CURRENT GUIDELINES FOR SCREENING, DIAGNOSIS AND TREATMENT OF CERVICAL CANCER.

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OUTLINE

- Introduction
- Epidemiology
- Patho-physiology
- Current guidelines on primary prevention
- Current guidelines on secondary prevention
- Diagnosis
- Treatment
- Prognosis
- Conclusion

INTRODUCTION

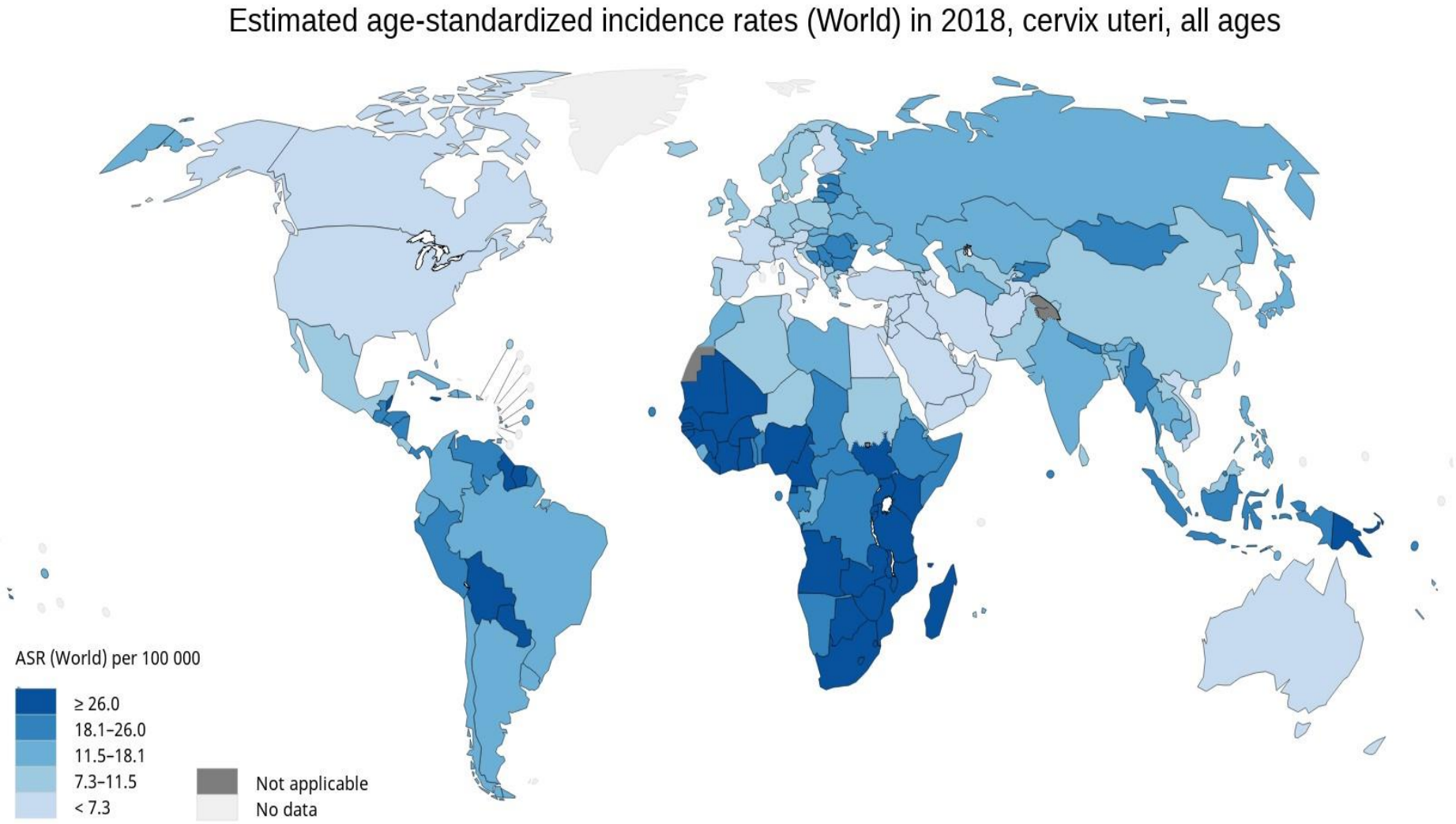
- Cervical cancer is a public health concern with a wide disparity between developed and developing countries.
- Globally, Cervical is the fourth most common cancer in women (6.6%) and the fourth most common cause of cancer – related deaths (7.5%) - 18.1 million new cases and 9.6 million deaths in 2018.
- Second most common cancer in developing countries but tenth most common in developed countries.
- It is a leading cause of cancer – related deaths for women in developing countries but relatively uncommon cause of cancer deaths in developed countries

