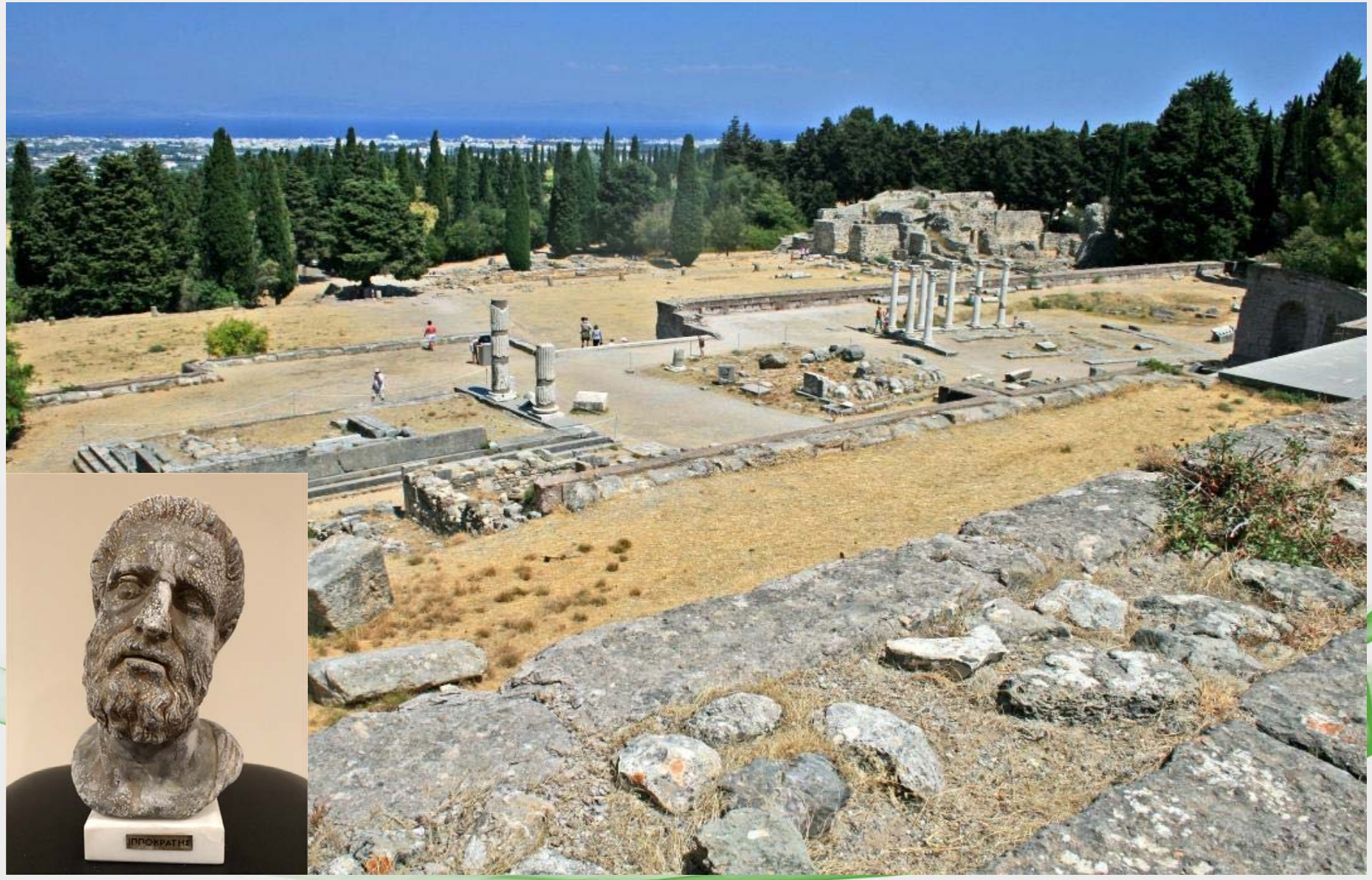
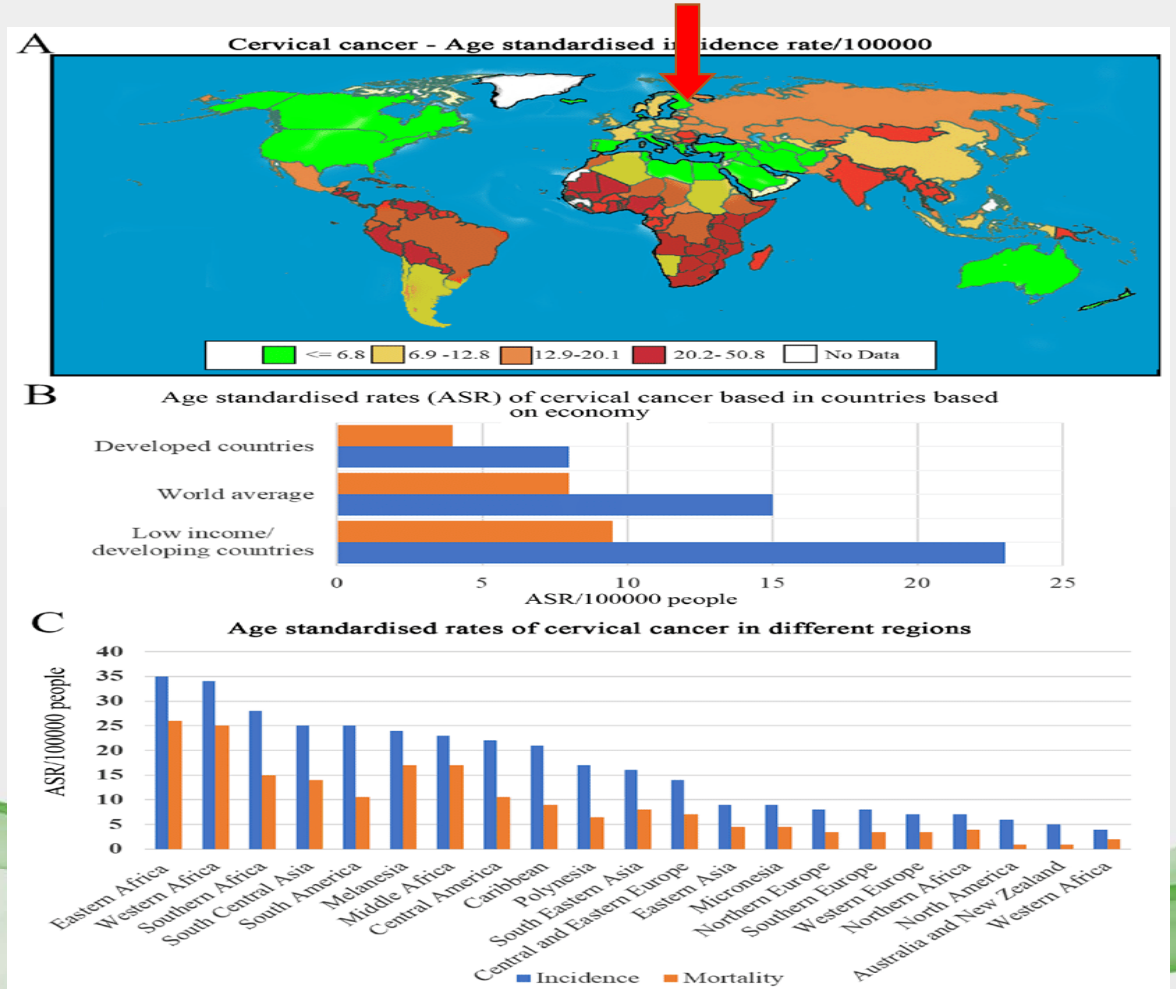
Cancerul de col uterin- cum îmbunătățim prevenția prin asumare și informare

