

**EVALUATION OF THE PROGRAM FOR THE PREVENTION AND EARLY  
DETECTION OF CERVICAL CANCER IN CASTILLA Y LEÓN (SPAIN)****Marta Capilla Díez<sup>1</sup>, Marta Domínguez-Gil<sup>2</sup>, Angel San Miguel<sup>3</sup> and Luis Inglada Galiana<sup>4\*</sup>**<sup>1</sup>Clinical Analysis Service. Rio Hortega Valladolid University Hospital. Valladolid. Spain.<sup>2</sup>Microbiology Service. Rio Hortega Valladolid University Hospital. Valladolid. Spain.<sup>3</sup>Department of Health Sciences International University of La Rioja (UNIR). Spain.<sup>4</sup>Internal Medicine Service. Rio Hortega Valladolid University Hospital. Valladolid. Spain.**\*Corresponding Author: Luis Inglada Galiana**

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**SUMMARY**

Cervical cancer screening is a check on the health of the cervix, the opening of the uterus into the vagina. And it helps prevent this cancer through the early detection of cellular abnormalities that can cause it. During screening, a small sample of cells is taken. These cells are tested for the human papillomavirus (HPV), which can cause abnormal cells in the cervix, and are visually examined for abnormalities.

In Spain, the health system carries out cervical cancer screening for all women who have a cervix, between 25 and 65 years of age. Between the ages of 25 and 34, they undergo screening or cytology every 3 years, and between the ages of 35 and 65, a human papillomavirus (HPV) test is performed every 5 years.<sup>[2]</sup>

**INTRODUCTION**

Human papillomavirus (HPV) belongs to the *Papillomaviridae* family, which generally infect the skin and mucous membranes. Within this family there are viruses that affect different vertebrates and are usually very specific in their replication, which usually takes place in a single animal species.<sup>[1-2]</sup>

HPV is a double-stranded DNA virus, small and non-enveloped, which makes it very stable, with long-lasting infection capacity and great resistance to numerous treatments, and with a capsid icosahedral with 72 capsomers.<sup>[3]</sup>

The HPV genome is made up of two types of genes, the E (*Early*) genes, encoded in the early stages of infection and the L (*Late*) genes, which are encoded during the late stages of the replication cycle. Both protein coding sequences are found on a single strand of DNA.<sup>[1]</sup>

Six early genes are known, which are proteins involved in viral replication and regulation, and some have transforming potential, which is why they are involved in the contagious characteristics of the virus. Of these proteins, E6 and E7 are the ones involved in the oncogenesis process; they already participate in the malignant transformation of cells.<sup>[3]</sup>

More than 200 different genotypes have been determined, which are divided into High Risk (AR) and Low Risk (BR) viruses.<sup>[1]</sup>

- High risk: genotypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59.
- Low risk: genotypes 6, 11, 32, 40, 42, 44, 54, 55, 61, 62, 64, 71, 72, 74, 81, 83, 84, 87, 89 and 91.

Low Risk cancers cause warts, genital condylomas and other benign skin and mucous membrane pathologies, while the association with cervical cancer (CCU) is quite rare, which is why, from a screening point of view, they are prioritized. detect High Risk viruses.<sup>[3]</sup>

The most frequent mode of transmission of human papillomavirus is sexual contact, through contact with infected epithelia. Contagion occurs through microscopic abrasions of the skin or mucous membranes, since the infection of cells by HPV requires a damaged or transitional epithelium that allows the virus to penetrate the basal layer of the epithelium, reach the cell nucleus and begin to replicate.<sup>[1]</sup>

Genital transmission routes other than sexual contact are likely, although less common. The risk of transmission through digital-genital or oral-genital contact appears to be minimal.<sup>[2]</sup>

In general, HPV infections are self-limited and usually resolve spontaneously in the first two years after infection, although in genotypes classified as high oncogenic risk they have an easier time disseminating and transforming the epithelium, giving rise to infections. persistent and can trigger cervical cancer over time.<sup>[1-2]</sup>

The worldwide prevalence of HPV infection in women with normal cytology is 11-12%, with the highest figures in sub-Saharan Africa (24%), Eastern Europe (21%) and Latin America (16%).<sup>[3]</sup>

The highest HPV prevalence rates are reported in women under 25 years of age with a decline at older ages in many populations, although a secondary uptick is seen in early peri-menopause or menopausal women. The five most common virus genotypes worldwide are HPV16 (3.2%), HPV18 (1.4%), HPV52 (0.9%), HPV31 (0.8%) and HPV58 (0.7%).<sup>[3]</sup>

