SEKCIJA ZA
ŠOLSKO, ŠTUDENTSKO
IN ADOLESCENTNO
MEDICINO

STROKOVNO SREČANJE

10 LET CEPLJENJA PROTI HPV

TOREK, 3. 9. 2019 HOTEL MONS, Ljubljana

Zbornik izročkov

SEKCIJA ZA
ŠOLSKO, ŠTUDENTSKO
IN ADOLESCENTNO
MEDICINO

9.00 – 9.05	Pozdravni nagovor predsednice Sekcije SŠŠAM	asist.**dr. Mojca Juričič**,dr.med.
9.05 – 9.15	Nagovor Ministrstva za zdravje	**Mojca Gobec, dr. med.,** Direktorat za JZ
MODERATORJA	Mario Poljak, Mojca Juričič	
9.15 – 10.15	12 let cepljenja proti HPV: zgodba o uspehu in kako naprej	**prof. dr. Mario Poljak, dr.med.**, UL MF, Inštitut za mikrobiologijo
10.15 – 10.45	HPV vaccine introduction in Scotland and data on HPV vaccine effectiveness in preventing pre-cervical cancer diseases	**prof. Maggie E Cruickshank,** Honorary Consultant in Gynaecology, Director of NHS Grampian Research and Development, and Co Lead Aberdeen Centre for Women's Health Research
10.45 – 11.15	Cepiva proti HPV: pregled najpomembnejših objav v obdobju september 2018 - september 2019	**dr. Anja Šterbenc, dr.med.**, UL MF, Inštitut za mikrobiologijo
MODERATORICI	Marta Grgič - Vitek, Janja Schweiger- Nemanič	
11.45 – 12.00	10 let programa cepljenja proti HPV v Sloveniji.	**Nadja Šinkovec, dr. med.** **dr. Veronika Učakar, dr. med.** **dr. Marta Grgič Vitek, dr. med.** NIJZ
12.00 – 12.50	Primeri dobre prakse iz različnih krajev Slovenije	**Jožica Mugoša, Majda Troha, Martina Mlaker, Miroslava Cajnkar Kac, Janja Schweiger-Nemanič, Barbara Pregl, Špela Žnidaršič- Reljič in Karmen Šparaš, Ana Keršič, Katarina Bole**
12.50 – 13.05	Genitalne bradavice	**Andreja Murnik Rauh, dr.med.**, UKC LJ, Dermatološka Klinika
13.05 - 13.20	Predstavitev knjige A. Grignolio Corsini Kdo se boji cepiv?	**doc.dr. Marko Pokorn,dr.med.** UKC- Klinika za infekcijske bolezni in vročinska stanja ; UL Medicinska fakulteta
MODERATORJA	Boštjan Mlakar, Majda Troha	
14.30 – 14.45	Eliminacija raka materničnega vratu – vloga Državnega programa ZORA	**dr. Urška Ivanuš, dr.med**. , **Mojca Florjančič, vms, dipl. org. inf.,** Onkološki inštitut Ljubljana
14.45 – 15.00	Okužbe s HPV pri mladih ženskah	**doc. dr. Nina Jančar, dr.med.,** UKC LJ, Ginekološka Klinika
15.00 – 15.15	Analni HPV- patologija	**doc. dr. Boštjan Mlakar, dr.med.,** Zasebna klinika, Zdrav splet Ljubljana, Maribor
15.15 – 15.30	HPV okužbe v področju glave in vratu	**asist. dr. Aleš Grošelj,dr.med.** UKC LJ , ORL klinika
15.30 – 16.00	Recidivantna respiratorna papilomatoza	**prof. dr. Irena Hočevar Boltežar, dr.med.** UKC LJ, ORL klinika

SEKCIJA ZA
ŠOLSKO, ŠTUDENTSKO
IN ADOLESCENTNO
MEDICINO

10 let neobveznega, brezplačnega cepljenja deklic proti HPV

ob sistematičnem pregledu v 6. razredu osnovne šole

sist.dr. Mojca juričič, dr.med.

Predsednica **Sekcije za šolsko, študentsko in adolescentno medicino**

pri Slovenskem zdravniškem društvu

UL- Medicinska fakulteta, **Katedra za javno zdravje**

mojca.juricic@mf.uni-lj.si

ŠOLSKA MEDICINA NA SLOVENSKEM – LETOS PRAZNUJE 110 LET

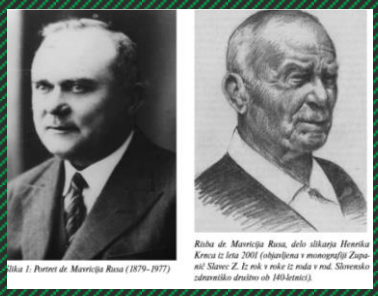
1909

Slovenski začetki šolske medicine sežejo v leto 1909, ko je Občinski svet mesta Ljubljane imenoval prva šolska zdravnika, dr. Mavricija Rusa in dr. Jerneja Demšarja.
Pred tem so od leta 1877 obstajale stalne šolske zdravstvene komisije

- 1909 prva šolska zdravnika
- dr. Mavricij Rus

in

- dr. Jernej Demšar



Slika 1: Portret dr. Mavricija Rusa (1879–1977)

Risba dr. Mavricija Rusa, delo slikarja Henrika Krnca iz leta 2001 (objavljena v monografiji Zupanič Slavec Z. Iz rok v roke iz roda v rod. Slovensko zdravniško društvo ob 140-letnici).

- Na prvem kongresu šolske higiene, ki je potekal v Nürnbergu leta 1904, Slovenci nismo imeli svojega zastopnika
- drugega kongresa v Londonu leta 1907 se je udeležil dr. Vladimir Prijatelj
- Mavricij Rus se je udeležil se je tretjega mednarodnega kongresa za šolsko higieno v Parizu leta 1910.

5.marca 1909 sprejme Mestni svet
NAVODILA ZA DELO ŠOLSKEGA ZDRAVNIKA

1. Šolski zdravnik za javne ljudske šole v Ljubljani je stalni nadzorovalni organ glede zdravstvenih razmer po šolah in zdravja dijaštva. Podrejen je mestnemu fizikatu, kateremu je dolžan podajati poročila.