Dr Raluca Gabriela Enciu


ΙΠΠΟΚΡΑΤΗΣ

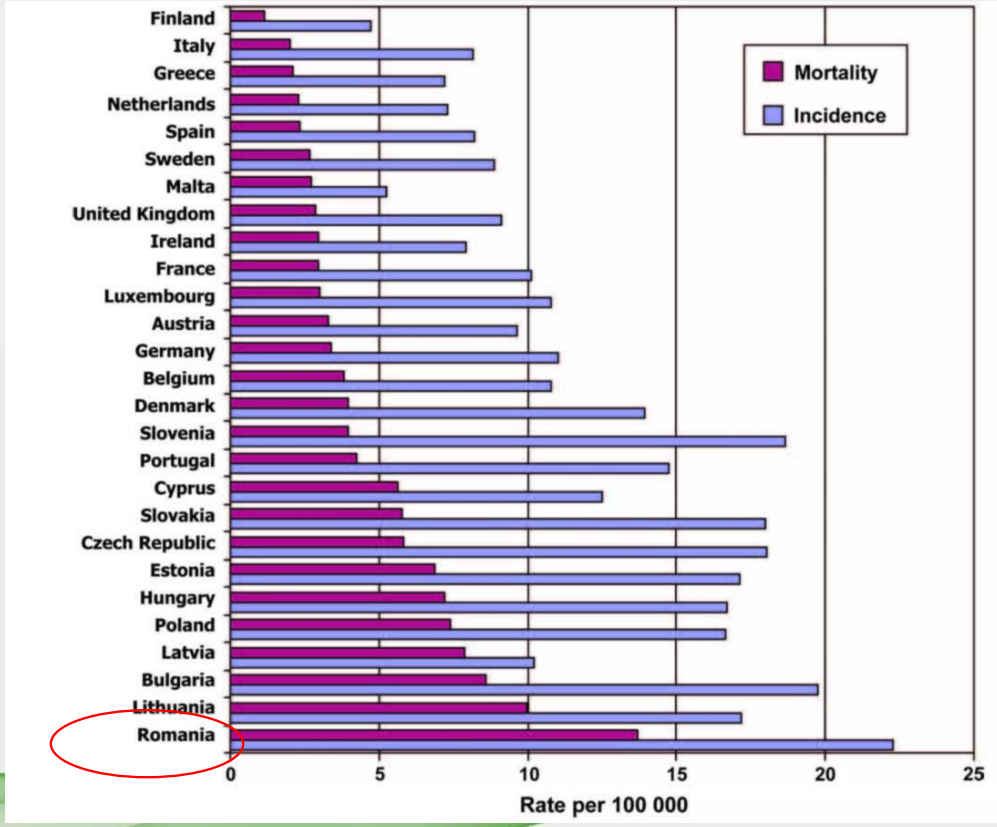
Situația cancerului de col în România vs în lume



Situația cancerului de col în România și în Europa

- Media incidenței cancerului de col in statele europene: 12.8 la 100 000 locuitori
- Finlanda : 6.7
- Italia , Suedia: 9.4
- România: 23
- Incidenta de 2,5 ori mai mare decât media UE
- 50% depistate în stadii avansate

Anual 3308 femei sunt diagnosticate cu neo de col în Romania, 1700 decedează



Plan de prevenție

3 mari piloni:

1. Informare medici și populație
2. Vaccinare
3. Screening

Informare medici și populație

PROGRAMELE NAȚIONALE DE IMUNIZARE ANTI-HPV DE SUCCES ÎN LUME

Informare medici și populație

O populație educată și informată corect medical este o populație mai sănătoasă

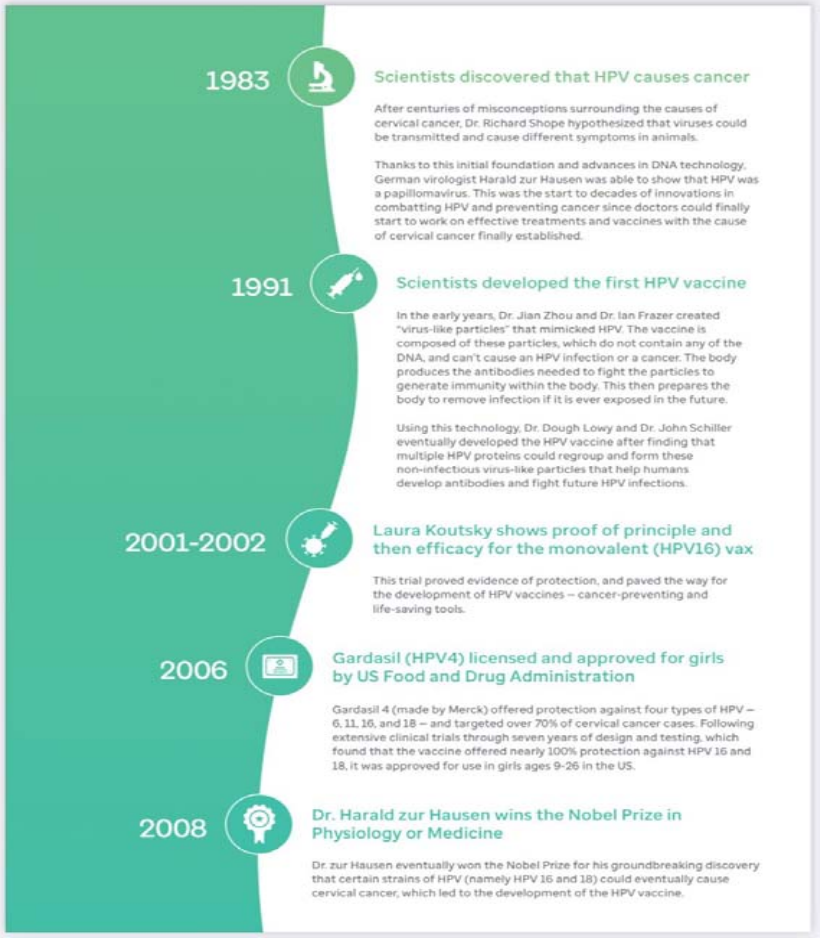
Dorința de informare a tinerei generații, iar mijloace mass media pot avea un rol crucial

Noi medicii care deținem informația corectă trebuie să o transmitem mai departe către pacienți chiar dacă poate părea o picătură într-un ocean.

