IMPLEMENTATION IN THE CAMPANIA REGION OF THE SCREENING FOR CANCER OF THE UTERINE CERVIX USING HR-HPV

Cimmino Olimpia[1], Cacace Simona[2], Falconio Lucio Marcello[3], Marzocco Adele Maria[2], Capasso Giusy[2], Cecere Nunzia[2], De Benedictis Andrea[2]

[1]degree in nursing sciences , coordination master's degree Integrated assistance master in hospital territory , regional contact person for SDO flow, Head of HUB VACCIBALI ASL NAPOLI 1 CENTRO
[2]degree in nursing Sciences HEAD OF ASL NAPOLI 1 CENTRO
[3]Falconio degree in Pharmacy ASL NAPOLI 2 NORD

KEYWORDS: oncological screenings, uterus's neck cancer, reduction of mortality, Campania

ABSTRACT

Oncological screenings: The screening program consists of the free and active offer (personal invitation) to the population, at risk by age, of practices that have proved to be able to significantly affect the natural history of the disease (reduction of morbidity and mortality) maintaining A convenient relationship between costs (economic, psychological, social) and the benefits (Omswilson, 1968). Oncological screenings organized currently active in our country are: The objective of oncological screening programs is the reduction of mortality.

According to the national guidelines (PNLG) "the assumptions that are the basis of the offer of an oncological screening test to a hypothetically healthy population are:

1. *that it is possible to identify the neoplasm, if present, when still asymptomatic;*
2. *that this anticipation of the diagnosis translates into a concrete benefit, first of all in terms of survival extension. Always the PNLG in the document at the evaluation of services stresses that:*

"Screening by nature is a tool that requires caution, because it proposes to asymptomatic people, who have a perception of their positive health, a diagnostic test that can reveal the presence of a cancer in its latency period". For this reason, another professional figure represented by the "psycho-oncologist" has also become part of the last decade. As we see below the screening of the uterus's neck cancer falls more than others in the two requirements (A and (B first mentioned. Tumors that affect the uterus must be distinguished in cervix cancers and body tumors based on the segment that comes Struck by neoplasm. This work will pay attention to the first group, which by natural history, risk factors, incidence, clinical trend, therapy and finally survival. For many years, it has been the subject of public health interventions aimed at its Primary and secondary prevention.

Incidence

Cancer of the uterine cervix ranks second in the world, after the breast, it is among the cancers that affect women.

It represents the first neoplasm to be recognized by the World Health Organization (WHO) as totally attributable to an infection. The etiological factor of this neoplasm consists, in fact, of a pool of high-risk strains of the sexually transmitted human papilloma virus (HPV), whose DNA has been found in almost all cases of carcinoma of the uterine cervix. (IARC Working Groupon the Evaluation of Carcinogenic Risks to Humans . IARC Monographs on the evalutation of carcinogenic risks to humans . Human Papillomaviruses . Vol 64.Lyon :

It is estimated that the risk of developing cervical cancer in a woman's lifetime is 1 in 158. The incidence trend appears to be slightly decreasing (-0.4% / year) and has North-South gradients, with slightly lower 6 values in the south.

Unfortunately, the South loses the advantage represented by the low incidence not only due to a diagnostic delay compared to the rest of Italy, but also due to the still poor adherence to organized Screening. Unfortunately, this diagnostic advantage is not realized in the screening of mother's cancer .

In fact, through mammography it is possible to identify only very small lesions, therefore it is not a question of prevention but rather of early diagnosis which is anything but. Especially in relation to the type of intervention, more or less demolishing, and to survival.

In Italy, there are approximately 51,100 living women diagnosed with cervical cancer. The prevalence rate is higher in the Northern Regions.

Over 80% of the prevalent cases have faced the diagnosis for over 5 years. The largest proportion of prevalent cases is observed in the 75+ age group (607 / 100,000), (Cancer numbers in Italy 2020 AIOM, AIRTUM, SIAPEC) The incidence is influenced not only by gender, but also by age. In females, breast cancer represents the most frequent malignancy in all age groups, albeit with different percentages (40% in the young vs 22% in the elderly). In young women, tumors of the thyroid gland, melanoma, colorectal and cervical cancer appear.

