WHO's comprehensive global guidance on cervical cancer control: new evidence, guidance and fundamentals for country-level success

Tuesday, January 20, 2015

Webinar panel

• **Dr. Debbie Saslow**, PhD, Director, Breast and Gynecologic Cancer, American Cancer Society (Moderator)

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• **Dr. Vivien Tsu**, PhD, MPH, Director, Director of the Cervical Cancer Prevention project and Associate Director, Reproductive Health at PATH

• **Dr. Mike Chirenje**, MD, FRCOG, Professor in the Department of Obstetrics and Gynecology, College of Health Sciences, University of Zimbabwe

• **Professor Lynette Denny**, PhD, MB ChB, MMed, FCOG, Chair and Professor of Obstetrics & Gynaecology, Groote Schuur Hospital, South Africa

• **Dr. Partha Basu**, MD, DNB, Associate Professor and Head, Department of Gynecological Oncology at Chittaranjan National Cancer Institute, India
New WHO guidance to prevent cervical cancer

Dr Nathalie Broutet
Reproductive Health and Research Department

January 20, 2015
Cervical Cancer Action webinar
What is a WHO guideline?

"Guidelines are recommendations intended to assist providers and recipients of health care and other stakeholders to make informed decisions. Recommendations may relate to clinical interventions, public health activities, or government policies."

WHO 2003, 2007
Recommendations and evidence

- Recommendations are judgements
  - Quality of evidence
  - Trade off between benefits and harms
  - Costs
  - Values and preferences
WHO Guidelines Review Committee

• Established in 2007 to develop and implement procedures to ensure that WHO guidelines are:
  • consistent with internationally accepted best practices
  • appropriately based on evidence.
  • transparent
• Members from headquarters and all 6 regions
• Decisions are made by consensus
Guideline development at WHO

1. Scoping the document
2. Setting up Guideline Development Group and External Review Group
3. Disclosure and management of secondary interests
4. Formulation of the questions (PICO) and choice of the relevant outcomes
5. Evidence retrieval, assessment and synthesis (systematic review(s))
6. Formulation of the recommendations (GRADE)
   - Including explicit consideration of:
     - Benefits and harms
     - Values and preferences
     - Resource use
7. Dissemination, implementation (adaptation)
8. Evaluation of impact
9. Plan for updating

Approval of guideline development proposal
- After completion of 1 and 2
- With draft of 4
- With plans for 3, 5-9

Approval of final guideline
- After completion of 6
- With plans for 7-9
Evidence not just about balance of benefits and harms
WHO Comprehensive approach: Programmatic interventions over the life course to prevent HPV infection and cervical cancer

**PRIMARY PREVENTION**

Girls 9-13 years
- HPV vaccination

From 10 years old and onward

Health education and services, for example:
- Sexual health education tailored to the age group
- Providing contraceptive counseling and services including condoms
- Prevent tobacco use and support cessation*

**SECONDARY PREVENTION**

Women > 30 years of age
- Screening and treatment
  - “screen and treat” with low cost technology VIA followed by cryotherapy
  - HPV testing for high risk HPV types (e.g. types 16, 18 and others)

**TERTIARY PREVENTION**

All women as needed
- Treatment of invasive cancer at any age – Palliative care
  - Ablative surgery
  - Radiotherapy
  - Chemotherapy

*WHO Comprehensive approach: Programmatic interventions over the life course to prevent HPV infection and cervical cancer

[Graph showing the progression of HPV infection, precancer, and cancer with age]
So, 2014: the new C4-GEP

- Chapter 1: Epi, Nat Hist, AnaPath
- Chapter 2: Programmatic issues
- Chapter 3: Heath Education
- Chapter 4: HPV Vaccination
- Chapter 5: Screen and Treat strat.
- Chapter 6: Diagnosis and Tx of cancer
- Chapter 7: Palliative care
Three key new issues

- Switch in communications paradigm
- Recommendation to vaccinate 9 to 13 year old girls with two doses of HPV vaccine.
- Recommendation on the use of HPV tests to screen women for cervical cancer prevention.
Comprehensive approach to Cervical Cancer Prevention and Control

http://www.who.int/reproductivehealth/topics/cancers/en/index.html
The issue

Overcoming the transfer and application of knowledge gap

To take evidence into practice
http://www.who.int/reproductivehealth/topics/cancers/en/
Primary prevention of cervical cancer through HPV vaccination

