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# Challenges to Cervical Cancer in the Developing Countries: South African Context

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## 1. Introduction

Despite the fact that cancer of the cervix is preventable, it is the commonest cancer cause of death in women in sub-Saharan Africa, Melanesia, South Central and South East Asia, the Caribbean and Latin America (Parkin et al., 2005). Southern Africa has one of the highest incident rates in the world, and in South Africa alone it caused the deaths of 3 700 women in 2002 (Denny, 2006). According to the International Agency for Research on Cancer (IARC), cervical cancer accounts for 23% of all cancers diagnosed in South Africa (International Agency for Research on Cancer, 2006 as cited in le Riche, 2006). Cervical cancer is the second most common cancer among South African women, with 1 in 41 women developing the disease in her lifetime (Sitas et al., 1998). Adar & Stevens (2000) noted that it was responsible for nearly 2% of deaths of women aged 15-44 years and 4% of women aged 45-59 years. In South Africa, the total age-adjusted incidence rate (ASIR) of cancer in Africans is far lower than that in the corresponding white population. According to the KwaZulu-Natal Department of Health (2004) in South Africa, cervical cancer accounts for 18.5% of female cancers, with approximately 5 000 new cases reported annually and black women being most at risk of getting cervical cancer compared to white and coloured women. African women seek help only when their particular disorder/disease is far advanced, thereby, as in the case of cervical cancer, rendering cure or control nearly impossible (Walker et al., 2002). A study done by De Jonge et al. (1999) found more aggressive tumours in black women compared to white women with cervical cancer in South Africa. In women of all race groups, the age specific cervical cancer rates for 1992 remained low up to 30 years of age, but thereafter increased rapidly until they peaked at 50 to 59 years (Denny, 2006). Similarly, Sitas et al. (1998) reported that the incidence of invasive cancer rises in the age group 35-39, with 87% of cases occurring in women over 35 years of age. It is a common cancer in poor women due to inadequate mass cervical cancer screening, and their cure rates are low as they present late (Denny, 2006).

The South African National Department of Health identified cervical cancer as a health priority and in 2000 introduced a national screening programme, based on models of the natural history of the disease (Department of Health, 2000). The cervical screening policy states that every woman attending public sector health services is entitled to three free smears from the age of 30 years at intervals of ten years provided no smears have been

taken within the previous five years and a total of three smears will be taken in a woman's lifetime. The starting age was based on the fact that the disease affects women in early to late middle age. The goal is to screen 70% of women in the target age group within 10 years of initiating the programme. This model aims to decrease cancer incidence by 64% (Miller, 1992 as cited in Smith et al., 2003). According to Walraven (2003), cervical cancer develops slowly. Invasive cancer is usually preceded by long phases of pre-invasive disease (Sankaranarayanan & Wesley, 2003) and high-grade dysplasia can generally be detected 10 years before cancer develops (Population Reference Bureau & Alliance for Cervical Cancer Screening, 2004). It is widely believed that that invasive cervical cancer develops from dysplastic precursor lesions, progressing steadily from mild to moderate to severe dysplasia, then to carcinoma in situ, and finally to cancer. Based on resource considerations and best available evidence, the policy adopted a public health approach by targeting the age group most at risk of developing high-grade, precursor lesions of the cervix. The policy conformed to the recommendations of the World Health Organization [WHO] (1999 as cited in Smith et al., 2003) for the screening protocol for regions with limited resource.

There has been much debate as to the most suitable screening policy, particularly with age commencement and appropriate time intervals between smears. A number of studies revealed that nurses were opposed to and misunderstood the screening policy, probably limiting the performance of screening (Smith & Hoffman, 2000; Smith et al., 2003; Sibiya & Grainger, 2010). They were of the opinion that women should have their first smears at the age of 20 and thereafter at intervals of five years because women become sexually active at an early age. Screening programmes are effective provided that they are well organized (le Riche et al., 2006; Gaym et al., 2007). The aim of cervical cytology screening programme is to detect pre-malignant lesions on the transformation zone of the cervix. Those patients with abnormal cytologic results are then referred for further management, usually at dedicated colposcopy clinics. The current referral criteria are a single smear with a high-grade squamous intra-epithelial lesion (HSIL) or two low-grade squamous intra-epithelial lesion (LSIL) smears. The aim of colposcopy is to detect the most abnormal area on the cervix and to direct the clinician to the area of biopsy.