INTRODUCTION 2

- 569,847 cases in 2018, about 80% of which occurred in developing countries
- 311,365 mortalities in 2018, about 90% of which occurred in developing countries

Globocan 2018, IARC

Estimated age-standardized incidence rates cervical cancer, 2018



Data source: GLOBOCAN 2018
Graph production: IARC (http://gco.iarc.fr/today)
World Health Organization

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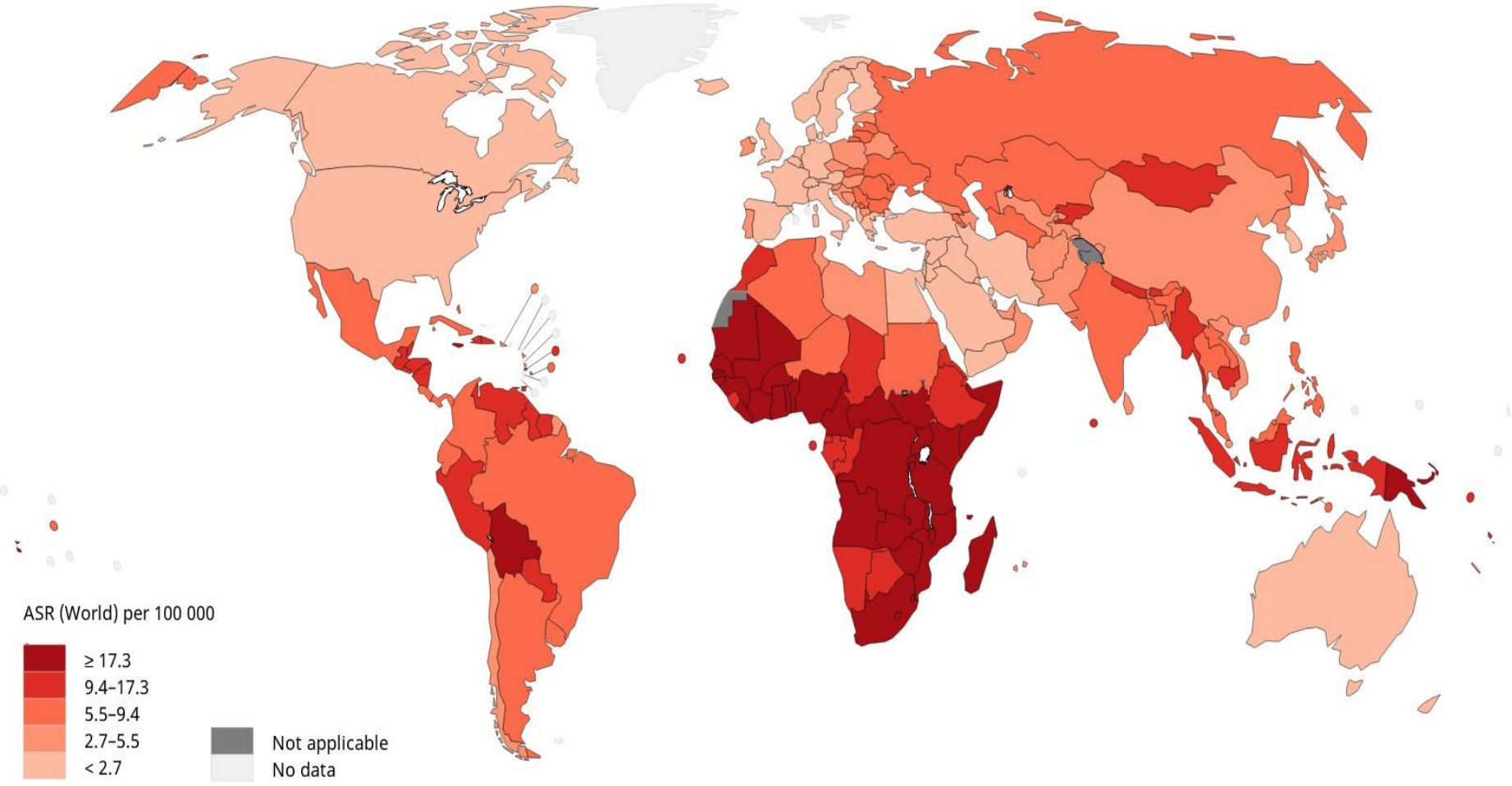

