



Massimo Rugge<sup>1\*</sup>, F.A.C.G<sup>1</sup>, Michele Cosentino<sup>1</sup>, Kebreab Mehari WG<sup>2</sup>, Paola Bassan<sup>1</sup>, Elisabetta Marcato<sup>1</sup>, Zewdi Ghebremedhin Andemicael<sup>2</sup>, Simon Gebrehiwet<sup>2</sup>, Kibrom Hailu Ghebremicael<sup>3</sup>, Tesfamariam Mehari Halki<sup>3</sup>, Egle A Insacco<sup>4</sup>, Gianlibero Onnis<sup>1</sup> and Daria Minucci<sup>4</sup>

<sup>1</sup>Department of Medicine (DIMED), Surgical Pathology & Cytopathology Unit, University of Padova; Padova, Italy

<sup>2</sup>Department of Gynecology & Obstetrics; Orotta National Referral Hospital, Asmara, Eritrea

<sup>3</sup>Department of Anatomic Pathology & Laboratory Medicine, Orotta National Referral Hospital, Asmara, Eritrea

<sup>4</sup>Department of Women's and Child's Health University of Padova Hospital, AOUP, Padova, Italy

**Received:** 08 January, 2018

**Accepted:** 16 January, 2018

**Published:** 17 January, 2018

**\*Corresponding author:** Massimo Rugge, Surgical Pathology & Cytopathology Unit, Department of Medicine (DIMED), University of Padova, Via Aristide Gabelli 61, 35121 Padova, Italy; Tel: (+39) 049 8218990; Fax: (+39) 049 8272277; E-mail: massimo.rugge@unipd.it

**Keywords:** Cervical cancer; Cancer prevention; Public health

<https://www.peertechz.com>

## Procedures

# Uterine Cervical Cancer Prevention in Eritrea: Development and Results of a Pilot Project

## Abstract

**Background:** Uterine cervical cancer (UCC) is the fourth most common cancer worldwide; almost 85%-90% of UCCs, and UCC-related deaths occur in low-income countries. No UCC prevention programs are currently running in Eritrea.

**Aims:** This manuscript describes a stepwise initiative aiming to establish an UCC prevention project in Eritrea, which combines Pap-smear and colposcopy.

**Methods:** In 2013, an Italian multidisciplinary team submitted a project to the Eritrean Ministry of Health with a view to establishing an Eritrean-Italian UCC prevention task force. The project's starting point was an educational initiative to train local technicians on both Pap-smear assessments and colposcopy.

**Results:** An intensive academic course organized by the University of Padova (Italy) under the patronage of the Eritrean Ministry of Health was successfully held in Asmara to train Eritrean technicians, nurses and midwives to conduct Pap-smear assessments. Two subsequent pilot projects (2014-2016; 2016-2018) monitored the diagnostic competence of the Eritrean cyto-screeners. These pilot schemes resulted in an initial assessment of 2,014 Pap-smears, which provided information on the main operative issues involved in newly establishing a cancer prevention initiative in a sub-Saharan country. They also generated preliminary data on the prevalence of cancer and precancerous cervical lesions. The second pilot study is additionally providing further insight on the problems faced in expanding the prevention project to the Asmara population as a whole.

**Conclusions:** Anti-HPV vaccination, the most efficient primary UCC prevention strategy, entails basic requirements that are not always available in low-income countries. In terms of secondary UCC prevention, this Eritrean experience suggests that the low cost of "Pap testing" and the availability of local human resources could lower the incidence of UCC and related deaths in Eritrea.

## Introduction

Of the 9 million people worldwide diagnosed with cancer in 2017, more than 60% live in Africa, Asia, or Central and South America. These regions also account for about 70% of the world's cancer-related deaths (Figure 1). Uterine cervical cancer (UCC) is the fourth most common cancer worldwide, and the second cause of cancer-related death. Almost 90% of UCC and UCC-related deaths occur in low-income countries, mostly affecting young women in critical socio-economic conditions [1].

