

# The epidemiological and preventive situation in Spain of causal human papilloma virus cancers

*Situación epidemiológica y preventiva en España de los cánceres causados por el virus del papiloma humano*

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## Abstract

The epidemiological circumstances in Spain of the oncogenic action of the human papilloma virus –3,376 cancers/year– and the primary and secondary preventive actions recommended and in application in Spain of these oncological pathologies are presented and discussed.

**Keywords:** Cancer, epidemiology, prevention, papilloma, virus.

## Resumen

Se presentan y discuten las circunstancias epidemiológicas en España de la acción oncogénica del virus del papiloma humano –3.376 cánceres/año– y las acciones preventivas primarias y secundarias recomendadas y en aplicación en España de estas patologías oncológicas.

**Palabras clave:** Cáncer, epidemiología, prevención, virus del papiloma.

## Epidemiology

Data for the year 2021 from the Cancer Observatory (CaOb) of the Spanish Cancer Association (SCA)<sup>1</sup> report that during the reference year, 285,530 cancers were diagnosed in Spain, 165,848 in men and 119,682 in women.

The human papillomavirus (HPV) maintains a causal relationship with all cervical cancers, with 90% of anal cancers, with 70% of vaginal cancers, with 40% of vulva and penis cancers, and with 30% of the oro-pharynx<sup>2</sup>.

The SCA CaOb registers for the year 2021 the incidence numbers in Spain of these cancers with the possibility of being HPV dependent which are summarized in **table I**. There are no data on the incidence of anal cancer in Spain: Spanish data available add cancer colon, rectum and anus<sup>3</sup>, but the estimate of the Catalan Institute of Oncology<sup>4</sup> is that between 350 and 400 are diagnosed per year.

Table I

Cancer	Cases
Cérvix	1.958
Oro-pharynx	1.203
Vulva	1.025
Penis	513
Anus	375
Vagina	151

Taking into consideration all these figures and relating them, the data expressed in **table II** are concluded, such as the causal HPV cancers that have been diagnosed in Spain in 2021.

Table II

Cáncer	Cases HPV +
Cervix	1.958
Oro-pharynge	360
Vulva	410
Penis	205
Anus	338
Vagina	105

A total of 3,376 cancers caused by HPV infection have been diagnosed in 2021 in Spain. This is a firm etiological relationship, neither estimated nor speculative, which places HPV as the second identified external cause of cancer, after smoking and slightly above sunlight and other types of radiation<sup>5</sup>.

### What is the trend of this incidence?

If the figures for 2012 are consulted 1, the global figures are 250,383 cancers diagnosed in Spain, 143,320 in men and 107,064 in women. For causal HPV cancers, the result is expressed in **table III**, except for anal cancer for the reasons mentioned above.

Table III

Cancer	Cases
Cervix	1.883
Oro-pharynge	1.065
Vulva	1.080
Penis	491
Vagina	139

If we apply the HPV causality percentages to these numbers, as was done previously for 2021, the result is detailed in **table IV**.

Table IV

Cancer	Cases
Cervix	1.883
Oro-pharynge	319
Vulva	432
Penis	196
Vagina	97

## Comments

A 14% increase in the total number of cancers, which in the case of those caused by HPV infection lead to a significant increase in cases of cervical and oropharyngeal cancer, and with similar figures, with slight variations, for the other cancers. Based on the following considerations, prevention work seems to be a priority, as a second preventive oncological action, behind the much-needed social, political and medical fight against smoking, the first cause of cancer identified<sup>6</sup>: 8 million smokers in Spain, with 52,000 deaths caused.

## Prevention

### Primary

Understood as the procedure that eliminates the cause of cancer, the primary prevention of the cancers in question will be to avoid HPV infection.

Knowing that HPV transmission occurs basically through sexual contact<sup>7</sup>, the use of a male condom will be the first measure to be proposed and adopted, given the

evidence that its use<sup>8</sup> considerably reduces the risk of contagion, although not totally, by 70%.

The most effective, efficient and safe way to prevent infection by HPV is vaccination against it. Currently there is a nonavalent vaccine –Gardasil9®– which guarantees according to its summary products characteristics<sup>9</sup> a greater than 97% prevention capacity for each of the HPV cancers that originate, under highly secure application conditions.

The coverage of HPV vaccination in Spain<sup>10</sup>, applied to girls aged 11-14 within the Public Health program, is 79%, with a range that ranges from 71% in Madrid to 91% in La Rioja and without including the data for Asturias, the Balearic Islands and the Canary Islands. The coverage in preventive-care recommendation in women between 15 and 55 years of age is 4%, with a very slight tendency to increase annually<sup>11</sup>.

### Comments

Establishing sex education programs and facilitating access to condoms in some simple way are two political-social actions that we consider very necessary. The beginning of sexual relations in Spain is located around 15-16 years<sup>12</sup>. This legislative and educational action would aim not only to avoid and / or control sexually transmitted diseases, but also to avoid the personal, family and medical drama that almost it is always an unwanted pregnancy in adolescents, which in Spain represent 3% of deliveries, an increasing figure<sup>13</sup>.

The level of vaccination coverage against HPV is satisfactory, at a level that allows to achieve herd immunity<sup>14</sup>. However, in line with the most current recommendations in application in neighboring countries, two actions should be recommended:

- Active rescue of unvaccinated women up to 26 years of age.
- Incorporation of men into vaccination programs.