The long preclinical phase of the disease and the possibility of diagnosing and thus intervening on precancerous lesions are the strengths of the Cervical Cancer Screening Program. Below is the representation of the latency of a precancerous lesion starting from the HPV infection and then the wide window in which it is possible to make the diagnosis, monitor and possi-

bly proceed with therapy. Carcinoma represents the final evolutionary phase of a series of progressively higher risk lesions, which, particularly in the initial phases, can also regress spontaneously.
So the advantage in the field of prevention represented by the Pap test consists in the fact that pre -cancerous lesions are diagnosed and even more today, thanks to the HR-HPV DNA Test, it is possible to identify **the type of HPV virus from which the woman is infected.**

Risk Factors

Cervical cancer ranks second in the world, after breast, among cancers that affect women. The etiological factor of this neoplasm is constituted by a pool of high-risk strains of the sexually transmitted human papilloma virus. Carcinogenesis is long-lasting and carcinoma represents the final evolutionary phase of a series of progressively higher risk lesions, which, particularly in the initial phases, may also regress spontaneously. Among the risk factors were identified:

1) low socio-economic level (with little access to prevention)
2) number of partners, sexual promisqueness
3) young age of onset of sexual activity and parity
4) immunosuppressive states
5) smoking of cigarette
6) hormonal contraception, the latter only if combined with the multiplicity of partners.

Prevention

Papillloma virus infection Cervical cancer represents the first neoplasm to be recognized by the World Health Organization as totally attributable to an infection.
The etiological factor of this neoplasm consists, in fact, of a pool of high-risk strains of the sexually transmitted human papilloma virus (HPV), whose DNA has been found in almost all cases of carcinoma of the uterine cervix. It is important to emphasize that only in a minority of cases does HPV infection lead to the development of cancer.
In fact, cervical cancer has been defined as the " **rare consequence of a common infection"**
Papilloma belongs to the Papovavirus family , it is a virus with a DNA genome that parasites the cells of the epidermis and mucous membranes. The human papillomavirus strains , over a hundred in total, can be divided, on the basis of the possible clinical consequences of the infection, 1) into low-risk HPV, which attack the skin without causing further damage (for example strains 6, 11, 42, 43, 44,) and 2) high-risk HPV, which attack mucous membranes (e.g. strains 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 , 68) and can cause benign tumors, such as genital warts, or malignant tumors, such as cervical cancer, oral cavity, anus, esophagus, larynx.
Of the high-risk HPV strains (or genotypes) 16 and 18 are the most frequently implicated in cervical cancer, accounting for approximately 60% and 10% of all cervical cancers, respectively. Other high-risk types are associated with cervical cancers, but less frequently, while low-risk HPVs (i.e. those not related to severe cancers) can still cause anogenital warts in both sexes.
HPV-related neoplasms in humans mainly concern the genital tract and the oropharyngeal district. 80-95% of anal cancers, at least 50% of penile cancers, and 45-90% of head and neck cancers are HPV-related.
Tumors of the oropharynx are 4 times more frequent in males than in females and are mainly caused, in at least 60% of cases, by HPV WHO GUIDANCE NOTE Comprehensive
cervical cancer prevention and control: a healthier future for girls and women (2013) schematically represents how early it is possible to intervene and above all how many interventions we now have to fight cervical cancer.

- **Primary prevention: Vaccination**
- **Secondary Prevention: Screening**
- **Tertiary Prevention: Treatment**

Vaccination

Already 12 years ago, the American Cancer Society stated that "the purpose of prophylactic vaccination is to reduce the incidence of all HPV-related genital pathology, including cancers and precancerous lesions of the uterine cervix, penis, vulva, vagina and anus". Vaccination against the human papilloma virus, offered today as reported below, protects against currently known oncogenic strains. However, since none of the currently available vaccines prevent all cervical cancers, it is still important to carry out regular checks even after vaccination. (Cochrane Library online 2018, published 9/5 DOI: 10.1002 / 14651858.CD009069.pub3)