The prevalence increases in women with cervical pathology in direct proportion to the level of evolution of the lesion determined by cytology. Retrospective investigations have shown that practically 100% of all cervical cancers are associated with HPV.<sup>[3]</sup>

According to the health portal of the health website of the Government of Castilla y León, the CCU prevention and early diagnosis program is “an organized screening program whose purpose is to reduce the incidence and mortality due to invasive cervical cancer. by identifying women with cervical precursor lesions at increased risk of progression to invasive cancer and/or human papillomavirus (HR-HPV) infection.”<sup>[4]</sup>

Screening is a secondary prevention activity that consists of “the examination of asymptomatic people to distinguish those who are probably sick and those who are probably not”.<sup>[5]</sup>

The World Health Organization (WHO) defines screening as “the systematic application of a test to identify individuals at sufficiently high risk of suffering from a particular health problem to benefit from further investigation or direct preventive action, including a population that has not sought medical attention for symptoms related to that disease” (WALD, 2001).

The latest UK National definition Screening Committee (NSC) introduces the key concept of balance between benefits and risks, as well as that of benefit understood as a reduction in risk and not as a guarantee of cure or non-appearance of the disease in the future. It defines screening as “a public health service in which members of a defined population, who do not necessarily perceive themselves to be at increased risk, or to be affected by a disease or its complications, are invited to undergo questions or tests to identify those individuals with a greater probability of obtaining a benefit than a harm,

caused by successive tests or treatment, to reduce the risk of the disease or its complications” (NSC, 2009).

Opportunistic screening is one in which there is no organization in the health system to invite the population to carry it out, but rather it is based on the initiative of the patient and the health professional. On the other hand, population screening is one in which all activities are planned and coordinated, in which the target population is invited in a protocolized manner.<sup>[5-6]</sup>

Consequently, we can affirm that in epidemiology, population screening focuses mainly on the early detection of diseases; classifying the participants based on the risk of presenting injury and thus facilitating the implementation of a more exhaustive control to prevent the progression of the biological injury or disease.

We must keep in mind that in the CCU screening process, depending on the phase we are in, different tests will be performed.

**Pap Test** It was introduced in the 1940s, but it was not until 1996 that the Hologic laboratory promoted ThinPrep. Pap Test with its cell counting chamber on a slide with cytology in liquid medium; unlike the old cytology collected directly with the brush on the slide for later staining. This test has clinical evidence from published, peer-reviewed studies that demonstrate benefits over the conventional Pap test. In addition to being approved by Health Canada and FDA. CLSI document GP15-A31 guidelines establish that it is important to obtain a sample without blood, mucus, inflammatory exudate or lubricant. The Papanicolaou stain uses hematoxylin, Orange G, Eosin Y, Light Green SF and Bismarck brown as dyes. This test detects potentially precancerous changes such as cervical intraepithelial neoplasia or cervical dysplasia, as well as infections and abnormalities in the endocervix or endometrium. A triple intake must be performed: endocervix, cervix and vagina. It has been shown that the old technique had low sensitivity (50-60%) and a high rate of false negatives (30%) due to errors in sample collection. The results are classified following the Bethesda system, introduced in 1988, later revised in 1991, 2001, and 2014, which is the classification in current use.<sup>[1]</sup>

- Squamous cell abnormalities (SIL)
  - Atypical squamous cells of undetermined significance (ASC-US).
  - High-grade suggestive atypical squamous cells (ASC-H).
  - Low-grade squamous intraepithelial lesions (L-SIL), mild dysplasia (CIN 1).
- High-grade squamous intraepithelial lesion (H-SIL): moderate (CIN 2) or severe (CIN 3/CIS) dysplasia; with recording of whether the lesions have features that suggest invasion.
  - Squamous cell carcinoma (SCC).

- Abnormalities of glandular epithelial cells (AGC).
  - Atypical glandular cells not otherwise specified (AGC-NOS).
  - Atypical glandular cells suggesting neoplasia (AGC-Neo).
  - Endocervical adenocarcinoma in situ (AIS).
  - Adenocarcinoma (AC).
- Other situations can be observed such as:
  - Reactive cellular changes associated with inflammation, radiation, or IUD use.
  - Microorganisms: *Trichomonas vaginalis*, *Candida*, bacterial vaginosis, *Actinomyces*, cellular changes compatible with HSV or CMV.
  - Non-neoplastic findings: atrophy or changes associated with pregnancy.

The Molecular Genotype Detection Test can detect infections and co-infections of the 49 types of HPV with greatest clinical importance (6, 11, 16, 18, 26, 31, 33, 34, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73, 74, 81, 82, 83, 84, 85, 86, 87, 89, 97, 101, 102, 103, 106, 150 and 151).