## **2. Cervical cytology screening programmes in developing countries**

Cervical cytology screening programmes have been introduced in low- and middle-income developing countries, but generally have achieved very limited success (WHO, 2001). Although cytological screening is being carried out in some developing countries, there are no organized programmes. As a result, there has been a very limited impact on the incidence of cervical cancer, despite the large numbers of cytological smears taken in some countries such as Cuba and Mexico (Sankaranarayanan et al., 2001). Only 5% of women in developing countries undergo cervical screening compared with 40-50% in the developed world. Substantial costs are involved in providing the infrastructure, manpower, follow up and surveillance for cervical screening programmes. Owing to their limited health care resources, developing countries cannot afford the models of frequently repeated screening of women over a wide age range that is used in developed countries (Sankaranarayanan et al., 2001). Cervical cancer has been described as "a disease of the economically disadvantaged" because even in developed countries such as the United States, cervical cancer mostly affects women of low socio-economic status, rural and poor women (Dickson-

Tetteh, 1998). Lower socio-economic status has been associated with higher risk of developing cancer probably due to lack of access to good health care and screening programmes (Mqoqi, 2003). Barriers to screening uptake include a lack of knowledge about the disease, the geographical and economic inaccessibility of care, the poor quality of services and lack of support from families. Abrahams et al. (1996) state that in order for the cervical screening programme to be successful, among other things, strategies in low-resource settings should be socially and culturally appropriate.

### **3. Cervical screening in South Africa**

South Africa, one of the better-resourced countries in sub-Saharan Africa provides opportunistic screening. Despite the existence of the guidelines, difficulties have occurred with the implementation of the South African cervical screening programme. A number of attempts were made in the past to introduce cervical screening programmes at national, provincial and local levels in South Africa. In the 1970s the Department of Health suggested that a Pap smear should be taken only if the cervix appears abnormal (Performance of the National Health System [NHS] Cervical Screening Programme in England, 1998 as cited by Hoffman et al., 2003). A number of cervical screening programmes that were introduced in the 1980s failed due to poor attendance of women at the health services. The findings of the study that was conducted by Abrahams et al. (1996) revealed that the poor attendance of women was due to lack of knowledge about cervical cancer and the significance of cancer screening. Fonn (2003) reported that implementation was slow, whilst Moodley et al., (2006) found that cervical screening in the public health service was conducted in an ad hoc manner and focused on younger women attending family planning and ante natal services. In South Africa, women have access to cervical screening at primary health care (PHC) clinics. The clinics serve a demarcated area and offer a variety of services. Due to the demand of services, it is not possible to concentrate on the prevention of cervical cancer, as cervical screening is one aspect of the total services rendered. This is a great concern given that the likelihood of reducing the incidence of cervical cancer is dependent upon a well-organized programme. A study was conducted in the eThekweni Region, previously named Ilembe in the province of KwaZulu-Natal on the evaluation of the implementation of the cervical screening programme in PHC clinics (Sibiya & Grainger, 2007). This study consisted of a record review, a clinic audit and focus group discussions with the nurses. The findings confirmed that follow-up of clients was problematic, referral hospital feedback was poor, record keeping was inadequate, and rural clinics lacked resources. Despite the positive aspects, such as the good quality of smears and adequate drugs, the problems overall would have resulted in an ineffective programme. The following factors have been identified as the contributory factors to ineffective screening in South Africa:

#### **3.1 Shortage of health care workers**

According to the South African cervical screening policy, all service providers are expected to participate in the screening programme (Department of Health, 2000). The South African screening policy states that women should have Pap smears at least once every 10 years as from the age of 30 years. Therefore, the annual number of women requiring a Pap smear is the total number in the province divided by 10. It is worth noting that the finding of the study that was conducted by Fonn (2003) revealed that in order to achieve 100% coverage of

women eligible for screening over a 10-year period, each nurse would have to perform on average less than one Pap smear per day. This author further argues that there is spare capacity and that any potential underestimate in the number of Pap smears required per year could be relatively easily accommodated. According to the Department of Health (2006) nurses constitute the largest professional group in South Africa's health care services and form the backbone of PHC in South Africa. Nurses provide the bulk of service provision in the public health sector. This emphasis is most striking at the primary care level. Given the emphasis the need for well-trained primary level staff is imperative. The South African yearbook (2004/05) states that patients visiting PHC clinics are treated mainly by PHC-trained nurses, or at some clinics, by doctors yet according to the Department of Health (2004) only about 40% of facilities have PHC qualified nurses. This means that the pace of training has been slower than planned. However, migration of nurses has also impacted on these figures. The gross shortage of health workers in developing countries may be a further limitation to effective screening.