Vaccination strategies in Italy

In Italy in December 2007 a State-Regions Agreement was formulated which recommended the active and free offer of vaccination against Hpv to girls during the twelfth year of life (from the age of 11 to the age of 12) .
Girls in the twelfth year were chosen as the primary target of the immunization program for:
ensure maximum effectiveness of vaccination, targeting girls before sexual debut to exploit the best immune response to the vaccine
addressing girls who attend compulsory school by facilitating both communication with families and active offerings to groups at risk of social deprivation.
The State-Regions Agreement left to the Regions the possibility of extending the population to be vaccinated, proposing 18 and / or 25 year olds as the recovery age (in this case exploiting access to the cervical cytological screening service).
The Pnpv 2017-2019 introduces in the vaccination calendar, and therefore in the LEA, in addition to the anti-meningococcal B, anti - rotavirus and anti-varicella vaccinations in the newborns; also anti-HPV in 11-year-old males. Twelfth year of life is the preferred age for actively offering HPV vaccination to the entire population (females and males).
Women who have undergone recent treatments for related HPV lesions, in order to reduce the risk of possible relapses, also fall within the expansion of free vaccination coverage.
The non-valent vaccine includes the main viral strains: seven of the nine HPV types (HPV 16, 18, 31, 33, 45, 52 and 58) at high oncogenic risk that cause about 90% of cervical cancers worldwide, 90% of anal cancer cases HPV related and approximately 80% of high grade cervical lesions. The two HPV types with low oncogenic risk 6 and 11, in addition to causing 90% of genital warts, are in third place among the HPV types that

cause cancer of the vagina or penis, fourth in cancer of the vulva and fifths in anus cancer.
On the basis of new and important scientific evidence, in fact, public health today aims to immunize adolescents of both sexes, for maximum protection from all related HPV diseases directly preventable with vaccination.
It is estimated that 70 to 80 percent of sexually active women and men are infected with HPV in their lifetime.
The virus tends to disappear after infection: in 70 percent of cases within one year and in 90 percent within two years.
The particularly affected age group ranges from 16 to 25 years. The frequency of HPV infections increases in proportion to the number of sexual partners; the risk of infection is highest at the start of sexual activity. The most appropriate solution is a vaccination before the start of sexual activity and therefore before any infection by the more dangerous human papilloma viruses.
preconceptional health of Italian university students conducted in the universities of Milan, Brescia, Padua, Rome, Cagliari, Messina, on 8,500 students between 18 and 30 years old, with an average age of 22, it appears that 20% of boys had their first sexual intercourse before the age of 15.
According to other sources, as much as 50% of young people under 15 are sexually active.
In the survey conducted by the ISS, 66% of sexually active students reported using a contraceptive, but 32% of them used an ineffective method against sexually transmitted diseases (STDs). Additionally, 15% of teens reported having sexual intercourse with casual partners .
22% of the girls said they had used emergency contraception on one or more occasions. It is important to underline, however, that while against AIDS, the use of so-called "barrier" contraceptive methods such as the male condom is sufficient o the female condom, protection by these devices against the HPV virus is limited, as transmission can also occur through contact between skin or mucous membranes.
Anyone who has many sexual partners should have regular checks for sexually transmitted infections.
In the case of persistent infection from a high-risk virus, a precancerous lesion can develop from which cancer can develop.
Therefore, the need to vaccinate adolescents before they start sexual activity is now consolidated by irrefutable evidence of efficacy.
Yet despite the fact that vaccination is free of charge, adherence to this important public health intervention falls into the exact same criticality as cancer screening, that is, low adherence.
The situation regarding the 2006 cohort sees Campania drop to 34.2% of membership.
The whole of Italy underwent a progressive worsening in relation to coverage; also Tuscany, which reached 82% of the 1998 cohort for the complete cycle, fell to 58.3% of the 2006 cohort (Data Ministry of Health 2018)

Screening

At the moment, screening for cervical cancer by means of colpocytological sampling and cytological Papanicolau test or Pap test is active in all AASSLL Campane.
In Italy, the 2014-2018 National Prevention Plan gave indications for the introduction of the new test within the screening protocol by 2019 in all Italian cervical screening programs.
Despite the Campania Region with DCA n. 36 of 01.06.2016 for the purpose: "Transposition of the observations of the Ministry of Health and Approval with amendments to the Regional Prevention Plan of the Campania Region for the years 2014 - 2018" approved action B3 under program B "Wellbeing in the Community" "Implementation of HPV-DNA Test for cervical cancer screening" with the aim of improving the early diagnosis of tumors covered by organized screening programs through the definition and implementation of innovative pathways for cervical cancer screening (HPV-DNA test), this implementation has not started yet. The possibility of performing the HR HPV-DNA test as primary has modified the diagnostic protocols of the Screening as shown below in the flow chart approved by the Italian Cervix Screening Group (GISCI)
HPV screening allows to reduce the incidence of invasive cervical cancer by 60% -70% compared to Pap test screening.
The study also made it possible to define the optimal screening methods with the HPV test: in particular, the results show that the increase in protection mainly affects women between the ages of 30 and 35 and that screening with HPV tests every 5 years is more protective than Pap smear screening every 3 years. (Ronco et al. 2014 reported in "The implementation of DNA-HPV as a primary test in the Italian cervicocarcinoma screening programs .
Indications from the results of the MIDDIR Methods for Investments / Disinvestments and Distribution of health project technologies in Italian Regions ") Screening based on HPV testing should not begin before the age of 30/35, given the higher prevalence of HPV infections compared to older women (Ronco et al. 2015).
There is evidence that under age 30 screening based on HPV testing leads to overdiagnosis of CIN2 which would spontaneously regress, with the consequent risk of overtreatment . Furthermore, some further overdiagnosis is also plausible between 30 and 34 years.
Cytological screening is currently recommended below this age. The examination of the available literature suggests that the introduction of a new method in organized screening programs requires a redefinition of the organizational and management processes of the companies and structures involved in screening.
The Regions listed below have enabled the transition from cytological to molecular using the primary HPV-DNA test