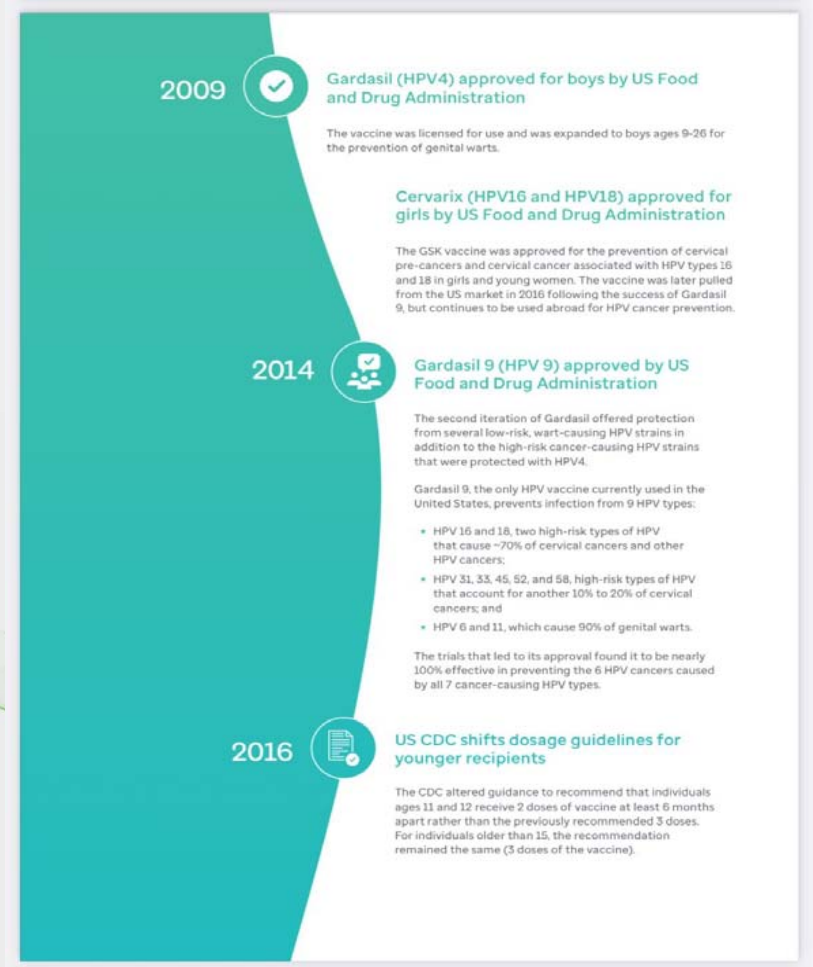
Consider esențiala informarea din surse corecte, distriburirea de materiale informative bazate pe ultimele studii, pentru ca mai apoi pacienții să adere la campaniile de vaccinare.

Informare prin intermediul medicului de familie –scrisoare la domiciliu prin poștă -despre beneficiile vaccinării

Istoria vaccinării anti- HPV



Istoria vaccinării anti- HPV



2009

Gardasil (HPV4) approved for boys by US Food and Drug Administration

The vaccine was licensed for use and was expanded to boys ages 9-26 for the prevention of genital warts.

Cervarix (HPV16 and HPV18) approved for girls by US Food and Drug Administration

The GSK vaccine was approved for the prevention of cervical pre-cancers and cervical cancer associated with HPV types 16 and 18 in girls and young women. The vaccine was later pulled from the US market in 2016 following the success of Gardasil 9, but continues to be used abroad for HPV cancer prevention.

2014

Gardasil 9 (HPV 9) approved by US Food and Drug Administration

The second iteration of Gardasil offered protection from several low-risk, wart-causing HPV strains in addition to the high-risk cancer-causing HPV strains that were protected with HPV4.

Gardasil 9, the only HPV vaccine currently used in the United States, prevents infection from 9 HPV types:

- HPV 16 and 18, two high-risk types of HPV that cause ~70% of cervical cancers and other HPV cancers;
- HPV 31, 33, 45, 52, and 58, high-risk types of HPV that account for another 10% to 20% of cervical cancers; and
- HPV 6 and 11, which cause 90% of genital warts.

The trials that led to its approval found it to be nearly 100% effective in preventing the 6 HPV cancers caused by all 7 cancer-causing HPV types.

2016

US CDC shifts dosage guidelines for younger recipients

The CDC altered guidance to recommend that individuals ages 11 and 12 receive 2 doses of vaccine at least 6 months apart rather than the previously recommended 3 doses. For individuals older than 15, the recommendation remained the same (3 doses of the vaccine).

2018

US Food and Drug Administration approved expanded use of Gardasil 9

The FDA expanded the vaccine's approval to include females and males 27-45 years old.

2019

HPV vaccination rates soar

By October 2019, 100 countries worldwide incorporated HPV vaccination into their regular vaccine schedule.

2020

US Food and Drug Administration approves expanded use of Gardasil 9

The FDA originally only approved the vaccine for cervical cancer prevention, but based on additional research in 2020, they expanded it to include cervical, vaginal, vulvar, anal, oropharyngeal, and other head and neck cancers.

2030

WHO hopes to meet milestones on path to eliminating cervical cancer

After meeting the 90-70-90 targets through a global focus on vaccination, screening, and treatment, the World Health Organization (WHO) hopes to eradicate vaccine preventable cervical cancer within the next century.

- 90% of girls fully vaccinated with the HPV vaccine by age 15;
- 70% of women initially screened with high-performance testing by age 35 and a secondary test at age 45; and
- 90% of pre-cancers treated and 90% of invasive cancers managed.

Want to Learn More?

Have a conversation with your or your child's healthcare provider, or another trusted, reliable source of medical information, and visit St.Jude.org/Bright-Future.

HPV vaccination is cancer prevention and offers protection today for a lifetime against HPV cancers.

References

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- Johns Hopkins Medicine www.hopkinsmedicine.org
- Kaiser Family Foundation www.kff.org
- Merck & Co www.merck.com
- National Cancer Institute at the National Institutes of Health https://hpvvaccinecancer.gov/
- The Noble Prize Organization www.nobelprize.org
- NOMAN Race to End HPV www.hathancampaign.org
- X Street www.xstreet.org

Prevenție primară- vaccin ani HPV

Vaccinul Gardasil®9 poate fi prescris în regim compensat

Pe data de 27 Noiembrie 2023, a fost publicat **Protocolul terapeutic** prin care se aprobă prescrierea vaccinului HPV, Gardasil®9, în regim compensat.[1]

Cine beneficiază de vaccinul HPV și care este nivelul de compensare?

Compensare **100%**

Băieți și fete cu vârsta ≥ 11 ani și < 19 ani[2]

- Se recomandă ca **prima administrare** a vaccinului să se realizeze **până la vârsta de 14 ani.**[1]
- Pentru persoanele cu vârsta ≥ 18 ani, dar < 19 ani la momentul primei administrări, **se va elibera rețeta pentru toate cele 3 doze** necesare pentru efectuarea schemei complete.[1]

Compensare **50%**

Femei cu vârsta ≥ 19 ani și ≤ 45 ani[2]

Cine poate prescrie vaccinul Gardasil®9?

Medici de toate specialitățile aflați în contract cu casele de asigurări de sănătate.[1]

Cine sunt medicii vaccinatori?[1]