A number of research studies have attempted to explore the 'push and pull' factors that lead to South African nurses working in other countries. Emigration is a commonly cited cause of PHC attrition rate in South Africa. Migration of health personnel, also dubbed the brain drain, partly from rural to urban areas, but more particularly out of the country, has become a debated issue in human resource circles not only in South Africa, but also on the continent of Africa itself. According to the Department of Health (2006) for many years before 1994 South Africa constituted a preferred destination for many health professionals, the majority being doctors from the African continent. This situation has however changed since the late 1990's when a policy of not recruiting from fellow developing African countries was adopted at the Southern African Development Community (SADC) Health Minister's level. The findings of the study that was done by Oosthuizen & Ehlers (2007) indicated that nurses' inadequate remuneration, poor working conditions, excessive workloads, lack of personal growth and career advancement possibilities were major factors that influenced nurses' decision to emigrate. Lucas (2005) argues that although African countries have a shortage of health workers, they continue to migrate from Africa to more developed countries. Tarimo (1991) argues that it is unrealistic to expect good performances under the difficult conditions from workers who are poorly rewarded. However, financial incentives alone are insufficient to improve health worker motivation. Investing in a functional health care system in which nurses feel motivated to work is an important part of human resource planning.

The capacity to read cervical smears at public sector laboratory level is limited in South Africa. The South African guidelines indicate that cyto-technologists reading population-based smears are expected to screen six smears per hour and to work for no longer than 8 hours per day, i.e. total of 48 smears per day. Thus if all technologists employed by the state only read cervical smears we would have just enough technologists employed in the public sector. However, they also have other smears to read (Fonn, 2003). It is important to note that if the first smear is done at the age of 20 years, it would mean that the annual number of smears would increase from 85 0740 to 127 5016. This would mean that cyto-technicians would have to read 69 smears per day. The capacity to read the cervical smears at public sector laboratory is limited (Fonn, 2003). In developing countries, because of lack of the trained cyto-technicians, there is often a long interval of 1-3 months between the Pap screening and when the test result is available (Jeronimo et al., 2005). This is further

supported by the findings of the study that was conducted by Moodley et al. (2006) which revealed that long cytology turnaround time is attributed to poorly functioning administrative and transportation systems. The study that was conducted by Denny et al, (2006) revealed that a large number of women did not return for the cervical screening results. Cytology-based screening programmes can only be successful if infrastructure is in place and laboratory quality assurance is consistent (Alliance for Cervical Cancer Prevention, 2004).

### **3.2 Poor system of follow up and referral process**

The South African policy on cervical screening maintains that a working follow-up system needs to be in place for effective implementation of the cervical screening programme (Department of Health, 2000). The policy further states that the time lapse between screening and follow-up should be 1–4 weeks depending on the circumstances and every attempt possible should be made to find those patients who do not return voluntarily. The results of the study that was done in the KwaZulu-Natal province of South Africa revealed that there was poor follow up of patients with abnormal smears and that if patients were referred to the hospital from the PHC settings there was no feedback that was provided to the clinic (Sibiya & Grainger, 2007). Lack of capacity in terms of infrastructure and human resources were cited as factors for poor follow up and referral process. However, the findings of the study that was conducted by Nene et al., (2007) showed that the lowest compliance rate with follow-up care was found among unmarried women, those with low level of education and those with a high number of pregnancies. Some studies have reported that women with abnormal screening results were confused and did not understand the information provided by the nurse (Kavanagh et al., 1997; Yabroff et al., 2000 as cited in by Nene et al., 2007).