- **Basilicata Region**
- **Emilia Romagna region**
- **Liguria Region**
- **Lazio region**
- **Piemonte region**
- **Tuscany region**
- **Autonomous Province of Trento**
- **Umbria Region**
- **Veneto region**

In Campania the HPV test is currently used only as a triage test in case of low grade cytological abnormalities (L-SIL). The organizational complexity linked to

the transition from the cytological to the molecular examination in a region such as Campania has added to a health context that has been suffering for years. Only last year did the Region exit the repayment plan thanks to the achievement of the Score provided for by the LEA grid.

But this delay is not responsible for the real criticality that characterizes all the Screening in Campania and we could say almost all the prevention interventions as we will see later, including the vaccination practice, that is the Low Adhesion. The table below confirms the significant difference in the various areas of our country Effective extent of cervical screening by geographical area (% of women aged 25-64 who receive the invitation letter compared to the target population in 2018) and participation (% of women who undergo the test following the invitation letter) (source survey ONS)

In fact, in the Southern Regions / Islands, where oncological screenings are still not very widespread, the reduction in mortality and the incidence of breast, colorectal and cervical cancer has not been observed as in the rest of the country. The data published in the 2018 ONS Report refer to the activity carried out by the screening programs in 2017 and tell us that, despite everything, progress continues in the development of organized programs, even if a merciless gap is confirmed between the Center, the North and the South. "The two sources: ONS universal survey and sample telephone interview Passi are different methods of investigation; in general, the ONS survey tends to underestimate the real coverage of organized programs, while the Passi survey tends to overestimate it. The combination of the two approaches offers a very realistic cross-section of the cancer prevention offer in the country "(ONS 2018).

In Italy, the monitoring of Screening activities is carried out by the National Screening Observatory (ONS), by the GISCI group and by the Istituto Superiore di Sanità, through the National Center for Epidemiology, Surveillance and Health Promotion (Cnesps) through the Studio Passi which is for Progress of the Health Authorities for Health in Italy. The Steps surveillance launched in 2006 is characterized as a public health surveillance with the aim of carrying out a 360-degree monitoring of the health status of the Italian adult population. It is based on sample surveys carried out on the Italian adult population (18-69 years) on lifestyles and behavioral risk factors related to the onset of chronic non-communicable diseases and on the degree of knowledge and adherence to the intervention programs that the country is implementing. for their prevention. The following table shows the data relating to the three-year period 2016-2019 regarding the screening of the cervix by pap-test inside and outside the Organized Program. The tests performed as part of the so-called "Spontaneous Screening" are therefore also considered, ie those Pap tests that are carried out at the request of the woman or on the recommendation of the private gynecologist who in any case do not fall within the path of Organized Screening which instead must respond to strict criteria, such as: Active Offer, Free, Quality Controls, Study Path, Monitoring, computerization of paths, etc. The indicators are monitored by the national GISCI Group. As you can see, Campania, like many other regions, declares a significant percentage of "spontaneous" exams, associated however with a low number of exams within the

Organized Screening

From this it can be deduced that there is a percentage of women who overexpose themselves to the test and another that does not undergo the test at all.

"The anti-HPV vaccination represents a sensational example of underutilization of a high value service: in fact, if in recent years, the evidence of efficacy has progressively consolidated and the monitoring of adverse events has shown that the anti-HPV vaccines have a adequate safety profile, vaccination coverage in Italy has plummeted, contributing to preventable morbidity and mortality, as well as an increase in health care costs.