2. O uspehu pregledovanja šolskih poslopij (šolske zgradbe, telovadnice, igrišča, notranjost šole – oprema, čistoča, razsvetljava, zračenje, kurjava,…) obvešča šolski zdravnik šolskega vodjo in mestnega fizika.

3. Šolski zdravnik naj šole pogosto obiskuje in preiskuje otroke glede vida, sluha, zobovja, izgovorjave, glede duševne sposobnosti, sposobnosti za telovadbo, ročna dela in risanje. Še posebno pa mora biti pozoren na nalezljive in »nagnusne« bolezni in skrbeti za redno cepljenje.

4. Pregledati je potrebno vse otroke, ki vstopijo v šolo in to čim preje po vstopu v šolo.

5. Preiskovanje otrok naj se vrši izven časa šolskega pouka in v prisotnosti učitelja.

SEKCIJA ZA
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NAVODILA ZA DELO ŠOLSKEGA ZDRAVNIKA

6. Zdravljenje bolnih šolskih otrok ni stvar šolskega zdravnika. Obvesti se starše, da otroke peljejo k pristojnemu zdravniku.

7. Če se pojavi sum na nalezljivo bolezen, mora šolski zdravnik takoj ukrepati, da obolel otrok ne obiskuje pouka, obolenje pa mora prijaviti mestnemu fizikatu.

8. Pri obiskih na šolah zdravnik ne sme motiti pouka.

9. Šolski zdravnik ni upravičen ukazovati učiteljem ali učencem, svojo sodbo more oddati pristojnemu uradu.

10. Šolski zdravnik mora imeti možnost prisostvovati konferenčnemu zborovanju učiteljev, če se razpravlja o šolskem zdravstvu.

11. Šolski zdravnik naj deluje v šoli sporazumno s šolskim vodstvom.

12. O nujnih zdravniških pomanjkljivostih mora šolski zdravnik poročati mestnemu fizikatu, drugače pa mu podaja ob koncu šolskega leta glavno poročilo o svojem delovanju.

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO PRI SZD

USTANOVLJENA 1981 kot Sekcija za šolsko in univerzitetno medicino

Sekcijo za šolsko, študentsko in adolescentno medicino pri SZD

- Kongresi: 1993, 1997, 2001, 2005, 2009, 2013,2017
- 3 do 4 strokovna srečanja na leto - **od leta 2009 na temo HPV**
- 2003 EUSUHM v Ljubljani – Carying of Europe Young Generatation
- 2008 IAAH v Portorožu – Reducing Inequalities among Youth Role of Adolescent, School Health
- Srečanja Alpe Adria: Portorož, Firence, Opatija
- 2008 Sodelovanje v mednarodnem projektu s Flamsko in Hrvaško – Implementation od a methodology for the development of evidence-based guidelines in school health care
- 2011, 2017 WHO GYTS –Odnos mladih do tobaka

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

10 let neobveznega, brezplačnega cepljenja deklic proti HPV

ob sistematičnem pregledu v 6. razredu osnovne šole

2009

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

SEKCIJA ZA ŠOLSKO IN VISOKOŠOLSKO MEDICINO PRI SLOVENSKEM ZDRAVNIŠKEM DRUŠTVU

VABILO

Sekcije za šolsko in visokošolsko medicino pri SZD,

na strokovni sestanek, ki bo v sredo, 9. 9. 2009, ob 15.30

v hotelu MONS, LJUBLJANA

V šolskem letu 2009/10 se prične cepljenje deklic proti okužbi s HPV, ob sistematskem pregledu v 6. razredu. Strokovno srečanje bo namenjeno izvedbi tega cepljenja.,

Sodelovali bodo: prof. dr. Poljak Mario, dr.med., prof. dr. Vrščaj Uršič Marjetka, dr.med. in mag. Marta Grgič Vitek, dr.med., ki vam bo tudi predstavila gradiva (obvestilo za starše o sistematskem pregledu, letak z izjavo o privoliti za cepljenje, izjavo o preklicu privolitve, predavanje za starše…), ki so jih pripravili na IVZ ob sodelovanju upravnega odbora naše Sekcije. Območni koordinatorji zdravstvene vzgoje so ta gradiva že posredovali šolskim zdravnikom ali v dogovoru s šolskimi zdravniki direktno v šole.

V želji, da bi dosegli čim večjo precepljenost in da bi bil potek cepljenja čim bolje organiziran, so poleg šolskih zdravnikov oziroma zdravnikov v šolskih dispanzerjih, otroško-šolskih dispanzerjih, medicinskih sester iz ŠD, vabljeni tudi območni koordinatorji cepljena in regijski koordinatorji zdravstvene vzgoje iz Zavodov za zdravstveno varstvo, ki so pomemben člen pri učinkoviti izvedbi cepljenja.

VLJUDNO VABLJENI!

Tajnica sekcije: Mojca Juričič, dr. med.
Predsednik sekcije: Jože Šumak, dr. med

2009/10

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

SEKCIJA ZA ŠOLSKO IN VISOKOŠOLSKO MEDICINO PRI SLOVENSKEM ZDRAVNIŠKEM DRUŠTVU

DATUM: MAREC 2010

SPOŠTOVANI STARŠI!

PONOVNO VAS OBVEŠNAMO, DA LAHKO ŠE DO KONCA ŠOLSKEGA LETA (JUNIJ 2010), CEPITE SVOJO DEKLICO PROTI HPV – HERPES PAPILOMA VIRUSU, KER JE V LETOŠNJEM LETU CEPLJENJE ZA DEKLETA V 6. RAZREDU BREZPLAČNO, JE DEL NACIONALNEGA PROGRAMA CEPLJENJA, A LE Z VAŠO PRIVOLITVIJO.

ZA VSA NADALJNJA POJASNILA IN VPRAŠANJA SE OBRNITE NA IZBRANEGA ZDRAVNIKA ŠOLE, KI JE ZADOLŽEN ZA OPRAVLJANJE PREVENTIVNIH PREGLEDOV NA ŠOLI KI JO OBISKUJE VAŠA DEKLICA OZIROMA MLADOSTNICA.