Different types of samples can be used: smears, cell suspensions, and tissue fixed in formalin or paraffin. It has been shown that there are interfering substances that inhibit DNA polymerase, therefore, the amplification reaction. These are the presence of hemoglobin or paraffin (because it contains non-visible remains of hemoglobin), as well as the acetic acid or iodine used in colposcopy. Inadequate sample conservation can also influence, for example, an excess of formalin fixation time also produces inhibition due to lack of amplification.

The test is based on PCR amplification of a fragment of the virus, followed by visualization on a low-density microarray. The chosen sequence is highly conserved between the different types of HPV, but presenting sufficient variations to be able to differentiate each type of HPV with specific probes. Subsequently, the results are analyzed and automatically interpreted with software designed and validated by GENOMICA. Analytical sensitivity was determined from samples from the evaluation program of laboratory tools for HPV typing, of the world health organization WHO (2015 WHO HPV LabNet Proficiency Study of HPV DNA Typing). The analytical specificity was determined by studies carried out in two Spanish hospitals (Microbiology Service of the Hospital Universitari Germans Trias i Pujol from Badalona and Virology Unit of the Virgen de la Arrixaca University Hospital) and one Portuguese (Department of Infectious Diseases of the Ricardo Jorge National Health Institute, IP Lisbon).

Currently, this test is undergoing a technological update because in 2019, a preliminary consultation is carried out on the market to learn about the latest technologies available, to subsequently only screen for HPV of high-risk genotypes.<sup>[1]</sup>

## MATERIAL AND METHODS

Was carried out based on a bibliographic review of CCU screening programs. It was decided to begin the search for information through the Pubmed platform, using the keywords “HPV AND Castilla y León” and “cancer AND cervix”, together with the search on the official pages of the public organizations of the Junta de Castilla y León. León (SACYL), and the Ministry of Health. Different associations are also consulted such as the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), the Spanish Association of Cervical Pathology and Colposcopy (AEPCC), the Spanish Association of Clinical Laboratory (AEFA), the Spanish Association of Medical Biopathology (AEBM) and the Spanish Society of Laboratory Medicine (SEQC). The official websites of the different autonomous communities are also consulted, as well as international organizations such as Centers for Diseases Control and Prevention (CDC) and European Center for Diseases Control and Prevention (ECDC).

## RESULTS AND DISCUSSION

At the national level there is no guideline for performing screening, the only thing that exists are some criteria to detect neoplasms early:

- Target population: asymptomatic women with sexual relations and ages between 25 and 65 years.
- Screening Test: cervical cytology.
- Recommended interval between examinations: 3 to 5 years after two normal initial cytology tests in one year.
- Objective: 70% of women between 30 and 60 years old have a screening cytology from the previous 5 years.

Since this design of the screening strategy does not exist, there are many differences between autonomous communities.<sup>[7]</sup>

### Screening in europe

According to the conclusions of the “Report on screening in Europe” (Von Karsa et al, 2008) made by the European Observatory on Health Systems and Policies at the initiative of the European region of the WHO and the European Commission together, it is noted that screening is very different between EU countries. There is no consensus between population or opportunistic screening, nor on the basic required criteria, and there is a lack of records for monitoring the target population. This report It is intended to be a first assessment of the impact of the 2003 EU Council recommendation on cancer screening.

### Screening in castilla and león

In Castilla y León the screening program began in 1986 using cytology as a test. Over the years the strategy changed and the target population changed. In 2008, human papillomavirus (HPV) detection was added to the program.<sup>[8-9]</sup>

A key moment in this prevention and diagnosis program is November 2012, since the program was updated, changing the target population to sexually active women residing in Castilla y León, without gynecological symptoms. Furthermore, this population was divided into two groups, women from 25 to 34 years old and women from 34 to 64 years old.<sup>[5]</sup>

The population group aged 25 to 34 years underwent cervical cytology every 3 years, but the first two cytology tests were performed at an interval of 12 months. The second age group, 35 to 64 years old, underwent the co - test, a cytology and an HPV detection test every 5 years.<sup>[8-10]</sup>

There are women who were excluded from the program, those who had a total hysterectomy permanently and temporarily those who had not had sexual relations or those who suffered from gynecological symptoms at the time of screening.<sup>[5]</sup>

In 2021, the program is modified again, changing screening from opportunistic, as it was until now, to population-based and establishing HPV determination as

the test of choice in the second age group, from 35 to 64 years. (eleven)

The annex includes an image of the brochure sent to the target population so that they have all the information related to this program.