There are also challenges regarding the referral process of women with abnormal smears for further investigation and management. When the protocol for cervical screening was evaluated in the province of KwaZulu-Natal, the results revealed that none of the 88 reviewed documents showed evidence of feedback from the referral hospital (Sibiya & Grainger, 2007). Interview data with nurses revealed that none of the referral hospital provided feedback to the referral hospital. This means that there was lack of effective liaison with referral centres for diagnosis and treatment to ensure follow-up and monitoring. According to Smith and Hoffman (2000) nurses work diligently to achieve good rates of follow-up but there is one group of women that they cannot monitor, namely those with high-grade lesions. Once a woman is referred for colposcopy, the nurses do not receive feedback regarding whether she kept her appointment, or what the outcome was. This is further supported by the findings of a study that was done by Abraham et al. (1996) where the health workers expressed disappointment that they continued to not receive feedback from hospital specialists to whom they referred women found to have abnormal smears, which merited further clinical investigations. The only way that feedback of a referral to a hospital was gained was that all patients were encouraged to report back to the clinic to give information as to the outcome of their hospital visit. Improving communication would allow the nurses to remain involved with their clients, and help to ensure that follow-up takes place. The referring doctor has a responsibility to the woman to ensure that she has fully understood the significance of her abnormal smear, the options for evaluation and management of that smear, and has been involved in the decision-making.

### 3.3 The impact of HIV and AIDS

The growing number of women in resource-poor areas, such as sub-Saharan Africa, who have immunodeficiency virus (HIV), appears to compound the problem because they have an increased risk of human papillomavirus (HPV) infection, the causal agent of cervical cancer (Goldie et al., 2001). South Africa remains one of the countries with a high HIV and AIDS prevalence rate - there are currently about 5.27 million people who are infected with HIV and AIDS in South Africa (UNAIDS, 2008). About 70% of the HIV positive pregnant women attending antenatal clinics are below the age of 30 years (Department of Health, 2007). The prevalence rate among young people aged 20-24 years was estimated to be 30%, with the highest prevalence rate of about 40% being among women aged 25-29 years. Cervical cancer is regarded as an important AIDS-related disease and since 1993 has been considered as an AIDS-defining illness in women with HIV virus (KwaZulu-Natal Department of Health, 2004). HIV positive women have a high rate of persistent HPV infections, and a higher rate than HIV negative women with the types of HPV that are associated with the development of high grade dysplasia and cervical cancer (Hoytt, 1998). HIV-positive women are almost five times more likely to present with dysplasia than HIV-negative women (KwaZulu-Natal Department of Health, 2004). One case-controlled case study reported that 60% of HPV positive women had initiated sex prior to reaching 16 years old. The report further stated that this may expose women to STIs, which may lower a woman's immune response and contribute to malignant transformation of HPV infections (Kenney, 1994).

Of particular concern was the lack of acceptance of the age at first screening criterion. According to the findings of the study that was conducted by Smith et al (2003), of the interviewed nurses, 90% were that some screening policy exists, and 57% could correctly state the policy. However, all the participants were of the opinion that women should have their first smear at the start of the sexual activity, which is at the age of 20 years, and the interval period should be five years due to high rate of HIV/AIDS in this province. They argued that there was an association between cervical cancer and HIV/AIDS and STIs hence younger women were at risk. This is in contrast with what the policy states as discussed above (Sibiya & Grainger, 2010). Many health professionals feel that as a result of the increased incidence of HIV/AIDS and sexually transmitted infections (STIs), younger women are at risk of getting cervical cancer (Kenney, 1994; KwaZulu-Natal Department of Health, 1999). Smith & Hoffman (2000) reported that approximately half of the nurses they sampled in Mitchell's Plain, Cape Town were of the opinion that women should have their smears done at the start of sexual activity, whilst a quarter thought that this should occur when the woman is under the age of 30 years. The participants in our study also believed that the age for first smear should be lowered to 20 years and that they should be repeated at five year intervals thereafter. They recommended this because of the high rate of HIV/AIDS in this province. Such sentiments have been criticized on the grounds that the nurses do not understand the natural course of the disease or the rationale behind the screening programme (Fonn, 2003; Smith et al., 2003). Worth noting are the results of the study that was conducted in the province of KwaZulu-Natal in South Africa by Gaym et al. (2007), which revealed that all the high-grade squamous intra-epithelial lesions occurred in women younger than 30 years of age, which is much lower than the usual age distribution for high grade lesions (around 35-40 years of age).