UCC is a preventable disease, and strategies for its primary (protected intercourse, HPV vaccination) and secondary prevention (detection and treatment of precancerous lesions) consistently result in lower rates of UCC incidence and related

deaths. Many (often concomitant) unfavorable conditions hinder the extensive implementation of secondary preventions programs for low-income populations. Cost is not the only issue. Other major "adverse situations" are fragile public healthcare networks (and the difficulty of establishing efficient links between diagnostic and therapeutic actions), poor connectivity (both logistic and digital), and the lack of educational projects. Running effective UCC screening programs also entails removing cultural and other barriers (the lack of information about UCC and Pap smears, negative attitudes to screening tests, etc.), which may interfere with women's chances of being tested [2-5].

In high-income countries, joint efforts by public and private healthcare networks usually do the operational groundwork needed to run oncological screening programs successfully. In

UCC secondary prevention, in particular, excellent results have been achieved by combining Pap smears with colposcopy [6]. Such favorable conditions are often unavailable in low-income countries, however. No established UCC prevention programs (be the primary or secondary) are currently running in Eritrea [7]. This manuscript describes an educational project that aimed to pave the way to locally-run screening programs for UCC secondary prevention in Eritrea [8].

The geopolitical landscape and early action undertaken in 2013–2017

#### - The geopolitical landscape

Eritrea is a sub-Saharan country (land area: 101,000 km<sup>2</sup>) with a population of five million (51% female). The median age of the resident population is 18.9 years, with a fertility rate of 4.32. The Eritrean population density is 50 per km<sup>2</sup>, and about one in three Eritreans live in urban areas. At the time of writing (2017), the country's annual per capita *gross domestic product* (GDP) was almost 1000 USD.

No reliable epidemiological information is available on the incidence of UCC in Eritrea [7]. In sub-Saharan Africa, 34.8 per 100,000 women are diagnosed with UCC each year, and 22.5 per 100,000 die of this disease [9].

### The project, teaching timetable, and available resources

#### - The project

In 2013, a team of Italian specialists (gynecologists, pathologists, and experienced cyto-screeners) submitted a project to the Eritrean Ministry of Health (Mrs. Amina Nurhussien) that proposed to establish a national UCC secondary prevention initiative (Figure 2). The first step in the project involved training local technicians to conduct Pap smear assessments. This step was considered crucial to the subsequent establishment of a screening-based secondary prevention program.

#### - Teaching program management and timetable (years 2013–2014)

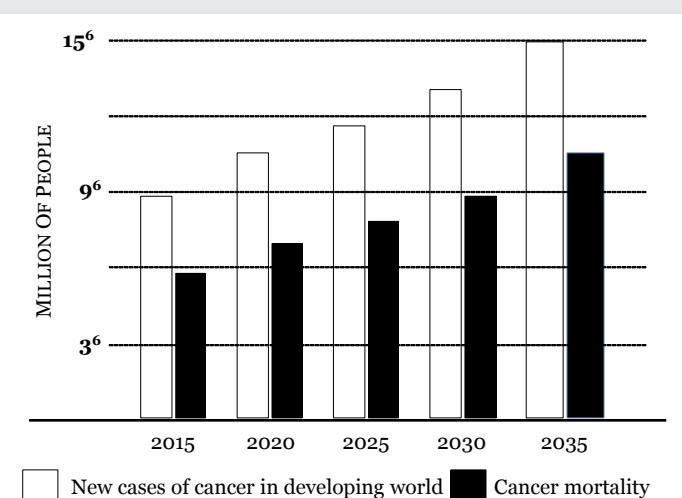


Figure 1: New cases of cancer in developing world (years 2015-2035) and associated cancer mortality.