The screening process has two phases. The first phase includes taking samples and the result, which can be positive, negative or non-determinative. If the result is negative, the woman continues in the program, having to repeat the tests according to the time interval that corresponds to her age. If the result is positive, diagnostic tests are carried out in specialized care or the second part of the screening. If the result is not decisive, the doses are repeated after 12 months.<sup>[5]</sup>

Cytology is performed on the group of women between 25 and 34 years old, and high-risk HPV is detected on the group between 35 and 64 years old. If the test is positive, cytology is performed. If the cytology is negative, another HPV detection is performed a year, if it is positive, the diagnostic tests are carried out. (eleven).



**Figure 1: Screening process in the Program of the government of Castilla y León.<sup>[5]</sup>**

The second part of the screening takes place in specialized care. Depending on the results of this part, the woman can leave the program or become part of a follow-up program, and may return to the program later.<sup>[5]</sup>

When comparing and seeing the evolution of the CCU prevention and early detection program, different indicators are used, of which we highlight:

- The number of cytology tests and positive results in the program.

- Human papillomavirus determinations and number of positive detections for viruses 16 and 18.
- Temporal evolution.<sup>[12]</sup>

In 2011, 85,750 cytology tests were performed in the Community of Castilla y León and 2,253 of them (2.6%) were positive. This year, 56,338 samples were taken to determine the virus, and 4,191 were positive for it. Of this 7.4% that were positive for HPV, 19.0%, 876 samples, were positive for viruses 16-18.<sup>[13]</sup>



**Table 1: Number of cytology tests and positive results in the Cervical Cancer Prevention and Early Detection Program, by province of Castilla y León. Year 2011.<sup>[13]</sup>**

	Citologías	Citologías positivas*	% Resultados sospechosos positivos
Ávila	4.190	100	2,4%
Burgos	12.980	401	3,1%
León	14.871	383	2,6%
Palencia	6.167	167	2,7%
Salamanca	11.332	282	2,5%
Segovia	5.007	140	2,8%
Soria	2.197	39	1,8%
Valladolid	22.504	587	2,6%
Zamora	6.502	154	2,4%
<b>Castilla y León</b>	<b>85.750</b>	<b>2.253</b>	<b>2,6%</b>

\* Las pacientes se derivan a atención especializada para que se realicen más pruebas y se confirme el diagnóstico

Fuente: Consejería de Sanidad de la Junta de Castilla y León.

In 2013, 55,621 cytology tests were performed in the Community of Castilla, of which 1,097 were positive, 2.0%. In this same year, 35,938 samples were processed,

of which 2,828 tested positive for HPV, 7.9%. Of these positives, 21.3% were positive in genotype 16-18.<sup>[12]</sup>

**Table 2: Number of cytology tests and positive results in the Cervical Cancer Prevention and Early Detection Program, by province of Castilla y León. Year 2013.<sup>[12]</sup>**

	Citologías	Citologías positivas*	% Resultados sospechosos positivos
Ávila	3.757	77	2,0%
Burgos	6.874	146	2,1%
León	9.500	220	2,3%
Palencia	4.473	82	1,8%
Salamanca	7.847	143	1,8%
Segovia	3.160	74	2,3%
Soria	1.978	27	1,4%
Valladolid	13.973	242	1,7%
Zamora	4.059	86	2,1%
<b>Castilla y León</b>	<b>55.621</b>	<b>1.097</b>	<b>2,0%</b>

\* Las pacientes se derivan a atención especializada para que se realicen más pruebas y se confirme el diagnóstico.

Fuente: Consejería de Sanidad de la Junta de Castilla y León.

**Table 3: Number of samples for HPV determination, number and percentage of positive HPV samples and number of positive samples for viruses 16-18. Castilla y León. Years 2008 to 2013.<sup>[12]</sup>**

	Nº muestras	Nº VPH (+)	% VPH (+)	Nº VPH 16-18	% VPH 16-18 / VPH (+)
2008	7.827	483	6,2%	82	17,0%
2009	55.098	3.561	6,5%	672	18,9%
2010	58.578	4.519	7,7%	797	17,6%
2011	56.338	4.191	7,4%	876	20,9%
2012	42.633	4.202	9,9%	678	16,1%
2013	35.938	2.828	7,9%	603	21,3%
<b>Total</b>	<b>256.412</b>	<b>19.784</b>	<b>7,7%</b>	<b>3.708</b>	<b>18,7%</b>

Fuente: Consejería de Sanidad de la Junta de Castilla y León.