VEČ INFORMACIJ O CEPLJENJU NAJDETE TUDI NA INTERNETNI STANI INŠTITUTA ZA VAROVANJE ZDRAVJA RS: HTTP://WWW.IVZ.SI/INDEX.PHP?AKCIJA=NOVICA&N=1170

IN NA STRANEH DRUŠTVA KALA: HTTP://NSI.VIRTUAPR.COM/INDEX.PHP?ID=3

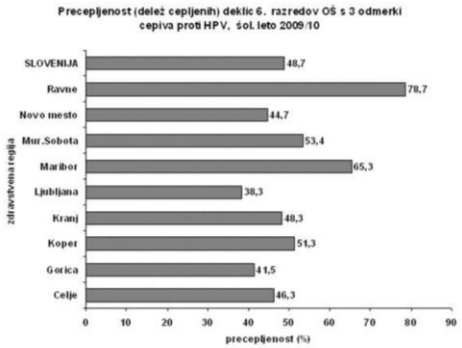
S SPOŠTOVANJEM,

Jože Šumak, dr. med

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

Precepljenost (delež cepljenih) deklic 6. razredov OŠ s 3 odmerki cepiva proti HPV, šolsko leto 2009/20010

26.11.2010



SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

Strah pred cepljenjem

Po uvedbi cepljenja proti okužbam s humanimi papiloma virusi

Kje tičijo vzroki za strah pred cepljenjem

Zakaj poseganje po zaščiti, ki lahko prepreči neprijetne, težko ozdravljive pa tudi smrtno nevarne bolezni rodil, (pri nas) tako zelo niha – Šestošolke se za cepljenje lahko odločijo še vse do konca šolskega leta

Letošnje šolsko leto je prineslo že nekaj časa pričakovano in tudi zahtevano novost: uvedbo cepljenja deklic proti okužbi s humanimi papiloma virusi (HPV), ki povzročajo neprijetne, težko ozdravljive pa tudi smrtno nevarne bolezni rodil, predvsem raka materničnega vratu in genitalne bradavice. Cepljenje, ki sicer ni obvezno, epidemiologi in šolski zdravniki staršem toplo priporočajo. Prof. dr. Marjetka Uršič Vrščaj z Oddelka za ginekološko onkologijo Onkološkega inštituta Ljubljana pravi, da cepljenje pomeni odlično dopolnitev rednim ginekološkim pregledom ter odvzemom brisov. »Za starše se morda odločitev za to cepljenje zdi nova in težka, a v resnici ne bi smelo biti tako. Veliko težja utegne biti čez nekaj let zavest, da niso naredili vsega, da bi svojo hčer obvarovali pred resno boleznijo.«

Rak materničnega vratu je najpogostejši rak pri ženskah do 34. leta. V Sloveniji vsako leto za to težko boleznijo zboli vsaj 150 žensk, okrog 40 jih umre. Tragične ljubljanske medicinske fakultete pravi, da je bilo doslej po svetu cepljenih že 60 milijonov deklic. Da bi ponazoril (različne) razsežnosti cepljenja, je spregovoril o izku-

PROF. DR. MARIO POLJAK

PROF. DR. MARJETKA URŠIČ VRŠČAJ

Fotografiji: Matic Prah

2010

Srečanje bo

3. septembra 2010 ob 14.30 uri

v Hotelu Mons

PROGRAM SREČANJA:

1. Program cepljenja proti HPV v šolskem letu 2010/11

prim. doc. dr. Alenka Kraigher, dr. med.; mag. Marta Grgič Vitek, dr. med.

2. Štirivalentno cepivo proti HPV okužbam: pregled znanstvenih objav v zadnjem letu

prof. dr. Mario Poljak, dr. med.

3. Leto dni po uvedbi cepljenja: katera vprašanja ostajajo najpogostejša?

prof. dr. Marjetka Uršič Vrščaj, dr. med.

4. šolska medicina

Prosimo vas, da se srečanja udeležite v čim večjem številu, saj bo to priložnost izmenjave mnenj in izkušenj o cepljenju proti HPV okužbam lanskega šolskega leta in priložnost kako izpeljati cepljenje v prihajajočem šolskem letu še bolje.

2011

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

Srečanje bo 2. septembra 2011 ob 14.30 uri , v Hotelu Mons v Ljubljani

PROGRAM SREČANJA:

1. **Cepljenje proti HPV-ključna sporočila**
   prim. doc. dr. Alenka Kraigher, dr. med; mag. Marta Grgič Vitek, dr. med.
2. **Štirivalentno cepivo proti HPV okužbam: pregled znanstvenih objav v zadnjem letu**
   prof. dr. Mario Poljak, dr. med.
3. **Svet in mi: kje smo glede cepljenja proti HPV?**
   prof. dr. Marjetka Uršič Vrščaj, dr. med.
4. **Praktične izkušnje pri cepljenju proti HPV**
   Majda Troha, dr. med. , spec. šol. med.

Prosimo vas, da se srečanja udeležite v čim večjem številu, saj bo to priložnost izmenjave mnenj in izkušenj o cepljenju proti HPV okužbam iz prejšnjih let, kako staršem in deklicam predstaviti pomembnost in dostopnost varnega in učinkovitega cepljenja proti okužbam HPV.

VABLJENI!

Tajnica sekcije:
Ksenija Goste ,dr.med.,l.r.
spec. šol.med.

Predsednica sekcije:
asis.dr. Mojca Juričič, dr.med.,
spec.šol.med. in spec.hig.