Using the new WHO guidelines

Vivien Tsu, PhD, MPH
CCA Webinar
January 20, 2015
Useful background information on current HPV vaccines

- 2 HPV types (16 and 18) account for the majority of cervical cancer cases in all regions (~70%).
- 2 vaccines are currently licensed in >120 countries and pre-qualified by WHO (Cervarix and Gardasil).
- Both vaccines have excellent safety records over 6+ years.
- Important to vaccinate girls (aged 9–13 years) before initiation of sexual activities, because vaccines prevent but do not treat infection.
- Screening still needed, since not all cancer-causing HPV types are included in the vaccines.
WHO recommendations for introduction of HPV vaccine

- Recommendations come from the WHO Strategic Advisory Group of Experts (SAGE) on immunization; 2009 position paper and 2014 revision.
- Countries should introduce HPV vaccination when:
  - Cervical cancer or other HPV-related diseases are a public health problem.
  - Vaccine introduction is programmatically feasible.
  - Sustainable funding is available.
  - Cost-effectiveness has been considered.
- Vaccination should be part of comprehensive strategy.
- Recommended for girls aged 9–13 years; can use 2-dose schedule if started before age 15 (with 6-month interval between doses).
Vaccine delivery

- Community volunteers and health care providers have important roles to play:
  - Educating community, countering rumors and misinformation, raising awareness.
  - Organizing and conducting vaccination sessions.
  - Maintaining records of girls vaccinated.
- If school-based, teachers and school officials also play critical roles of education, identification of eligible girls, logistics, and (sometimes) record-keeping.
What is known so far from vaccine experience and continuing research?

• Chapter summarizes current knowledge on vaccine effectiveness and safety and identifies remaining gaps in knowledge.
• Modeling currently shows that vaccinating boys is less cost-effective than using those resources to reach more girls.
• Tools and methods are available for monitoring coverage and adverse events.
Vaccine delivery strategies

• Basically 2 types of strategies: facility-based or outreach, either can be continuous or pulsed (set times for each dose).

• School-based is example of outreach, requires coordination with school schedule, mobilization of transport, and (sometimes) travel allowances.

• Often need a combination of strategies to cover school and out-of-school girls.

• Strategies should be tailored to local conditions.
Experience in Gavi-eligible countries so far

- Gavi, the Vaccine Alliance, provides support for both demonstration projects (as opportunities to learn and plan) and national introductions of HPV vaccine.
- Since Gavi began offering HPV vaccine support in 2012, 29 of 47 countries have applied; 24 have been approved (as of Oct 2014).
- 3 are approved for national introductions (Rwanda, Uganda, and Uzbekistan).
- 21 are approved for 2-year demonstration projects—usually in 1 or 2 districts, mostly 10- or 11-year-old girls, multiple strategies being tried; evaluation of coverage, cost, and feasibility required after year 1.
Global introduction of HPV vaccines

Global Progress in HPV vaccine introduction

Source: Cervical Cancer Action

September 2014
Many resources available

- Practical experience guides for implementation and evaluation
- WHO HPV vaccine Portal
  http://www.who.int/immunization/hpv/en/
- On-line library – www.rho.org
Conclusions

• HPV vaccination is now recognized as a critical component in any comprehensive strategy to prevent cervical cancer.

• New WHO guidelines provide all the essential information needed for country health planners, managers, and advocates.

• Need to move ahead now with implementation to protect our coming generations of girls and women.
Thank You

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2014 C4-GEP Guidance: Secondary Prevention through screening and treatment of cervical pre-cancer

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Key Points from Chapter 5 in the WHO C4- GEP

- I will be presenting a summary of KEY POINTS from chapter 5 of the newly launched C4-GEP
- This new chapter 5 consolidates screening for cervical pre-cancer and its treatment into one chapter as revision and update from the 2006 edition
- To support this evidence that WHO endorses, I will briefly discuss current recommendations for screening and treatment strategies
Cervical cancer takes 10-20 yrs. to manifest therefore provides us opportunity to screen and detect pre-cancer cells.

Effective treatment modalities should be offered to all women identified with cervical pre-cancer.

