A BRIEF REPORT ON CERVICAL CANCER IN INDIA
I. Cervical Cancer

Cervical cancer starts in the cells on the surface of the cervix, the lower part of the uterus (womb) that opens at the top of the vagina. Most cervical cancers are squamous cell carcinomas with adenocarcinomas that involve the glandular epithelial cells, being the second most common type. Cervical cancer usually develops very slowly and starts as a precancerous condition called dysplasia. This condition can be detected by a Pap smear and is 100% treatable. The early stages of cervical cancer are completely asymptomatic and it can take years for precancerous changes to turn into cervical cancer (NCBI, 2012).

Human papillomavirus (HPV) infection is a well-established cause of cervical cancer and there is growing evidence of HPV being a relevant factor in other anogenital cancers (anus, vulva, vagina and penis) and head and neck cancers. HPV infection is common among women but it usually goes away on its own. Persistent HPV infections, however, can cause cellular abnormalities that sometimes develop into cervical cancer if not treated. High risk HPV genotypes includes HPV-16, HPV-18, HPV 31, HPV 33, HPV 35, HPV 39, HPV 45, HPV 51, HPV 52, HPV 56, HPV 58, HPV 59, HPV 68, and HPV 69 out of which 70% of cervical cancer are caused by HPV 16 and 18 worldwide. In India about 7.9% of women in the general population are estimated to harbor cervical HPV infection at a given time and 82.5% of invasive cervical cancers are attributed to HPVs 16 or 18 (WHO 2010).

II. Burden of Cervical Cancer

Cervical cancer is an important public health problem in women in many developing countries. It is a major cause of morbidity and mortality among women in resource-poor settings. Majority of cancers in developing countries like India are detected in late stages, predominantly due to lack of awareness about the condition, lack of availability of screening programs and prevention services (Diaz M et al, 2008). In India, cervical cancer is the most common cancers among women between 15 and 44 years of age, followed by breast cancer. Current estimates report the age adjusted incidence rate of cervical cancer per year is 27.0 per 100,000 women with an age adjusted mortality rate of 15.2 per 100,000 women (according to the WHO/ICO 2010).
Fig. 1: States with a higher age adjusted incidence and mortality rate of cervical cancer in India

ICMR, 2006-2008
III. Risk factors associated with Cervical Cancer

Several risk factors increase the chance of developing cervical cancer. Most common risk factor for developing cervical cancer is infection of HPV. There are some risk factors that may influence the progression of cervical cancer such as leaving the HPV infection untreated and allowing it to persist for a long period of time, smoking cigarettes, weakened immune system, multiple partners etc.

- Human Papillomavirus (HPV specially 16 &18)
- Overweight or obese
- Smoking
- Family history of cervical
- Weekend immune system (i.e. HIV)
- Multiple partners

*WHO, 2010

Hussain H et al, 2012; Dutta S et al, 2012; Franceschi S et al, 2003*
IV. Cervical Cancer Prevention

Prevention and control of cervical cancer requires primary prevention with vaccination of high-risk patients, secondary prevention with regular screening and treatment of precancers, and availability of cancer treatment and palliative care. (WHO/UNFPA, 2006) While epidemiological data is useful and necessary to identify populations at high risk for cervical cancer, an understanding of the knowledge and attitudes regarding HPV and cervical cancer prevention of racial/ethnic groups are critical for the implementation of effective, targeted educational efforts. Inequities in cervical cancer screening, diagnosis and treatment and HPV vaccination may arise from a number of barriers including access to healthcare, cultural beliefs and limited awareness. To address the issue of limited vaccine uptake, it may be beneficial to develop culturally-relevant interventions at the individual and community levels. That coupled with an increased educational program regarding HPV-related cervical disease, transmission and risk, as well as vaccination as a preventative measure, may help to diminish existing disparities in cervical cancer incidence and mortality.

An awareness program initiated by the National Cancer Registration Program at Barshi, a rural area in India, showed improvement in the stage at diagnosis of cervical cancer from 1988-89 to 1990-92, with a control site (no awareness program) showing no such improvement. The methodology consisted of educating the general population about the symptoms of the cancer, and encouraging women who had such symptoms to undergo screening (Jayant et al, 2006). Similar findings were reported by a study in a district in Western India (Sankaranarayanan et al, 2001). These studies demonstrate the importance of incorporating health education in a national screening program.

### Barriers to Screening Programs in India

- Age- older women are less likely to undergo screening
- Women who did not use contraception
- Low education levels (> primary school)
- Reluctance to undergo testing in the absence of symptoms
- Costs
- Anxiety and fear related to the testing procedure and results
- Apprehension at sight of instruments
- Long waiting time

### Health Promotion & Education

- Cervical cancer is preventable
- About the signs and symptoms of the disease
- What they should do if signs and symptoms are present
- Regular screening is essential to detect the cancer early and avoid disability and death from the disease

### Recommendations to Increase Participation in Screening Programs in India

- Sustained and focused public awareness campaign
- Health education activities
- Easy access to clinics for target women
- Testing and treatment in the same session
V. Screening Strategies

Despite the fact that more than 80% of cervical cancer cases are in developing countries, only 5% of women in these countries have been ever tested for abnormalities of the cervix (WHO 2006). Cytology screening programs have resulted in a marked decline of this disease in developed countries. However this method of screening requires excessive use of resources in terms of laboratories, equipment, trained personnel, etc. Furthermore, a large proportion of the Indian population resides in the rural areas where a very small percent of women undergo cytology-based screening every year. In addition, the costs associated with these tests have prevented cytology-based screening programs from being effectively implemented in low-resource setting countries.