#### **4. Recommended measures to improve screening programmes in developing countries**

Many low-income developing countries currently have neither the financial and manpower resources nor the capacity in their health services to organize and sustain a screening programme of any sort (Sankaranarayanan et al., 2001). Efforts to organize effective screening programmes in developing countries will have to find adequate financial resources, develop the infrastructure, train the needed manpower, and elaborate surveillance mechanisms for screening, investigating, treating and follow-up of the targeted women. The following measures need to be put in place in order to improve cervical screening in developing countries:

##### **4.1 Effective screening tests**

The developing countries should consider cost effective screening test to use. Newer alternative methods for cervical screening have being developed and tested (Denny, et al., 2000; Goldie et al., 2006; Sankaranarayanan et al., 1998). These include DNA testing for HPV and visual inspection with acetic acid (VIA). The most promising of these being DNA testing for HPV as cervical cancer is caused mainly by HPV. The key barriers to HPV testing in developing countries are the costs and technical requirements associated with the test (Sankaranarayanan et al., 2005). VIA also called cervicospoty, consists of naked eye visualization of the uterine cervix after the application of diluted acetic acid, to screen for cervical abnormalities. A solution of 3% to 5% acetic acid is used, and the cervix is illuminated with a light source and the purpose is to identify aceto-white areas which may indicate tissue undergoing precancerous changes (Sankaranarayanan et al., 1998). A study of the cost effectiveness of several cervical cancer screening strategies, based on the South African experience, indicated that strategies using VIA or HPV DNA testing may offer attractive alternatives to cytology-based screening programmes in low-resource settings (Goldie et al., 2001). In developing countries, because of the lack of trained cytotechnologists and cytology laboratories, there is often a long interval (1-3 months) between the Pap screenings and when the test result is available. VIA has the advantage of requiring only low-technology equipment and the result is available immediately (Jeronimo et al., 2005). Therefore, the treatment of abnormal lesions can be done during the same consultation. This is further supported by the findings of the study that was conducted by Goldie et al., (2005) which revealed that VIA or HPV DNA testing offer cost-effective alternatives to conventional cytology-based screening in low resource settings as these require only one or two clinical visits. The results of the study that was conducted by Maree et al. (2009) revealed that VIA screening is acceptable to women due to the fact that the results are available immediately. The use of VIA as a screening tool should be considered as it is a realistic alternative for low-resource settings. VIA training should be instituted and registered nurses trained to perform it effectively. Part time registered nurses, possibly including the retired registered nurses, could perform VIAs at primary health care clinics, together with breast examinations. The major drawback of this approach that was identified by Sankaranarayanan et al. (1998) is that lesions are not detected early enough to prevent invasion because of a large proportion of the cancers detected are relatively advanced, requiring complex medical therapy that is difficult to provide in many settings. Cytology remains the best method available in screening for cervical cancer. However, in countries

with limited resources, an inexpensive and easy alternative is needed. Choosing a suitable screening test is only one aspect of a screening programme. A more fundamental and challenging issue is the organization of the programme in its totality. Whichever screening test is to be used, the challenges in organizing a screening programme are more or less the same. However, screening tests that require additional recalls and revisits for diagnostic evaluation and treatment may pose added logistic difficulties and these may emerge as another barrier for participation in low-resource settings (Sankaranarayanan et al., 2001).

#### **4.2 Improving health human resources**

Due to task shifting, cervical screening previously the exclusive domain of doctors and family planning nurses was extended to all registered nurses in the public sector (Department of Health, 2000). This led to the greater availability of screening services as well as increasing the demand for additional competent nurses to do Pap smears. Making the registered nurses the primary cervical screening providers is logical, given the need to increase the services. However, Kawonga & Fonn (2008) argues that this solution fails to recognize that a screening programme entails more than just taking Pap smears. These authors further argue that there are several components that should be well-co-ordinated including the facilities for follow-up and referral of women with abnormal smears. South Africa has not invested sufficiently in health systems strengthening nor in building the management capacity to co-ordinate and monitor the screening programme (Moodley et al., 2006). In South Africa, registered nurses have an important responsibility for the implementation of the programme. Health workers in South Africa are poorly distributed, being concentrated in urban areas, private sectors and hospitals (Wadee & Khan, 2007). In order to ensure efficient utilization of registered nurses, appropriate skills mix at the PHC clinics must be ensured.