2012

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

SEKCIJA ZA ŠOLSKO IN VISOKOŠOLSKO MEDICINO
PRI SLOVENSKEM ZDRAVNIŠKEM DRUŠTVU

VABI NA STROKOVNO SREČANJE **NEOBVEZNA BREZPLAČNA CEPLJENJA,**

KI BO V SREDO, 5.9.2012, OB 15.00, V HOTELU MONS

DNEVNI RED:

15.00- - 15.30 **Novosti na področju cepljenja proti HPV** -prof. dr.. Mario Poljak, dr.med. ; UL MF, Inštitut za mikrobiologijo

15.30 – 16.00 **Bolezni, ki jih HPV povzroča pri ženskah, in preprečevanje s cepljenjem** - as. dr. Nina Jančar, dr. med. ;UKC Ljubljana, Ginekološka klinika,

16.00 -16.30 **Cepljenje proti HPV - krepitev partnerstva med šolskimi zdravniki in starši** - doc.dr. Alenka Kraigher,dr.med., mag.Marta Vitek, dr.med., Veronika Učakar,dr.med.;IVZ RS

16.30 – 16.50 **Vprašalnik o HPV za starše in rezultati** – Majda Troha, dr.med.; ZD Idrija, Šolski dispanzer

16. 50 – 17.10 **Spolnost mladostnikov in njihovo poznavanje spolno prenosljivih bolezni** – Miroslava Cajnkar. Kac, dr.med, MC KAC dispanzer za otroke in mladostnike, Slovenj Gradec

17.10- 18.00 Razprava

Registracija od 14.30 dalje. Strokovno srečanje smo prijavili ZZS za pridobitev točk.

VABLJENI!

2013

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

VABI NA STROKOVNO SREČANJE

NOVOSTI IN IZZIVI NEOBVEZNIH CEPLJENJ

V PETEK, 6.9.2013 OB 14.00, V HOTELU MONS

DNEVNI RED

14.00 – 14.45 -***Registracija***

14.45 -15.45 - ***HPV program implementation : where are we in Europe? Sharing best practices from Spain;*** - Federico Martinón-Torres MD, PhD, Assoc Prof, Pediatrician, PICU medical attending, Pediatric Critical, Intermediate and Emergency Care ,

15.45- - 16.15 –***Novosti na področju cepljenja proti HPV*** - prof. dr. Mario Poljak, UL MF Inštitut za mikrobiologijo

16.15 -16.45 ***Rutinsko cepljenje proti HPV v Sloveniji - kaj smo se naučili?*** - prof.dr.Alenka Kraigher, dr. Marta Vitek, Veronika Učakar. IVZ RS

16.45 -18.00 ***Razprava***

VABLJENI!

Kotizacije ni. Pri ZZS je postopek za pridobitevkreditnih točk

2015

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO


CEPLJENJA – ALI SO RAZLIKE MED DEKLICAMI IN DEČKI

PETEK, 4. 9. 2015
HOTELU MONS

1


13. 30 - 14. 30 – **Registracija**

14. 30 - 15. 00 **Novosti v Programu cepljenja proti HPV (v Sloveniji) v šolskem letu 2015/2016;**
prof. dr. Alenka Kraigher, dr. med, dr. Marta Vitek, dr. med., - NIJZ RS

15. 00 - 15. 45 **Novosti na področju cepljenja proti HPV v zadnjem letu (september 2014 - september 2015;** prof. dr. Mario Poljak, dr. med. - UL MF, Inštitut za mikrobiologijo

15.45 - 16.00 Razprava

2


16.00 - 16.20 **Uz medijsku kampanju do veće procijepljenosti djevojčica protiv HPV-a u Zagrebu**
prim.dr.sc.Marina Kuzman, prof.vš. dr.med., Marija Posavec dr.med – Nastavni zavod za javno zdravstvo "Dr. Andrija Štampar", Zagreb

16.20 - 16.40 **Cepljenje proti HPV v Sloveniji – cepljenje dečkov v ZD Idrija**
Majda Troha, dr.med. -ZD Idrija

16.40 - 17.00 **Predstavitev delavnic po šolah in predstavitev knjižice**
Katja Čehovin s sodelavci, Društvo študentov medicine Slovenije – projekt Virus

17.00 - 18.00 **Razprava in zaključki**

3

2014

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

VABI NA STROKOVNO SREČANJE

V SREDO, 3. 9. 2014 OB 14. 00, V HOTELU MONS

CEPLJENJA - DOMAČE IN TUJE IZKUŠNJE

DNEVNI RED:

13. 30 – 14. 00 **-Registracija**

14. 00 - 14. 30 **Cepljenje proti okužbam s HPV v novem šolskem letu**; dr. Marta Vitek, dr. med., Veronika Učakar, dr. med., prof. dr. Alenka Kraigher, dr. med, - NIJZ RS

14. 30 - 15. 15 **Novosti na področju cepljenja proti HPV/Recent advances in HPV vaccination: literature review of the last year;** prof. dr. Mario Poljak, dr. med. - UL MF Inštitut za mikrobiologijo

15. 15 - 15. 45 **Cepljenje proti HPV – hrvaške izkušnje/Cijepljenje protiv HPV infekcije – kakva su hrvatska iskustva;** prim. prof. dr. Marina Kuzman, dr. med., mag. Vesna Juhovic Markus, dr. med, Marija Posavec, dr. med., Zavod za javno zdravstvo "Dr. Andrija Štampar", Zagreb, Nataša Dragaš Zubalj, dr. med. - Nastavni zavod za javno zdravstvo Primorsko-goranske županije

15. 45 -16. 15 - **Cepljenje proti HPV – kakšne so makedonske izkušnje**; prim. dr. Mimi Karovska, Specijalist školske i univerzitetske medicine, Služba za Preventivna Zdravstvena Zaštita na Učilisni Deca i Mladina, Zdravstven Dom Kavadarci, Republika Makedonija

16. 15 -16. 45 - **Cepljenje proti HPV – slovenske izkušnje;** Janja Schweiger Nemanič, dr.med, Jožica Mugoša, dr. med, Miroslava Cajnkar Kac, dr.med, Majda Troha, dr.med,

16. 45 – 17. 10 – **Cepljenje proti HPV pri študentkah UL** – Irena Kirar Fazarinc, dr. med., Zdravstveni dom za študente Univerze v Ljubljani

