

## GLOBAL BURDEN OF CERVICAL CANCER: A LITERATURE REVIEW

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### ABSTRACT (250 words)

**Background:** Cervical cancer is the fourth most common cancer in women, and the seventh overall. As with liver cancer, a large majority of the global burden occurs in the less developed regions, where it accounts for almost 12% of all female cancers. This article reviews the global burden of cervical cancer, and the distribution of the disease according to various regions.

**Materials and Methods:** An electronic literature search through Google Scholar and ProQuest Central was undertaken to determine the best estimates on cervical cancer incidence and mortality using recently compiled data from cancer and mortality registries since 2008. Additional information was gathered from manual search of relevant articles in the reference lists of selected resources. Altogether, 19 references were used in this review.

**Result:** There were an estimated 528,000 new cases of cervical cancer and 266,000 deaths in 2012. It is the fourth most common cancer globally. The incidence of cervical cancer varied widely among countries with world age-standardized rates (ASR) ranging from 4.4 to 75.9 per 100 000 population. About 85% of all new cervical cancer cases and 87% of all cervical cancer deaths occur in the less developed regions. High-risk regions, with estimated ASRs over 30 per 100,000, include Eastern Africa (42.7), Melanesia (33.3), Southern (31.5) and Middle (30.6) Africa. Rates are lowest in Australia/New Zealand (5.5) and Western Asia (4.4). Cervical cancer accounts for 7.5% of all female cancer deaths. Mortality varied 18-fold between the different regions of the world, with rates ranging from less than 2/100,000 in Western Asia, Western Europe and Australia/New Zealand to more than 20/100,000 in Melanesia (20.6), Middle (22.2) and Eastern (27.6) Africa.

**Conclusion:** Despite of effective screening methods, cervical cancer continues to be a major public health problem. New methodologies of cervical cancer prevention should be made available and accessible for women of all countries through well-organized programs.

**Keywords:** cervical cancer, global estimates, HPV, human papillomavirus, incidence, mortality

## 1.0 Introduction

Cervical cancer ranked the fourth most common cancer among women worldwide. In many low-income countries, it was the most common female cancer (Ferlay et al., 2012). Compared with other cancers, screening for cervical cancer is the most effective, as it has the ability to detect through Pap smear pre-cancerous stage and high-risk type HPV that cause 70% cervical cancers (World Health Organisation, 2012). However, cytology-based cervical cancer screening requires having an infrastructure, skilled human resources, and quality assurance in place (Miller et al., 2002). It is now established that virtually all cases of cervical cancer follow from an infection by oncogenic human papillomavirus (HPV) types, therefore screening opportunities using alternative HPV-based strategies give further hope to expanding and simplifying screening strategies, pending availability of low-cost tests (Arbyn et al., 2010). Additionally, there are two HPV vaccines available that can prevent human papillomavirus type 16 and human papillomavirus type 18 infections, which jointly cause 70%–75% of all cervical cancers and 40%–60% of its precursors (Clifford et al., 2006). Currently, it is seen that the countries with the highest burden of cervical cancer are those not able to implement HPV vaccination due to its high costs and also effective screening practices due to lack of infrastructure, expertise and so on (Goldie et al., 2008)

Now more than ever, effective cervical cancer control planning requires having access to the most accurate statistics (Arbyn et al., 2009). According to the World Health Organization (WHO), one of the fundamental steps in the action plan for non-communicable diseases is to establish a high-quality surveillance and monitoring system that should provide, as minimum standards, reliable population-based mortality statistics and standardised data on non-communicable diseases (WHO, 2008). The aim of this review is to describe the current patterns of incidence and mortality of cervical cancer alongside corresponding HPV prevalence data.

## 2.0 Materials and Methods

### 2.1 Identification of publications

Three strategies were used in the review of literature. First, an article search in the ProQuest Central and Google Scholar was undertaken with the aim to identify published studies on worldwide burden of cervical cancer. The key words used were cervical cancer, global estimates, HPV, human papillomavirus, incidence, mortality. While the search focused on publications from year 2006 to 2016, several valuable articles published earlier were also included in the review. Secondly, reference lists of useful review articles and meta-analyses in the area of cervical cancer among women were combed and manually searched to identify relevant references related to the field. The third strategy was by reviewing all related reports, working papers and government policy documents, as well as surveillance data from the WHO cancer and mortality registries since the year 2008 and the GLOBOCAN cervical cancer information compiled by the International Agency for Research on Cancer (IARC, 2012).

## 2.2 Inclusion and exclusion criteria

Duplicate references and those without abstract or not related to cervical cancer were excluded. A further selection of article was performed by reading the abstract thoroughly for information related to the global burden of cervical cancer.

## 3.0 Result

In total 45 articles and reports were found but only 19 were found eligible for this review. The 19 articles and reports were analyzed and the findings are discussed according to incidence rates, mortality and the global trend of cervical cancer.

