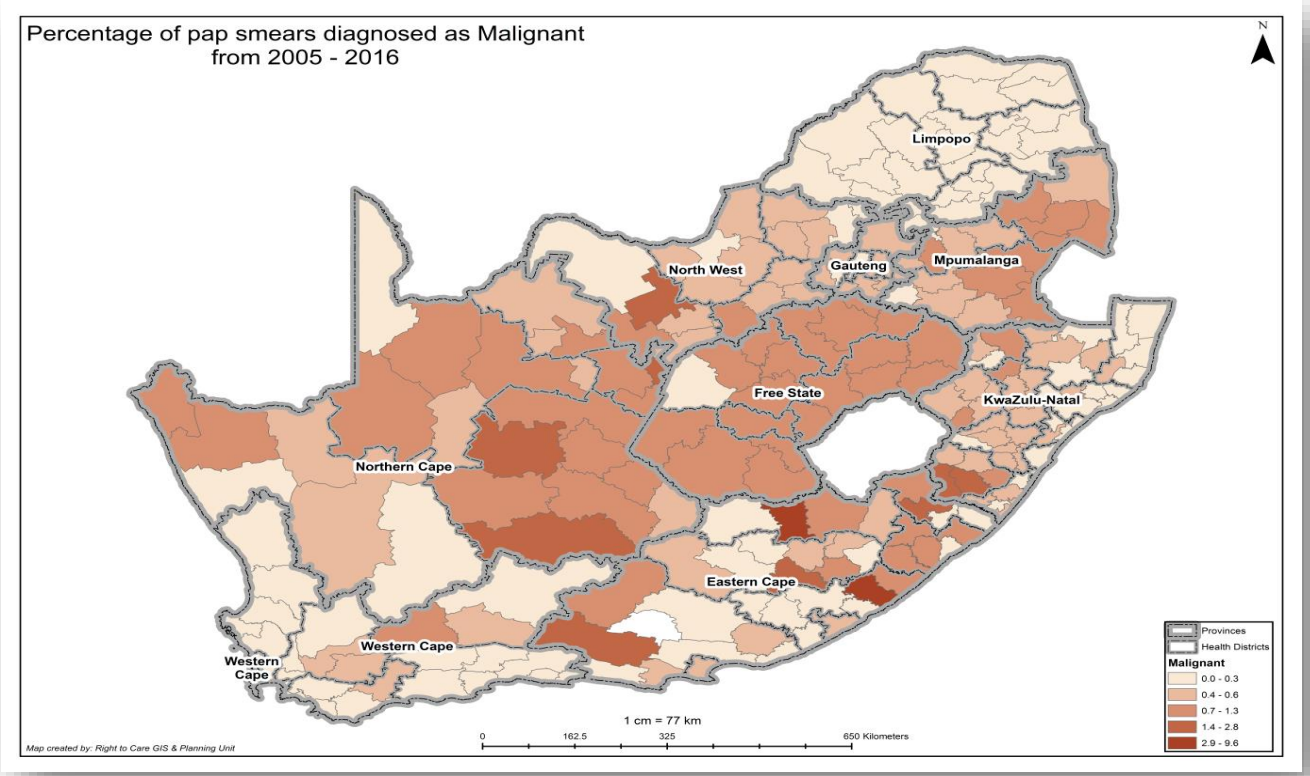
Choropleth map: Districts and sub-districts – cervical malignancy



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Gauteng Province: District and sub-district

City of Tshwane Metro							
Sub District	Smears	% Adequacy	% ASC-US	% LSIL	% HSIL	% MAL	% Unsuitable
Tshwane 1 Health Sub-District	107.489	79%	0.9	6.2	3.6	0.2	1
Tshwane 2 Health Sub-District	37.871	72%	1.6	5.4	3.5	0.2	1
Tshwane 3 Health Sub-District	113.808	74%	3.7	4.6	6.3	0.8	1
Tshwane 4 Health Sub-District	33.512	78%	4.5	3.7	7.1	0.5	1
Tshwane 5 Health Sub-District	4.492	46%	4.6	4.5	6.5	0.3	1
Tshwane 6 Health Sub-District	66.587	73%	5.3	4.8	8.2	0.6	1
Tshwane 7 Health Sub-District	10.367	58%	5.1	4.8	7.8	0.4	1
City of Tshwane	2.201	69%	3.5	7.1	5.1	0.0	1

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Western Cape province

Central Karoo								
Sub District	**Urban/ Rural**	**Cases**	**% Adequacy**	**% ASC-US**	**% LSIL**	**% HSIL**	**% MALIG**	**% Unsuitable**
Laingsburg	**Suburban**	**1.456**	**85%**	**5.2%**	**6.6%**	**4.1%**	**0.9%**	**4%**
Prince Albert	**Rural**	**2.193**	**64%**	**2.4%**	**5.6%**	**2.3%**	**0.5%**	**2%**
Beaufort West	**Urban**	**9.343**	**70%**	**2.5%**	**7.6%**	**3.3%**	**0.2%**	**1%**