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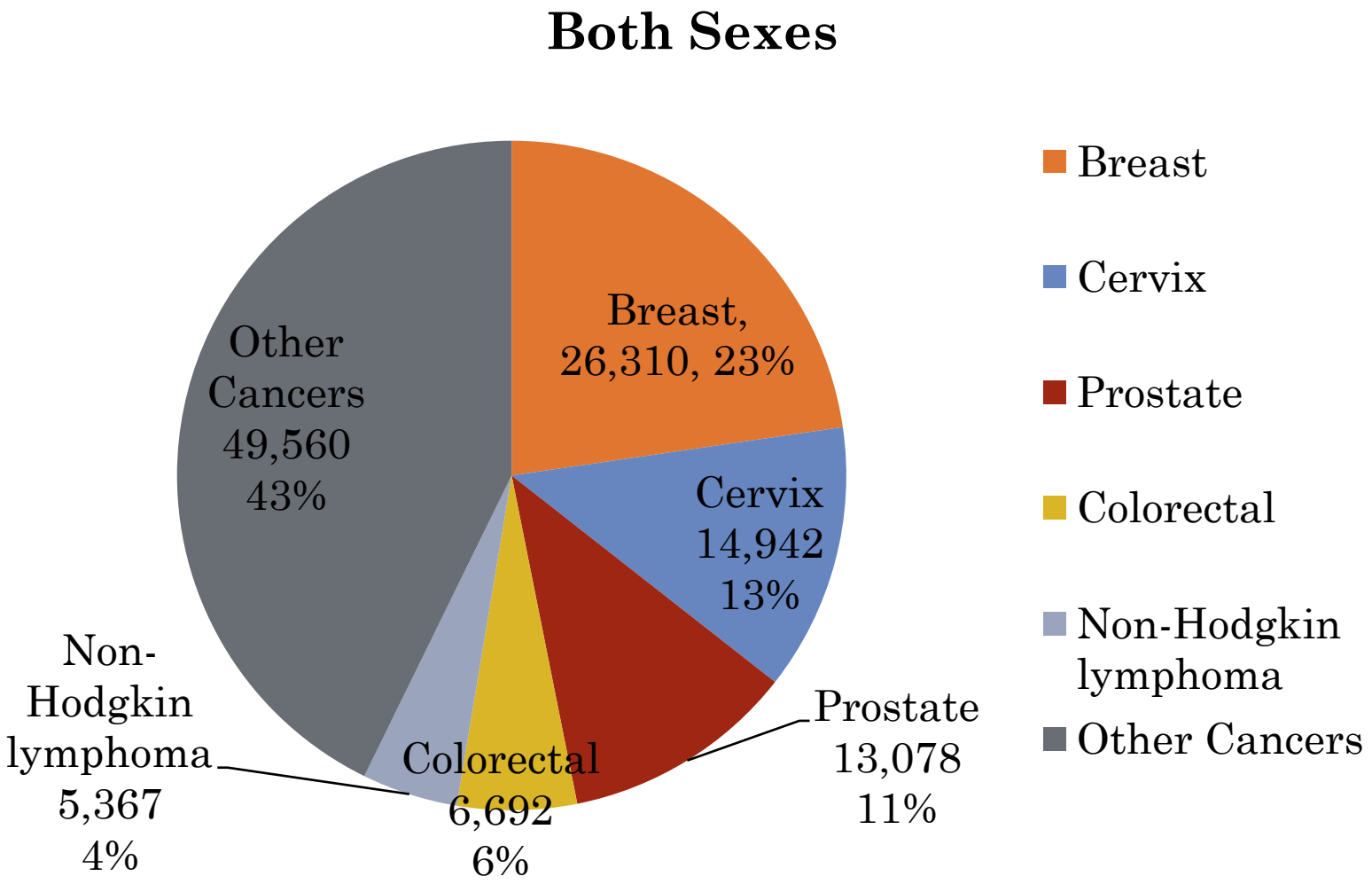
20 MOST AFFECTED COUNTRIES

S/No	Country	Age-Related Standardized rate/100,000
1	Swaziland	75.3
2	Malawi	72.9
3	Zambia	66.4
4	Zimbabwe	62.3
5	Tanzania	59.1
6	Burundi	57.4
7	Uganda	54.8
8	Lesotho	52.1
9	Madagascar	51.6
10	Comoros	50.9
11	Guinea	45.5
12	Burkina Faso	45.1