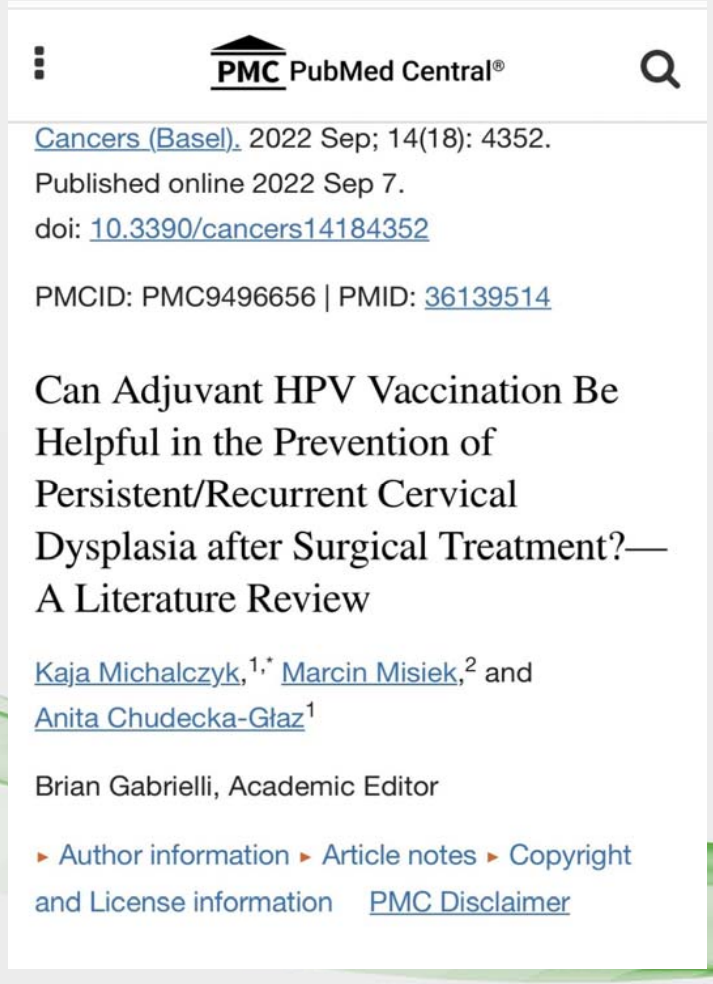
Medicii vaccinatori

- medici de familie, epidemiologi, boli infecțioase, pediatrie;
- medici din orice altă specialitate care au un atestat de vaccinologie.

Toți medicii vaccinatori trebuie:

- să fie în contract pentru furnizarea de servicii de vaccinare cu direcția de sănătate publică județeană sau a municipiului București,
- să dețină cont în RENV și au obligația înregistrării administrării vaccinului și raportării RAPI.

Vaccin ani HPV cu rol terapeutic



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PMCID: PMC9496656 | PMID: 36139514

Can Adjuvant HPV Vaccination Be Helpful in the Prevention of Persistent/Recurrent Cervical Dysplasia after Surgical Treatment?—A Literature Review

Kaja Michalczyk,[1,*] Marcin Misiek,[2] and Anita Chudecka-Głaz[1]

Brian Gabrielli, Academic Editor

tients diagnosed with HSILs; however, attempts have been made to determine the use of HPV prophylactic vaccination to reduce recurrent HSILs and prevent cervical cancer. The aim of this review was to analyze the up-to-date literature concerning the possible use of secondary human papilloma virus (HPV) vaccination as an adjuvant method to surgical treatment in patients diagnosed with cervical HSILs. Adjuvant HPV vaccination after surgical treatment may reduce the risk of recurrent cervical dysplasia.

Keywords: HPV, vaccination, cervical dysplasia, CIN, HSIL, conization, LEEP

1. Introduction

Go to: ▸

Each year, more than half a million women are diagnosed with cervical cancer [1]. Despite the advances in cancer screening and prevention, it remains one of the leading causes of cancer deaths. Chronic human papilloma virus (HPV) infection is responsible for 99.7% of cervical cancer diagnoses [2].

Vaccin anti HPV cu rol terapeutic

pathogens

MDPI

Article

Post-Conization HPV Vaccination and Its Impact on Viral Status: A Retrospective Cohort Study in Troms and Finnmark, 2022

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† These authors contributed equally to this work.

Abstract: Human papillomavirus (HPV) is associated with cellular changes in the cervix leading to cancer, which highlights the importance of vaccination in preventing HPV infections and subsequent cellular changes. Women undergoing the loop electrosurgical excision procedure (LEEP), a treatment for high-grade cervical intraepithelial neoplasia (CIN2+), remain at risk of recurrence. This study assessed the effect of post-conization HPV vaccination on the viral status of women at six months post-conization, aiming to evaluate the vaccine's effectiveness in preventing recurrence of CIN2+. A retrospective cohort study was conducted among women in Troms and Finnmark who underwent conization in 2022. Using the SymPathy database and the national vaccination register (SYSVAK), we analyzed the vaccination statuses and HPV test results of women born before 1991, who had not received the HPV vaccine prior to conization. Out of 419 women undergoing conization, 243 met the inclusion criteria. A significant association was found between post-conization HPV vaccination and a negative HPV test at six months of follow-up (ARR = 12.1%, $p = 0.039$). Post-conization HPV vaccination significantly reduced the risk of a positive HPV test at the first follow-up, suggesting its potential in preventing the recurrence of high-grade cellular changes. However, the retrospective design and the insufficient control of confounding variables in this study underscore the need for further studies to confirm these findings.

Keywords: human papillomavirus (HPV); HPV vaccine; conization; LEEP; recurrence; post-conization recurrence; HPV status; cervical cancer prevention; vaccination efficacy; cervical intraepithelial neoplasia

check for updates

Citation: Rykkelid, M.; Wennberg, H.M.; Richardsen, E.; Sørbye, S.W. Post-Conization HPV Vaccination and Its Impact on Viral Status: A Retrospective Cohort Study in Troms and Finnmark, 2022. *Pathogens* **2024**, *13*, 381. https://doi.org/10.3390/pathogens13050381

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1. Introduction

In Norway, the National Cervical Screening Program aims to prevent cervical cancer through early identification and treatment of high-grade cervical intraepithelial neoplasia (CIN2+) before it progresses to malignancy and to reduce the incidence and mortality of cervical cancer [1,2]. The program, managed by the National Cancer Registry of Norway, was established as a national initiative in 1995 and targets women aged 25 to 69.

As of July 2023, women now undergo high-risk HPV testing every five years, where positive results are followed up with microscopic examination of the cervical smear [3,4]. This represents a shift from the prior triennial microscopic evaluations that contributed to the observed decline in cervical cancer mortality since the 1980s [2]. Notably, in Norway, more than half of cervical cancer cases arise in individuals who were non-compliant with the screening recommendations.

Persistent infection with HPV can cause cervical intraepithelial neoplasia (CIN) [5], also known as cervical dysplasia or precancerous abnormal cells, and more than 99% of cervical cancers are linked to HPV [6]. The conventional management of CIN2+ involves conization, specifically the loop electrosurgical excision procedure (LEEP), which removes

a higher prevalence of 75% HPV positivity was observed after conization. The disparity in HPV positivity rates between participants younger than 60 years and those aged 60 and above was statistically significant ($p < 0.001$, Fisher's exact test, one-sided).

The analysis of vaccination coverage revealed that the highest rates were among the three youngest age groups. Specifically, the age groups 30–39 and 50–59 years demonstrated similar vaccination rates of 37.0% and 36.7%, respectively, whereas the 40–49 age group exhibited a vaccination rate of 27.4%. Notably, vaccination coverage was markedly lower in the oldest age groups, with 12.5% in the 60–69 age group and 0% in the 70–79 age group.

Table 2 outlines the categorization of participants based on whether they received the HPV vaccine post-conization (YES or NO) and their HPV test results approximately six months after the procedure (HPV+ or HPV−).

Table 2. Frequency table that compares the HPV vaccination status (no/yes) with the result of the HPV test taken at the six-month follow-up (HPV−/HPV+).

Vaccinated (after Conization)	HPV− ($n = 166$)	HPV+ (%) ($n = 77$, 31.7%)	Total ($n = 243$)	*p*-Value
No	107	59 (35.5)	166	0.039
Yes	59	18 (23.4)	77	

Out of the 243 participants included in this study, 77 had been vaccinated post-conization. This represents less than one-third of the sample. A considerable proportion, 77 out of 243 (31.7%), tested positive for HPV at about six months post-conization. The incidence of HPV positivity was 23.4% in the vaccinated group compared to 35.5% in the unvaccinated group, resulting in an absolute risk reduction (ARR) of 12.1 percentage points. The significance of the vaccination's effect was evaluated using a one-sided Fisher's exact test, yielding a *p*-value of 0.039, which indicates a significant correlation between post-conization vaccination and a negative HPV test at the six-month follow-up. The number needed to vaccinate (NNV) to prevent a single positive HPV test six months post-conization was calculated to be 8.22.