2016

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

VABI NA STROKOVNO SREČANJE

V SREDO, 7. 9. 2016 OB 14. 00 V HOTELU MONS

CEPLJENJE PROTI HPV TER SPOLNO PRENOSLJIVE BOLEZNI PRI MLADOSTNICAH, MLADOSTNIKIH IN MLADIH

14. 00 – 14. 30 **Registracija**

14. 30 - 14. 50 **Program cepljenja, precepljenost in neželeni učinki po cepljenju proti HPV v Sloveniji;** dr. Marta Grgič Vitek, dr. med., dr. Veronika Učakar, dr.med., prim. izr. prof. dr. Alenka Kraigher, dr.med. - NIJZ

14. 50 - 15. 35 **Novosti na področju cepljenja proti HPV v zadnjem letu (september 2015-september 2016);** prof. dr. Mario Poljak, dr. med. - UL MF, Inštitut za mikrobiologijo

15.35 – 15. 55 **Pomen cepljenja proti HPV z vidika ginekologa;** doc. dr. Nina Jančar, dr.med. - UKC, Ginekološka klinika

15. 55 – 16. 15 **Cepljenje proti HPV v Sloveniji – izkušnje s terena**: Janja Schweiger Nemanič, dr.med., Jožica Mugoša, dr.med., Majda Troha, dr.med, Canjkar Kac Miroslava, dr.med.

16.15 – 16.25 Razprava

16.25 – 16.45 **Spolno prenosljive okužbe v Sloveniji - rezultati epidemioloških spremljanja;** izr. prof. dr. Irena Klavs, dr.med., mag. Tanja Kustec, univ. dipl. soc. – NIJZ

16. 45 – 17. 15 **Novi načini življenja in vpliv na spolne navade med mladimi** – prof. dr. Janez Tomažič, dr.med. UKC, Infekcijska klinika.

17. 15 – 17.25 **Novi izzivi za zdravo spolnost;** Evita Leskovšek, dr. med. - NIJZ

17.25 – 17. 45 Razprava in zaključki

Kotizacije ni. Kreditne točke so v postopku pri ZZS. Predprijava na srečanje ni potrebna.

Vabljeni!

Tajnica Sekcije:
Ksenija Gorše ,dr.med.,Ln.
spec.šolske med.

Predsednica Sekcije:
asist. dr. Mojca Juričič, dr.med
spec.šolske med. in spec. javnega zdravja

2017

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

VABIMO VAS NA STROKOVNO SREČANJE

V PETEK, 1. 9. 2017 OB 14.30 URI

V HOTELU MONS, Four Points by Sheraton Ljubljana

14.30-15.00 Novosti na področju cepljenja proti HPV – prof. dr. Mario Poljak, dr.med.; UL MF, Inštitut za mikrobiologijo

15.00-15.20 Podatki v Sloveniji –NIJZ

15.20-15.50 HPV na področju glave in vratu – asist. Aleš Grošelj dr. med.; UKC Ljubljana, Klinika za otorinolaringologijo in cervikofacialno kirurgijo

15.50-16.20

16.20-17.00 Izkušnje pri cepljenju – Majda Troha, dr.med., ZD Idrija, Šolski dispanzer, Janja Schweiger, dr.med., ZD Ljubljana – Siska, Miroslava Canjkar Kac –MC Kac, Dispanzer za otroke in mladostnike – Slovenj Gradec

2018

2019

SEKCIJA ZA ŠOLSKO, ŠTUDENTSKO IN ADOLESCENTNO MEDICINO

IN ADOLESCENTNO MEDICINO

VABIMO VAS NA STROKOVNO SREČANJE - HPV CEPLJENJE

V PONEDELJEK, 10. 9. 2018 OB 15.00 URI, V HOTELU MONS, Ljubljana

15.00 - 15.10 Cepljenje proti HPV v Sloveniji - dr. Marta Vitek, dr. med., NIJZ

15.10 - 15.40 Novosti na področju cepljenja proti HPV v zadnjem letu - prof. dr. Mario Poljak, dr.med., UL MF, Inštitut za mikrobiologijo

15.40 -16.00 S HPV povzročene spremembe analne regije - doc. dr. med. Boštjan Mlakar, dr.med., Zasebna klinika Zdrav splet Ljubljana, Maribor

16.00 - 16.15 Vključevanje cepljenih deklet v program Zora - Urška Ivanuš, dr.med., Onkološki inštitut, Ljubljana

16.15 - 16.30 Okužbe s HPV pri mladih ženskah - doc.dr. Nina Jančar, dr.med., UKC Ljubljana, Ginekološka klinika

16.30 -16.40 Razprava

16.40 -16.55 ODMOR

16.55 - 17.15 Nacionalna raziskava Komuniciranje ob cepljenju - Mitja Verdelja, mag. odn. jav., univ. dipl. kom., NIJZ

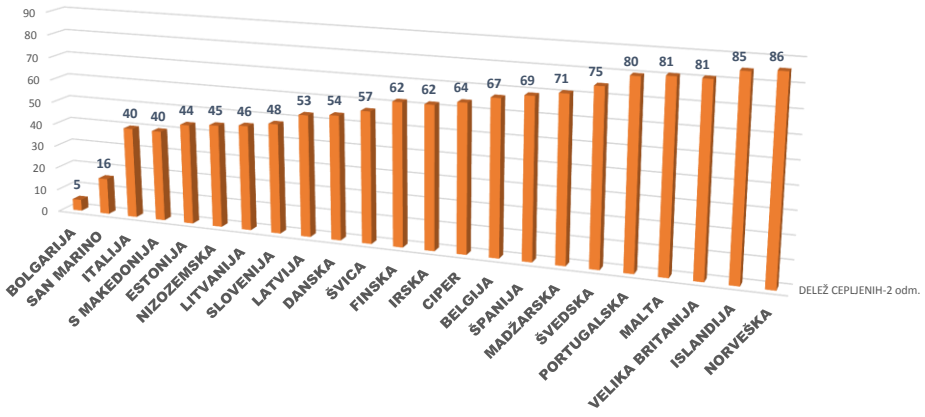
17.15 - 17.30 HPV okužbe in cepljenje: razlike v stališčih med šolskimi zdravniki/pediatri in gnekologi - Majda Troha, dr.med., ZD Idrija,

17.30 - 17.40 Kaj se dogaja na področju cepljenja dečkov s HPV/GNV cepivom, Janja Schweiger Nemanič, dr.med., ZDL

17.40 - 17.50 Projekt Virus: Izkušnje s predavanji na Srednjih šolah. Lucija Neudauer, štud.med. MF Ljubljana

17.50 Razprava

DELEŽ CEPLJENIH DEKLET z 2 odmerkoma, po državah, leto 2018



cepljenje deklic

cepljenje deklic in dečkov

Program cepljenja po državah

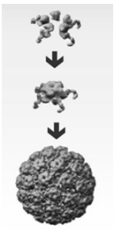
Zbrano in povzeto iz programov cepljenja posameznih drzav.