This paradox testifies that the process of transferring the best evidence to clinical practice, the organization of health services, professional decisions and the choices of citizens and patients is an obstacle course, often unpredictable and not always adequately managed at the institutional level. "

(Anti-HPV vaccine: evidence of efficacy, safety profile and vaccination coverage in Italy FondazioneG-IMBE Evidence 2018; 10 (7): e1000184 doi : 10.4470 / E1000184 Published: 9 July 2018)

The two public health interventions taken into consideration for the prevention of Cervical Cancer, Screening and Vaccination, both free for the population at risk by age, are however little exploited by the reference community as shown by the data presented. This low adhesion involves not only an increase in the incidence and mortality from cervical cancer, but also an increase in public health costs which sees a double expenditure commitment for the same woman: the organizational structure of screening modulated on the number of target population 25-64 years, regardless of whether the target is fully achieved or not, and also the cost of surgical and / or medical therapy that the woman will have to resort to for a late diagnosis. While for the pap-test it is now established that the use of private individuals is justified in some cases by the need for a more "confidential" relationship for the execution of the colpocytological sampling , the low adherence to vaccination practice apparently does not find justification. Yet free in a context of high social risk such as that of Campania should be a sufficiently captivating element. "The socio-economic gradient appears to be probably the most important explanatory factor of the quality and quantity of life and this regardless of the cultural humus in the broad sense in which an individual or a population is immersed. As happened on the occasion of the sinking of the Titanic, where survival was positively correlated with the boarding class, so in civil society those who are in a condition of greater socio-economic well-being, will benefit from greater longevity and therefore will have mortality rates. lower. (G. Domenichetti: For a Public Health policy centered on the needs of the population and not on that of services.) But it is also true that extreme social deprivation means that "The less educated and low-class people are less confident about effects that could derive in the future from the change in health-related behaviors, since other risk factors are still beyond their control, such as the adverse conditions of income, home, environment, work that are more widespread in these groups. "

From the data of the Passi Study we talked about previously, it is confirmed that the lowest socio-economic levels of the population use Screening.
Avoidable Mortality If, as previously mentioned, in the South we do not see a decrease in mortality from cervical cancer, as in the rest of the country, it means that there is a slice of the population that escapes both primary and secondary prevention. Since these are deaths that could be avoided thanks to interventions such as vaccination and screening, the latter can fall into the group of so-called Avoidable Mortality. Avoidable deaths are those deaths that occur at certain ages (within 60 years of age) and from causes that could be actively countered with primary prevention, early diagnosis and therapy, hygiene and health care interventions. The graph below shows the relationship between 5-year survival after cancer diagnosis and adherence to screening in the various regions.
"This is a geographical gap entirely within the Italian territory, which does not find a similar response in most European countries. The North-South gradient therefore remains an unsolved node, despite the enormous effort put in place by public health in terms of efficiency and appropriateness. Searching for the root causes of this gap is a complex operation, which goes far beyond the reach of epidemiology or health care, and for which social, political and historical analysis tools would be needed. Certainly, the current crisis of confidence gripping institutions can further jeopardize the participation of the population in public health initiatives such as screening, especially in areas of the country where trust in services and in the state has always been very low " . Evaluating Avoidable Deaths from Cervical Cancer, identifying the main reasons "is the first, indispensable, tool to remedy them. The reasons are linked to a lack of primary and secondary prevention and to responsibilities linked to health planning and organization " A.Panà
Just at a time when political planning in Campania had begun to pay attention to two critical issues typical of the region, namely the incidence of Improper Caesarean Section and the spread of cancer screening, also to be included in the LEA indicators. the CoViD -19 pandemic has been brought down, which has momentarily shifted attention to other emergencies. The latest MEV-2019 Report shows that "The component of avoidable mortality that identifies deaths linked to the quality of health services is the one that marks the greatest distances and divides Italy in two: all and only the central-northern regions, Excluding Lazio, they are better than the national average. " However, the death toll due to lifestyle causes remains higher: smoking, alcohol, incorrect eating habits. At the regional level, the minimum values are recorded in Veneto and Marche, while Campania is confirmed at the other end of the ranking as the region with the maximum number of days lost per capita due to avoidable mortality, an indicator adopted by MEV (i) for the regional and provincial rankings which take into account not only the number of the phenomenon but also the age at death, with the deaths occurring at a younger age weighing more heavily. Among the provinces, Treviso is the one with the lowest value, below 15 lost days, followed by Siena, Florence, Rimini, Monza Brianza, Modena, Trento, all below 16.
It is evident that the low adherence to screening and / or vaccinations fall within a much broader dimension that makes the regional health system a patient who needs urgent and no longer postponable interventions. It is necessary to rebuild a public health system, aimed at a community made up of people aware of the management of their health that has gradually disappeared in recent decades, giving way to an economic-financial vision of "health" no longer understood as an objective. to be achieved, but rather as a "good to sell and therefore to buy", the person from patient has therefore become a customer. And, while the good health became part of the investments of the Finance, inexorably, public health, especially the territorial one, was sucked into the vortex of inadequacy up to the delegitimization, thanks to the equally inexorable reduction of the resources allocated, especially in those Regions, victims of an at least improper interpretation of Fiscal Federalism.
The current pandemic has unequivocally highlighted the strategic role of public health and territorial medicine in particular, with its low-access services (pediatricians, family doctors, continuity of care doctors, family clinics, vaccination centers , diabetes centers, social and health services for the elderly, the disabled, the mentally ill, drug addicts, etc.) which represents that advanced point of health that many countries envy us. The social emergency that is emerging post -CoviD opens up difficult scenarios for the future, for our country and in particular for Campania. This moment can represent an opportunity to redefine skills, roles and responsibilities in our very precious Health System. First of all, the requalification of territorial medicine by restoring that widespread distribution of its Agencies which in the past represented its strength by welcoming needs but above all by monitoring the state of health of the community, but the real process of renewal passes through recovery. of that de-legitimization by a non-negligible slice of society which has ended up considering the quality of the healthcare offer as a function of its cost. Furthermore, a stabilization of the regional health planning is indispensable, which pursues the pre-established objectives, whose path indicators are evaluated and monitored in time in order to be able to make appropriate changes in the procedures and that the outcome indicators are achieved. The organizational structure of Oncological Screening, of all three oncological screenings, represents a real revolution not only for the reference community, but also and above all for public health. The Screening path is nothing more than a PDTA, i.e. a therapeutic diagnostic path that starts from the territory, in the case of the Family Consultants where the colpocytological sampling is performed up to the Colposcopic Study Centers and finally to the III level Centers for surgical or chemotherapy therapy . For the path not to be an obstacle course for the patient, that is, not a performance but experienced as a service, it is necessary that there is professional recognition among the various operators involved in the different levels of assistance. Furthermore, it is necessary to identify a communication strategy suited to the needs of that particular context, and above all that the most effective strategy, that is empowerment , is put in place.