### 3.1 Incidence rates

Cervical cancer was the fourth most commonly diagnosed cancer in women in 2012, with an estimated 527,600 new cases worldwide. The highest incidence rates were in Central and South America and sub-Saharan Africa. Where about 35 cervical cancer cases are diagnosed for every 100,000 women, compared with only about 7 cases for every 100,000 women in North America. About 23 women per 100,000 die from cervical cancer in Sub-Saharan Africa, compared to about 3 per 100,000 in North America. Rates were lowest in the Middle East, Northern America, Australia and New Zealand, China, and parts of Western Europe (Table 1 and Figure 1). The disproportionately high burden of cervical cancer in sub-Saharan Africa, parts of Latin America and the Caribbean, and elsewhere in medically underserved populations is mainly due to lack of screening (WHO, 2012).

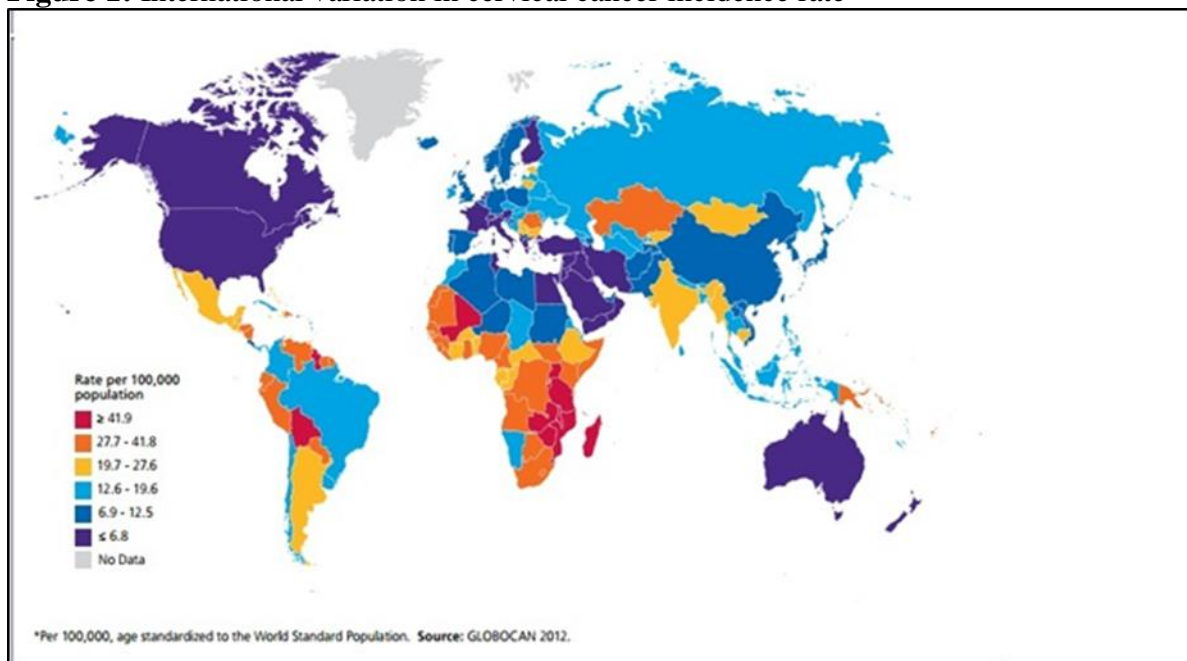
**Table 1:** Countries with the top 20 highest incidence of cervical cancer in 2012

Rank	Country	Age-Standardized Rate per 100,000 (World)
1	Malawi	75.9
2	Mozambique	65.0
3	Comoros	61.3
4	Zambia	58.0
5	Zimbabwe	56.4
6	Tanzania	54.0
7	Swaziland	53.1
8	Burundi	49.3
9	Bolivia	47.7
10	Guyana	46.9
11	Madagascar	44.6
12	Uganda	44.4

Rank	Country	Age-Standardized Rate per 100,000 (World)
13	Mali	44.2
14	Rwanda	41.8
15	Senegal	41.4
16	Kenya	40.1
17	Guinea	38.4
17	Lesotho	38.4
19	Suriname	38.0
20	Fiji	37.8

Source: Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. GLOBOCAN 2012 v1.1, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11