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Eastern Cape province

Amathole			
Sub District	**Urban / Rural**	**Cases**	**% MALIG**
Mnquma	**Rural**	**18.031**	**9.6%**
Mbashe	**Rural**	**22.903**	**0.8%**
Amahlati	**Rural**	**25.973**	**0.2%**
Nkonkobe	**Rural**	**21.667**	**0.2%**

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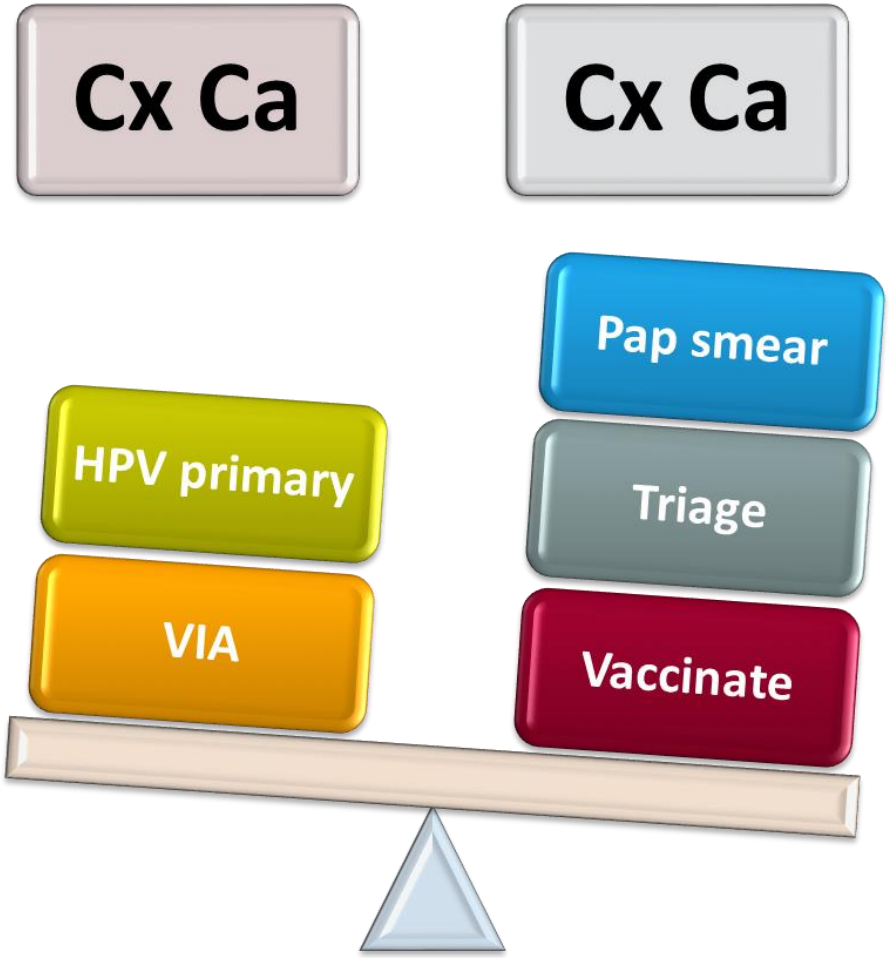
Cervical cancer prevention in SA: what do we do now?



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What have we learnt?

- Before a successful screening program is introduced one needs to have some base-level data e.g. number of women in target population; rates of cervical lesions nationally as well as district and sub-district level, risks e.g. prevalence rates of HPV, HIV etc.

- Appropriate new technologies for SA include platforms that offer good detection rate of abnormalities, faster TAT, ability to perform ancillary studies, COST.

- Do not repeat previous screening mistakes, e.g. poor coverage, lack of staffing and equipment, screening but no treatment.

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Results of LBC tender

- The Hologic ThinPrep system was found to be more suitable for the NHLS.
  - Ease of use
  - Automation
  - Better turn around time
  - Easier to screen – mono-layered smear
  - Automated screening

Hologic autoloader

Comparison of HPV equipment

Equipment evaluated for HPV	Batch size	Measured throughput per 8hr day	Walk-away time per 8 hr. day	Ability to do HIV or TB tests on this platform
Panther – IlexSA	16	278 500 in 12hr	SurePath – 2hrs ThinPrep – 4hrs	HPV, HIV
BD Viper™ LT	30	60 90 in 12hr	NIL	HPV
Qiagen - QiaSymphony and Rapid Capture System (RCS) Hybrid Capture II	88	176	NIL STM – 2 hrs.	HPV