A program that directly links cervical screening to treatment of pre-cancer cells has maximum observed reduction to cervical cancer cases.
Cervical pre-cancer screening is an intervention that targets healthy women, without symptoms.

Maximum impact is screening women 30-50 yrs.

Molecular testing for HPV DNA high risk types, Visual Inspection With Acetic Acid (VIA), Cervical Cytology testing (Pap smears) are all recommended screening tests.

A reliable screening test must be accurate, reproducible, affordable, available, acceptable, safe, sustainable.
Molecular testing for high risk HPV DNA types

- HPV DNA testing should be offered to women above 30 yrs. to avoid detection of transient HPV infection
- HPV test must be standardized and clinically validated
- Women who test HPV positive can be offered immediate treatment or undergo a second screening test such as VIA to reduce number of women who may receive unnecessary treatment
- Women with test negative results can be invited for repeat HPV DNA screening after 5 yrs.
Visual Inspection with Acetic Acid (VIA)

- VIA testing is detection of early cervical cell changes that occurs after application of dilute (3-5%) acetic acid to cervix (“aceto-white changes”)
- VIA is applicable to women <50yrs (before menopause) when squamo-columnar junction is still visible
- A woman with VIA positive test can be offered immediate treatment
- A woman with a negative VIA test result should be offered repeat testing after 3-5 yrs.
- VIA is a subjective test, requires training and refresher courses
- VIA test does not require laboratory services, can be implemented in resource limited settings
Cervical Cytology Testing (Pap Smears)

- Cytology based screening has been successfully implemented in high resource settings past 6 decades.
- Involves taking a sample of cells from transformation zone of cervix that are fixed on a slide (Pap smear) or transported in a liquid medium to a laboratory for cells to be examined under a microscope by cytotechnologist.
- Women must be scheduled for follow up appointment to receive test results.
- If test is negative, repeat after 3-5 yrs, if positive woman is referred for further evaluation with colposcopy.
Treatment for cervical pre-cancer

- Effective treatment modalities are cornerstone for successful cervical pre-cancer screening program.
- Cryotherapy treats cervical pre-cancer cells by freezing (an ablative method) the identified abnormal cells commonly after VIA screen test positive test ("aceto-white lesion").
- Cryotherapy should only be applied if entire lesion is visible and invasive cancer is not suspected.
- Cryotherapy does not require electricity or laboratory facility, is suitable low resource settings.
Loop electrosurgical excision procedure (LEEP) and Cold Knife Conization (CKC)

- LEEP is removal of abnormal areas of cervix (entire transformation zone) using a loop made up of thin wire powered by electro generator unit.
- Procedure is performed under local anesthesia and removed specimen is transported to laboratory for histological analysis.
- CKC is removal of a cone from cervix, done under general or regional anaesthesia, specimen is transported to laboratory for histological analysis.
- The caregiver performing CKC must be surgically skilled.
Introducing screening and treatment programs at country level

- Accurate country specific data on cervical pre-cancer screening with population coverage is scanty.
- There is a wide variation in crude population coverage from less than 1% in many low resourced countries to as much as 45% in middle income countries.
- In a substantial number of low resourced countries, many women (30—50yrs) have never had pelvic exam.
- In the past decade, many low resourced and middle income countries have introduced cervical pre-cancer screening starting in mainly urban population before scaling up.
Introduction of cervical pre-cancer screening programs in developing countries has been challenging from the 1960’s

Zambia successfully introduced low cost nurse driven VIA and cryotherapy in its public sector clinics co-housed with HIV/AIDS programs

CCPZ started with 2 public clinics in Lusaka, now operates in 33 Gvt. facilities across 10 provinces

Between 2006-2013, screened 102,942 F, 71.7% in the target 25-49 age group, 28% HIV positive
Cervical pre-cancer burden was demonstrated to be high with a 20%(20,401 F) VIA positive rate. 56% (11,508 F) of VIA screen positive received cryotherapy, 44%(8,911) were ineligible for cryotherapy and referred to University Hospital for LEEP and biopsy for suspected cancer cases. Among the referred group, 710 women who confirmed histologically positive for ICC. A big congrats and thank you to Professor Groesbeck Parharm and his team who have established a highly successful screening program tightly linked to a treatment access.
Diagnosis, treatment and palliative care of cervical cancer