The efficacy of Gardasil9® is documented without gender difference and from 9 years of age, with no upper limit<sup>9</sup>. Capturing 30% of unvaccinated women to offer them the undoubted benefits of vaccination is a task of great health impact, as well as incorporating boys into HPV vaccination, in order to cut off the main source of HPV transmission to women and to protect them from causal HPV cancers<sup>15,16</sup>. The SCA is preparing a document of position<sup>17</sup> that will be forwarded to the Ministry of Health, requesting that children be vaccinated against HPV, in which it is recalled that more than 50 countries in the world have already made this decision.

### Secondary

In Spain, secondary preventive regulations related to recommendations for the early diagnosis (screening) of

cancer, issued by the Ministry of Health<sup>18</sup> (Order SCB / 480/2019), include cervical, female breast and colon cancer, for be the only three that meet the conditions dictated and published by the European Union in the year 2000<sup>19</sup>, which have not been modified.

The current recommendation in Spain 18 on the prevention of cervical cancer is specified as follows:

- Target population: women between the ages of 25 and 65.
- Primary screening test and interval between examinations:
  - 25-34 years: Cytology every 3 years.
  - 35-65 years: Determination of high-risk HPV (HPV-HR).
  - If HPV-HR Negative: Repeat HPV- HR test at 5 years.
  - If HPV-HR positive: Triage with cytology. If HPV-HR positive and cytology negative: repeat HPV-HR one year.
- The Autonomous Communities and Cities have 5 years to initiate the change in the program and 5 more years to achieve coverage close to 100% of the population.

The current situation in Spain can be summarized as follows<sup>20</sup>:

- They do not communicate news about updating programs: Balearic Islands, Valencian Community, Asturias, Cantabria, and Extremadura.
- Budgeting and looking for options: Canary Islands.
- With poblational screening pilot programs: Galicia and Andalusia.
- Trying to agree on strategies: Catalonia, Madrid.
- Resuming previous programs suspended by the pandemic: La Rioja.
- Poblational screening trying to improve them: Castilla y León and the Basque Country.
- Screened with local initiatives: Aragón.
- Evolving to poblational screening: Castilla La Mancha, Murcia, Navarra.

There are no public application programs for secondary prevention of the other HPV-dependent cancers in progress or in the project.

## Comments

- The criterion that cervical cancer is not an oncological priority for Public Health can be accepted. It is the breast and the prostate, more incidents in women and men, respectively, the colon, more population incident, and the lung, the one with the highest mortality. Tumors with low incidence but very high mortality could be added to the list, cancers of the central nervous system (glioblastomas) or of the pancreas<sup>1</sup>, of

which we do not know their oncogenic history and, consequently, we do not have at the moment of preventive or diagnostic capacity early<sup>21,22</sup>. Cervical cancer occupies the 22nd place in the cancer incidence classification in 2021<sup>1</sup>, 1,958 cases, which have caused 676 deaths, also number 22 on the list.

Comparing 2012 with 2021, a slight increase in its frequency is observed, bad news and even more so if we remember that it is a cancer that the World Health Organization has declared the first with a certain possibility of being eradicated<sup>23</sup>, as has been the case of our socio-sanitary world infections such as polio or smallpox. The joint application of highly effective strategies of primary prevention –vaccination against HPV– and secondary – redesigned poblational screening– does it, it should make it possible. If we do not do it –and it is also a warning from the WHO<sup>23</sup>– cervical cancer will present a 30% increase in its incidence by 2030.

- In the registries that record it, anal cancer shows a consolidated tendency to increase its incidence and mortality<sup>24</sup>, both in women and in men. Maintaining anal sex is a circumstance that increases the risk, but not doing so does not eliminate it<sup>25</sup>. High-quality information highlights that anal cytology and / or HPV determination, followed by high-resolution anoscopy, offer very good efficacy in preventive control and in the early diagnosis of anal cancer<sup>26</sup>, a cancer with an established and detectable oncogenic history, very similar to that of cervical cancer, low and high grade intraepithelial lesions of the anus<sup>27</sup>. All this information will make it feasible and necessary in the near future incorporate into clinical practice and Public Health policies regulated strategies for the secondary prevention of anal cancer, reinforcing the primary prevention that vaccination against HPV has already demonstrated<sup>9</sup>.
- One in three oro-pharyngeal cancers is causal HPV: its natural history and oncogenic process have not been established, although its relationship is, in addition to HPV infection, smoking, alcoholism and poor oral hygiene<sup>28</sup>. The calls for attention in the medical literature follow one another, demanding attention to this pathology, which still does not receive, in general terms, the necessary investigative and healthcare attention<sup>29</sup>, to correct the increasing trend that the comparison 2012 - 2021 shows
- Preventive procedures for cancers of the vulva and vagina, which are causative HPV in a high proportion, are well established. The Spanish Association of Cervical Pathology and Colposcopy has done, does and will surely do a great job in promoting clinical practice guidelines in this regard<sup>30,31</sup>. The impact that this educational work

is going to have will be reflected in the incidence rates of these two cancers recorded in the registries. The aforementioned data points to a slight decrease and, therefore, to an initial success of this initiative.

In short, and as described and proposed very recently<sup>32</sup>, it is

urgent to establish adequate preventive mechanisms in our environment for the prevention of HPV-dependent cancers, a group of cancers that represent a serious health problem.

### Interests conflict

The researchers declare that they have no conflict of interest.

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