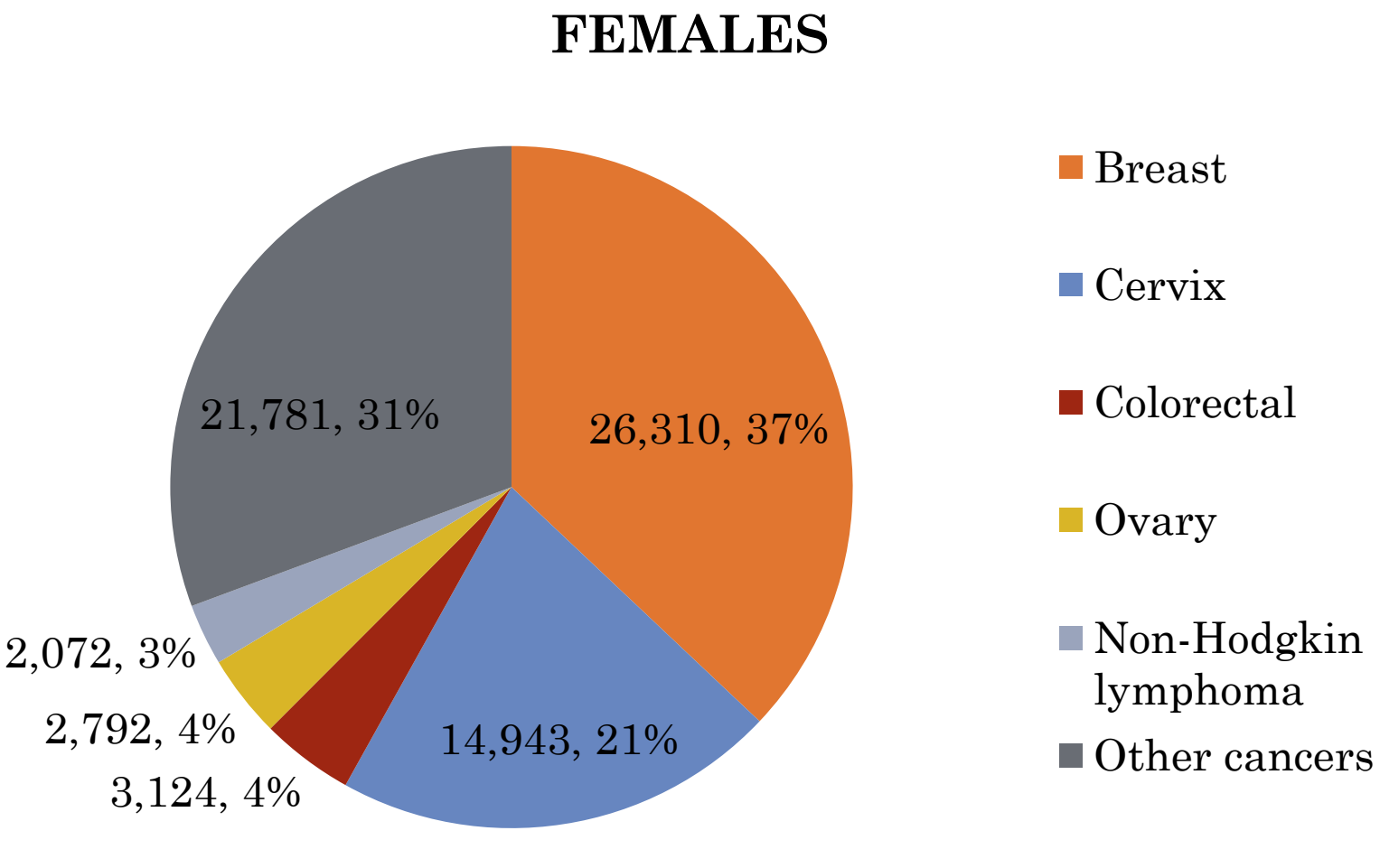
NIGERIA IN PERSPECTIVE

- In Nigeria
- 2nd most common cancer in women
- 14,943 new cases and 10,403 death annually
- Cervical cancer is preventable and curable
- Main aetiological agent is Human Papillomavirus (HPV)
- Vaccine for HPV is available
- Screening for Cervical cancer is readily available
- Early diagnosed Cervical cancer is treatable

INCIDENCE OF CERVICAL CANCER IN NIGERIA



INCIDENCE OF CERVICAL CANCER IN NIGERIA 2



NIGERIA IN PERSPECTIVE 2

- No routine immunization programme for HPV
- Statistics of those immunized not available
- Less than 10% vaccinated
- Poor attitude to prevention
- Less than 10% of all women ever screened for cervical cancer
- Poverty
- High Out-of-pocket health expenditure
- Poor awareness
- Low budgetary allocation to health
- Competing health challenges