In 2022, 27,464 cytology tests have been performed, with 950 of them being positive (3.46%). For the detection of HPV, 60,015 samples were taken, of which

5,563 were positive (9.27%) and, of these 1,000 (17.98%) were positive for subtypes 16-18. This year, 79,652 women participated in the program. (14)

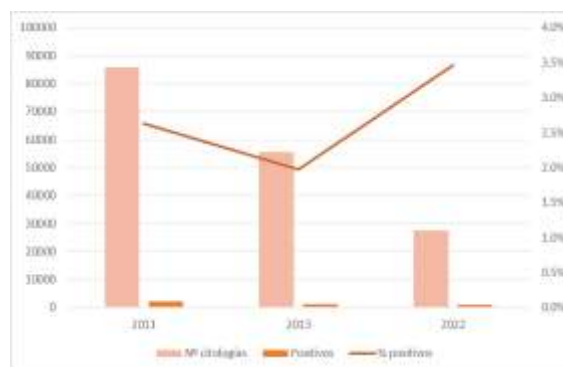
**Table 4: Number of total cytology tests and positive results, in the Cervical Cancer Prevention and Early Detection Program, by province of Castilla y León. Year 2022.<sup>[14]</sup>**

	Citologías	Citologías positivas	% Pruebas positivas
Ávila	1.779	53	2,98
Burgos	3.736	152	4,07
León	5.304	173	3,26
Palencia	1.889	50	2,65
Salamanca	3.623	131	3,62
Segovia	1.768	97	5,49
Soria	976	20	2,05
Valladolid	6.612	215	3,25
Zamora	1.777	59	3,32
<b>Castilla y León</b>	<b>27.464</b>	<b>950</b>	<b>3,46</b>

Fuente: Consejería de Sanidad de la Junta de Castilla y León.

**Table 5: Cytologies and positive results for the years 2011, 2013 and 2022.**

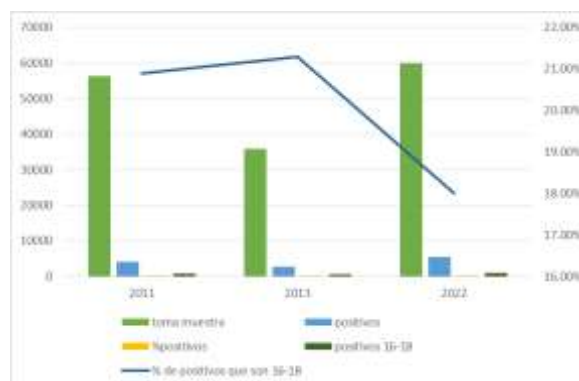
Year	No. cytology	Positives	% Positive
2011	85720	2253	2.6
2013	55621	1097	2
2022	27464	950	3.5



**Figure 2: List of cytology tests and positive results for the years 2011, 2013 and 2022.**

**Table 6: Taking samples for HPV determination and positive results for the years 2011, 2013 and 2022.**

Year	No. tests	Positive No.	% Positive	Positive for HPV 16 and 18	% of positives that are HPV 16 and 18
2011	56338	4191	7.4	876	20.9
2013	35938	2828	7.9	603	21.35
2022	60015	5563	9.3	1000	18



**Figure 3: Relationship between sampling for HPV determination and positive results for the years 2011, 2013 and 2022.**

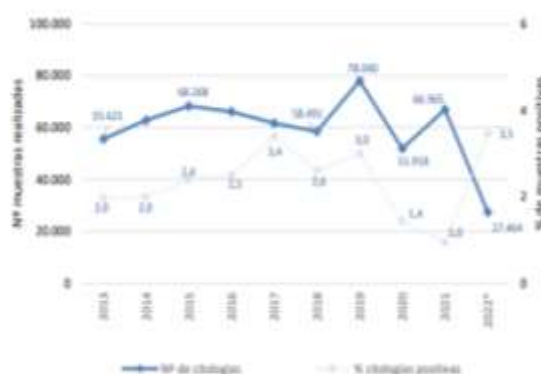
### Screening in the pandemic years

In 2020, the Program update began to be introduced, as cytology becomes the test of choice in women over 35 years of age. Although the establishment had to be delayed until 2021 due to the COVID-19 pandemic.

Previous data and data during the years of the SARS-CoV-2 virus pandemic are presented.