4. Discussion

Evidence from multiple studies indicates that post-conization HPV vaccination may play a preventative role in the recurrence of high-grade intraepithelial neoplasia (CIN2+) [16–18]. Our research identified a notable reduction in HPV positivity rates at six months after conization, from 35.5% in the unvaccinated group to 23.4% in the vaccinated group. This translates to an absolute risk reduction (ARR) of 12.1 percentage points in the likelihood of testing positive for HPV among vaccinated individuals compared to their unvaccinated counterparts. This outcome not only underlines the vaccine's potential in reducing the likelihood of future CIN2+ but also its role in mitigating cancer risk due to HPV.

The disparity in conization rates across age demographics can likely be linked to the prevalence of CIN2+ within the population. Data from Norway in 2022 reveal a median conization age of 36 years, with a noteworthy observation that only 149 out of 6393 women who underwent conization were aged 70 or above [9]. This trend suggests a decrease in conization procedures with advancing age. Notably, our study found the highest HPV positivity rates post-conization among the eldest cohorts. A contributing factor might be the minimal vaccination coverage observed in these groups, with only 2 out of 24 (8.3%) women aged 60 or above receiving the HPV vaccine post-conization. An alternative explanation could be the diminished immune response and weaker immune system prevalent in older populations [21]. However, the small sample size warrants caution in drawing definitive conclusions regarding this observed difference.

Less than one-third of the study population opted for vaccination post-conization. This phenomenon is potentially due to the lack of explicit national guidelines on post-conization HPV vaccination. While our analysis did not delve into how economic, educational, or other socio-economic factors might influence vaccination decisions, the high cost of the

Take-home message

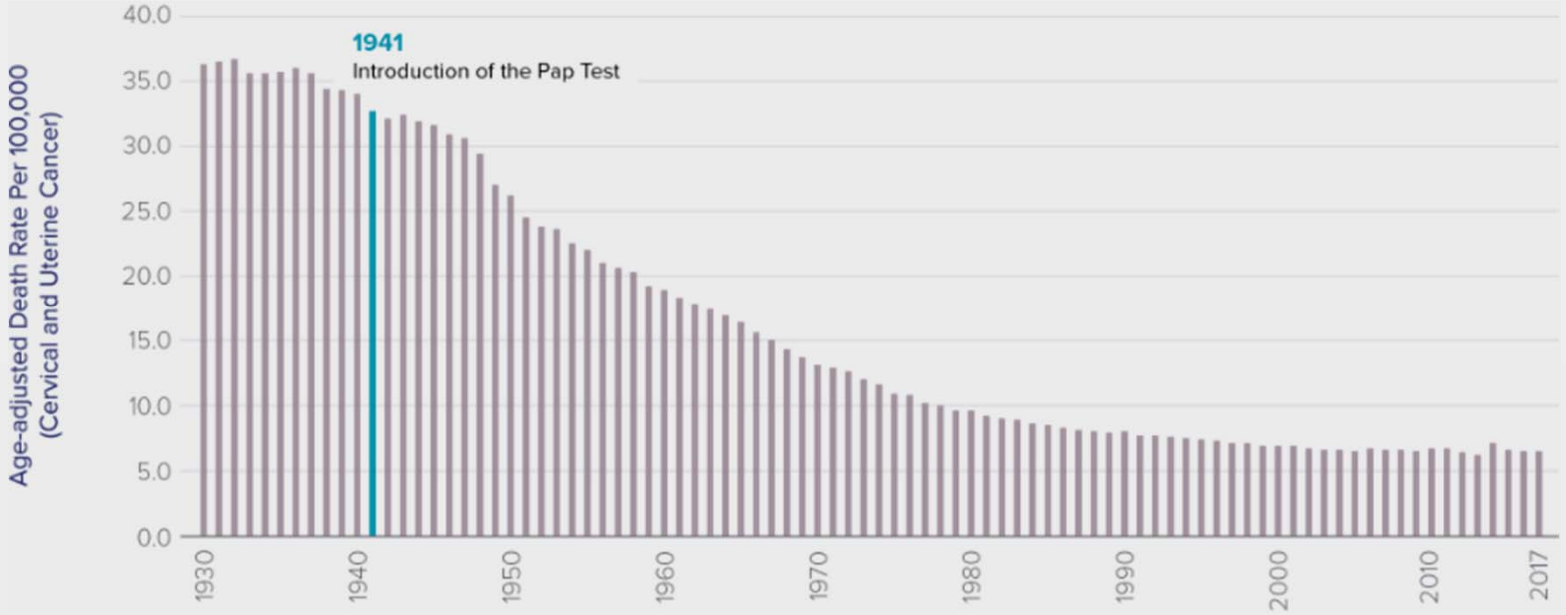
- Deziderat vaccinare 11-14 ani

- Recomandare vaccinare tuturor femeilor şi bărbaţilor < 45 de ani indiferent dacă au început viaţa sexuală sau au contactat HPV

- Recomandare vaccinare persoanelor cu leziuni cervicale CIN 1 sau CIN 2,3

- Creşterea numărului de medici vaccinatori

Prevenție secundară- screening- Babeș-PAP



Prevenție secundară- screening- Babeș-PAP

- **Programul național de screening pentru cancerul de col uterin a fost introdus în 2012:**

„Femeile cu vârste cuprinse între 25 și 64 de ani sunt invitate să facă un test Babeș-Papanicolau o dată la cinci ani, indiferent dacă sunt asigurate sau neasigurate.

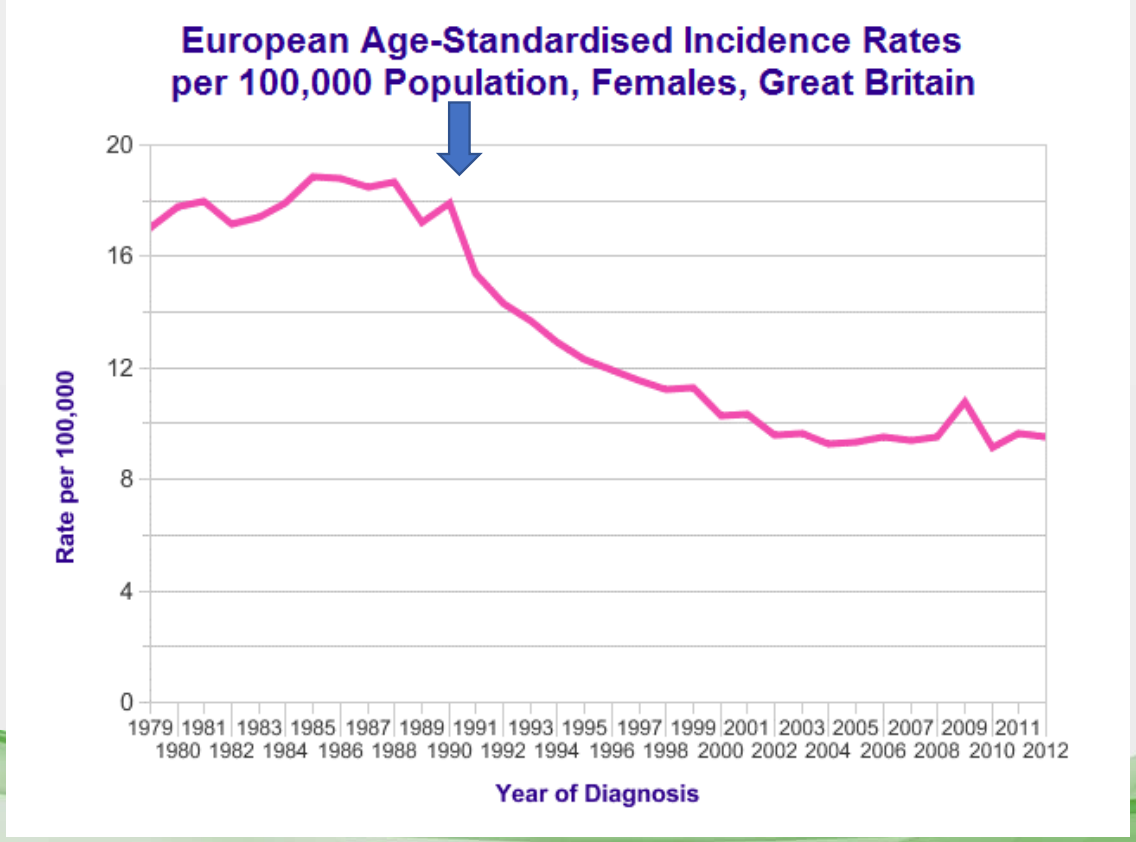
- **În primii cinci ani, au fost testate în cadrul programului 12% dintre femeile eligibile**, iar restul (până la 30%) au optat pentru testarea oportunistă. Pentru a mări gradul de participare, autoritățile de sănătate publică au desfășurat mai multe inițiative. Strategia de testare primară HPV pe baza Ghidurilor europene de asigurare a calității în programele de screening pentru cancerul de col uterin se află în faza de pilotare. Autoritățile investesc în unități mobile și în echipamente de diagnostic și tratament”.