PATHO-PHYSIOLOGY

- HPV – aetiological agent
- HPV is the most common sexually transmitted disease and occurs in high percentage of sexually active women
- Risk factors
  – multiple sexual partners or partner with multiple sexual partner
  – early onset of sexual intercourse
  – history of other sexually transmitted disease
  – partner with HPV infection

PATHO-PHYSIOLOGY 2

- Over 170 serotypes of HPV have been isolated
- Serotype 16 is the most carcinogenic
- Serotypes16 and 18 responsible for 70% of all cervical cancers
- High risk HPV (hr HPV) has been isolated in 96.6% of all invasive cervical cancers. This include HPV serotypes 16, 18, 31, 33, 35. 45, 52 and 58
- 90% of HPV infections clear spontaneously
- 95% resolve spontaneously or low grade Squamous intraepithelial lesion (SIL)
- 5% will result in CIN 2 or 3 (CIN 2+)
- 20% 0f CIN 3 will progress to invasive cancer in 5 years. 40% within 30years

HPV PROGRESSION

- Factors influencing progression of HPV

1. Type and duration of HPV infection
2. Immune compromise e.g HIV, Immunocompromised due to organ transplant
3. Diet – Diet rich fruits and vegetables appears to lower risk of progression
4. Environmental factors e.g smoking
5. Oral contraceptives
6. Genetic susceptibility – less than 1% of cervical cancer. Association with single nucleotide polymorphism (Caucasian population) - 2 fold relative risk increase with 1st degree relations or twin.

Primary prevention

- Primary prevention of Cervical Cancer involve education and vaccination
- Education

1. Delay onset of sexual intercourse
2. Safe Sex practices
3. Benefit of immunization

- Vaccination - 3 vaccine types available

1. Bivalent Vaccine – HPV 16 and 18 (Cervarix) – Offer 70 % protection
2. Quadrivalent Vaccine – HPV 6, 11, 16, 18 (Gardasil)
3. Nonavalent Vaccine – HPV 6, 11, 16, 18, 31, 33, 45, 52, 58. (Gardasil-9)
   Offer 87 % protection

CURRENT GUIDELINES ON VACCINATION

- Bivalent and Quadrivalent vaccines licensed in Nigeria
- Focus
  – HPV naive individuals.
  – Young girls age 9 or 10 to 13.
  – For girls < 15 years: 2 doses 6 months apart.
  - For 15 – 26 years: 3 in 6 months
  – Cervarix: 0, 1, 6 months.
  – Gardasil: 0, 2, 6 months.
- No vaccination for pregnant women
- Booster dose is not necessary
- Cervical cancer screening is still necessary

Secondary prevention

- Screening for detection and timely treatment of precancerous lesions
- Methods of screening

1. Cytology
2. Visual Inspection
3. HPV testing

- HPV testing has the highest sensitivity

CYTOLOGY

- Cytology – traditional or Modification
- Traditional (Conventional) Papanicolaou (Pap Smear) – introduced in 1941
- Modification
  - Liquid based – Thin layer Cytology (Thin Prep)
  - Computerized rescreening using neural network technology (Papnet)
- Bethesda 2014 Classification
  – Negative
  – Positive

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CYTOLOGY – ABNORMALITIES

EPITHELIAL CELL ABNORMALITIES		
A. SQUAMOUS CELL		
1	Atypical Squamous cells	• of undetermined significance (ASC-US) • cannot exclude HSIL (ASC-H)
2	Low-grade squamous intraepithelial lesion (LSIL)	• HPV induced changes • Mild dysplasia •CIN 1
3	High-grade squamous intraepithelial lesion (HSIL)	• Moderate and severe dysplasia •Carcinoma Insitu • CIN 2 and CIN 3
4	Squamous cell carcinoma	
B. GLANDULAR CELL		
1	Atypical	Not otherwise specified

VISUAL INSPECTION

- Visual Inspection

i. With Acetic acid (VIA)

ii. 3 – 5 % Acetic acid

iii. Abnormal tissue turns white - Acetowhite reaction (Sharp, distinct, well defined, dense white area)

iv. The reaction results from the coagulation of the abnormal load of protein in the cell by acetic acid making it an opaque and white segment.

v. Acetowhite reaction – VIA positive

VISUAL INSPECTION 2

- Visual inspection

i. With Lugol's iodine (VILI)
ii. Lugol's iodine react with glycogen in normal mature squamous epithelium to turn brown or black
iii. Abnormal epithelium contains little or no glycogen hence turns yellow
iv. Yellow portion on the brown or black cervical epithelium – VILI positive