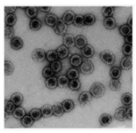
12 let cepljenja proti HPV:
zgodba o uspehu in kako naprej

Mario Poljak

Inštitut za mikrobiologijo in imunologijo
Medicinska fakulteta, Univerza v Ljubljani

Prophylactic HPV vaccines





L1 viral like particles

2vHPV: 16 and 18 with ASO4

4vHPV: 6, 11, 16 and 18 with aluminium

9vHPV: 6, 11, 16, 18, 31, 33, 45, 52 and 58 with aluminium

WHO statement on cervical cancer elimination Director-General call to action

World Health Organization

"Today I am calling for coordinated action globally to eliminate cervical cancer, one of the greatest threats to women's health. We have the tools and, crucially, the political commitment to achieve it"

www.who.int/reproductivehealth/DG_all-to-action.pdf

Dr Tedros Adhanom Ghebreyesus
WHO Director General - 19 May 2018

Cervical cancer as best human cancer candidate for elimination

important public health issue (569'847 cases per year; 311'365 deaths)
GLOBOCAN 2018

infectious origin, no reservoirs outside humans

long clinical latency

acceptable and valid screening tools available

precursors lesions can be treated in a safe, effective and acceptable way

safe and effective vaccines against main etiological factor - HPV

secondary prevention (screening)
(cytology, HPV, cytology+HPV)

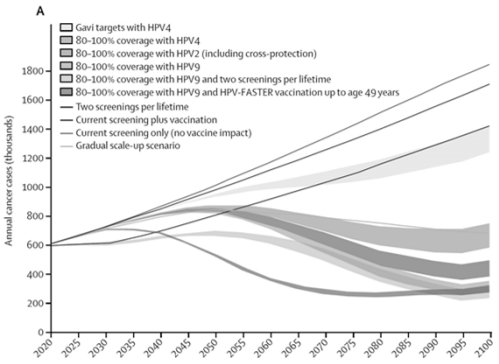
+

primary prevention (HPV vaccination)

Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020–99: a modelling study

Lancet Oncol 2019;20:394-407

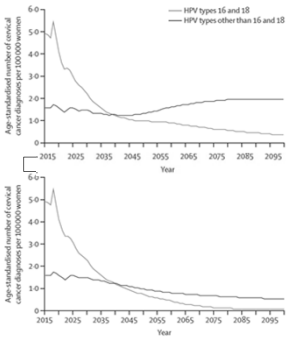
Kate T Simms, Julia Steinberg, Michael Caruana, Megan A Smith, Jie-Bin Lew, Isabelle Soerjomataram, Philip E Castle, Freddie Bray, Karen Canfell



The projected timeframe until cervical cancer elimination in Australia: a modelling study

Lancet Public Health 2018; 4:e19-e27

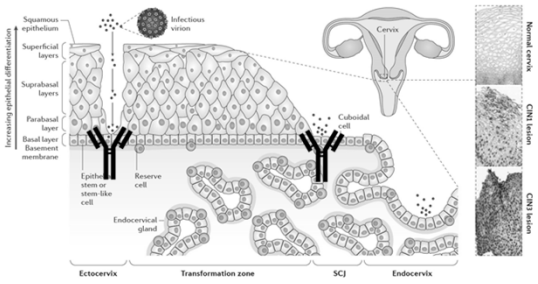
Michaela T Hall, Kate T Simms, Jie-Bin Lew, Megan A Smith, Julia ML Brotherton, Marion Saville, Ian H Frazer, Karen Canfell



vaccination of women with the 9v vaccine from 2018 onwards and discontinuation of cervical screening in women offered this vaccination

continuing vaccination with the 9v vaccine and continuation of screening as per the existing National Cervical Screening Program

secondary and primary prevention act additively by intervening at different points in the natural history of cervical cancer and imply actions in women of different ages



- IgG antibodies (transudation and exudation)
- heterogeneous mixture of neutralizing and non-neutralizing antibodies
- an immunologic correlate with protection not established yet !!!

Natural HPV infection

women:

- 54%–69% seroconvert
- low-level antibodies
- partial protection against reinfection

men:

- 7%–10% seroconvert
- low-level antibodies
- no protection against reinfection

BUT: nearly 100% seroconversion following HPV vaccination in both genders !

Why are vaccines "better" than nature ??

Natural infection
- no viraemia, poor access of virus to lymph nodes

HPV vaccines
- delivered intramuscularly
- rapid access of VLPs to blood vessels and local lymph nodes

BONUS

VLPs are very immunogenic:
- display many neutralising epitopes (more than native virion)
- induce good T-cell helper responses for B-cells
  - important for robust antibody and B-cell memory responses

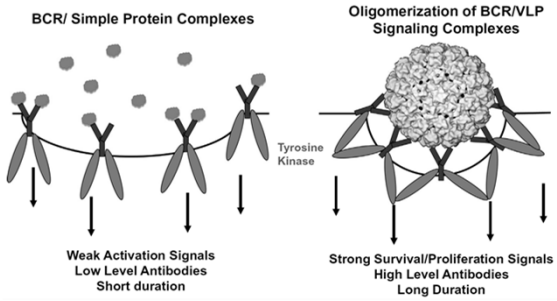
Explanations for the high potency of HPV prophylactic vaccines

John Schiller*, Doug Lowy

Laboratory of Cellular Oncology, Center for Cancer Research, NCI, Bethesda, MD, USA

Vaccine 2018;36:4768-73

B cell recognition of dense repetitive protein arrays promotes the induction of exceptionally potent and durable antibody responses



98-100% efficacy against anogenital lesions (cervical, vulvar, vaginal, and anal) caused by targeted HPV types in several large international randomized, double-blind trials

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Recommended Childhood and Adolescent Immunization Schedule—United States, 2017

COMMITTEE ON INFECTIOUS DISEASES

Annals of Internal Medicine — CLINICAL GUIDELINE

Recommended Immunization Schedule for Adults Aged 19 Years or Older, United States, 2017*

Two doses are recommended for persons starting the series before their 15th birthday.