Conclusions

The systematic review identified several interventions that proved effective in all contexts, some of which

with minimal economic and organizational impact. One of the factors that most influences the effectiveness of cancer screening programs in reducing cancer mortality and / or morbidity is the participation of the target population in the program. High participation rates must be achieved to achieve a significant impact on the health of the affected population. This objective must be achieved by encouraging an informed participation of the individual who, before joining, must be made aware of the benefits, limitations and disadvantages of the screening program.

Among The Improvement Strategies Of Non-Organized Screening:

- there is solid evidence for systematic reminders to GPs in which people who have not undergone screening are reported;
- there are very heterogeneous results for information and education campaigns aimed at the individual;
- very intensive face-to-face promotion interventions proved effective, but were mainly tested in groups of deprived or at risk population;
- there are indications of the effectiveness of mass campaigns, but they have shown many objective difficulties in the evaluation methodology;
- there is solid evidence of the effectiveness of interventions to remove economic barriers, specifying that a woman will carry out the blood sampling increases participation in cervical screening. You must never abandon the practice of Screening in the course of adult life.

The State Of The Art In Campania

The identification of human papillomavirus as a necessary cause of cervical cancer has opened up new opportunities for prevention: the vaccine to prevent infection and the HPV test to detect infections and treat pre-invasive lesions early . Some large population trials conducted in Europe have shown that the HPV test is more sensitive than the Pap test; the follow up of these studies has then shown that this greater sensitivity translates into greater diagnostic anticipation of preinvasive lesions , finally in greater efficacy in the prevention of invasive cancer. In light of these findings, many pilot projects have begun to evaluate the feasibility of organized screening programs based on HPV as the primary screening test.