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Comparison of HPV equipment

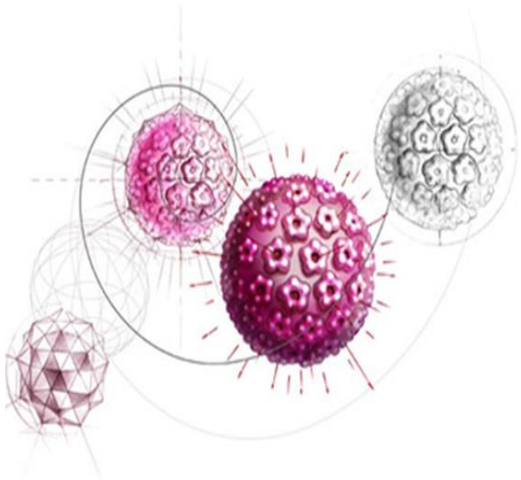
Equipment evaluated for HPV	Batch size	Measured throughput per 8hr day	Walk-away time per 8 hr. day	Ability to do HIV or TB tests on this platform
Roche Cobas 4800 and Z4800	24	88 110 in 12hr	3hrs	HPV,HIV
Cepheid -GeneXpert	1 per module	8 per module	Depends on nr of modules	HPV,TB, HIV
ABBOTT - m2000sp and m2000rt	94	188	NIL Prolonged Prep time	HPV, HIV

HPV tests

HPV DNA / mRNA

Discriminatory

Non-discriminatory



HPV test requirement

HPV test would be required which has been clinically validated, robust, fully automated, fast, affordable, single assay with an adjustable cut-off for detection, having a cell control and preferentially linked to a genotyping method.

HPV prevalence – Study KZN 2004 -2007

- Study in KZN – rural setting - samples were collected from all 224 enrolled Black African women – 57% of women from rural area. HPV prevalence was 76.3% (171/224) overall and 70.5% in the rural setting. The prevalence of high-risk genotypes in this study was 54.5%. HPV prevalence was high both among women <18 years (70.3%) and >18 years (77.5%) old. The overall HPV prevalence of 76.3% in this study is almost 3–4 fold higher than other reported estimates. The proportion of women infected with the high-risk vaccine genotypes (HPV16 and/or 18) was 21% (47/224)

HPV prevalence – GP - 2013

- 1 472 women from the Gauteng Province attending five urban and peri-urban public health sector clinics.
- In this study, the prevalence of HPV DNA was 74.6% with high risk HPV (hrHPV) DNA in 54.3%.
- HPV type 16 and/or 18 was found in 19.5% of women. Specimens for HPV genotyping were either healthcare worker-collected dry cervical swabs (N=951) or patient-collected tampon specimens (N=573).

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HPV prevalence – CT - 2014

- showed a much lower overall prevalence of HPV DNA of 25.4% of 9429 study participants.

- One or more high-risk HPV genotypes was present in 78.5% (1848/2 354) of the HPV positive women tested which is an overall hrHPV prevalence of 19.6%.

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Way forward

- Establish Strengths, Weaknesses, Opportunities and Threats (SWOT)
- Establish the population, prevalence rates per age groups
- Learn from cervical cancer screening program
- Decide whether to strengthen what we have or implement new technologies
- Evaluate new technologies for suitability

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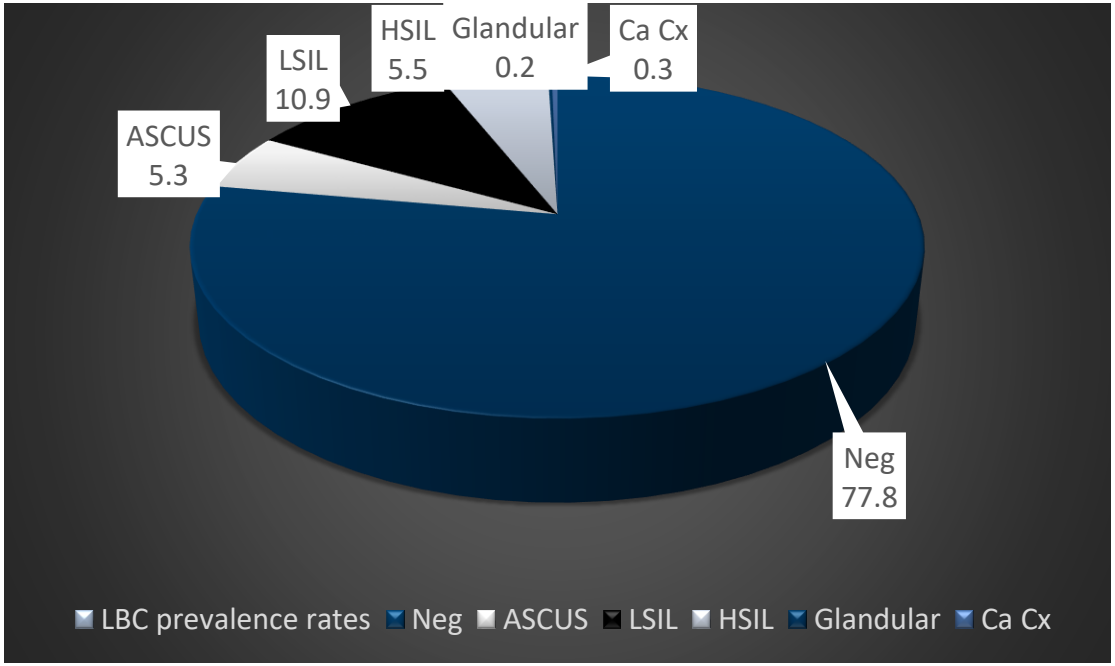
Prevalence rates -LBC



