Cervical Cancer Prevention
South East Asia Region of WHO

Prof. Surendra Shastri MD
Head, WHO Collaborating Centre for Cancer Prevention, Screening and Early Detection
Department of Preventive Oncology
Tata Memorial Centre, Mumbai
India
shastri@vsnl.com
Cervical Cancer Burden

- Cervical cancer is the third most common cancer in women worldwide with an estimated 530,000 new cases and 275,000 deaths each year.

- Over 85% of the global burden occurs in developing countries, where it accounts for 13% of all female cancers.

- SEAR records 188,000 new cases and 102,000 deaths from cervical cancer each year contributing to over 35% of the global burden of the disease.
Cancer incidence and mortality among women in SEAR
Estimated age-standardised incidence rate per 100,000
Cervix uteri, all ages

International Agency for Research on Cancer
Organization

< 7.0  < 12.9  < 20.2  < 29.6  < 56.3

GLOBOCAN 2008 (IARC) - 12.6.2013
Estimated age-standardised incidence rate per 100,000
Cervix uteri, all ages

GLOBOCAN 2008 (IARC) - 12.6.2013
Estimated age-standardised mortality rate per 100,000
Cervix uteri, all ages

GLOBOCAN 2008 (IARC) - 12.6.2013
Estimated age-standardised mortality rate per 100,000
Cervix uteri, all ages
Cervical cancer Incidence and mortality in Asia

Cervix uteri, all ages

ASR (W) per 100,000

Nepal, Bangladesh, Mongolia, Cambodia, India, Kyrgyzstan, Myanmar, Thailand, Lao PDR, Bhutan, Pakistan, Kazakhstan, Malaysia, Armenia, Maldives, Indonesia, Sri Lanka, Philippines, Viet Nam, Timor Leste

Incidence
Mortality

GLOBOCAN 2008 (IARC) (12.6.2013)
No cervical cancer screening programmes

Pap smear screening is not feasible

- Inadequate infrastructure
- Lack of trained human resource
- Logistic difficulties
- Relatively high cost


Presented by: Surendra Shastri MD
Pap smear (conventional cytology)

- On the other hand, cervical cancer is the most preventable cancer and large population-based cytology (Pap smear) screening programmes have been in place for several years in Nordic countries, UK, USA, Australia and New Zealand leading to a drastic reduction in cervical cancer incidence and mortality.
Cancer incidence trends in NORDIC countries
Cervical cancer incidence trends in a few other European countries.
Pap smear

- Although screening using the Pap smear has never been rigorously tested in a randomized clinical trial in developed countries, the marked differences in the incidence and mortality figures for cervical cancer before and after the introduction of screening has been interpreted as “robust” evidence favoring the efficacy of these screening programmes.

- Observed that for the large population of India the infrastructure and resources do not permit Pap smear-based national screening programmes, and alternative strategies that are feasible and scientifically valid should be identified.
Pap smear

- It is however quite clear that from the perspective of public health the success of a cytology screening programme is strongly influenced by the percentage coverage of “at-risk” women, the quality of the infrastructure for screening, and compliance with regular follow-up. In LMICs however, organization of such systematic screening programmes is not feasible for economic and socio-demographic reasons.

- Cytology screening has failed to significantly reduce the cervical cancer burden in the Latin American countries due to a combination of several factors including poor coverage of at-risk women, suboptimal follow-up/treatment of screen-positive women, inadequate infrastructure and quality assurance measures.
An expert committee constituted by the Government of India, in 2006, to develop national guidelines for cervical cancer screening in India observed that for the large population of India the infrastructure and resources do not permit Pap smear-based national screening programmes, and alternative strategies that are feasible and scientifically valid should be identified.

A large cluster randomized trial in rural India reported that HPV testing alone was associated with a significant reduction in the numbers of advanced cervical cancers and deaths from cervical cancer. There was no reduction in cervical cancer mortality in the group undergoing screening by cytology despite the strict quality control and follow up procedures adopted in the study. The results also suggested that VIA was more sensitive, slightly less specific and significantly less costly than Pap smear.
Visual Inspection with Acetic Acid (VIA)

- Simple visual test, does not require laboratory
- Results available immediately
- Paramedical workers can be trained in 4 weeks

VIA Chart developed by IARC

VIA Negative

- Acetowhite areas far away from the TZ
- Faint acetowhite areas without a sharp outline
- Streak-like acetowhitening
- Line-like acetowhitening
- Dot-like pale areas in the endocervix

VIA Positive

Thick well-defined acetowhite areas, near the Transformation Zone (TZ) either on the endocervix or ectocervix (or both) are VIA positive

Presented by: Surendra Shastri MD
Visual inspection of the cervix after application of acetic acid has emerged as the optimal screening tool for LMICs, since it is economical and provides immediate results.