Lynette Denny
Groote Schuur Hospital/University of Cape Town
Diagnosis and treatment of cervical cancer

- Women diagnosed with early stage invasive cervical cancer can be cured with effective therapy
- Health workers at all levels of care should be able to recognise and promptly manage the symptoms and signs of cancer
- The definitive diagnosis of invasive cervical cancer (ICC) is made by histopathological examination of a biopsy
- ICC is best treated in tertiary hospitals or regional cancer centres
- Treatment modalities include:
  - Surgery – conservative or radical
  - Chemotherapy
  - Radiation
  - Or a combination of the above
Diagnosis and treatment of cervical cancer

- Patients should be counselled about possible side-effects of treatment of ICC which include:
  - Infertility
  - Onset of menopause
  - Discomfort or pain with sexual intercourse
  - Inflammation of the bowels or bladder
- Long term follow up is essential as even after treatment cancer can recur and there are often still options for either curative or palliative treatment
- There should be excellent communication between the tertiary and primary care institutions on the nature of the post-treatment follow-up and clear instructions as to when to refer the patient back to the tertiary institution
- Untreated ICC is nearly always fatal
Diagnosis

- May be detected through screening – microinvasive (early) disease
- Most women present with symptoms related to the local growth of the tumor which include:
  - Abnormal bleeding (irregular, post-coital, postmenopausal, prolonged, heavy)
  - Associated with offensive vaginal discharge which if often offensive and profuse
  - Lower abdominal pain
Diagnosis

• More advanced disease:
  • Symptoms related to urinary tract and/or rectum, including malignant fistulae
  • Pain
    • pelvic
    • back or
    • related to metastases e.g. to bone, liver or lung
  • Weight loss
  • Lumps in areas such as the neck and the groins
  • Shortness of breath due to anaemia or metastases
Diagnosis

• Mandatory to visualise the cervix in any woman complaining of symptoms related to ano-genital tract
• If cervix is abnormal, histological sample should be obtained by performing punch biopsy
  • It is mandatory to confirm diagnosis as cervical cancer can mimic other conditions such as TB of the cervix, schistosomiasis, herpetic infection, or other cancers that have metastasised to cervix e.g. lymphoma
• If patient needs referral to higher level of care for diagnosis and management, interim treatment should be instituted after careful consultation with patient e.g.
  • Antibiotics, analgesia, iron and folate if anaemic, tranexamic acid if bleeding significant
• Referral to next level of care should be considered **urgent**
Treatment

• According to stage
• Early stage disease (cancer is confined to cervix and less than 4 cms in diameter) treated with either conservative or radical surgery, with or without lymph node dissection
• If no surgical facilities available then primary chemoradiation
• For more advanced disease, primary chemoradiation is treatment of choice
• Staging is clinical by performing pelvi-rectal examination and determining the degree of local spread
• Complemented by supporting investigations which include;
  • CXR, U/S ureters and liver, renal and liver tests, Blood Count, HIV and VDRL
  • Other investigations should be tailored to patient symptoms e.g. bone scans or scans other areas of the body
Palliative care

- Palliative care is an essential element of cervical cancer control
- Should improve the quality of life of patients and their families facing a life-threatening illness
- Consists of the prevention and relief of suffering by means of early identification, assessment and treatment of pain and other forms of physical, psychosocial and spiritual suffering
- Should enable dignity and peace during the difficult and final phases of life
- Best provided by multi-disciplinary teams which involve the patient, the family and close supporters, community health workers and if available, special palliative care workers and health care providers at all levels of care
Palliative care

• Palliative implementation requires access to appropriate medication (e.g. analgesia) as well as educated patients, communities and health care workers
• Most symptoms at the end of life such as pain can be effectively controlled using a combination of medical and non-medical interventions
• It should be possible for nurses to prescribe opioid analgesia according to national norms, rules and regulations
• Quality of palliative care requires adequate training of health care and community health care workers on an ongoing basis
• Access to all necessary medicines, equipment and supplies is critical for symptom management both at the health care facility and the patient’s home
Palliative care