HPV TESTING

- HPV testing – high sensitivity
- Cervical smear collected
- Polymerase chain reaction (PCR) test
- Genotyping for HPV type
- Home Testing

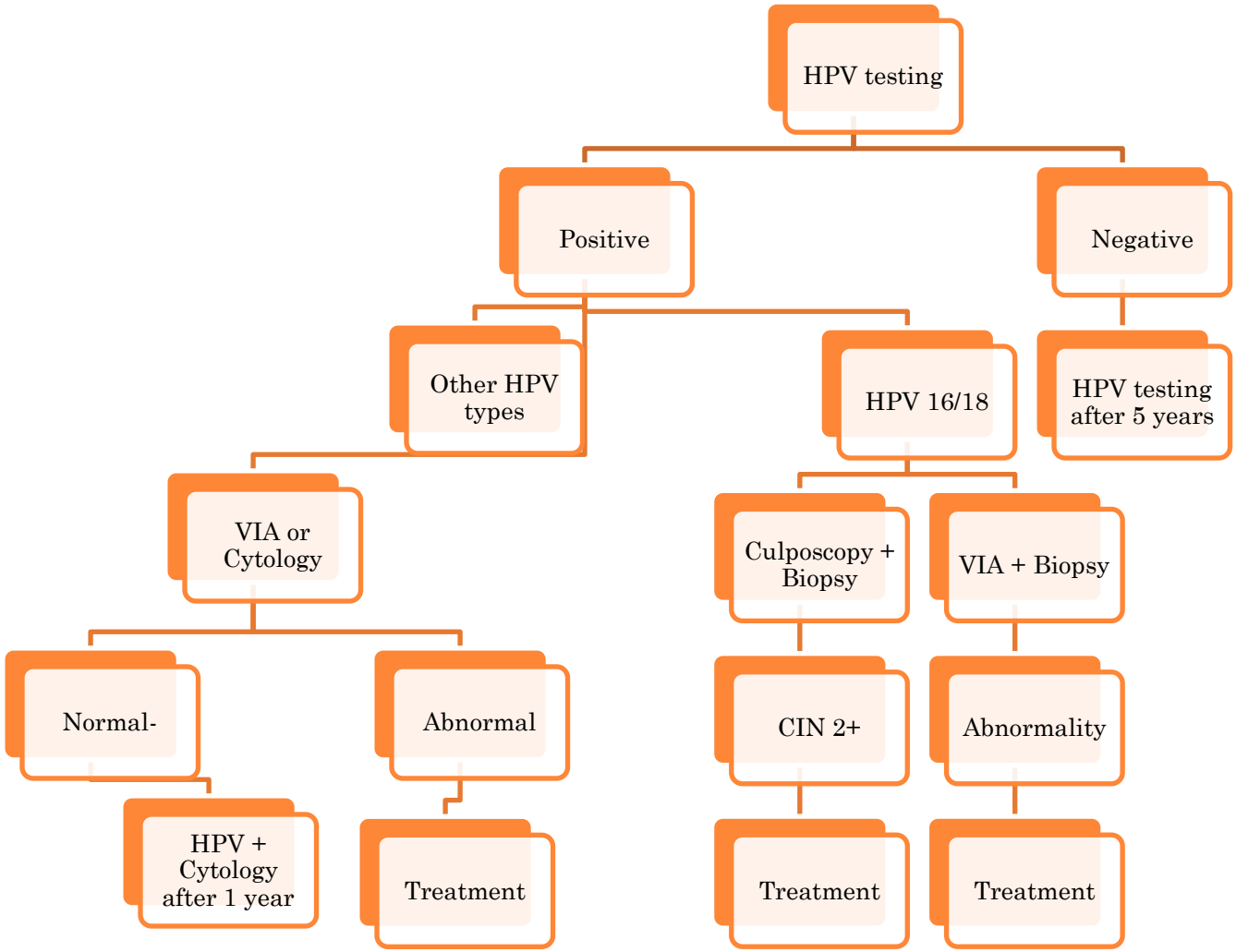
HPV Home Test Kit

Recent guideline on screening

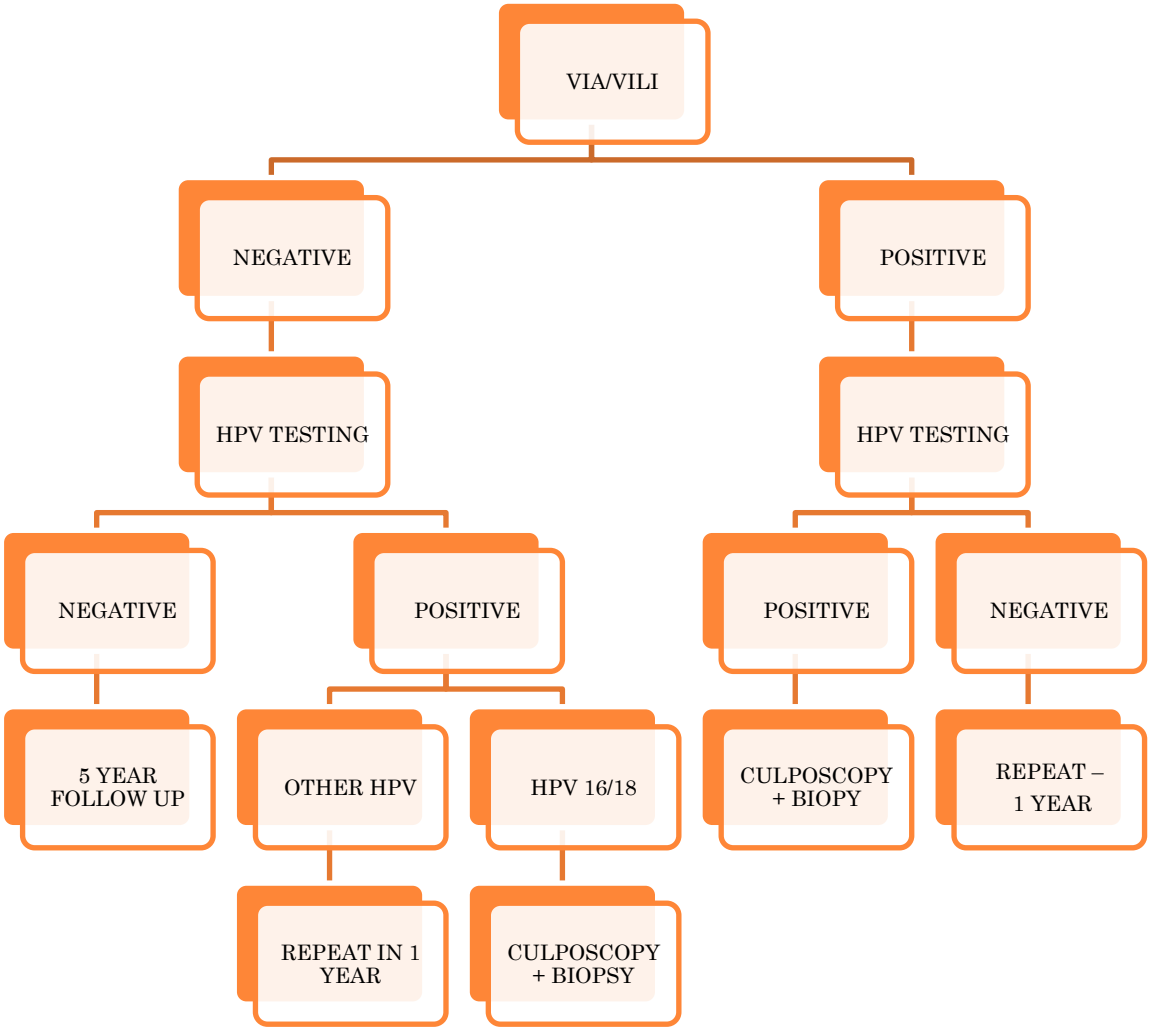
- SOGON Guideline (2015)

1. Target population
   – all women age 25 – 65 years.
   – Women < 25 at high risk of cervical cancer.
2. HPV testing: Primary screening strategy
   - HPV negative for repeat in 5 year
   - HPV positive for follow up protocol
3. Alternative screening path
   - Visual Inspection as Primary test.
   - Refer Positive for HPV testing

SOGON GUIDELINE – ALGORITHM 1



SOGON GUIDELINE – ALGORITHM 2



SOGON GUIDELINE – RECOMMENDATIONS

- Testing to stop at 60 years with previous negative result
- No previous testing – perform screening test ≤ 65years
- Recommended treatment option – Excisional
- Special consideration – HIV Positive patient

- HPV testing every 3 years

WHO GUIDELINE

- WHO GUIDELINE (2013)
- Standard practice
  - Cytology → Positive → Culposcopy + Biopsy → CIN2+ diagnosed histologically → Treat
  - Cytology → Negative → Repeat 3 – 5 Years
  - HPV Testing → Positive → Culposcopy + Biopsy → CIN2+ diagnosed histologically → Treat
  - HPV Testing → Negative → Repeat at least 5 Years