**Table 7: Number of total cytology tests, number of positive cytology tests and % of positive tests between 2018 and 2022, in the Cervical Cancer Prevention and Early Detection Program, by province of Castilla y León. Year 2022.<sup>[14]</sup>**

Cytology test			
Year	No. screening tests	No. positive tests	% positive tests
2018	58,311	2,134	3.66%
2019	78,040	2,348	3.01%
2020	51,918	744	1.43%
2021	66,965	634	0.95%
2022	27,464	950	3.46%



**Figure 4: Temporal evolution of the number of cytology tests performed and percentage of positive tests in the last 10 years, in the Cervical Cancer Prevention and Early Detection Program, by province of Castilla y León. Year 2022.<sup>[14]</sup>**

The graph shows an increase in 2019 in the number of tests carried out compared to the previous year of 33.4% due to the change in the program with a personalized invitation to women in the target population. During 2020, and due to the effects of the pandemic, the Program had to be suspended for 2 months. The slow and progressive recovery of rhythm is reflected in the number of screening tests performed. The percentage of

positive women in the first phase of screening is 1.43% in the Community as a whole for the year 2020.

In 2022, participation increases and the figure is comparable with the data for 2019. The expected forecast is also met after the establishment of the new program in November 2021. By establishing more specific criteria, a smaller number of cytology tests in the target population and the average positivity percentage is around 3.5%.<sup>[14]</sup>

**Table 8: Number of total HPV molecular tests, number of positive tests and % of positive and % genotypes 16-18 between the years 2018 and 2022, in the Cervical Cancer Prevention and Early Detection Program, by provinces of Castilla and Leon . Year 2022.<sup>[14]</sup>**

HPV molecular test				
Year	No. tests	No. positive tests	% positive tests	% genotypes 16-18
2018	40,517	3,593	8.8	18.7
2019	57,710	4,226	7.3	18.2
2020	36,284	2,888	7.96	17.24
2021	64,693	5,095	7.88	18.12
2022	60,015	5,563	9.27	18



**Figure 5: Temporal evolution of the number of HPV determinations and percentage of positives in the last 10 years, in the Cervical Cancer Prevention and Early Detection Program, by provinces of Castilla y León. Year 2022.<sup>[14]</sup>**

The following graph shows a recovery in 2019 with an increase of 42.4% in the number of samples compared to the previous year. However, due to the pandemic situation in 2020, tests decreased by 33.5%, so this atypical global situation must be taken into account when interpreting the time series. The percentage of positive HPV samples ranges between 6% and 10%. In the last 5 years it has been in an interval between 7.3% and 9.3%. These values are within the range of expected percentages.<sup>[14]</sup>

### Screening in Spain

Castilla y León, together with La Rioja, is the only community in Spain that carries out population screening. The rest carry out opportunistic screening, except for the Valencian Community, which carries it out in both ways (making an active invitation and systematically offering it to women who go to health services and who meet the target population requirements). The Balearic Islands carry out opportunistic screening, but with active recruitment of women who meet certain established criteria. (fifteen)

Andalusia is the only community that carries out a different screening strategy depending on the established risk groups. Other communities carry out different strategies depending on age. (fifteen)

Asturias, the Canary Islands, the Valencian Community, Extremadura, Madrid and Murcia establish, apart from the starting age of participation in screening, that 3 years after the first sexual relationship you can begin to participate in the program. (fifteen)

La Rioja is another community that divides the target population into groups according to age, Castilla y León divides it into two age groups as we have seen, while La Rioja divides the population into three groups, 25 to 42 years old, from 43 to 51 and from 52 to 65.<sup>[15]</sup>

In 2019, Order SCB/480/209 was published, which modifies the screening programs, including them in the common portfolio of services of the National Health System, as part of the public health programs. This order

establishes that screening must be population-based and incorporate the HPV detection test as a primary screening test in a part of the target population. This program confirms the target population (women aged 25 to 65) and establishes two target population groups: 25 to 34 years, for whom cytology is performed every 3 years; and 35 to 65 years old, for whom high-risk HPV (HR-HPV) is determined, repeating the test after 5 years. This second group is triaged with cytology if the HR-HPV test is positive.<sup>[16]</sup>

In this order, the autonomous communities are given 5 years to make the change in the program, and 5 more years to obtain coverage close to 100% of the population.<sup>[16]</sup>

Some communities have progressively adapted their screening programs to adapt to the indications of the aforementioned ministerial order.