- Role for anti-cancer therapies e.g.
  - Chemotherapy for multiple metastases may improve quality of life
  - Radiation to localised metastases
  - Urinary or bowel diversion surgery for fistulae
- Careful assessment of patient’s symptoms and what her priorities are – make no assumptions
- Impeccable understanding of the cause and source of pain and how to treat appropriately
- Treat patient holistically with equal attention to physical, psychological, emotional, spiritual needs and concerns
- Main purpose of palliative care is to provide Quality, not Quantity of Life
ADAPTING WHO GUIDANCE (2ND ED) INTO NATIONAL CERVICAL CANCER CONTROL PROGRAMS

Comprehensive Cervical Cancer Control
A guide to essential practice
Second edition

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Adaptation & Implementation of New Guidelines

- WHO Guidance is a generic global document to cover all country situations
- Needs & capabilities vary between and within the countries
- The guideline has to be adapted to the country’s needs, circumstances & context
- This may require updating of existing national guidelines & other tools
Process of Introduction of New Guidance

Plan & Advocate

Analyze Situation

Adapt to Local Situation

Plan Implementation Strategy

Do Pilot Test

Advocate & Scale up

Comprehensive Cervical Cancer Control

Adapted from: Introducing WHO’s sexual and reproductive health guidelines and tools into national programs
Planning & Advocacy

• Identify interventions that are feasible and sustainable
• Determine how best they can be introduced & implemented
• Check for the key differences between the new & existing (if any) guidelines
• Approach relevant health authority who can involve more stakeholders
• Advocate for political & financial commitments
Situation Analysis to Collect Information on -

- Existing policies & guidelines
- Capabilities of health systems to provide service related to screening & vaccination
- Availability of trained human resources & possible options for their training
- Attitude & practices of clients & providers
- Supervisory mechanisms & tools
Adaption to Local Situation

- Review Guidance Document & identify the interventions applicable
- Modify based on:
  - Epidemiological context
  - Health system context
  - Legal & policy issues
  - Available resources
- Introduce the locally adapted guidelines in training programs, medical school curricula
Designing Implementation Strategy

• Plan logistics of service delivery & referrals
• Develop strategies to train all providers & modify training materials if required
• Make provision for adequate staff & funding
• Plan community mobilization strategies
• Select process & outcome indicators for different levels of care
• Plan quality assurance & supportive supervision
Planning Cervical Cancer Screening Program

- **Input**
  - Protocol
  - Finance
  - Facilities
  - Human Resources
  - BCC

- **Process**
  - Community Mobilization
  - Screening
  - Diagnosis/Treatment
  - Follow up

- **Output**
  - Early Detection & Treatment

- **Outcome**
  - Reduction in Mortality

**FEEDBACK**
Pilot testing & evaluation to Know

- Are the interventions based on the guidelines -
  - Feasible to implement?
  - Effective?
- Is the training effective?
- How to do supportive supervision?
- Are the interventions acceptable?
- What additional inputs are required to scale up?
Stepwise implementation

Core Interventions

Expanded Interventions

Desirable Interventions
Implementing new WHO Cervical Cancer Program Guidance in your Country

In December 2014 the World Health Organization launched an updated edition of its popular 2006 publication “Comprehensive Cervical Cancer Control: A Guide to Essential Practice.” Also known as the "Pink Book," the new, 364-page volume explains recent technical and strategic developments for improving access to cervical cancer prevention and control services, and it identifies key opportunities throughout a woman's life when interventions can be put into action. The guide is available as a free download—see the Resources section at the end of this paper. French and Spanish versions of the book will be produced in 2015.

Tailoring strategies for specific situations

The published guidelines are global in nature and discuss a variety of cervical cancer prevention interventions that can be implemented in countries. Some of the tools are more appropriate than others for low-resource countries, so effective use of the guidelines should be tailored to specific national, and sub-national, needs and capabilities. This requires a thoughtful process of analyzing the local situation and selecting relevant solutions, using local evidence whenever possible.

To strengthen health programs and to determine which strategies make the most sense in your country, it is a good idea to involve a variety of stakeholder groups in the decision-making process, including relevant Ministry of Health staff, private providers such as NGO clinics, professional societies, women's groups, cancer and reproductive health advocates, and others. And even though many interventions may be introduced as pilots and in limited geographic areas, scale-up and sustainability should be planned from the beginning. You may wish to review the WHO strategic approach document listed in Resources.