



Pesquisa, Teoria e Metodologia

A Case Study: Uterine Cancer and HPV Infection

Um estudo de caso: cancer uterino e infecção por HPV

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ABSTRACT - Statistical correlations remain a source of mis-information and of false causal relationships and of spurious correlations of data. The relationship of uterine cancer with HPV (Human papiloma virus) provides a good example of the difficulties we face when trying to establish a causal relationship. Several of the commonly associated factors may interfere with the proper interpretation of statistical data. They are widely used as independent demographic categories in epidemiological analyses. This paper refers to Age, Behavior and Number of partners in HPV research.

Keywords: Causality, Epidemiology, Human papillomavirus 6.

RESUMO - As correlações estatísticas podem constituir fonte de informação errada, falsas relações causais e de correlações de dados espúrias. A relação de câncer uterino por HPV (papilomavírus humano) é um bom exemplo das dificuldades que enfrentamos ao tentar estabelecer uma relação causal. Vários dos principais fatores associados podem interferir com a correta interpretação de dados estatísticos. Eles são amplamente utilizados como categorias demográficas independentes em análises epidemiológicas. Esse artigo trata da idade, comportamento e número de parceiros na pesquisa com HPV.

Palavras-Chave: Causalidade, Epidemiologia, Papillomavirus Humano 6.

Statistical correlations remain a source of mis-information and of false causal relationships and of spurious correlations of data. The relationship of uterine cancer with HPV (Human papiloma virus) provides a good example of the difficulties we face when trying to establish a causal relationship.

It is now generally accepted that there is a proven association involving uterine cancer and infection with HPV. While some authors accept the causal nexus of HPV and uterine cancer as fully demonstrated, others claim that HPV infection is important but not sufficient for the evolution of the disease.

A host of contributing etiological factors for uterine cancer has been suggested: frequent conceptions and deliveries, infection with herpes simplex virus type 2, Chlamydia, smoking habits frequent intake of animal fat, obesity or being overweight, infertility, history of diabetes mellitus, and hypertension. It has also been suggested that infrequent intake of vegetables and fruits may be related to the increased risk of cervical cancer by supporting persistent infection of HPV through

impaired immunological function. Polycystic ovary syndrome has been reported to be a risk factor for endometrial cancer. A variant of a tumor suppressor gene like p53 has been assessed in terms of the risk of cervical cancer but its role is not so far fully explained.

Moreno¹ warned that

In view of the discrepancy between the high frequency of HPV infections in young sexually active women and the relatively low occurrence of lesions of the cervix, doubts were raised concerning the viral etiology of the disease, and it was accepted that the infection is a necessary but “not sufficient cause for the development of the disease”, given that virtually only a fraction of the women harboring the virus develop the disease.

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Analysis of categories and correlations

In 1949 a Greek pathologist, Georgios Papanikolaou, developed a non-invasive method for the detection of cancer cells in body fluids. As a follow-up, the association of uterine cancer with sexual activity was established and the possibility of the existence of a viral etiological agent has been raised. Eventually a numerical coincidence between uterine cancer and infection with HPV virus became apparent.

1. IS THE STATISTICAL CORRELATION A MERE COINCIDENCE?

To answer this query we must search first for a hypothetical explanation. In order to do so, we need to be familiar with the biological, ecological, and sociological aspects of the problem.

2. WHAT COMES FIRST?

We must to establish first and foremost the sequence of events or the direction of the causative equation. Does HPV infection lower organic resistance allowing for uterine cancer to develop and evolve? Or does a cancerigenous growth of cells makes it possible for the HPV to colonize the uterus?

Recently² published an instigating article on the evidence for a viral cause for chronic fatigue syndrome. In the preceding year a study in *Science* had showed that 67% of persons suffering from chronic fatigue syndrome had a retrovirus which occurred in 3.7 % in healthy controls. Those findings could not be reproduced by independent researchers.

In 2006, Hopman et al³ cautioned that

Recently proposed events associated with the progression of cervical intraepithelial neoplasia (CIN) 2/3 to cervical carcinoma include integration of human papillomavirus (HPV) into the host genome, genomic instability, and an increase in chromosome 3q copy number. In particular, the gene coding for the RNA component of telomerase (TERC) at 3q26 has been implicated as a possible candidate gene.[...] it is not known to date how these events are temporally related during cervical carcinogenesis [...]

3. PREVENTIVE MEASURES AGAINST HPV

As history shows, public health control do not always depend upon the correct explanation or of any explanation at all of a problem. From Roman times to the late 19th century the control of malaria as made under the belief that the disease resulted from the

exposure to a miasmatic atmosphere. In the present case, the role of sexual transmission of HPV is the factor we must have in mind in order to establish a preventive program against HPV, irrespective of what comes first. The prevention of uterine cancer though, depends on the identification of its causal factor. If it results from a HPV infection, the control of HPV is essential. If it has another etiology, we must search for its source and etiology.

Prevention against HPV may be achieved by: **Vaccination.** Religious beliefs may act as a negative factor. Anthroposophists, for instance, oppose vaccination².

Early diagnosis and prompt treatment. Intervening factors are the availability of diagnostic services and control programs and social/individual behavior, both feminine and masculine. It is a known fact that husbands in many cultures often oppose their wives submitting themselves to regular consultations with both masculine or feminine gynecologists.

Use of preservative condoms. It is considered as the most effective means of prevention. Intervening factors are the availability and price of condoms, religious intolerance and cultural mores surrounding its use. Eventually, the “now or never” and “only this once” decisions lead to infection. The role of preservatives is now well known and widely used as a contraceptive, but frequently ignored as protective against infections.

4. CONFOUNDING VARIABLES.

Several of the commonly associated factors may interfere with the proper interpretation of statistical data. They are widely used as independent demographic categories in epidemiological analyses:

Age. The older a woman, the greater chance of her being married, of being exposed to HPV infection, and of having consorted with more than one partner.

Behavior. Must be taken into account when interpreting the significance of the beginning of sex life and **number of partners.** A preponderant factor is masculine behavior towards the use of preservatives.

Number of partners. Depends upon behavior. Infections, as pregnancy happens with “only one” sexual relation.

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