In 2018, the Basque Country began the “Oncology Plan of Euskadi 2018-2023”, where they proposed the change from opportunistic to population screening and including the determination of HPV as a screening test.<sup>[17]</sup>

Castilla-La Mancha began in 2018, with a pilot plan, the adaptation to population screening and currently complies with national guidelines.<sup>[18]</sup>

Aragón continues with opportunistic screening, but it has adapted to the differentiation of tests according to age groups.<sup>[19]</sup>

The Community of La Rioja began the new screening program at the end of 2022, while the Community of Madrid began the program at the beginning of this year.<sup>[20-21]</sup>

Currently, Cantabria is also undergoing this progressive change, still maintaining opportunistic screening, but adapting the two types of tests depending on age.<sup>[22]</sup>

Catalonia maintains opportunistic screening and is progressively implementing differentiation into two age



groups when choosing the screening test. This community is a pioneer in establishing an agreement with the college of pharmacists to carry out screening using self-samples delivered by the target population in community pharmacies. This program is currently under evaluation.<sup>[23-24]</sup>

Navarra and Extremadura have published documents in 2023 with the new protocols to be implemented this year to adapt to the guidelines of the Order.<sup>[25-26]</sup>

The Valencian Community has developed a pilot study to comply with national indications and, throughout this fall, will begin to implement the new population screening plan and two age groups with different tests throughout the community.<sup>[27]</sup>

The Balearic Islands and Canary Islands have not yet implemented new plans while Murcia is implementing a pilot plan.

## CONCLUSIONS

- Regarding screening in Europe, the conclusion drawn is the need for agreement between the Member States and the Commission on the priority of establishing population screening to improve accessibility, effectiveness and cost-effectiveness, as well as adherence to the European Guidelines for cervical cancer.
- In the section on screening in Castilla y León, from the data analyzed we can see in Figure 2 that the number of cytology tests has been decreasing, but not the percentage of positive tests. From 2011 to 2013, there was a reduction in the percentage of positive cytology tests, from 2.3% to 2%, also reducing the total number of samples taken. The great decrease in the number of cytology tests in 2022 is due to the change in the test of choice for screening in the age group of 35 to 65 years, since it is no longer the co -test and becomes only the determination of HPV. Therefore, in Figure 3 we can see how the sampling for HPV determination increases significantly in the year 2022. We also see that from 2013 to 2022 there is a marked decrease in the percentage of positives that correspond to the genotypes 16 and 18.
- Regarding the screening data in the pandemic years, the Program had to be suspended for 2 months (April and May). The slow and progressive recovery of rhythm is reflected in the number of screening tests performed. The change in the program due to the establishment of the new population screening criteria in November 2021 must be taken into account. The data is not directly comparable with previous years, but we will be able to compare the figures for 2021 and 2022 and observe this evolution over the coming years.
- After analyzing the screenings in other communities, we can see that the screening model that was followed until 2019 was opportunistic, except in our

community and La Rioja. We can also verify that the target population coincides, from 25 to 65 years old and that in all communities the end age is 65 years, complying with the recommendations established by the Screening Guide of the Spanish Association of Cervical Pathology and Colposcopy. (fifteen)

- With these data we can see that Castilla y León is the community that previously adapted to the recommendations, since in 2012 it already divided the target population into two groups (25 to 34 years, 35 to 65 years) and carried out two tests different, with two different year intervals.
- We can verify that Castilla y León has been one of the communities that has previously adapted to the indications of order SCB/480/209, while many communities have not yet implemented all the points of this order or are in the process of implementation.
- For this reason, the screening program of Castilla y León is one of those that most closely aligns with the European screening recommendations (*European Guidelines for quality assurance in cervical cancer screening*) and the Spanish companies (AEPP and SEGO).

## REFERENCES

1. Douhal Y, Benito V. Human papillomavirus. present past and future. Continuing training course, 2022-2023 Updates in the Clinical Laboratory, Spanish Association of Medical Biopathology -Laboratory Medicine (AEBM-ML).
2. Soler RM, HPV Course: Cervical Cancer Screening. Institute of Health Technology, 2021.
3. Mateos ML, Pérez-Castro S, Pérez-Gracia MT, Rodríguez-Iglesias M. Microbiological diagnosis of human papillomavirus infection. Procedures in Clinical Microbiology. Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), 2016
4. Health Portal of the Government of Castilla y León. Cervical cancer prevention and early detection program in Castilla y León [internet]. Valladolid: Junta de Castilla y León. Available at: <https://www.saludcastillayleon.es/profesionales/es/programas-guias-clinicas/programas-salud/programa-prevencion-deteccion-precoz-cancer-cuello-utero-ca>
5. Santos J. HPV detection in cervical cancer screening programs. Results of the screening program in Castilla y León. In: SEAPSEC Symposium. XXXVII annual meeting of the Spanish society of pathological anatomy.
6. Ministry of Health. Cervical cancer prevention and detection program in Castilla y León Update, 2021 [internet]. Valladolid: Junta de Castilla y León.
7. Torné A, et al. Cervical cancer screening guide in Spain, 2014. Rev Esp Patol, 2014; 47(1): 1-43.
8. Ministry of Health of the Government of Castilla y León. Cervical cancer prevention and early detection program in Castilla y León (2021 edition) [internet]. Valladolid: Junta de Castilla y León. Available at: <https://www.saludcastillayleon.es/profesionales/es/p>