The test characteristics of VIA have been evaluated in several cross-sectional studies in LMICs and the results of these studies strongly suggest that VIA screening would be a useful alternative to conventional cytology.

The pooled estimates of VIA sensitivity to detect high-grade CIN vary from 62-80% and specificity from 77-84%.
VIA

- A large cluster randomized trial in Southern India, where VIA was performed by trained nurses, showed that a single round of screening with VIA reduces cervical cancer incidence and mortality by 25% and 35% respectively.

- Another large cluster randomized study, from urban low socio-economic populations in Western India, recently reported that four rounds of biennial VIA screening performed by trained primary health workers reduced cervical cancer mortality by a significant 31%. The study had an inter-observer variability (kappa) coefficient of 0.84 between the primary health workers and an expert. This study also reported an almost zero over-diagnosis rate, which is very crucial for overburdened public health systems in LMICs. (ASCO 2013, Plenary Abstract No. 2).
Cost effectiveness studies based on data from India, Kenya, Peru, South Africa, and Thailand indicate that the most cost-effective strategies for cervical screening are those approaches requiring the fewest visits, leading to improved follow-up testing and treatment.

The analyses reports that screening women once in their lifetime, at the age of 35 years, with a one- or two-visit screening strategy involving VIA or HPV testing reduced the lifetime risk of cancer by approximately 25–36%, and costs less than 500 dollars per year of life saved.
HPV testing

- HPV causality for cervical cancer is now firmly established and is considered a necessary cause of the disease. HPV 16 and 18 account for 70% of cervical cancer cases.

- All reviews of the HPV-based screening have shown a significantly improved sensitivity (by 30-35%) and a slightly reduced specificity (by 8-12%) compared to conventional cytology.

- The large cluster randomized trial from rural India showed that a single round of HPV screening can reduce mortality from cervical cancer when compared to controls that received only health education. Mortality reduction was not seen in the groups that received one round of cytology or one round of VIA.
HPV testing

- Similar results were reported by a large trial in Italy, where the first screening round identified almost double the number of CIN 2+ in the HPV arm as compared to the cytology arm, with an almost equal number of invasive cancers in both arms. In the second screening round (at 3-year interval), the number of CIN 2+ in the HPV arm was significantly less as compared to the cytology arm. In the second round the cytology arm had incident cases of invasive cancers, while the HPV arm showed no incident cases.

- Studies suggest that when women over 30 years are offered HPV-based screening, there is minimal over-diagnosis and that HPV screening is useful even when carried out less frequently.
HPV testing

- Early results from E6/E7 screening (RNA test) and triage studies have shown a further gain (over HPV DNA test using Hybrid Capture II) of 5-6% in specificity for CIN 2+ and CIN 3+ at same levels of sensitivity. Both assays showed 20% superiority compared to liquid-based cytology.

- A more recent entry in cervical cancer screening tool is the “Care HPV” test. This is a HPV DNA test adapted for use in LMICs for primary screening and triage. Care HPV has the benefits of low cost, simple technology and short reporting period that allows for strategies incorporating the see-and-treat approach.
HPV Vaccine

- Currently two HPV vaccines are commercially available: Quadrivalent (HPV 16,18,6 and 11) vaccine and Bivalent (HPV 16 and 18) vaccine.

- The results of Phase III clinical trials are now available and these two vaccines are now licensed in some 120 countries. Many HICs (High Income Countries) have introduced HPV vaccines into routine vaccination programs.

- These two vaccines have so far shown high efficacy with reference to the predefined end point lesions (HPV 16 or 18-related CIN 2 or more, CIN 2+), adequate safety and tolerability, high immunogenicity, long-term protection (currently 7-8 years) and strong indications of its ability to induce immune memory.
HPV Vaccine

- None of the vaccines has shown therapeutic activity.

- Very high coverage rates (65-70%) are seen in Australia and in UK.

- The limitations of current vaccines i.e. the lack of therapeutic effect and the limited impact of cross-protection effect requires the continuation of screening programs in the vaccinated women. The cost of the vaccine is very high and is currently unaffordable in LMICs.
Cervical cancer prevention strategy for SEAR

Screening
- Primary screening with VIA among women aged 35-64 years, 2-3 times.
- Triage with HPV DNA, Pap smear, colposcopy.
- Treat CIN 2 and above with: Cryotherapy, LEEP, Conisation, Hysterectomy.

Vaccine
- Pilot studies on safety and efficacy of different dosage schedules in girls aged 9-15 years, before introducing countrywide vaccination programmes.

Indicators: Percentage coverage of eligible women/ girls (at least 70%)

Targets: Reduction of cervical cancer mortality by 30% by 2025
Thank You for Your Attention

Presented by: Surendra Shastri MD