WHO GUIDELINE 2

- WHO GUIDELINE
- ALTERNATIVE PRACTICE
- Screen and treat
- No prior histological diagnosis before treatment
- Treatment provided soon, ideally immediately after a positive screening test
- VIA → Positive → HPV testing → Positive → Treat
- VIA → Positive → HPV testing not available → Treat
- HPV test → Positive → VIA → Treat

WHO GUIDELINE 3

- Recommendation
- Screening priority from age 30 – 49 years
- Screening even once in a lifetime is beneficial
- Screening interval may depend on financial, infrastructural and other resources.
  Ideally, follow up
  - after Cytology or VIA: 3 – 5 years.
  – after HPV testing: at least 5 years
  – HIV positive or Unknown status in area of high HIV endemicity: within 3 years
- Screening should be done as soon as a woman test positive for HIV

WHO GUIDELINE 4

- Consideration for treatment
- Cryotherapy – first choice
- Loop electrosurgical excision procedure (LEEP) – when cryotherapy is not available
- Cold Knife Conization (CKC) – Not recommended

Eligibility for Cryotherapy

- Established by VIA
- The entire lesion is visible
- The squamo-columnar junction is visible
- Lesion does not cover more than 75% of the ectocervix
- The lesion does not extend beyond the cryoprobe being used

ACOG GUIDELINE

- ACOG (USPSTF) GUIGELINE 2018

Patient Status	Recommended screening	Comment
< 21 years	No screening	Sexual history not a consideration
21 – 29 years	Cytology alone every 3 years	
30 – 65 years	HPV + Cytology (Co-testing) every 5 years – preferred Cytology alone every 3 years - acceptable	
> 65 years	Screening can be	History of CIN

DIAGNOSIS

- Early diagnosis
- Signs and symptoms de-emphasized
- Histological diagnosis

STAGING – FIGO CLASSIFICATION

STAGE	Surgico – Pathological Findings
I	Cervical cancer confined to the cervix (disregard extension to the corpus)
IA	Invasive cancer diagnosed only by microscopy; stromal invasion with a maximum depth of <5.0mm, measured from the base of the epithelium; vascular space involvement, venous or lymphatics , does not affect classification.
IA1	Measured stromal invasion <3.0mm in depth
IA2	Measured stromal invasion ≥ 3.0 mm and < 5.0 mm
IB	Invasive carcinoma with measured deepest invasion ≥ 5 mm (Greater than stage 1A), lesion limited to the cervix
IB1	Invasive carcinoma with ≥ 5 mm depth of stromal invasion and < 2 cm to in greatest dimension
IB2	Invasive carcinoma, 2cm to < 4cm in greatest dimension

TREATMENT

- Based on staging
- Stage IA1
  – Without lymphovascular space invasion
  - Fertility Sparing: Cone biopsy
  - Otherwise: Simple hysterectomy
  – With lymphovascular space invasion
  - Cone biopsy or hysterectomy with lymphadinectomy
  - Post operative pelvic irradiation (with or without Cisplatin chemotherapy)

TREATMENT 2

- Stage IA2
  - Fertility Sparing: Radical trachelectomy and pelvic lymph node dissection
  - Otherwise: Modified radical hysterectomy and bilateral lymph node dissection
  - Pelvic irradiation
- Stage IB and IIA
- Fertility Sparing: Radical trachelectomy and pelvic lymph node dissection – only for IB1with tumour $\leq$ 2cm ($\pm$ Chemotherapy)
- Stage IB1 or IIA1: Radical Hysterectomy and bilateral lymph node dissection

TREATMENT 3

- Stage IB2 or IIA2: Concurrent Chemoradiation is preferred
- Advanced Disease IIB – IVA
  - Concurrent Chemoradiation and brachytherapy (Standard of care)
  - Cisplatin based chemotherapy regimen
- Stage IVB or recurrent tumour
  - Chemotherapy (Cisplatin or Carboplatin)
  - Palliative radiotherapy
    - Concept of palliative care

PROGNOSIS

- Stage I – Greater than 90%
- Stage II – 60 to 80%
- Stage III – Approximately 50%
- Stage IV – Less than 30%

CONCLUSION

- Cervical cancer is preventable and treatable
- Routine HPV immunization has significantly reduced incidence of cervical cancer and can achieve same if implemented in Nigeria
- Cervical screening is critical both for prevention and down staging of cervical cancer
- Cervical cancer with available cost effective interventions for prevention should no longer kill our women if we care enough to act now.

THANK YOU

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