- rogramas-guias-clinicas/programas-salud/programa-prevencion-deteccion-precoz-cancer-cuello-utero-ca
9. García S, Domínguez -Gil M, Gayete J, Rojo S, Muñoz JL, Santos Salas J, et al. Rev Prevalence of human papillomavirus in Spanish women from a population screening program *Esp Chemioter*, 2017; 30(3): 177-182.
  10. Sanjosé S, García AM. Human papillomavirus and cancer: epidemiology and prevention. Prevention of cervical cancer in Spain. 4th Monograph. Spanish Society of Epidemiology.
  11. Domínguez-Gil M. HPV: the value of population screening, 25 years of experience. Microbiology Service. Río Hortega University Hospital. Valladolid.
  12. Public health prevention programs Castilla y León 2013. Decree 79/2013, of December 26, which approves the Statistical Plan of Castilla y León, 2014-2017 Statistical operation no, 11025: 1007014.
  13. Public Health Prevention Program Castilla y León, 2011. Decree 87/2009, of December 17, which approves the Statistical Plan of Castilla y León 2010-2013. Statistical operation n<sup>a</sup> 11027, rev 14022013
  14. Public health prevention programs Castilla y León, 2022. Decree 26/2022, of June 16, which approves the Statistical Plan of Castilla y León, 2022-2025. Statistical operation no. 11024, rev 07072023
  15. Torné A, Saladríguez MP, Gimferrer MC, Quítle FA, Ortiz DA, Piqué XC et al. Cervical cancer screening guide in Spain, Spanish Association of Cervical Pathology and Colposcopy (AEPCC), 2014.
  16. Order SCB/480/2019, of April 26, which modifies annexes I, III and VI of Royal Decree 1030/2006, of September 15, which establishes the portfolio of common services of the National System of Health and the procedure for its update. BOE-A-2019-6277[internet]. Available at: <https://www.boe.es/eli/es/o/2019/04/26/scb480>
  17. Osakidetza -Department of health. Cervical cancer population screening program in Euskadi. Version 2.0. New protocol, 2022. Basque Government
  18. Del Campo M, Villarín A. The implementation of population screening for cervical cancer in Castilla-La Mancha. SCAMFYC Publishing. *Rev clin Med. Fam* 2018; 11(3): 125-127.
  19. Padín M, González JV, Muñoz AF, Mateos FJ, Alfaro J. Recommendations for the development of the Cervical Cancer Screening Program in Aragón General Directorate of Health Assistance. General Directorate of Public Health. Health Department. Government of Aragon.
  20. Riojasalud. Cervical cancer early detection program [internet]. Logroño: Riojasalud.es. Available at: <https://www.riojasalud.es/ciudadanos/informacion/programas-de-deteccion-precoz-de-cancer/cervix>
  21. Health Community of Madrid. Cervicam program [internet]. Madrid: Comunidad de Madrid, 2023. Available at: <https://www.comunidad.madrid/servicios/salud/cervicam>
  22. Ajo P, Flor V, Gómez I, Gómez JJ, Jubete Y, Martín Y, et al. Risk-based opportunistic cervical cancer screening algorithms with cytology as primary test. October. Cantabrian Health Service. Ministry of Health. Government of Cantabria, 2022.
  23. Health Channel. Cervical cancer early detection program [internet]. Barcelona: Generalitat de Catalunya. Available in: <https://canalsalut.gencat.cat/ca/salut-az/c/cancer/deteccio-precoc/programes/coll-uter/>
  24. Global E. Catalan pharmacies introduce a new cervical cancer screening circuit [internet]. The global. 7/6/2023. Available at: <https://elglobal.es/farmacia/las-farmacias-catalanas-introducen-un-nuevo-circuito-de-cribado-de-cancer-de-cuello-uterino/>
  25. Institute of Public and Occupational Health. Cervical cancer early detection program. Early detection section. Government of Navarra, 2023.
  26. General Directorate of Public Health. Cervix screening program in Extremadura. Extremadura Health Service. Extremadura joint, 2023.
  27. Generalitat Valenciana communication office. Health will begin in the fall with the mass mailing to invite all women between 25 and 65 years old to participate in cervical cancer screening. Press release dated 02-17-2023. [internet] Valencia: Generalitat Valenciana. Available at: <https://comunica.gva.es/es/detalle?id=369926627&site=174859789>