According to the South African cervical screening policy, all nurses at the clinics are expected to conduct screening but this is not happening, mainly because nurses have not been equipped with knowledge and skills (Moodley et al., 2006; Sibiya & Grainger, 2007; Smith et al., 2003). In order for the nurses to be knowledgeable about the disease and understand, accept and comply with the programme, they must be trained through continuing professional development system. Education concerning the rationale of the policy, and the natural history of the disease, may encourage nurses to perform more screening tests. Zweigenthal (1998) found a correlation between a high level of screening and nurses' knowledge or a personal interest in the level of nurses' education. This researcher reported that the screening rates increased with an increase in the level of nurses' education. If nurses have a positive attitude towards the cervical screening programme, they are likely to motivate women to have a smear done. According to the cervical screening policy, all service providers must have access to information and be technically competent to perform adequate smears with effective management of abnormal results. The policy further states that the adequacy rate of a screening facility must reach at least 70% and if the facility consistently achieves below 70%, the programme stipulates that the staff will have to be re-trained (Department of Health, 2000). Smith et al. (2003) suggested that low coverage may be due to nurses' opposition to and poor understanding of the programme. Given that the participants disagreed with the starting age and intervals for smears, and mentioned inappropriate criteria, there is a clear need for further training.

In order to address the limited capacity to read cervical smears, the alternative methods for cervical screening, for example the DNA testing for HPV and VIA will relieve pressure on the cyto-technicians. Additional posts will have to be established or, in addition, methods of contracting private sector resources could be investigated (Fonn, 2003).

#### **4.3 Good follow up and referral systems**

It is unethical to offer screening without ensuring that follow-up and treatment services are available for women with abnormal smears (Sackett, 1975 as cited in Kawonga & Fonn, 2008). The WHO (2002) states that for success, the cervical screening programme must have the ability to "ensure high levels of coverage of the target population, to offer high quality, caring services, to develop and monitor good referral systems that ensure good patient follow-up and to ensure that the patients receive appropriate, acceptable and caring treatment in the context of informed consent." The manner in which the health professionals perform can have a profound effect on the achievement of these. The relationship between primary and referral sites and good monitoring systems is essential in order for a screening programme to be effective. The fact that screening services offered at PHC settings are not available outside office hours can also be seen as an obstacle. A system must be put in place to ensure that working women have access to the clinics even after office hours. A booking system can also be used to increase access of the screening services.

#### **5. Conclusion**

The South African government has produced a commendable screening programme and made a commitment to reduce cervical cancer. However, there are still challenges with the implementation of the cervical screening policy. South Africa is better placed than most sub-Saharan countries, but will not attain a successful screening programme without increased effort. An important consideration that needs to be taken into account is the cost. Frequent screening of women has considerable cost and resource implications. The limited health care budgets in most developing countries preclude initiating and sustaining such programmes. Despite calls for screening, implementation difficulties include shortages both of health funds and of number of skilled personnel. Strategies to reduce the burden on registered nurses may include training of less skilled cadres of nurses, like enrolled nurses and enrolled nursing auxiliaries for cervical screening. In order for a cervical cancer screening programme to succeed in South Africa, there must be greater political commitment so as to improve resources that are required for implementing the policy. The political will to see a national screening programme implemented is required from government, the health sector, the various medical, nursing and allied health and professional boards. Communication methods and delivery strategies aimed at encouraging women from developing countries are needed in order to increase screening uptake.

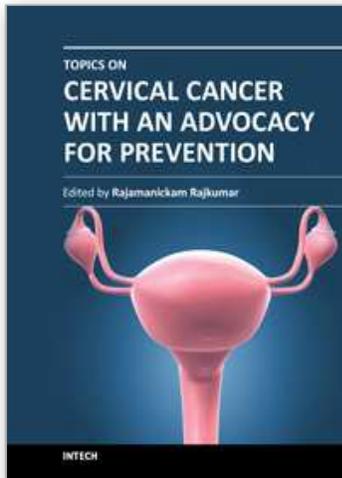
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## **Topics on Cervical Cancer With an Advocacy for Prevention**

Edited by Dr. R. Rajamanickam

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Cervical Cancer is one of the leading cancers among women, especially in developing countries. Prevention and control are the most important public health strategies. Empowerment of women, education, "earlier" screening by affordable technologies like visual inspection, and treatment of precancers by cryotherapy/ LEEP are the most promising interventions to reduce the burden of cervical cancer. Dr Rajamanickam Rajkumar had the privilege of establishing a rural population based cancer registry in South India in 1996, as well as planning and implementing a large scale screening program for cervical cancer in 2000. The program was able to show a reduction in the incidence rate of cervical cancer by 25%, and reduction in mortality rate by 35%. This was the greatest inspiration for him to work on cervical cancer prevention, and he edited this book to inspire others to initiate such programs in developing countries. InTech - Open Access Publisher plays a major role in this crusade against cancer, and the authors have contributed to it very well.

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