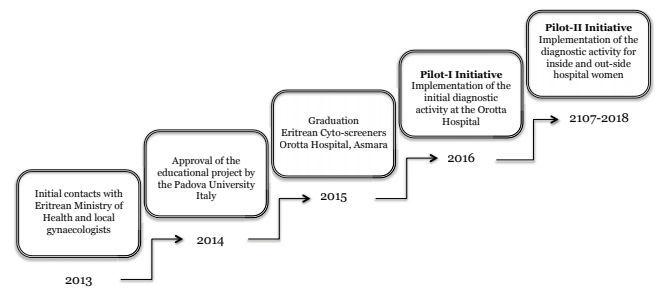


Figure 2: Timetable of the educational campaign.

Before starting the training activities at the Asmara Orotta Hospital, the gynecologist (KM) acting as the Eritrean promoter of the project spent 2 months in charge of the UCC screening activities at the Gynecology Unit at Padova University Hospital in Italy. During this period, he also attended a course on colposcopy organized by the Italian Society of Colposcopy and Cervical Pathology.

A structured academic course organized by the University of Padova was then held in Asmara. The course was structured and formally recognized by the University of Padova (Decree of the Rector of the University of Padova: July/22<sup>nd</sup>/2013). The teaching team consisted of 7 Italian specialists (2 cyto-screeners, 3 gynecologists, and 2 pathologists). An Eritrean gynecologist (KM) appointed by the Eritrean Minister of Public Health was in charge of local organizational matters.

Twelve Eritrean nurses, midwives, and laboratory technicians, selected from among the healthcare personnel at the Orotta National Referral Hospital in Asmara, attended the residential course, which was held at the Orotta National Referral Hospital. The course included: (a) formal lectures to provide a basic theoretical knowledge of the pathology of the female genital tract; and (b) microscopy tutorials to provide the basic diagnostic criteria to apply in Pap smear assessments.

#### - Formal lectures

The following topics were addressed in 8 days (70 hours) of intensive teaching activity: i) anatomy of the female genital tract; ii) physiopathology and basic pathology of the female genital tract, iii) diagnostic cytopathology/microbiology techniques; iv) histological-cytological correlations; and v) diagnostic cytopathology laboratory management.

#### - Diagnostic Laboratory of Pap smears assessment.

In all, 180 hours of training on real Pap smear slides were delivered as practical microscopy sessions. Informal group tuition with one-to-one discussion of cases at a multi-vision microscope was also included.

After completing these teaching activities, the students were shown a series of 75 pre-assessed Pap-smears representative of normal and pathological, neoplastic and non-neoplastic conditions (all obtained using conventional thick layer methods). They were also given a pre-set diagnostic frame (Figure 3), consisting of a checklist of the most significant cytological changes potentially encountered in a Pap smear

assessment. This teaching set of cytology slides was circulated among all the students over a period of two months, and the students were asked to complete the diagnostic checklist on the slides in order to test their diagnostic skills. After they had assessed the Pap-smears, new sessions of informal group tuition were conducted to critically review each student's diagnostic performance (one-to-one discussion of cases at a multi-vision microscope). A final test of their performance was based on the discussion of a series of 50 newly selected cases. Eleven students passed the proficiency test (November 2014), three of them also with a special mention. The graduation ceremony was held at the Orotta National Referral Hospital, involving the General Manager of the Orotta Hospital, the Dean of the School of Medicine of the Asmara University, the Director of the Health care National Office and the teaching team.

- Human resources and logistics, technical instruments, and teaching material

The training initiative required both local and Italian resources.

The Eritrean Government provided:

- human resources: dedicated personnel from the Orotta National Referral Hospital in Asmara;
- facilities/instruments: classroom and microscopes.

The Italian team provided:

- the teaching project as formally recognized by the Padova University (including free registration, formal certifications of attendance and graduation);
- facilities/instruments: teaching material, including cytology slides, books, and digital media (CD-ROMs).

The Italian team lived in Asmara for a total period of 160 person/days. All the teaching activities were conducted on a voluntary basis (as part of the Padova University institutional mission).