**Figure 1:** International variation in cervical cancer incidence rate



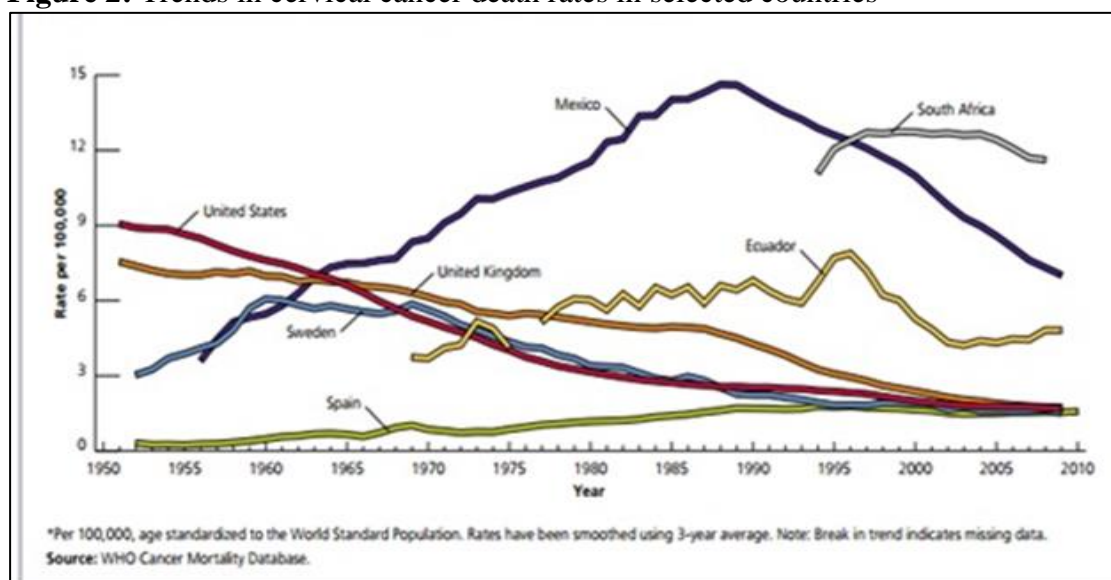
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### 3.2 Mortality

Cervical cancer was the fourth leading cause of cancer death in women worldwide in 2012, with an estimated 265,700 deaths. Nearly 90% of cervical cancer deaths occurred in developing parts of the world: 60,100 deaths in Africa, 28,600 in Latin America and the Caribbean, and 144,400 in Asia. India, the second most populous country in the world, accounted for 25% (67,500) of cervical cancer deaths. In Eastern, Middle, and Southern Africa, as well as Melanesia, cervical cancer is the leading cause of cancer death in females

(WHO, 2012). The trend of cervical cancer death rates comparing several developed and developing countries is shown in Figure 2. The rates were noted to be decreasing in the United States of America, Sweden and the United Kingdom, while remain unchanged or slightly increasing over the years in Ecuador and Spain. This difference in mortality rate is mainly as a result of lack of effective screening programs aimed at detecting and treating precancerous conditions, in the developing countries (Hakama et al., 1986). Comprehensive pap smear screening-based programs have not been properly implemented in most developing countries because, in most of these developing countries where pap smear screening is available, it often is accessible to only a small proportion of women through private health care providers, or it is offered primarily to young women through maternal or child health clinics or family planning clinics where the population being screened generally is not at high risk. Therefore, these approaches have had little effect on morbidity and mortality in developing countries compared to most developed countries that has long implemented comprehensive Pap smear screening-based programs (WHO, 2012).

**Figure 2:** Trends in cervical cancer death rates in selected countries



Source: WHO cancer mortality Database (2012)

### 3.3 Global trends

The large geographic variation in cervical cancer rates reflects differences in both the availability of screening, which can detect and allow for the removal of pre-cancerous lesions. In addition, screening also allows for the detection of HPV infection which can be treated accordingly. The death rates from cervical cancer have reduced by 65 percent over the past four decades in most developed world such as several Western countries, where screening programs have long been established (Ferlay, 2010; WHO, 2012). For example, in Norway, cervical cancer mortality rates decreased from 6.3 per 100,000 in 1970 to 1.5 per 100,000 in 2011 (WHO, 2012). Rates have also decreased in some high-incidence areas, including Colombia, the Philippines, and India, likely due to improved screening activities and better socioeconomic conditions (WHO, 2012). The reason for the decrease in mortality in these developed worlds is the availability of a simple screening test called the “Pap test”. The Pap test detects precancerous changes of the cervix before they progress to invasive cancer. In

contrast to this favorable trend, a wide variations exists between high- and low income countries, with incidence rates ranging from 4.4 to 75.9 per 100 000. These contrasts are believed to reflect both differences in exposure to risk factors such as high- risk HPV 16 & 18 as well as protection from screening. Sexually transmitted infection with high-risk HPV types is the main etiological factor for cervical cancer (WHO, 2012). This high risk HPV types is widely spread among people with multiple sexual partners, than those with only one sexual partner, hence the differences in exposure to risk factors (HPV 16 & 18) of cervical cancer. Cervical cancer rates have been reported to be rising in Uganda and in some countries of Eastern Europe such as Estonia, Lithuania, and Bulgaria (Bruni et al.; WHO, 2012). Most affected are younger women in several countries, including many in Europe, Central Asia, Japan, and China; this cohort-driven trend is thought to reflect increases in high-risk HPV prevalence from changing sexual behaviors. The exceptionally low overall cervical cancer rates in the Middle East and parts of Asia are thought to reflect low prevalence of HPV infections due to societal disapproval of extramarital sexual activity. Table to shows the general trend of cervical cancer by cases, deaths and prevalence globally and some selected WHO regions.