Three doses are recommended for those who start the series on or after their 15th birthday and for persons with certain immunocompromising conditions.

Durability of Protection Afforded by Fewer Doses of the HPV16/18 Vaccine: The CVT Trial

J Natl Cancer Inst 2018;110:djx158

Mahboobeh Safaeian, Joshua N. Sampson, Yuanji Pan, Carolina Porras, Troy J. Kemp, Rolando Herrero, Wim Quint, Leen Jan van Doorn, John Schussler, Douglas R. Lowy, John Schiller, Mark T. Schiffman, Ana Cecilia Rodriguez, Mitchell H. Gail, Allan Hildesheim, Paula Gonzalez*, Ligia A. Pinto*, Aimée R. Kreimer*; for the Costa Rica HPV Vaccine Trial (CVT) Group

Can a single dose of human papillomavirus (HPV) vaccine prevent cervical cancer? Early findings from an Indian study

Rengaswamy Sankaranarayanan [a,e], Smita Joshi [b], Richard Muwonge [a], Pulikottil Okkuru Esmy [c], Partha Basu [c], Priya Prabhu [d], Neerja Bhatla [e], Bhagwan M. Nene [f], Janmesh Shaw [g], Usha Rani Reddy Poli [h], Yogesh Verma [i], Eric Zomawia [j], Sharmila Pimple [k], Massimo Tommasino [l], Michael Pawlita [m], Tarik Gheit [l], Tim Waterboer [m], Peter Sehr [n], Madhavan Radhakrishna Pillai [d], for the Indian HPV vaccine study group [1]

Vaccine 36 (2018) 4783–4791

Dose-related Effectiveness of Quadrivalent Human Papillomavirus Vaccine Against Cervical Intraepithelial Neoplasia: A Danish Nationwide Cohort Study

Freija Verdoodt,[1,2] Christian Dehlendorff,[2] and Susanne K. Kjaer[1,3]

Clin Infect Dis 2019;1-7

Background. A reduced, 2-dose schedule of human papillomavirus (HPV) vaccination has been endorsed for preadolescent women on the basis of immunogenicity data from randomized trials, and limited data suggest that even 1 dose may provide sufficient protection. Surveillance of the impact of <3 vaccine doses on clinical endpoints in the targeted age group is warranted.

Methods. We conducted a nationwide cohort study of all women aged 17–25 years, living in Denmark between 2006 and 2016. From nationwide registries, we extracted individual-level data on vaccination with the quadrivalent HPV (qHPV) vaccine at 16 years or younger, number of doses administered, diagnoses of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) or grade 3 or worse (CIN3+), and potential confounders. Using Poisson regression, we estimated incidence rate ratios (IRRs) with 95% confidence intervals (CIs) for CIN2+ and CIN3+, according to vaccination status.

Results. The cohort comprised 590 083 women, of which 215 309 (36%) women were vaccinated at ≤16 years, and among these, 40 742 (19%) received <3 vaccine doses. A total of 5561 women had a diagnosis of CIN3+. We found considerable vaccine effectiveness against CIN3+ after 1 (IRR, 0.38 [95% CI, .14–.98]), 2 (IRR, 0.38 [95% CI, .22–.66]), or 3 (IRR, 0.37 [95% CI, .30–.45]) vaccine doses, compared to unvaccinated women. Results were similar for CIN2+.

Conclusions. We find substantial effectiveness of qHPV vaccination against high-grade cervical precancerous lesions, among women vaccinated with 1, 2, or 3 doses at ≤16 years of age. One-dose vaccination appeared to provide similar protection as 3-dose vaccination.

Randomized controlled efficacy trial in Costa Rica to test efficacy of 1 dose vs. 2 doses (NCI & Gates Foundation)

4-arm non-inferiority trial in 12-16 year old girls:

- 1 dose and 2 doses of bivalent vaccine and 9-valent vaccine
- unethical to have a placebo arm

Main hypothesis:

- protection induced by 1 dose is not inferior to 2 doses

Second hypothesis:

- protection will be similar for 1 dose of either vaccine
- potential difference due to adjuvant: alum vs. AS04

clinicaltrials.gov: identifier NCT03180034

Avis sur le calendrier de vaccination contre les virus du papillome humain (VPH)

Dépôt légal – 2e trimestre 2018

COMITÉ SUR L'IMMUNISATION DU QUÉBEC

a two-vaccine mixed schedule:
- one dose of 9v vaccine followed by one dose of 2v vaccine

rationale: to maximize the immune response against HPV-16 and HPV-18 while ensuring good immunity against the other seven HPV types included in 9v-vaccine

only for girls and boys aged 9 to 17 years in good health

for individuals aged 18 and over as well as for other groups (e.g. immunocompromised), the vaccination schedule remains unchanged (2 doses of 9v vaccine)

Immunogenicity and safety of a mixed vaccination schedule with one dose of nonavalent and one dose of bivalent HPV vaccine versus two doses of nonavalent vaccine – A randomized clinical trial

Vladimir Gilca [a,b,*], Chantal Sauvageau [a,b], Gitika Panicker [c], Gaston De Serres [a,b], Manale Ouakki [a], Elizabeth R. Unger [c]

[a] Quebec Public Health Institute, Quebec, Canada
[b] Laval University Research Hospital Center, Quebec, Canada
[c] Centers for Disease Control and Prevention, Atlanta, USA

Vaccine 2018;36:7017-24

371 girls and boys aged 9–10 years were randomized 1:1 to receive: (i) two doses of 9vHPV or (ii) a mixed schedule of 2vHPV + 9vHPV or 9vHPV + 2vHPV with a 6 month interval

100% seropositivity to all 9 HPV types in all vaccinated groups

anti-HPV16 and anti-HPV18 GMTs were higher in subjects with the mixed schedule and for the other 7 HPV types higher in subjects who received two doses of 9vHPV vaccine

Mixed HPV vaccination schedules are immunogenic and have an acceptable safety profile.