### The first pilot project (Pilot-I: 2014-2016): tutored training

To consolidate the diagnostic skills gained by the Eritrean graduate cyto-screeners, a new intervention was planned to explore the feasibility of setting up a Pap smear clinic at the Orotta National Referral Hospital in Asmara. The goal of this pilot scheme (Figure 2) was to collect at least 2000 Pap-smear samples from outpatients at the hospital.

The project involved: i) setting up a colposcopy clinic and a cytology laboratory at the Orotta hospital; ii) monitoring, in the real life, how the graduated technicians could deal with a Pap smears clinic (quality, identification, and assessment of the cytological samples); iii) establishing structured clinical pathways for women revealing precancerous lesions or cancer.

The project was run under the supervisions of a local gynecologist (KM) between 2016 and 2017. All cytological samples had to be obtained, handled technically, and examined microscopically by Eritrean nurses or midwives. The Italian team assessed the technical adequacy of the specimens obtained.

A total of 2,042 women were enrolled. The women's distribution by age is shown in figure 4. The results of the cytology according to the Bethesda system are shown in table 1, which also shows the mean age (and range) of the women in each of the diagnostic categories considered [10].

Among the 2,042, in 50 cases (2.45%) the slides were incorrectly identified or lost and in 198 cases (9.68%) the quality of Pap-smear did not allow any consistent cytology assessment.

Beyond the above-mentioned weaknesses, the results demonstrate that the educational initiative had succeeded in producing a local task force of cyto-screeners capable of managing the diagnostic phase of the UCC secondary prevention strategy efficiently. This was an important step towards ensuring the feasibility of a UCC prevention project.

Major weaknesses emerged in this phase, however, relating particularly to the difficulty of establishing a comprehensive secondary prevention program that could encompass both the initial diagnostic assessment of the neoplastic lesions and the subsequent therapeutic steps.

### The second pilot project (Pilot-II: 2017-2018): real-life testing

To preserve the professional competence gained by the Eritrean technicians, and improve the operational link between the diagnostic and any necessary therapeutic steps, a Pilot-II project was developed and is still underway (Figure 2).

The aims of this Pilot-II initiative are:

- to monitor the quality of the cytology samples and the laboratory's functional organization (including its technical performance);

**OROTTA NATIONAL REFERRAL HOSPITAL – ASMARA –**  
**OBSTETRICS & GYNECOLOGY DEPARTMENT: CERVICO-VAGINAL CYTOLOGY REPORT**

---

NAME _____	SPECIMEN	IDENTIFICATION NUMBER
DATE OF BIRTH _____	Vagina <input type="checkbox"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
ADDRESS _____	Exocervix <input type="checkbox"/>	<b>SPECIMEN ADEQUACY</b>
PHONE _____	Endocervix <input type="checkbox"/>	Satisfactory <input type="checkbox"/> Unsatisfactory <input type="checkbox"/>
	Other <input type="checkbox"/>	

**GENERAL CATEGORIZATION**

Negative for intraepithelial lesion or malignancy

Epithelial cells abnormality

**SQUAMOUS CELLS ABNORMALITIES**

Atypical squamous cells undetermined significance= **ASC-US**

Atypical squamous cells, cannot exclude HSIL= **ASC-H**

Low-grade squamous intraepithelial lesion (including HPV)= **LSIL**

High-grade squamous intraepithelial lesion= **HSIL**

Squamous cell carcinoma

**GLANDULAR CELLS ABNORMALITIES**

Atypical glandular cells: **AGC**

Atypical glandular cells (favour neoplastic)

Adenocarcinoma

L. Menstruation: \_\_\_\_\_

**ORGANISMS**

L. No inflammation      L. Fungi (Candida)

L. Doderlein Bacillus    L. Bacterial vaginosis

L. Bacteria                L. Herpes Simplex V.

L. Trichomonas v.        L. Other

NOTES: \_\_\_\_\_

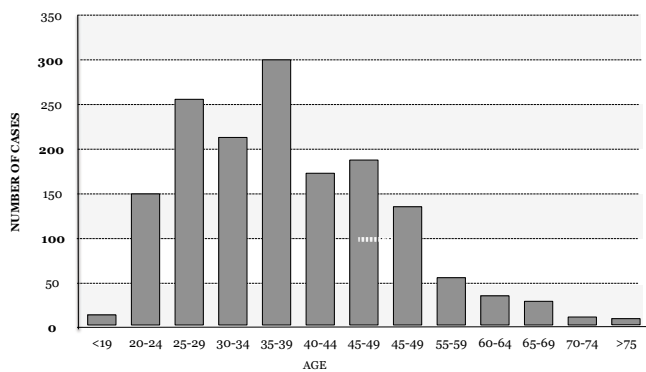
\_\_\_\_\_

\_\_\_\_\_

DATE: \_\_\_\_\_

SIGNATURE: \_\_\_\_\_

Figure 3: Frame for the Pap-smear diagnostic reporting as applied in the screening pilot study.



**Figure 4:** Age distribution of 2042 Pap smears as obtained in the Pilot-I phase of the intervention (year 2016).

**Table 1:** Pap smears assessment (according to the Bethesda criteria) in 2042 cases enrolled at the Orotta Hospital, Amara (year 2016).

2042 PAP-SMEARS: FINAL ASSESSMENT (according to Bethesda criteria).

Diagnosis	Number	Percentage %	Mean Age (Range)
Normal	1,653	80.9	-----
Low-Risk Lesions	67	3.28	39.7 (20-70)
High-Risk Lesions	38	1.86	42.0 (21-80)
CANCER (Invasive)	36	16.7	46.6 (28-70)
INADEQUATE (Sampling)	198	9.69	-----
Lost	50	2.45	-----
<b>Total</b>	<b>2,042</b>	<b>100</b>	<b>59 (20-80)</b>

- to establish the colposcopy clinic;
- to test the procedures for enabling outpatients to access Pap testing;
- to obtain more reliable information on the prevalence of the target disease in the outpatient population.

The goal of Pilot-II is thus to collect at least 5,000 Pap-smears, half of them from patients admitted to the Orotta Hospital in Asmara, and the other half from women recruited from the population of Asmara. The project is still ongoing, and should be concluded by the end of 2018. The whole Pilot-II project is under the responsibility of Eritrean physicians and cyto-screeners, with the Italian team only monitoring the activities and serving in an advisory role (where needed).

## Conclusions

Before the extensive implementation of screening programs, the UCC-related mortality rates were much the same in high- and low-income countries. This is no longer the case, however, now that the incidence and mortality rates for UCC in Europe and North America have been drastically lowered. It is generally acknowledged that we have to thank cervical cytology (Pap-smear) combined with colposcopy for the significant improvements made in this setting [11,12].

The results emerging from this Eritrean experience suggest a high prevalence of UCC in the population of Asmara, although no dependable information has been obtained as yet on the UCC incidence in Eritrea as a whole. The only (albeit

weak) information potentially comparable with other African experiences concerns the association between an older mean age of the women screened and an increasing severity of the cases of cytologically identified cervical disease.

As for the educational effort, our initiative demonstrates that an intensive training program can produce efficient cyto-screeners capable of covering all the diagnostic steps of a Pap smear procedure successfully [13].

Secondary prevention strategies offer the opportunity to lower the incidence of UCC in developing countries too, even though certain practical issues may hinder the broad implementation of screening programs [14]. In 2015, a USA task force asked to design cancer prevention strategies for developing countries identified two major lines of intervention for preventing UCC: i) preventing HPV infection by making vaccines more readily available; and ii) implementing screening methods “more compatible than Pap smear” with the resources available in developing countries [15].

Vaccinating against HPV is currently the most efficient strategy for eradicating the main causative agent behind UCC, but the cost of national vaccination campaigns seems to be hardly compatible with the resources available in some areas.

As concerns secondary prevention strategies, this Eritrean experience demonstrated – despite significant weaknesses (related largely to shortcomings of the health system infrastructure) – that most of the obstacles are potentially manageable. On balance, the “cons” of “Pap testing” are largely counteracted by two significant “pros”, i.e. low cost and the availability of local human resources [16-19].

## Eritrean team

Kebreab Mehari, M.D. (Eritrean Cervical Cancer Prevention Project Director)

Kibrom Hailu Ghebremicael (course graduate)

Zewdi Ghebremedhin Andemicael (course graduate)

Rahel Tesfamicael Yohannes (withdrawn)

Berzelin Adugna Haile (course graduate)

Amanuel Mahari Tesfamariam (withdrawn)

Mihreteab Tekie Zewoldi (withdrawn)

Saba Haile Abraha (course graduate)

Absera Woldu Haile (course graduate)

Abrehet Weldemicael Weldemariam (course graduate)

Tesfamariam Mehari Halki (course graduate)

Nahom Amanuel Asfaha (course graduate)

Selam Haileab Estifanos (course graduate)

Samson Fisehatsion (laboratory technician)



Simon Gebrehiwet (laboratory technician)  
 Tesfamariam Mehari Halki (laboratory technician)  
 Kibrom Hailu Ghebremicael (laboratory technician)  
 Zewdi Ghebremedhin Andemicael (laboratory technician)

### Italian team in Eritrea

Paola Bassan, BMSc in Diagnostic gynecological cytology, Padova University Teaching Hospital

Michele Cosentino, MD, Gynecologist, Padova University Teaching Hospital

Egle A Insacco, MD, Gynecologist, Padova University Teaching Hospital

Elisabetta Marcato, BMSc in Diagnostic gynecological cytology; Master's Degree in Diagnostic Technical Sciences; Padova University Teaching Hospital

Daria Minucci, MD, Associated Professor of Obstetrics Gynecology, currently senior scholar at Padova University

Gianlibero Onnis, MD, Pathologist, Padova University Teaching Hospital

Massimo Rugge, MD, Head of the Pathology Department (AOUP), and Course Director, University of Padova

### Acknowledgment

This manuscript is in memory of Mrs. Sara Debesai Sebhatsu (1927-2010), a native of Eritrea, who generously worked in Asmara to improve Eritrean women's quality of life.

### References

1. Fidler MM, Gupta S, Soerjomataram I, Ferlay J, Steliarova-Foucher E, et al. (2017) Cancer incidence and mortality among young adults aged 20-39 years worldwide in 2012: a population-based study. *Lancet Oncol* 18: 1579-1589. [Link: https://goo.gl/uGm8SG](https://goo.gl/uGm8SG)
2. WHO (2012) Cervical Cancer Screening in Developing Countries: report of a WHO consultation. World Health Organization. 2002. [Link: https://goo.gl/kQSVho](https://goo.gl/kQSVho)
3. Williams KP, Mullan PB, Fletcher F (2007) Working with African American women to develop a cancer literacy assessment tool: a cancer-specific literacy assessment in measuring women's functional cancer literacy. *J Cancer Educ* 22: 241-244. [Link: https://goo.gl/9AwhL3](https://goo.gl/9AwhL3)
4. Navarro AM, McNicholas LJ, Cruz M, McKennett M, Sánchez O, et al. (2007). Development and implementation of a curriculum on cancer screening for small groups of Latino women. *J Cancer Educ* 22: 186-190. [Link: https://goo.gl/gRC38z](https://goo.gl/gRC38z)
5. Lavelle AE, Su D, Kahesa C, Soliman AS (2017) Needs for professional education to optimize cervical cancer screenings in low-income countries:

a case study from Tanzania. *J Cancer Educ*. [Epub ahead of print] [Link: https://goo.gl/cVQvVq](https://goo.gl/cVQvVq)

6. Viviano M, De Beudrap P, Tebeu PM, Fouogue JT, Vassilakos P, et al. (2017) A review of screening strategies for cervical cancer in human immunodeficiency virus-positive women in sub-Saharan Africa. *Int J Womens Health* 9: 69-79. [Link: https://goo.gl/jTRJaU](https://goo.gl/jTRJaU)
7. Finocchiaro-Kessler S, Wexler C, Maloba M, Mabachi N, Ndikum-Moffor F, et al. (2006) Cervical cancer prevention and treatment research in Africa: a systematic review from a public health perspective. *BMC Womens Health* 4: 16:29. [Link: https://goo.gl/2uFx9v](https://goo.gl/2uFx9v)
8. Peters LM, Soliman AS, Bukori P, Mkuchu J, Ngoma T (2010) Evidence for the need of educational programs for cervical screening in rural Tanzania. *J Cancer Educ* 25: 153-159. [Link: https://goo.gl/vfX6TS](https://goo.gl/vfX6TS)
9. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, et al. (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 136: E359-E386. [Link: https://goo.gl/qU14BF](https://goo.gl/qU14BF)
10. Nguyen HN, Nordqvist SR (1999) The Bethesda system and evaluation of abnormal Pap smears. *Semin Surg Oncol* 16: 217-221. [Link: https://goo.gl/V8vWcW](https://goo.gl/V8vWcW)
11. Mbumba Bouassa RS, Prazuck T, Lethu T, Meye JF, Bélec L (2017) Cervical cancer in sub-Saharan Africa: an emerging and preventable disease associated with oncogenic human papillomavirus. *Med Santé Trop* 27: 16-22. [Link: https://goo.gl/oGSYnF](https://goo.gl/oGSYnF)
12. Mukakalisa I, Bindler R, Allen C, Dotson J (2014) Cervical cancer in developing countries: effective screening and preventive strategies with an application in Rwanda. *Health Care Women Int* 35: 1065-1080. [Link: https://goo.gl/yR55bF](https://goo.gl/yR55bF)
13. Catarino R, Petignat P, Dongui G, Vassilakos P (2015) Cervical cancer screening in developing countries at a crossroad: emerging technologies and policy choices. *World Journal of Clinical Oncology* 6: 281-290. [Link: https://goo.gl/s2yu0q](https://goo.gl/s2yu0q)
14. Akinfolarin AC, Olusegun AK, Omoladun O, Omoniyi-Esan GO, Onwundiegwu U (2017) Age and pattern of Pap smear abnormalities: implications for cervical cancer control in a developing country. *Cytol* 34: 208-211. [Link: https://goo.gl/nKmgwX](https://goo.gl/nKmgwX)
15. Bollyky TJ, Andridge D (2015) Cancer prevention and Treatment in developing Countries: recommendations for action. *Cancer Control Planning. Cancer Control*. [Link: https://goo.gl/hhAC4e](https://goo.gl/hhAC4e)
16. Anorlu RI, Ola ER, Abudu OO (2007) Low-cost methods for secondary prevention of cervical cancer in developing countries. *Niger Postgrad Med J* 14: 242-246. [Link: https://goo.gl/9rdVbf](https://goo.gl/9rdVbf)
17. Park IU, Diaz ML, Bowey C, Magaril R, Ferris DG (2007) On behalf of the INCCA Foundation. Cervical cancer prevention in the developing world. *Journal of Lower Genital Tract Disease* 11: 273.
18. Navarro AM, Rock CL, McNicholas LJ, et al. (2000) Community-based education in nutrition and cancer: the Por La Vida Cuidándose curriculum. *J Cancer Educ* 15: 168-172. [Link: https://goo.gl/MKcpQE](https://goo.gl/MKcpQE)
19. Otulo P, Ngotiek P, Yiaiale AL, Serrem CK, Menge D, et al. (2017) An Assessment of the Need to Establish a Nursing Training Institution in Narok County, Kenya. *Arch Community Med Public Health* 3: 008-016. [Link: https://goo.gl/TK7Npc](https://goo.gl/TK7Npc)