Prevenție secundară- screening- Babeș-PAP

- Rata de participare la screeningul pentru cancerul de col uterin este cea mai scăzută din UE Astfel, în 2019, sub 30% dintre românce au declarat că au făcut un test Babeș-Papanicolau în ultimii trei ani, proporția fiind la jumătatea mediei europene.

- Rata de participare – calculată pe baza declarațiilor – a fost de
- 45% în rândul femeilor cu venituri mari,
- 13%, femeile cu venituri mici
- 51% în cazul femeilor cu un nivel de educație ridicat
- 11% în cazul femeilor cu nivel scăzut de instruire.
- 2.5 ori mai multe răspunsuri au fost obținute de la femeile care locuiau la oraș.

Cancerul de col situația în Marea Britanie- program screening



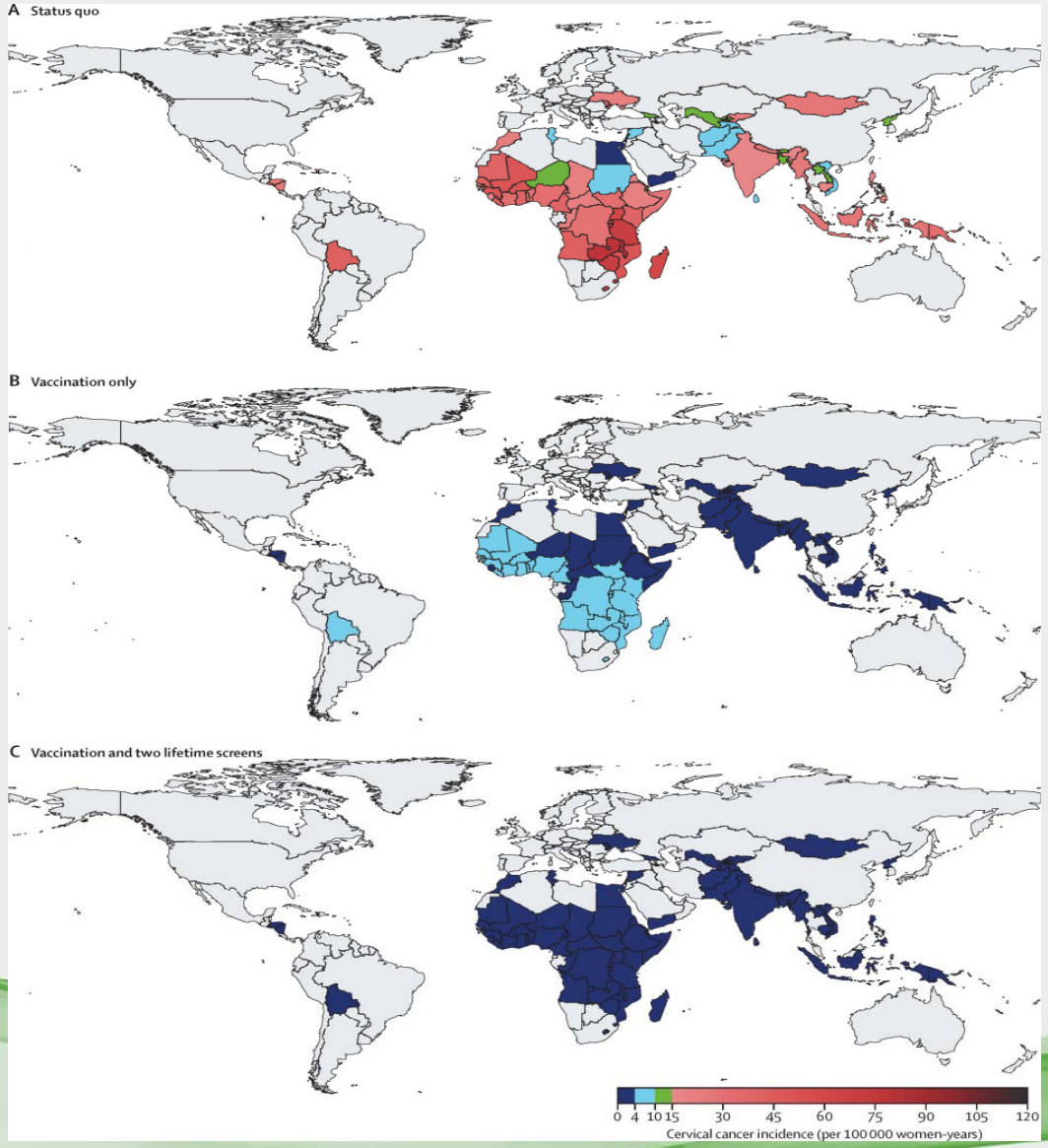
Strategia Globală pt eliminarea cancerului de col

- Lansată de OMS în 2020
- Scop eliminare cancerului de col ca problemă de sănătate publică
- Rezoluție adoptată de 194 de țări
- Obiectiv : scăderea incidenței neo de col sub 4 la 100 000 femei până în 2030
- Posibil prin:

- 90% din fetițe să fie vaccinate < 15 ani
- 70% din femei să beneficieze de PAP de 2 ori între 35-45 ani
- 90 % din femeile depistate cu leziuni să beneficieze de tratament

Strategia Globală pt eliminarea cancerului de col

- 2021 55% din cele 194 state membre OMS au introdus vaccinarea anti HPV la niv național
- Doar 41% din țările cu venituri mici și mijlocii au optat pt vaccinare
- Țări precum Rusia, China, India, Nigeria, Pakistan, Indonezia, Bangladesh NU prevăd vaccinul în schema vaccinală gratuită
- România a demarat programe de vaccinare în 2011, 2012, și 2015 , ulterior acesteau au fost oprite până în 2020 când s-a reluat programul de vaccinare. În 2021 s-a prelungit vârsta de vaccinare gratuită până la 18 ani
- În 2024 s-a introdus compensația de 50 % pentru femeile 19-45 de ani