The Italian HTA report anticipates the indications of the European guidelines, the recommendations of the report were adopted by the Ministry of Health, after hearing the opinion of the Health Commission of the State Regions Conference, as a support tool to the Regions for planning cervical screening 15 . Therefore, despite the excellent results of the use of the Pap Test as the main method of screening, in recent years, numerous studies have addressed the problem of overcoming the current screening procedures 40 for cervical cancer, with the aim of verifying whether , new methods, generated by the advancement of diagnostic techniques in molecular biology, could lead to improving the management and results of this prevention path. In the context of this complex topic, which would require a discussion that goes beyond the boundaries of this work, we can simplify, underlining the acquisition of at least three basic points in the scientific literature:

- There is clear scientific evidence that screening with clinically validated DNA tests for oncogenic HPVs (HPV tests), as a primary screening test and with an appropriate protocol, is more effective than cytology-based screening in preventing invasive neck cancers of the neck. ‘uterus.
- HPV screening allows to reduce the incidence of invasive cervical cancer by 60% -70%, compared to Pap test screening, with an interval between two tests of 5 years instead of 3 (Ronco et al. 2014).
- A protocol centered on the HPV test reduces the referral to second level assessments and the overdiagnosis of spontaneously regressive lesions, affecting the containment of costs and the percentages of adherence to the path.

In view of these evidences, in Italy the 2017-2019 National Prevention Plan gave indications for the introduction of the new test within the screening protocol by 2019 in all Italian cervical screening programs.

The Campania Region with DCA n. 36 of 01.06.2016 for the purpose: “Transposition of the observations of the Ministry of Health and Approval with amendments to the Regional Prevention Plan of the Campania Region for the years 2014 - 2018” approved action B3 under program B “Wellbeing in the Community” “Implementation of HPV-DNA Test for cervical cancer screening” with the aim of improving the early diagnosis of tumors covered by organized screening programs through the definition and implementation of innovative pathways for cervical cancer screening (HPV-DNA test) 14. Following these assumptions, to date in some regions the HPV test is progressively replacing the Pap test; in situations where the latter is still being used, the HPV test is used as a triage test in case of low-grade cytological abnormalities.

General objectives of the intervention:

- Adapt the clinical and organizational path of cervical cancer screening in the Campania Region to the quality standards recommended at national level.
- Improving the early diagnosis of tumors covered by organized screening programs through the definition and implementation of innovative pathways for cervical screening (HPV-DNA test), in order to promote a homogeneous extension of early diagnosis and an acceptable / desirable adhesion. specific to the intervention.
- With a regional guiding document, define the methods and times for introducing the new procedure.

Define and organize the reference centers responsible for taking care of the different steps of the path.

- Promptly initiate training for the operators involved in the program.
- Promptly activate awareness / empowerment / information campaigns for the target population.
- Update the operational / technological levers of the program, through the revision of the regional screening software and moving the invitation system of the target population entirely to the web- based telematic platform , guaranteeing with the same tool the informative feed-back to citizens and treating doctors .

Project Proposal

Essential elements for the preparation of an appropriate protocol The consolidated definitions and techni-

cal-scientific costrains for the implementation of the intervention must be assumed in advance, considering the evidence present in the literature. These can be summarized as follows:

- The screening test of choice for the diagnosis and prevention of cervical cancer is the Pap test, with a three-year interval for women aged between 25 and 29, and the HPV test, with a five-year interval, for women aged between 30 and 64.
- The Pap test is also used as a triage test in HPV positive women, during the follow - up post second level CIN2 + negative tests and post treatment.
- HPV positive women are not to be sent directly for colposcopy but it is necessary to use cytology (Pap test) as a triage system. If the cytology is positive, the woman is sent for colposcopy. If the cytology is negative, the woman is asked to perform
- The Pap test is also used as a triage test in HPV positive women, during the follow - up post second level CIN2 + negative tests and post treatment.
- HPV positive women are not to be sent directly for colposcopy but it is necessary to use cytology (Pap test) as a triage system. If the cytology is positive, the woman is sent for colposcopy. If the cytology is negative, the woman is asked to perform a new HPV test one year later. If this test is still positive, the woman is sent for colposcopy while, if it is negative, she is invited to a new screening round within the scheduled intervals.
- Validated oncogenic HPV DNA tests for sensitivity and specificity for high grade lesions should be used, as reported in the European Guidelines (Antila et al. 2015).
- There is no evidence that dual cytology and HPV testing is either more protective than HPV alone as a primary test or that it increases sensitivity. The double test strategy, on the other hand, determines a substantial increase in referral for colposcopy. For this reason, when using the HPV test as the primary test, it is recommended not to add cytology in parallel.
- The HPV test to be used for primary screening must be a clinically validated test according to the criteria defined by the guidelines for the clinical validation of HPV DNA tests for screening.