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“ONE SIZE DOES NOT FIT ALL”

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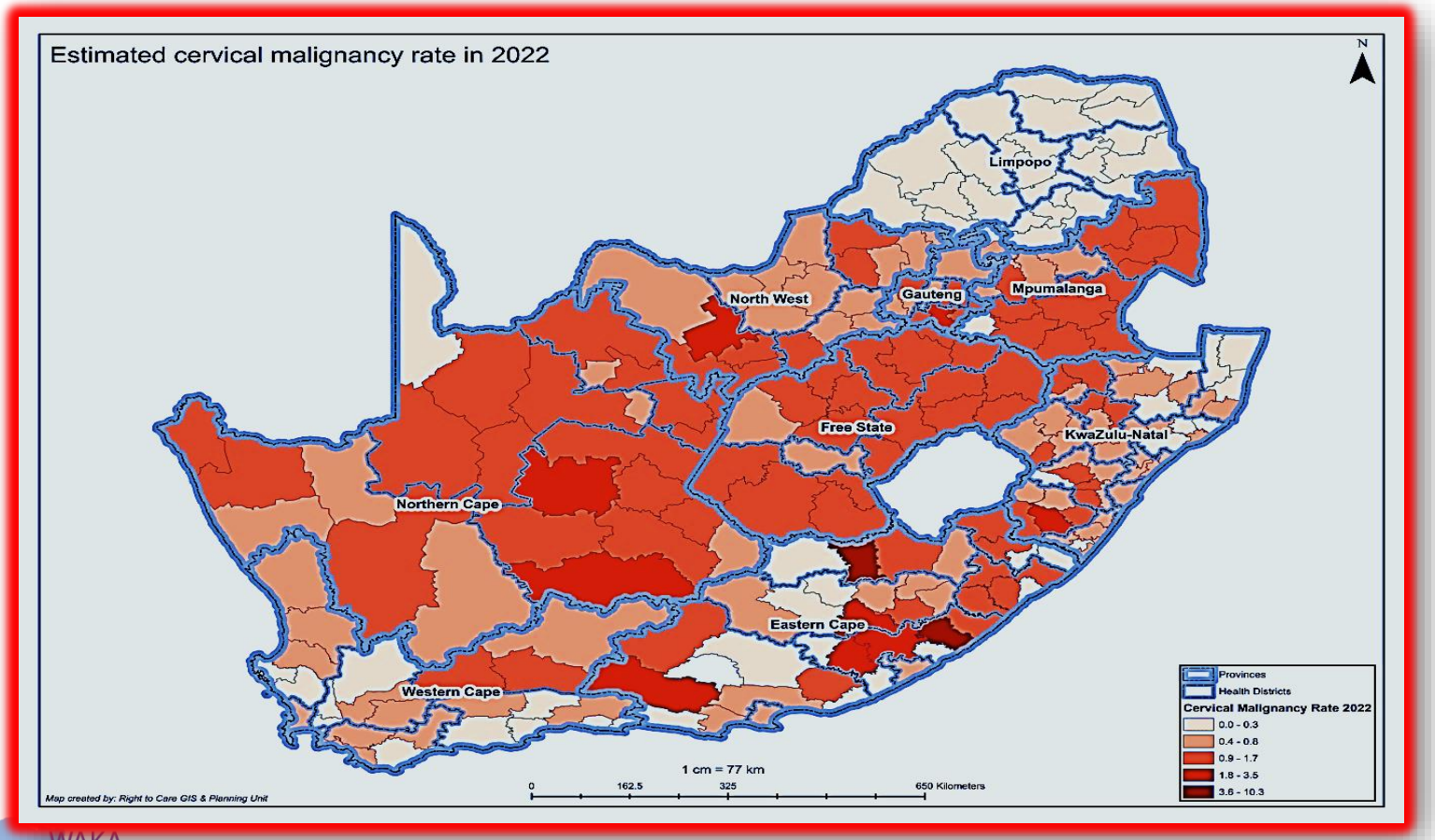

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Thank you

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