A clinical perspective on cervical cancer screening in the Pacific region.

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BACKGROUND

It has been recognised for many decades that women in low-resource settings (which include most Pacific islands) suffer the burden of morbidity and mortality associated with the universal life experience of reproduction.¹ In accordance with WHO Millennium Development Goal (MDG) 5,² attention has been paid to improving maternity care and access to contraception. There has been less focus by governments on how these earlier life experiences affect the health of women beyond their reproductive years. It is surprising that women’s cancers are not specifically addressed by any of the MDGs, when 200 000 more women die each year from breast and cervical cancer than from complications due to pregnancy and childbirth.²,³

Cervical cancer is the second most common cancer in women worldwide affecting 1.4 million women, with 493 000 new cases, and 273 000 deaths each year. More than 80 to 85% of new cases occur in developing countries, where cervical cancer is also the most common cancer in women.¹,³ The cervical cancer burden in the Pacific Region is substantial as shown in Table 1, with age standardized incidence rates ranging from 8.2 to 50.7 and age standardized mortality rate ranging from 2.7 to 23.9 per 100 000 women per year.⁴ In the recent Global Burden of Disease study, cervical cancer was ranked the eighth leading cause of death among women in the Pacific in 2010, which is by far the highest ranked cancer.⁴

Australia and New Zealand have some of the lowest incidence for both morbidity and mortality from cervical cancer because of well-organised cervical screening programmes implemented since 1991 and 1990 respectively.

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence†† (per 100 000)</th>
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</thead>
<tbody>
<tr>
<td>Fiji</td>
<td>39.5 §</td>
</tr>
<tr>
<td>Papua New Guinea</td>
<td>40.4</td>
</tr>
<tr>
<td>Samoa</td>
<td>28.8</td>
</tr>
<tr>
<td>Tonga</td>
<td>12.7</td>
</tr>
<tr>
<td>Guam</td>
<td>9.4</td>
</tr>
<tr>
<td>New Zealand</td>
<td>7.0</td>
</tr>
<tr>
<td>Australia</td>
<td>6.9</td>
</tr>
</tbody>
</table>

† Fijian statistic is based on current study data from 2004 to 2007 for all ages; other countries' data sourced from GLOBOCAN 2002.¹
†† Standardised to the WHO world population.
§ The rate increases to 60.5 per 100 000 (WHO STD) for 20-69 years old.

How should we address the cervical cancer problem in the Pacific region? A comprehensive approach to cervical cancer prevention should be two pronged, primary prevention with HPV vaccination and secondary prevention by diagnosing and treating precancerous lesions.

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Received: 26.04.2016; Published: 01.07.2016


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HUMAN PAPILLOMAVIRUS VACCINATION – Primary Prevention

HPV vaccination has been shown to be extremely safe and efficacious. Worldwide experience has shown that well-designed immunisation programmes can achieve high coverage among young adolescent girls both in low and middle-income countries. This has been shown in the Pacific region with Fiji initiating a HPV vaccination programme with a reported 95% coverage. New Zealand National Cervical Screening Programme (NCSP) reports the highest uptake of 70% amongst Pacific island teenagers compared to the national rate of 50%. This means that a well implemented vaccination programme will most likely have a more than 90% uptake, and long term is our best approach for cervical cancer prevention. High vaccine costs which has been a significant barrier for many Pacific Island government have steadily been reduced as a result of the efforts of the GAVI (Global Alliance for Vaccine and Immunization). The poorest countries now have access to a sustainable supply of HPV vaccines for as little as US$4.50 per dose. The same vaccines can cost more than US$100 in high-income countries. The vaccine will have a positive impact on cervical cancer rates but this impact will not be appreciable for another 20 years.

CERVICAL SCREENING PROGRAMME – Secondary Prevention

Cytology-based screening has resulted in dramatically lowered cervical cancer rates in developed countries including Australia and New Zealand. However, most developing countries lack the resources, infrastructure and trained personnel needed to implement such programmes effectively. Pacific Island countries need to look at evidence based alternative approaches that have been successfully implemented around the world in similar low-resource settings. The question of whom, when, and how you would implement these need to be answered.

Before implementing any screening programme, the need for education and communication about the disease, screening methods available as well as the implications of abnormal results is essential for it to be successful. Recent research conducted in rural Fiji indicated that 70% of women did not know about cervical cancer and 40% did not know about a “cervical smear”. A Fijian audit on cervical cancer management by Sikiti highlighted that patients’ lack of knowledge was an important factor in the low coverage. Local communities and local health workers’ involvement can be an effective solution in dealing with these issues.

Geographical isolation is a common and significant problem throughout the Pacific Islands. This can lead to decreased access to screening and also contribute to low uptake in those areas. It might well be that different segments of the population may need to be screened differently in order to overcome various barriers.

Infrastructure and resources required to implement such screening programmes includes:

1. Manpower – nurses, community health workers/educators.
2. Education and training of personnel.
3. Education material – pamphlets, videos, media.
4. Bundle with the HPV vaccination programme – educate the mother via daughter (mother and daughter programme).
6. Information technology that enables personnel to establish a call, recall system for screening but, more importantly to allow data collection which will help identify areas for improvement.