**Table 2:** Estimated Incidence, Mortality and Prevalence Worldwide in 2012

Estimated numbers (thousands)	Cases	Deaths	5-year prevalence
World	528	266	1547
More developed regions	83	36	289
Less developed regions	445	230	1258
WHO Africa region (AFRO)	92	57	236
WHO Americas region (PAHO)	83	36	279
WHO East Mediterranean region (EMRO)	15	8	42
WHO Europe region (EURO)	67	28	225
WHO South-East Asia region (SEARO)	175	94	465
WHO Western Pacific region (WPRO)	94	43	299
IARC membership (24 countries)	206	103	595
United States of America	13	7	47
China	62	30	190
India	123	67	309
European Union (EU-28)	34	13	115



## 4.0 Discussion

Cervical cancer is the only cancer that is almost completely preventable by safe, simple and inexpensive methods. Yet, every two minutes, one woman dies an unnecessary death from this cancer in the world. Unlike other cancers that occur in older age, cervical cancer peaks between the ages of 35-65 years and not only takes the life of young women, but devastates families with young children along the way. From the mortality and incidence rates, it is seen that the developing countries are with higher burden than the developed countries. These countries with a higher burden are not able to implement a successfully organized, population-based cervical cancer screening programs despite the greatest burden of cervical cancer in these countries (Yang, 2004), which is largely related to poverty, lack of resources and infrastructure and disenfranchisement of women. Even in some countries such as the developed countries where screening programs are free of charge and widely available, the uptake is still very low among the women. This low uptake has being found to be due to lack of knowledge about the disease and screening practices (Ncube et. al, 2015).

There is being a major breakthrough in cervical cancer control since the development of an effective prophylactic vaccine against the two main carcinogenic HPV types, i.e., HPV 16 and 18 (Andrus et al., 2008; Paavonen et al., 2009). However, this inflicts a very high cost burden on the developing countries (Goldie et al., 2008). Therefore, an effective screening practice still remains the best option in reducing incidence and mortality of cervical cancer. A large randomized study conducted in India demonstrated that screening with a high-risk HPV DNA assay once in a lifetime results in a reduction of the incidence of advanced cervical cancer as well as the cause-specific mortality by about one-half (Sankaranarayanan et al., 2009). In Europe, four randomized trials consistently showed, in the second screening round, a significant reduction of CIN3+ (cervical intraepithelial neoplasia of grade III or worse) by screening with a validated HPV assay compared with cytology (Arbyn et al., 2009), and one trial showed even a significant reduction in the cumulative incidence of invasive cervical cancer (Ronco et al., 2013). In China, a rapid and low-cost HPV assay, easily applicable in field conditions, demonstrated an accuracy for cancer precursors that was similar to the clinically validated Hybrid Capture-2 assay (Qiao et al., 2008). These findings should now be translated into effective prevention strategies, applicable in developing countries (Arbyn et al., 2011]. These include one or two HPV tests, in a lifetime followed by visual inspection and cryotherapy of eligible lesions among HPV-positive women for generations already sexually active and completed with immunisation of young girls with an affordable prophylactic HPV vaccine (Arbyn et al., 2011). Many of these interventions are being introduced in Africa, a continent with a low number of cancer registries. If these major breakthroughs are successfully implemented, careful thought and consideration should be given to the investment in adequate monitoring systems and developing cancer registries in target areas to measure the impact on incidence and mortality of cervical cancer (Arbyn et al., 2011).

## 5.0 Conclusion and recommendation

Cervical cancer continues to be a major public health problem that mostly affects developing countries and young women in particular, killing approximately a quarter of million women every year. There is a large geographic variation in cervical cancer rates reflected by differences the availability of screening and prevalence of high risk HPV infection. While the

incidence of cervical cancer in developed countries has reduced in accordance to effective screening practices, developing countries still suffer a greater burden of cervical cancer. Surveillance, including high-quality cancer registries, linked to screening and vaccination registries is essential to track the impact of these prevention strategies and to provide the foundation for advocacy, national policy and global action.

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## Declaration

The authors have no conflict of interest to declare.

## Authors contribution

Author 1: Article search, article review and writing the manuscript

Author 2: Reviewing the manuscript, organisation of ideas, organizing the references and final editing

Author 3: Reviewing and editing the manuscript

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