The difficulties in organizing cytology screening in developing countries have prompted the assessment of alternative methods which may be more suitable and readily implemented in developing countries (Table 1). Visual inspection-based screening tests (VIA) and visual inspection post application of Lugol’s iodine (VILI) are a couple of screening tests that have been used in low-resource settings, including in India (Sankaranarayanan et al, 2004). These methods have many advantages: they are less expensive than cytology based screening, easy to administer and train appropriate health care workers, and provides real-time results. Thereby, enabling those eligible for treatment can receive treatment of the precancerous lesions using cryotherapy or loop electrosurgical excision procedure (LEEP) on the same day and in the same health facility. This "single visit see and treat" method ensures adherence to treatment soon after diagnosis, hence stemming the problem of women lost to follow-up. (Singla S et al, 2012)

Recent studies have demonstrated that visual inspection with acetic acid (VIA) and visual inspection with Lugol’s iodine (VILI) to be sensitive and effective screening alternatives that are less expensive and can be performed by paramedical staff in low resource settings (Sankaranarayanan et al, 2003; Goldie et al, 2005). Although the sensitivity and specificity of VIA has been found to vary considerably from study to study (Sankaranarayanan et al, 2004), the general finding has been that the sensitivity of VIA and VILI is comparable to that of cytological screening, but its specificity is lower for detecting CIN2 or worse lesions (Sankaranarayanan et al, 2004). Results from an Indian cluster randomized control trial based in Tamil Nadu suggests that screening using the VIA method substantially reduces the incidence of, and mortality from, cervical cancer [incidence hazard ratio of 0.75 (0.55–0.95) and mortality hazard ratio of 0.65 (0.47–0.89)],(Sankaranarayanan et al, 2007)

Another screening method is HPV DNA testing, which although expensive, can be cost-effective in the long run, as it has higher sensitivity than cytological screening, can detect CIN lesions at an earlier stage than cytology. Sankaranarayanan et al (2009) found that a single round of HPV DNA testing in a rural setting in India to result in a decrease in incidence of, and death from, advanced cervical cancer.

### Table 1: Sensitivity and specificity of screening tests used to detect cervical cancer

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<thead>
<tr>
<th>Parameters</th>
<th>Screening Methods</th>
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<tbody>
<tr>
<td></td>
<td>VIA</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>78.7%</td>
</tr>
<tr>
<td>Specificity</td>
<td>94.8%</td>
</tr>
<tr>
<td>NPV</td>
<td>99%</td>
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VIA - Visual inspection with acetic acid; VILI - Visual inspection with Lugol’s iodine; NPV - Negative predictive value

*Deodhar K et al, 2012; Sankaranarayanan et al, 2004; Diaz M et al, 2008*
VI. Vaccines

HPV is largely asymptomatic, making it difficult to recognize and detect among the general population, which limits any behavior modification (Singh, 2005). Vaccinations may thus provide a solution for prevention. HPV vaccines that prevent against HPV 16 and 18 infections are now available and have the potential to reduce the incidence of cervical and other anogenital cancers (WHO, 2010). These two prophylactic HPV vaccines have shown excellent efficacy against persistent HPV infections and related cervical lesions among HPV-naive women in proof-of-principle studies. Additionally, these two vaccines have shown potential benefits in males, younger age groups, HIV-infected patients, and pregnant women. (WHO/UNFPA, 2006)

VII. Guidelines for Cervical Cancer Screening in India

As cytology based screening is highly resource intensive and cannot be implemented in resource poor areas of India, the guidelines for implementing a cervical cancer screening program developed by National Cancer Control Program and WHO-India in 2006 recommend the use of alternative screening strategies, in particular VIA, at the primary health care level, followed immediately by a single visit to the district hospital (DH) for further management. All women, who on the basis of their VIA results are referred to the DH, should be diagnosed using colposcopy, and treatment should be offered to the women during the same visit itself, to avoid loss to follow up. Confirmation of diagnosis using pap smears and biopsy should be done subsequently. The guidelines strongly recommend that information, education and communication activities should be incorporated into the screening program. In addition the guidelines provide details of the roles of different healthcare professionals, training of personnel, preparation and procedures for screening, equipments required, protocols for referrals and follow up, and procedures for monitoring and evaluation as well as quality control. (WHO/NCCP, 2006)

Table 2: Comparison of HPV vaccines

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<th>Gardasil</th>
<th>Cervarix</th>
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<tr>
<td><strong>Target population</strong></td>
<td>Girls 9 through 26 years of age</td>
<td>Girls 9 through 25 years of age</td>
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<tr>
<td><strong>Active against</strong></td>
<td>HPV 6, 11, 16 and 18</td>
<td>HPV 16 and 18</td>
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<tr>
<td><strong>Prevent against</strong></td>
<td>Cervical cancer, Vulvular cancer, Vaginal cancer, Anal cancer, Genital warts, Precancerous Cervical, Vaginal, Vulvular and Anal lesion.</td>
<td>Cervical cancer, CIN1, CIN2 or worse grade diseases and Adenocarcinoma.</td>
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*Merck & co, 2009; GSK, 2009
References: