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Pharmacoeconomic Analysis of Cervical Cancer Cases Specific to Serotypes 16 and 18 Based on the Analysis of Protective Determinants and Risk Factors Based on Activity-Based Accounting in Morocco

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Abstract - With 2057 new cases of cervical cancer and 923 deaths each year in Rabat, and most of the cases (80%) occur at the age of 45, Morocco is facing a public health problem that absorbs huge expenses from the health system and that requires reflection to minimize costs and reduce premature deaths of married women of childbearing age. Method: Faced with this emerging problem, a cohort study was carried out on 250 women over 5 years in the Rabat region to study the risk and protective factors against cervical cancer. Results: The study found two protective factors: diet rich in vitamin A and C (RR: 2.9 [1.69 to 4.18]) and use of progestin-only injectable contraceptives (RR :0.5[0.36 to0.75]), as well as risk factors, mainly smoking (RR :9.8[9.51 to 9. 93]), Menopause (RR :1.3[1.21 to 1.76]), Post coital metrorrhagia (RR :4.83[1.63 to 5.01]), Previous history of clamidiya (RR :3.9[1.67 to 6. 01]), Hemoglobin level≤10g/dl (RR :6.8[4.13 to6.01], use of oestro-progestins≥10 years (RR :5.9[4.36 to 7.01], multiple partners (5.6[1.56 to6.75]. In addition, the study used the analysis of their cost per activity approach to allow a better diagnosis of the causes of direct and indirect costs as well as the search to reduce the burden on the health system and to reduce premature mortality in the working population. Conclusion: The cost to meet the expenses of cervical cancer is estimated at 12 783 138 907 160 €, while the cost of vaccination that will cover the entire female Moroccan population aged 10 to 14 years is 1526000 is estimated 67 296 600 €, and the cost of vaccine is estimated 44.9 € which will save the health system a cost minimization that is around 12 783 071 610 560 €. Conclusion: the cost to meet the expenses of cervical cancer is estimated at 12,783,138,907,160 €, while the cost of vaccination that will cover the entire female Moroccan population aged 10 to 14 years is 1526,000 is estimated 67,296,600 €, and the cost of vaccine is estimated 44.9 € which will save the health system a cost minimization which is around 12,783,071,610,560 €.

Keywords: Cancer of the cervix, Human papillomavirus, Activity Based costing, and Vaccine.

1.Introduction

According to the latest World Health Organization estimates, cervical cancer is the fourth most common cancer in women worldwide, with an estimated 604,000 cases and 342,000 deaths in 2020[1]. It is a special cancer because it is a sexually transmitted infection that can be caught at the first intercourse. In low- and middle-income countries, access to treatment for cancerous lesions is expensive and may prevent economically disadvantaged women without social security coverage from accessing care. With 90% of cervical cancer cases occurring in low- and middle-income countries [2]. In the eastern Mediterranean region, a systematic review of data collected from 26,536 women with normal cytology from 13 countries in the eastern Mediterranean region countries found that the average prevalence of human papilloma virus (HPV) was 9.3%, with HPV 16 and HPV 18 being the most common types with a reported prevalence of 2.3% and 0.7%, respectively [3]. The highest prevalence was recorded in Saudi Arabia (19.0%) among Asian countries and in Morocco (19.0%) among African countries. Women in

Kuwait and Sudan had the lowest HPV prevalence (2.0% and 3.0%, respectively) among Asian and African countries in the region [4]. According to World Health Organization estimates on the incidence of cancer in Morocco in 2020, breast cancer is the leading cancer in women with 6,650 cases, followed by cervical cancer (2,258 cases), and ovarian cancer (735 cases) [5]. Cervical cancer is the second most common cancer in women, with 3,300 new cases and almost 2,500 deaths recorded, and age-standardized mortality rates of 17.2 and 12.6 per 100,000 women respectively [6]. Regarding the cost of treatment of cervical cancer according to The International Federation of Gynecology and Obstetrics (FIGO) stages, an estimate was concluded in Tunisia, ranging from (431 to 4,143 €) with an average of (1,766 ± 772 €) [7]. In Morocco, no economic evaluation has been conducted to estimate the cost and expenses inherent in the management of cancers patients and particularly those with cervical cancer. A significant proportion are reluctant to undergo treatment for fear of the expense of chemotherapy and radiotherapy, and rely on traditional medication until serious complications arise.

Almost all cervical cancers are attributable to high-risk oncogenic viruses (HR-HPV), with serotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68 considered "carcinogenic", and types 16 and 18 being the most potent of these [8]. HPV is responsible for almost all cervical cancers, 88 HPV is ubiquitous and is the most common sexually transmitted infection in the world. About 200 HPV genotypes are responsible for 78% of uterine cancers, 50% and 25% of vulvar cancers [9]. It should be recalled that papillomaviruses belong to the family Papillomaviridae, which is composed of a variety of ancient DNA viruses that spread on a wide range of hosts, including mammals, birds, reptiles and fish [10]. Over the past century, more than 200 different genotypes of human papillomavirus have been discovered, and they have been classified according to their genomic sequence, tropism or carcinogenic potential [11,12]. For classification based on genomic sequence, HPVs are divided into five genera (alpha, beta, gamma, mu and nu), which have less than 60% L1 sequence homology between them. Within each genus, HPVs are divided into four categories (Figures 1 and 2): species (60-70% homology), types (71-89% similarity), subtypes (90-98% homology) and finally variations (90-98% homology) [12].

2. Methods: Study setting

With regard to HPV classification based on tropism, the alpha genus infects both cutaneous and mucosal epithelia and includes genotypes described as causing cancer, whereas Beta and Gammapillomavirus infections are for 8 years, we recruited women aged 17 years or older who consulted for cervical cancer screening. Two subgroups were formed at any stage of carcinogenic status discovery, diagnosed as HPV positive by either visual inspection with acetic acid, Pap smear, colposcopy, magnetic resonance imaging and on the basis of laboratory confirmation and/or radiological findings suggestive of precancerous lesions or invasive carcinoma 258 women were recruited to study exposure factors for cervical cancer. On the costing side of cervical cancer management, using the cost accounting method. The study aims to calculate the costs of management that ensures patient safety with an efficient quality assurance system, while meeting the generally asymptomatic, but immunosuppressive conditions allow these types to produce skin papilloma's or increase the propensity for skin cancer [13].

Regarding classification based on oncogenic potential, according to the International Agency for Research on Cancer (IARC), twelve high-risk types (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59) have been identified as carcinogenic to humans. However, the low-risk types, such as HPV 6 or HPV 11, often cause benign diseases such as genital warts [14]. Regarding the structure and genome of HPV, the genetic structure and mode of organization of the HPV family is similar [15]. They have a circular double-stranded DNA genome of 8 kb, which encodes for 8-10 proteins. The genome consists of three main sections. (I) An essential role in cell transformation is played by the early (E) region (E1, E2, E4, E5, E6 and E7). (ii) The capsid proteins L1 and L2 are encoded by the late (L) region. (iii) The upstream regulatory protein (UPR), sometimes called the long control region (LCR), is a non-coding region located between L1 and E6/E7 and includes transcription factor binding sites. It controls viral gene transcription and DNA replication [16]. In a context of scarce resources, the analysis of cervical cancer costs is directly involved in the management of the activity of hospital organizations, it provides information on their efficiency and informs the decision-making processes of the Ministry of Health in order to cope with expenditure related to hospitalisation and to promote screening and vaccination in order to reduce the number of exposures. The present study aims to investigate the epidemiological profile and economic evaluation of the costs of managing women with positive cervical cancer status using the activity-based costing method. In the face of a rapidly changing environment characterized by increased budgetary constraints, economic evaluation

contributes directly to the management of the activity of health establishments, which provides information on their efficiency and rationalizes the decision-making process [17]. According to the WHO, low- income countries can save 12 to 24% per year on their total health expenditure by improving the efficiency of hospitals [18]. However, the management of cervical cancer in Morocco lacks financial and human resources, which leads to a rapid turnover of medical resources, resulting in huge expenses in terms of providing care for all patients. However, cervical cancer care in Morocco lacks financial and human resources. This lack leads to a rapid turnover of medical resources, thus causing enormous expenses in terms of ensuring care for all patients. The objective is to gather as much information as possible on the functioning, the resources consumed and the procedures followed within the oncology department.

Implementation

This is a cohort study conducted between 2013 and 2023 at the Sidi Mohamed Ben Abdallah National Oncology Center, with two subgroups. Women with positive cervical cancer status at any stage and their disease-free peers. Population characteristics were compared between the two groups: 1) age, 2) age of first pregnancy, 3) body mass index, 4) menstrual cycle, 5) menopausal status, 6) diet, 7) smoking status, 8) reasons for referral to the oncology center, 9) biopsy results, 10) depression, 11) parity, 12) metrorrhagia.

Regarding the economic evaluation of cervical cancer management by Activity Based Coasting. The method chosen for the cost evaluation is a technique that responds to the limits that certain organizations, in this case hospitals, encounter in the analysis of costs and activities, as long as it breaks down the hospital into activities and establishes the traceability of indirect charges in order to focus on the costs of activities that are allocated to the services provided to patients. The study was conducted from the perspective of the oncology center in Rabat.

Ethics

The research ethics committee at the Faculty of Medicine and Pharmacy in Rabat and the local center's ethics committee approved the study (No. 48/13), which did not interfere with clinical management. Written informed consent was obtained from the study participants in accordance with local requirements. The investigators adhered to the Helsinki declaration9 and good clinical practice guidelines during the development of the study protocol, including the laboratory tests used during the investigation.

3.Results

With 2057 new cases of cervical cancer and 923 deaths each year in Rabat [19], the study was conducted to investigate the incidence of HPV in women in the Rabat region as well as the risk and protective factors of exposure to the virus. The women with a positive diagnosis of human papillomavirus, 154 (58.6%) had confirmation by positive Ana pathology examination and magnetic resonance imaging and 96 (36.5%) had symptoms without laboratory confirmation. Of those confirmed positive, they were reconfirmed positive by polymerase chain reaction 32(20.7%) and. The two subgroups with and without diagnosis showed similar socio-demographic characteristics. Women with a positive HPV diagnosis had a high rate of recreational smoking, early sexual intercourse due to age of first pregnancy, high parity, carnivorous diet, BMI above 30 (85.8%) of cases, as well as exposure to Chlamydia Trachomatis (94%), bacterial vaginosis (39%) and genital herpes (15%).Adjusting for cervical cancer, risk factors and two protective factors were identified that were associated with the occurrence of UCC. The risk factors were Tobacco (RR: 9.8 [9.51 to 9.93]), which is at the top of the risk factors, as it is a 9-fold risk for cervical cancer, Recurrent leucorrhoea (RR: 2.5 [2.16 to 2. 70]), body mass index ≥30 (RR:1.7[1.06 to 2.75]), Parity (3.6[3.51 to 4.21]), Low level of education(RR :5.3[3.13 to 8.10]), Sponsored metrorrhagia (RR :2.7[2.13 to 4.10]), Post-coital metrorrhagia(RR : 4. 83[1.63 to 5.01]),Age at first pregnancy≤17years(RR :2.3[1.56 to 2.51]),Menopause (RR :1.3[1.21 to 1.76]), Previous history of clamidiya trachomatis(RR : 3.9[1.67 to 6.01]), History of genital herpes(RR : 2. 2[2.87 to 3.04]), HIV positive (RR :6.5 [6.42 to 7.45]), Bacterial vaginosis(RR :1.6 [1.27 to 2.43]), Irregular menstrual cycle(RR :2.7[1.52 to 3.27]),Hemoglobin level <10 g/dl (RR :6.8[4. 13 to 8.10]), Depression (RR :1.8[1.23 to 6.01]), Multiple partners (RR: 5.6[1.56 to 6.75]), Use of oestro-progestins≥10years (RR: 5.9[4.63 to 7.01]), Access to cancer screening≥10km (RR :9.7[5. 63 to 9.81]), Unmarried women (RR :2.9[1.69 to 4.18]), Infections requiring antibiotics (RR :3.5[3.43 to 7.21]), C-reactive protein ≥6mg/L, (RR :5.9[4.63 to 6.01]). Regarding protective factors, the study identified the use of depot-medroxyprogesterone acetate (RR: 0.5[0.36 to 0.75]), as well as Diet rich in vitamin A and C (RR: 0.6[0.74 to

0.87]), see table1.The multiple correspondence analysis generated correlations of the transformed variables, showed strong correlations between Ana pathology results (R :0.705) and cervical cancer, as well as for sexually transmitted infections (R:0.894), see graph1. Weak correlations were found for the correlation of menstrual cycle irregularity with exposure to cervical cancer (R :0.224), see table2.

With regard to the analysis of costs attributable to cervical cancer management, the study of international experiences shows that cost analysis contributes to a change in organizational culture, since the question is no longer to reason in terms of expenditure, but also in terms of the value of resources intended for cervical cancer management. In this respect, cost accounting is of great importance for hospitals, especially as the real cost of public hospitals is not well known [20] ; it enables hospitals to identify the cost prices of their "products" and to record operations relating to the hospital's activity.

The economic evaluation of cervical cancer management by Activity Based Coasting. This involved calculating the direct and indirect costs associated with the management of patients. It concerned those attributable to the purchase price of treatment, consumables, equipment, hospitalisation and other indirect costs relating to the depreciation of the building, electricity, water, disposal of waste from Care Activities with Infectious Risks. It will also allow the internal and external comparison of the evolution of production costs in relation to activity.

For direct costs, it amounts to 11454.79 € per capita, broken down by length of stay in hospital, (486.01 €), X-ray Examinations (120.88 €), Further tests (111.43 €), Biological tests (7066.07 €), Drug (4017.94 €), see Table3. For indirect costs, staff costs, medical costs, depreciation costs (hospital, maintenance and administrative) were identified. Broken down as follows, Annual staff costs (489599.73 €), Chemotherapy unit room (53099.79 €), Total depreciation (319525.2 €), see Table4. In total, the sum of expenses charged to the health system directly and indirectly per woman with cervical cancer is estimated at 1506912.52 €. Noting that the female population in Morocco aged 15-45 years is around 84830,00(21), the cost of meeting the expenses of exposure to cervical cancer is estimated at € 12,783,138,907,160. While the cost of vaccination that will cover the entire female population aged 10-14 years (1526000) is estimated to be ↪Lu_67 296 600, and the cost of vaccine is estimated to be 44.9 € which will save the health system a cost minimization that is around 12 783 071 610 560 €. Finally, vaccination remains the public health intervention with the best cost-benefit ratio to address the catastrophic expenditure of cervical cancer.

The depreciation charges are charges related to wear and tear due to the use of the premises, biomedical equipment and furniture. In order to calculate these expenses, we have opted for the linear depreciation method, by calculating the equivalent annual cost of the initial investment expenditure. The annual equivalent cost is the division of the investment expenditure by the number of years of life of the good or equipment, while making an adjustment with a discount rate of 5%. The high depreciation charge is due to the fact that the hospital is still new, and the equipment is expensive and recently acquired. The formula used for its calculation is: k=E×1-(1+ r)-n/ r =EA (n, r), A: present value of an annual instalment, K: initial investment, E: equivalent annual cost, n: years of life of the capital good, r: interest rate [22].

It should be remembered that the strength of the ABC approach is that it allows for a better diagnosis of the causes of costs and performance within an organization and the allocation of resources consumed to the different activities [23] Furthermore, its aim is to identify the drivers, which make it possible to explain the costs and performance. Knowing that the resource driver, also called level 1 driver, is the best measure of the quantity of resources consumed by a given activity, it links the resources and the activity under analysis [24]. For our analysis, the drivers adopted for activities relate to resources. This is the key to attributing the resources consumed to the different activities. The drivers chosen to link resources to activities are: the direct charge for equipment maintenance, the surface area in m^2 for premises, the number of telephone sets, the quantity used for medical expenses, the full-time equivalent for the activity of health professionals.

4.Discussion

Globally, cervical cancer is the second most common cancer among women, with an estimated 630 million women infected with HPV, 80% of whom are in low-income countries. The study highlighted two protective factors against high-risk HPV (16,18). These were a vegetarian diet rich in vitamin A and C and the use of contraception

depot-medroxyprogesterone acetate.

In this regard, the study established a significant association between the diet rich in vitamin A and C with a relative risk (RR:0. 6), these results corroborate with several studies dedicated to the study of the influence of various nutritional factors such as folates, vitamin C, vitamin E and carotenoids on the cervical epithelium it appears that a diet rich in fruits and vegetables would have a protective effect against UCC, thanks to the micronutrients provided (vitamin A, C, E, Folates), this protection is exerted mainly during the early stages of carcinogenesis [25,26].

Regarding the protective effect of depot-medroxyprogesterone acetate adopted as a long-term contraceptive, the study established a protective link against uterine UCC with a relative risk (RR :0.5), A cohort study conducted in Australia in 30 years confirmed the protective effect of DMPA in women of reproductive age against UCC, in addition, women who have used DMPA for a period of ten years, do not have any advantage of developing breast cancer [27]. In terms of risk factors that increase the risk of cervical cancer, recreational smoking tops all risk factors (RR: 9.8).

As smoking affects the body's defense mechanisms, it can prevent the human papillomavirus (HPV) from clearing on its own and causing the development of cervical cancer. Experimental studies have shown a strong association between both forms of smoking (passive and active) and exposure to many cancers, in this case cervical cancer, which is among the most identified environmental co-factors in all cancers [28]. For the present study, smoking is at the top of all factors, recording a relative risk of (RR :9.8). J. BRISSON's group conducted a case-control study of 247 female cervical cancer patients and 137 controls, the results of which clearly show a significant increase in the risk of developing cervical cancer in female smokers [29]. In addition, several studies have shown that the risk of dysplasia and invasive cancer is twice as high in smokers as in non-smokers, taking HPV infection into account [30].

With regard to the occurrence of spontaneous and post-coital metrorrhagia, the study recorded significant relative risks in favour of an association (RR :2.7) and (RR :4.83) with cervical cancer exposure. This corroborates with the literature, they can be spontaneous without any trauma or be sudden and considerable if the neoplastic ulceration has eroded a cervical vessel [31]. It is the main symptom of cervical cancer, they can be spontaneous or post-coital, its occurrence is due if the neoplastic ulceration has eroded a cervical vessel. With regard to parity, an analysis by the International Agency for Research on Cancer based on several studies of HPV-positive women found that the risk increased manifold with the number of pregnancies, with women who had completed 7 pregnancies having a 4-fold higher risk than nulliparous women; furthermore, the risk increased linearly with the number of pregnancies. Although this association is well established, the explanatory mechanism is not yet clear [32]. In the present study, hemoglobin <10 g/dl was associated with the occurrence of cervical cancer, with a significant relative risk (RR:6.8). Anemia is considered both a risk factor and a complication that exacerbates hypoxia in cervical tumour, and hypoxia is a prognostic factor inextricably linked to cancer. However, it is known that oxygenation of these tumors is directly related to hemoglobin concentration [33]. The study found a strong association between both forms of smoking (passive and active) and exposure to many cancers, in this case cervical cancer, which is among the most identified environmental co-factors in all cancers. For the present study, smoking is at the top of all factors, recording a relative risk of (RR:9.8). J. BRISSON's group conducted a case-control study of 247 female cervical cancer patients and 137 controls, the results of which clearly show a significant increase in the risk of developing cervical cancer in female smokers. In addition, several studies have shown that the risk of dysplasia and invasive cancer is twice as high in smokers as in non-smokers, taking HPV infection into account [34]. With regard to the occurrence of spontaneous and post-coital metrorrhagia, the study recorded significant relative risks in favour of the association (RR :2.7) and (RR :4.83) with exposure to cervical cancer. This corroborates with the literature, they can be spontaneous without any trauma or be sudden and considerable if the neoplastic ulceration has eroded a cervical vessel [35]. It is the main symptom of cervical cancer, they can be spontaneous or post-coital, its occurrence is due if the neoplastic ulceration has eroded a cervical vessel. With regard to parity, an analysis by the International Agency for Research on Cancer based on several studies of HPV-positive women found that the risk increased manifold with the number of pregnancies, with women who had completed 7 pregnancies having a 4-fold higher risk than nulliparous women; furthermore,

the risk increased linearly with the number of pregnancies. Although this association is well established, the explanatory mechanism is not yet clear [36]. In the present study, hemoglobin <10 g/dl was associated with the occurrence of cervical cancer, with a significant relative risk (RR:6.8). Anemia is considered both a risk factor and a complication that exacerbates hypoxia in cervical tumours, and hypoxia is a prognostic factor inextricably linked to cancer. However, it is known that oxygenation of these tumours is directly related to hemoglobin concentration [37].

With regard to co-infection of HPV and other sexually transmitted infections, markers of exposure to other STIs have been found to be associated with cervical cancer successively, clamidiya trachomatis, genital herpes and bacterial vaginosis (28,34,35). this is consistent with the results of the clamidiya trachomatis (RR:3.9), genital herpes (RR:2.2) and bacterial vaginosis (RR:1.6) study. The results are consistent with findings from a case-control study, which showed that in HPV-positive women, the presence of antibodies to Chlamydia trachomatis was associated with twice the risk of cervical cancer compared to women without these antibodies [36]. A second similar study showed that infection with herpes simplex virus type 2 was also a Co factor for HPV infection (37). It should be remembered that women living with HIV have a six-fold increased risk of cervical cancer compared to HIV-negative women [38].

In Morocco, a study conducted on risk factors in women with cervical cancer, the results of a case-control study showed that women reporting high to very high habitual stress and those reporting medium habitual stress were significantly higher in cases than in controls (37.0% vs. 21.6% and 47.4% vs. 32.9% respectively). These results corroborate with the results of the study that found the association between depression and cervical cancer exposure [39]. With regard to the effect of body mass index greater than 30, it was found to be a significant risk factor for cervical cancer exposure, the study recorded a relative risk of (RR: 1. This is confirmed by the strong results reported by the World Health Organization which confirms the strong association between cervical cancer and body mass index above 30 [40].

The survey found that use of estrogen-progestin contraceptives for more than ten years increases the risk of cervical cancer (RR: 5.9). These results corroborate with the findings of an international multicenter case-control study published in the Lancet, which found that the risk of cervical cancer increased by a factor of four if HPV-positive women had been using an oral contraceptive for at least ten years. Regarding the effect of multiple partners and the risk of cervical cancer, the present study found a risk of (RR: 5.6) of exposure to cervical cancer and a risk of (RR: 2.9) for unmarried women (single, divorced, widowed). This is in line with the results of a national study in Fez which found that multiple partnering beyond two was significantly higher in cases than in controls (20.8% vs. 11.4%; P≤0.05) recording (OR=2.1; CI95%= [1.2-3.8]) [41].

5.Conclusion

Cervical cancer remains a problem of female reproductive health and public health that requires special attention by addressing the causal factors, especially in developing countries where it ranks second among all cancers in Morocco among women of reproductive age and incurs catastrophic costs to systems that can be prevented through screening and vaccination. Sexual transmission of the human papillomavirus is the main cause of cervical cancer. Smoking, young age of sexual debut, multiple sexual partners, and multiparity are the main risk factors that can potentiate the power of HPV. Despite screening efforts, the proportion of locally advance. Cervical cancer remains a problem of female reproductive health and public health that requires special attention by addressing the causal factors, especially in developing countries where it ranks second among all cancers in Morocco among women of reproductive age and incurs catastrophic costs to systems that can be prevented through screening and vaccination

Table 1. Risk and protective factors in women with and without an HPV positive diagnostics

	No. (%)

Characteristics	Woman with HPV diagnostic (n =154)	Woman without HPV diagnostic (n=96)	Relative Risk (95% CI)
Age over 45	125 (83.3%)	50(20%)	1.9 (1.8 to 2.3)
Recurrent leucorrhoea	135(87.6%)	13(13,5%)	2.5(2.16 to 2.70)
BMI≥30	96(62.33%)	15(15.6%)	1.7(1.06 to 2.75)
Tobacco	135(87.6%)	15(9.7%)	9.8(9.51 to 9.93)
Parity≥5	125(81.1%)	26(27.03)	3.6(3.51 to 4.21)
Low level of education	95(61.3%)	43(44.7%)	5.3(3.13 to 8.10)
Sponsored metrorrhagia	73(46.79%)	21(21.8%)	2.7(2.13 to 4.10)
Post coïtal metrorrhagia	97 (62.9%)	13 (13.5%)	4.83(1.63 to 5.01)
Age at first pregnancy≤17years	60 (38.9%	23(23.3%)	2.3(1.56 to 2.51)
Menopause	35 (22.7%)	16(16.6%)	1.3(1.21 to 1.76)
Previous history of clamidiya trachomatis	86 (55.8%)	12(12.5%)	3.9(1.67 to 6.01)
History of genital herpes	34(22%)	11 (11.4%)	2.2(2.87 to 3.04)
HIV positive	26 (16.8%)	3(3.12%)	6.5 (6.42 to 7.45)
Bacterial vaginosis	34 (22%)	10 (9.6%)	1.6 (1.27 to 2.43)
Irregular menstrual cycle	82(53.2%)	5 (5.2%)	2.7(1.52 to 3.27)
Hemoglobin level <10 g/dl	132(85.7%)	19(19.7%)	6.8(4.13 to 8.10)
Use of depot-medroxyprogesterone acetate	35(25.9%)	56 (58.3%)	0.5(0.36 to 0.75)
Depression	57 (37%)	11(11.4%)	1.8(1.23 to 6.01)
Multiple partners	36(23.3%)	8(8.3%)	5.6(1.56 to 6.75)
Use of oestro-progestins≥10years	120(77.9%)	50(52 %)	5.9(4.63 to 7.01)
Access to cancer screening≥10km	39 (25.32%)	8(8.3%)	9.7(5.63 to 9.81)
Diet rich in vitamin A and C	23 (14.9%)	80(86.4%)	0.6(0.74 to 0.87)
Unmarried women	72 (46.7%)	11(11.4%)	2.9 (1.69 to 4.18)
Infections requiring antibiotics	126 (81.8%)	12(12.5%)	3.5(3.43 to 7.21)
Protein C reactive≥6mg/L	68(44.15%)	7(7.21%)	5.9(4.63 to 6.01)

Table2 : Multiple correspondence analysis : Correlations of transformed variables

Dimension : 1

	Menstrual c ycle	Medical_ History	Ana findings	pathReference_	STI_history	Cervical tumor
Menstrual Cycle	1,000	,135	,173	,310	,177	,224
Medical History[a]		1,000	,160	,181	,048	,116
Ana path findings		.	1,000	,381	,626	,705
Reference motif[a]		.		1,000	,291	,369
STI_history[a]		.		.	1,000	,894
Cervical tumor[b]		.		.		1,000

Ana path findings : CIN1, CIN2, CIN3, CEMD few KI, CEMD no KI, CE, MIAC, AdCC, MCP

Medical_Historya : STI, Diabetes, Hypertension, Cardiac disease, Chronic_Renal_Insufficiency, Basdow_ disease, Hepatitis C

Reference motif : Abnormal cervico-vaginal smear, Positive acetic acid visual inspection, Rebel Vaginitis, Metrorrhagia, Pelvic pain, Spontaneous metrorrhagia, Microinvasive carcinoma, The atypia of squamous cells undetermined significance

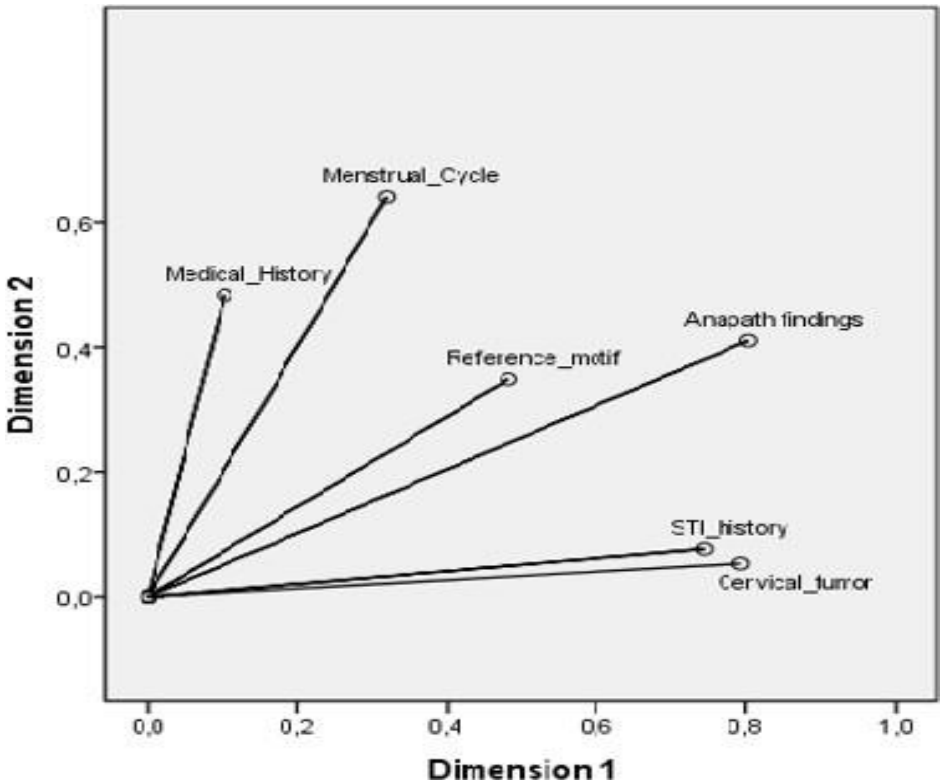

Figure 1 : Main variable normalisation

Table 3: Direct costs of treating cervical cancer

Designation	Amount in MAD	Amount in (€)	%
Length of stay in hospital	5400,16	486.01	4.24
Biological tests	78511.99	7066.07	59.68
X-ray examinations	1 343.17	120.88	1.04
Further tests	1238.13	111.43	0.97
Drugs			
*Weekly cisplatin at a dose of 40mg/m2/week	1680	151	1.28
*Cisplatin 50mg/m2 on D2 + paclitaxel 135mg/m2 on D1 every 21 days (6months)	14862	1337.58	11
*Cisplatin 50mg/m^2 on D2 + paclitaxel 135mg/m^2 on D1 + bevacizumab 15mg/kg every 21 days	10814	937.26	8.2
*Paclitaxel 175mg/m^2 + bevacizumab 15mg/kg every 21 days	17690	1592.1	13
Total	131539.45	11454.79	100

Table 4: Indirect costs of cervical cancer treatment

Designation	Amount in MAD	Amount in(€)	%
Electricity and water	1391240	125406.37	73.61
Telephone	57408	5174.76	3,30
Waste disposal	12376.8	1115.64	0.7
Guarding	61884	5578.22	3.5
Laundry	169099.4	15242.62	7,69
Hygiene products	16703.4	1505.64	9.6
Office supplies	28350	2555.47	1,6
Total	1725922.6	155333.03	100
Management administrative expenses charged to the chemotherapy unit			
	Annual cost in MAD	2.3% to the chemotherapy unit in MAD (€)	%
Annual staff	2 365 216,20	5439997.26 (489599.73 €)	36

costs				
Chemotherapy unit room	2565 216,40	5899997.72 (53099,79 €)	3.9	
Total depreciation	1543600	3550280 (319525.2 €)		60.1
Total	6474032,6	14890274.98 (1340124.7 €)	100	

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