References

1. International Agency for Research on Cancer . IARC Monograph on the evaluation of carcinogenic risks to humans : Human Papillomaviruses . IARC, Lyon 1995 (updated 1997). http://monographs.iarc.fr/ENG/Monographs/vol64/volume64.pdf Redburn JC, Murphy MFG.
2. Hysterectomy prevalence and adjusted cervical and uterine cancer rates in England and Wales. Brit J ObstetGynaecol 2001; 108: 388-95. AIRTUM Working Group. Tumors in Italy - 2016 Report. Survival. EpidemiolPrev 2017; 41 (2): Suppl . 1. AIRTUM Working Group. Italian cancer figures , Report 2014. Prevalence and recovery from cancer in Italy. Prev - alence and cure of cancer in Italy . Italian cancer figures , Report 2014. Prevalence and cure of cancer in Italy . EpidemiolPrev 2014; 38 (6 Suppl . 1): 1-144. National Screening Observatory.
3. http://www.osser-vatorionazionalescreening.it/content/i-numeri-degliscreening Jeong BK, Choi DH, Huh SJ, et al. The role of squamous cell carcinoma antigen as a prognostic and predictive factor in carcinoma of uterine cervix . RadiatOncol J 2011; 29: 191-8. Burghardt E, Holzer E. Diagnosis and treatment of micro -invasive carcinoma of the cervix uteri. ObstetGyne - with 1977; 49: 641-53. Shepherd JH, Crawford RAF, Oram DH. Radical tra- chelectomy : a way to preserve fertility in the treatment of early cervical cancer ? Br J
4. ObstetGynaecol 1998; 105: 912-6. Song S, Rudra S, Hasselle MD, et al. The effect of treat - ment time in locally advanced cervical cancer in the era of concurrent chemoradiotherapy . Cancer 2013; 119 (2): 325-31. Gupta S, Maheshwari A, Parab P, et al. Neoadjuvant Chemotherapy Followed by Radical Surgery Versus Concomitant Chemotherapy and Radiotherapy in Patients With Stage IB2, IIA, or IIB Squamous Cervical Cancer : A Randomized Controlled Trial. J ClinOncol . 2018 Feb 12: JCO 2017759985. Tewary K, Sill M, Long IIIH, et al. Improved survival with bevacizumab in advanced cervical cancer . NEJM 2014; 370 (8): 734-43. Frenel JS, Le Tourneau C, O'Neil BH, et al. Pembroli - zumab in patients with advanced cervical squamous cell Cancer : Preliminary results from the phase Ib KEY- NOTE-028 study . J ClinOncol 2016; 34 (Suppl ., Abstr 5515). Antoine Hollebecque , Tim Meyer , Kathleen N. Moore et al. An open- label , multicohort , phase I / II study of nivolumab in patients with virus- associated tumors (CheckMate 358): Efficacy and safety in recurrent or metastatic (R / M) cervical , vaginal , and vulvar cancers . JCO 2017 abst 5504 Campania Region: DCA n. 36 of 01.06.2016 for the purpose: "Transposition of the observations of the Ministry of Health and Approval with amendments to the Regional Prevention Plan of the Campania Region for the years 2014 - 2018" Document "HTA reports on cervicocarcinoma screening " Epidemiol , Prev 2012; 36 (3-4.5) suppl 1
5. Ronco et al. 2014, Ronco et al. 2015, Antila et al. 2015 Italian Group of Head and Neck Cancer Screening (GISCI): Triage cytology in screening programs with HPV as primary test – 2013
6. SurveyGISCi on follow - up activities of cervical screening programs - 2013 report
7. Use of the HPV- hr test in the triage of ASC-US, LSIL in women over 35 years, in the follow-up of women with ASC-US + cytology after a second level study negative for CIN2 + and in the follow-up after treatment of CIN2-3 lesions: 2012 update
8. Recommendations on the HR-HPV test as primary screening test and review of the role of the Pap test. Approved by the GISCi assembly , 2010 edition
9. 2nd level manual-Recommendations for quality in the diagnosis, therapy and follow-up of cervical lesions, within the screening programs, 2009 edition
10. GISCI operating document for application in the programs of screening of the Bethesda System 2001, 2009 edition
11. "HTA reports on cervicocarcinoma screening " Epidemiol , Prev 2012; 36 (3-4.5) suppl 1