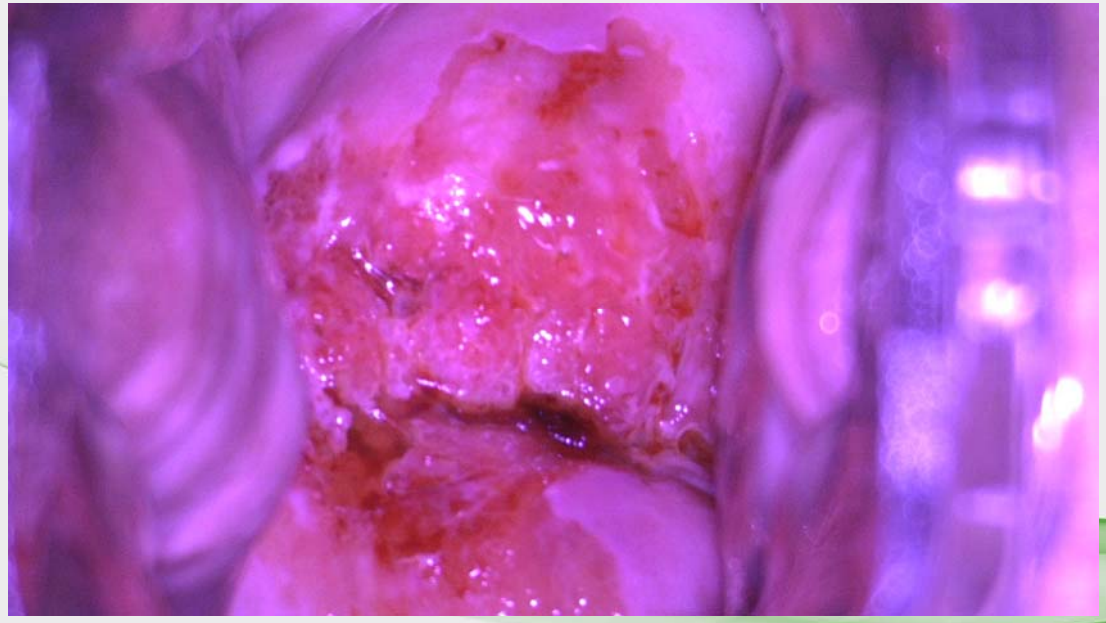

A Status quo
B Vaccination only
C Vaccination and two lifetime screens
0 4 10 15 30 45 60 75 90 105 120
Cervical cancer incidence (per 100 000 women-years)

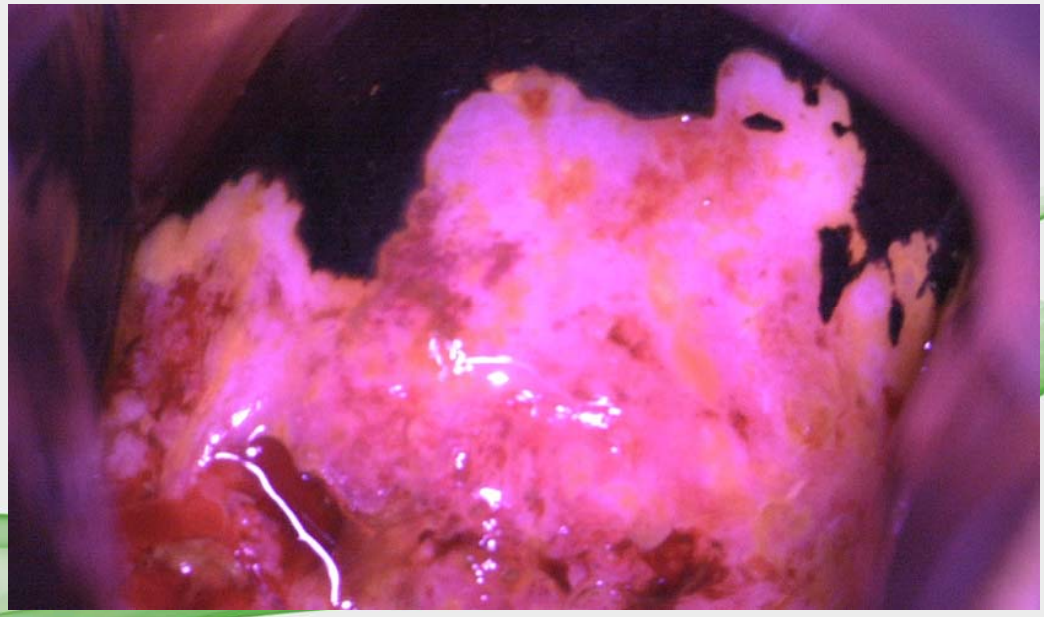
Propuneri

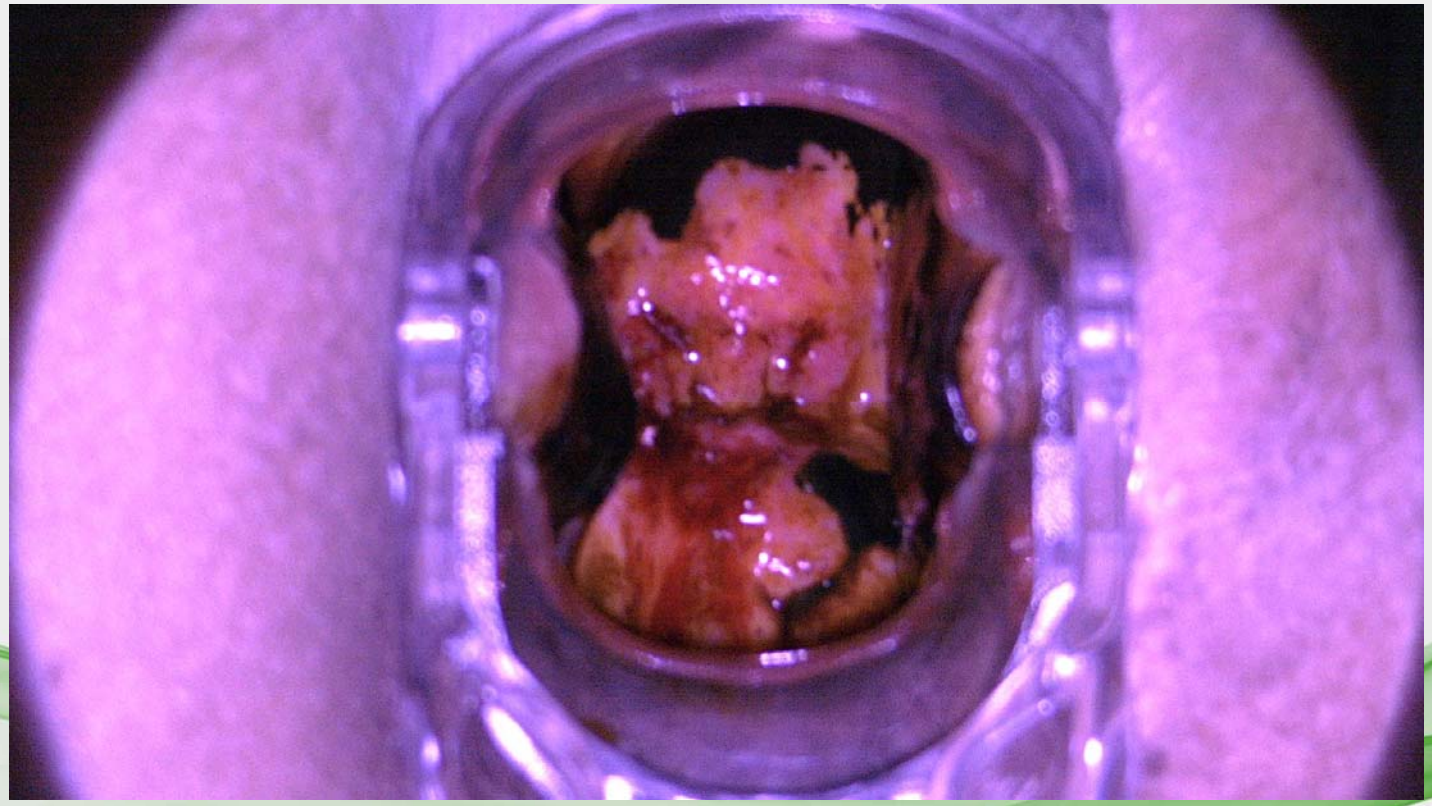
- Campanii Naționale de informare a populației despre siguranța și eficacitatea vaccinului
- Suplimentarea nr de doze de vaccinuri gratuite
- Reintroducerea vaccinării în școli
- Program obligatoriu de screening prin Casa de asigurări, afectarea dreptului de asigurat prin neprezentare