The most efficient and effective strategy for detecting and treating cervical cancer precursors in low-resource settings is to screen using either Visual inspection with acetic acid (VIA) and/or HPV DNA testing and then to treat using cryotherapy. This strategy is optimally achieved in a single visit and can be carried out by competent physicians and non-physicians, including nurses and midwives. If a woman was screened for cervical cancer only once in her lifetime between the ages of 30 to 40 years old, her risk of cancer would be reduced by 25-36%. Screening women twice, at ages 35 and 40, was predicted to reduce lifetime cancer risk by 65%-76%.

A single visit approach decreases the risk of women not turning up for subsequent treatment appointments. In the TATI project in Peru only 8% of women in the single visit group did not have treatment, but when they were referred elsewhere for treatment 48% did not have treatment. There is evidence to support single visit treatment, as efficacy measured at 12 month and 36 months showed that prevalence of CIN 2-3 is much lower in the group that had
immediate treatment.\textsuperscript{12,13,14} Similarly with the TATI Peru study, 88\% of CIN 1 were cured and 70\% CIN 3 were cured within three years.

HPV testing has emerged as a new option for cervical cancer prevention with many countries taking it up as their primary screening tool. Persistent infection with high-risk types of HPV (especially 16,18) can lead to the development of cervical cancer so testing for high risk HPV has the potential to identify women at increased risk. A large body of evidence, including randomised controlled trials, has shown HPV testing in primary screening is superior to cytology with greater sensitivity and better reproducibility but lower specificity.\textsuperscript{15} Analysis of four European randomised controlled trials found that, compared with cytology, HPV-based screening provided 60–70\% greater protection against invasive cervical cancers.\textsuperscript{15} The randomized controlled trial run in India by IARC showed that a single round screening with HPV decreased cervical cancer mortality by 50\%, not seen with VIA or cytology.\textsuperscript{12} It can be done 10 yearly and is recommended by WHO in low resource countries.

Commercially available HPV tests such as Hybrid Capture 2 (QIAGEN Inc.), Cobas (Roche) and Aptima (Hologic) are expensive and involve sophisticated equipment and processing in a laboratory. Fortunately a new, rapid, low cost HPV DNA test called \textit{care}HPV has been introduced for developing countries like the Pacific Islands. \textit{Care}HPV specimens can be self-collected which will overcome one of the barriers to screening. Using antibody bound paramagnetic beads, it can quickly and quantitatively detect 14 types of high risk HPV (16,18,31,33,35,39,45,51,52,56,58,66,68). The system can process 80 specimens in 2.5 hours, powered by dry battery obviating the need of water or electricity. A healthcare worker with basic training can run it. Hong Ying et al showed there is good clinical accuracy with sensitivity for CIN 2+ of 85.7\% (cytology 53\%) and specificity of 76.7\% (compared to cytology 90\%). It has a higher false positive rate.\textsuperscript{18,19} Some studies have shown that VIA screening can decrease cervical cancer incidence by 31\%. These visual tests require simple equipment and relatively brief training, and can be performed by midlevel health personnel. Results can be communicated to the patient immediately. Data in Thailand and Ghana have shown that 99\% of newly trained screener’s assessment of the cervix was equivalent to that of the trainer and remained high regardless of the time elapsed negating concerns about the skill levels if they are trained.\textsuperscript{19} Like cytology, one of the limitations of VIA is that results are highly dependent on the individual’s interpretation. This means that initial training and ongoing quality control is of paramount importance. Another limitation of visual tests is that they are not reliable in postmenopausal women because of changes in the transformation zone of the cervix, the area in which precursors of cervical cancer arise.

DISCUSSION AND CONCLUSION
The goal is that all women regardless of where they live in the Pacific should be screened for cervical cancer at least once in their lifetime. We are all well aware that most Pacific Islands have limited funds and many health initiatives are in competition for these scarce funds. However, with the burden of cervical cancer in the region remaining amongst the highest in the world, we all have the duty to continue to advocate for cervical cancer prevention to be a priority.

The evidence on the effectiveness and feasibility of a single visit approach with HPV testing followed by VIA and cryotherapy treatment in low resource communities like the Pacific Islands is presented above. We believe that this approach can overcome some of the barriers in implementing a successful cancer prevention programme. It addresses issues of cost,
accessibility, lack of resources, loss to follow up and buy in from the women.

Concerns about overtreatment have been raised with single-visit approaches but this can be countered with the low morbidity associated with cryotherapy as well as the overall programme benefit that is gained by ensuring higher rates of treatment. Some evidence also suggests that cryotherapy may be protective against the future development of cervical disease among women infected with HPV. Given the effectiveness and relative ease of administering cryotherapy, we view this technology as the most promising method for treating CIN at the primary health care level in most low-resource settings. Presently, cryotherapy equipment is not universally available, and concerns have been raised about the quality of some of the equipment that is in use. Strategies must be explored to ensure that adequate numbers of effective, affordable cryotherapy units are available to cervical cancer prevention programmes.

It is crucial that women, their families, community organisations and other stakeholders understand the vision and objectives of the cervical cancer prevention programme and any concerns that may discourage participation are actively addressed. Robust programmes also require mechanisms for effective training, supervision and continuous quality improvement and support from the government.

REFERENCES:


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