Cazuri clinice

1. V. E 51 de ani , sangerare –spotting in menopauza , nu a mai efectuat consult ginecologic de 35 de ani



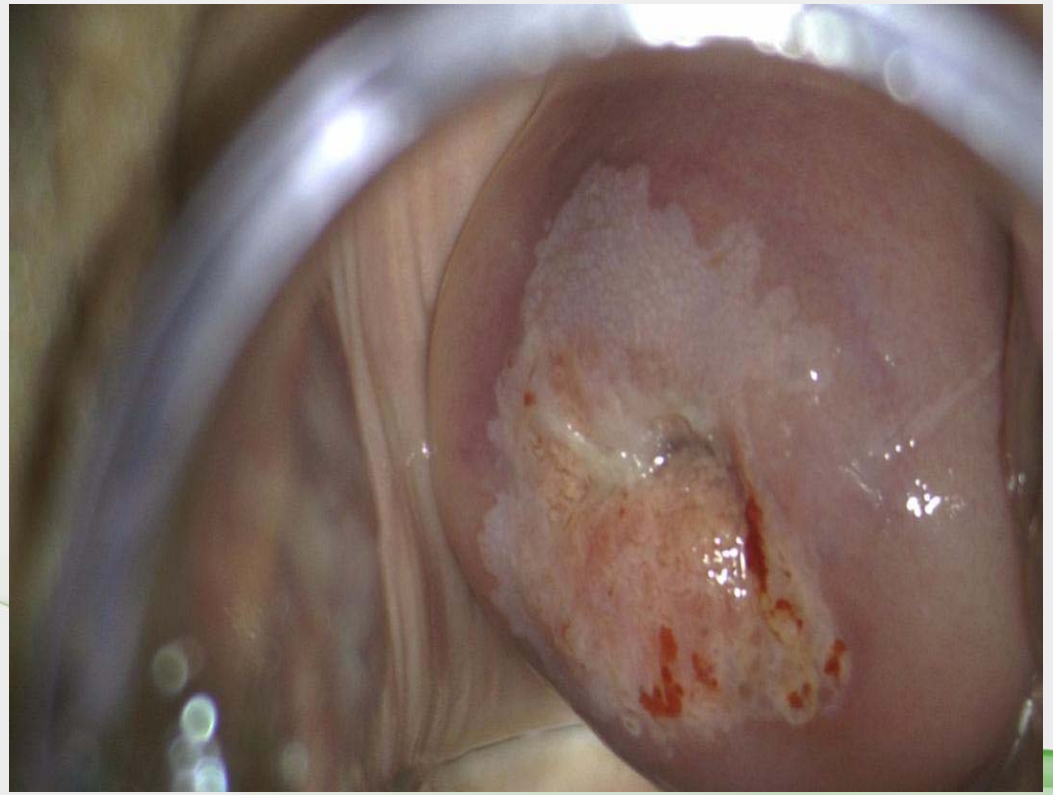


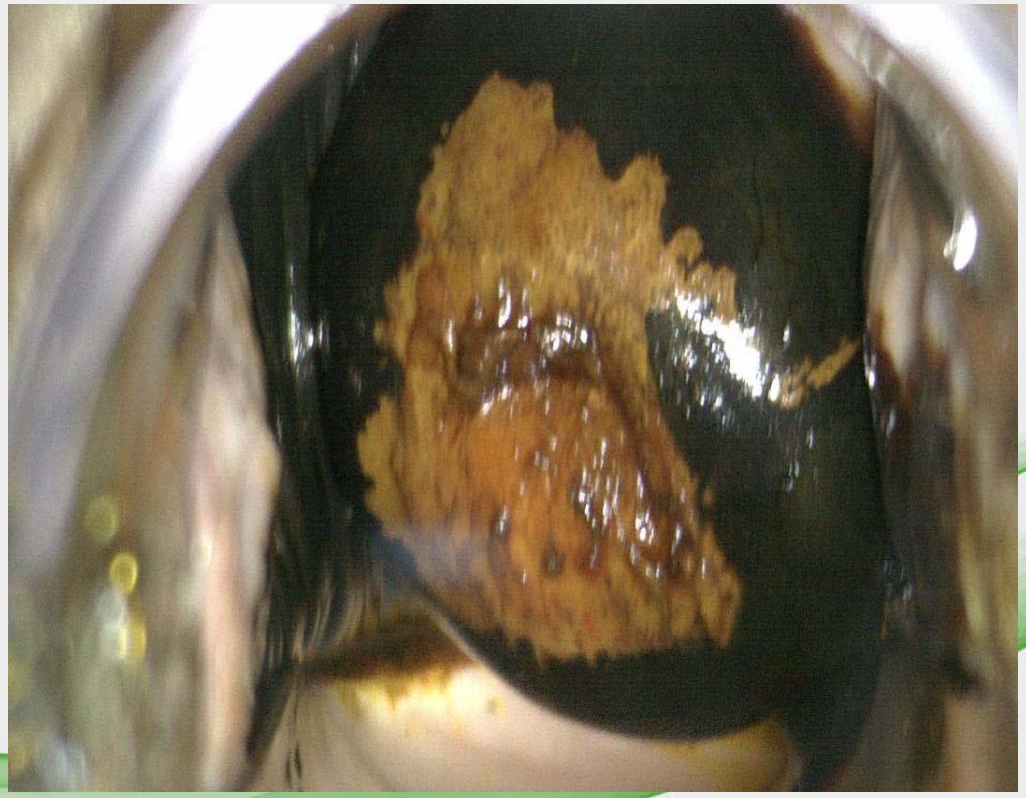


Cazuri clinice

2. B.C 20 de ani primul consult ginecologic, debutul vieții sexuale la 17 ani,fumătoare, dorește să se vaccineze anti-HPV

- PAP- HSIL
- Colposcopie –leziune de grad înalt
- Conizație CIN 3
- Vacccinare post-conizație





Răspunsuri la întrebări neadresate direct

1. Pentru o pacientă cu histerectomie totală se mai recomandă testare PAP sau genotipare HPV?
2. După cât timp de amenoree se consideră că o pacientă a intrat la menopauză?
3. O pacienta diagnosticată cu cancer al colului uterin pentru care s-a practicat HTAB și a intrat la menopauză indusa chirurgical prematur sau precoce poate urma tratament de substituție hormonala?
4. O pacienta cu cancer de sân sau cancer de ovar în antecedente poate urma tratament de substituție hormonală?