Real life efficacy data

Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis

Mélanie Drolet, Élodie Bénard, Norma Pérez, Marc Brisson, on behalf of the HPV Vaccination Impact Study Group

Lancet 2019;394:497-509

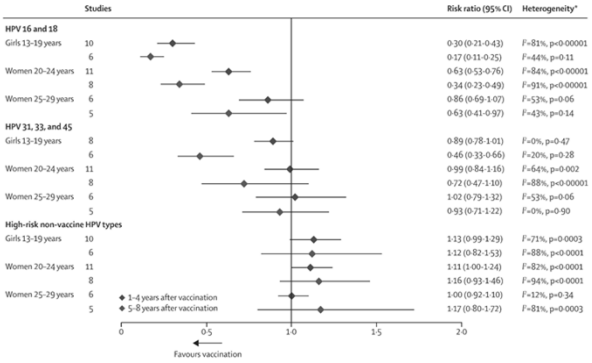
studies published between Feb 1, 2014, and Oct 11, 2018

updated systematic review and meta-analysis includes data from 60 million individuals and up to 8 years of post-vaccination follow-up

HPV infections (vaccine types)

time

Changes in the prevalence of HPV infections between pre-vaccination and post-vaccination periods



Drolet M et al. Lancet 2019;394:497-509.

Quadrivalent vaccine-targeted human papillomavirus genotypes in heterosexual men after the Australian female human papillomavirus vaccination programme: a retrospective observational study Lancet Infect Dis 2017;17:68-77

Eric P F Chow, Dorothy A Machalek, Sepehr N Tabrizi, Jennifer A Danielewski, Glenda Fehler, Catriona S Bradshaw, Suzanne M Garland, Marcus Y Chen, Christopher K Fairley

Retrospective, observational study of urine and urethral swab specimens from heterosexual men aged 25 years or younger (2004-2015), who tested positive for *Chlamydia trachomatis*

Australian-born men:
4vHPV-targeted genotype prevalence decreased from 20% to 3%

Australian-born men aged 21 years or younger:
4vHPV-targeted genotype prevalence decreased from 31% to 0%

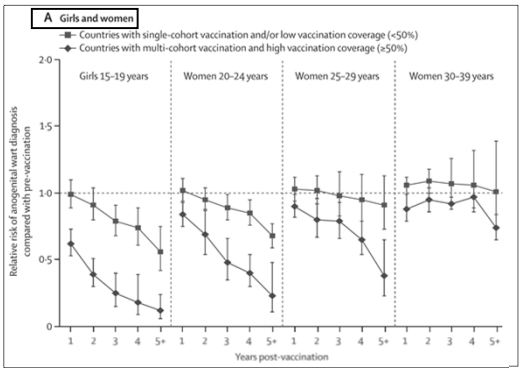
herd protection of mainly unvaccinated men from the vaccinated females

HPV infections (vaccine types)

genital warts

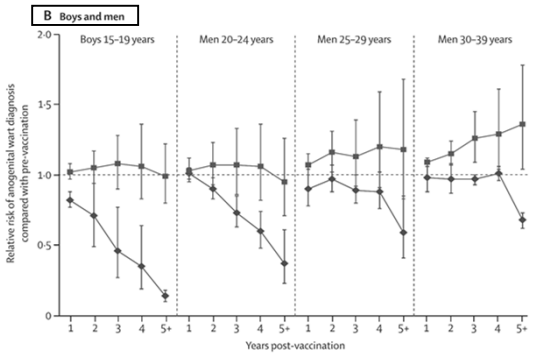
time

Changes in anogenital wart diagnoses during the 8 years after the introduction of girls-only HPV vaccination in countries using the quadrivalent vaccine



Drolet M et al. Lancet 2019;394:497-509.

Changes in anogenital wart diagnoses during the 8 years after the introduction of girls-only HPV vaccination in countries using the quadrivalent vaccine



Drolet M et al. Lancet 2019;394:497-509.

Condylomata Acuminata (Anogenital Warts) Contain Accumulations of HIV-1 Target Cells That May Provide Portals for HIV Transmission

J Infect Dis 2019;219:275-83

Jeffrey Pudney,[1a] Zoon Wangu,[1a] Lori Panther,[3] Dana Fugelso,[4] Jai G. Marathe,[2] Manish Sagar,[2] Joseph A. Politch,[1] and Deborah J. Anderson[1,2]

Immunohistologic staining to identify HIV target cells in anogenital warts (*AGW*) and control specimens.

CD1a+ dendritic cells, CD4+ T cells, and macrophages were significantly more abundant in the epidermis of *AGW* specimens than control specimens.

Compared with normal skin, *AGW*s contain significantly higher concentrations of HIV target cells that may be susceptible to HIV infection.

Condylomata may thus promote HIV transmission, especially in the setting of typical lesion vascularity and friability.

Prevention or treatment of *AGW*s may decrease the sexual transmission of HIV.

HPV infections (vaccine types)

genital warts

CIN 2/3

time

A 12-Year Follow-up on the Long-Term Effectiveness of the Quadrivalent Human Papillomavirus Vaccine in 4 Nordic Countries

Clin Infect Dis 2018;66:339-45.

Susanne K. Kjaer,[1,2] Mari Nygård,[1] Joakim Dillner,[4] J. Brooke Marshall,[5] David Radley,[5] Meng Li,[5] Christian Munk,[1] Bo T. Hansen,[3] Lera G. Sigurdardottir,[6] Maria Hortlund,[7] Lauley Tryggvadottir,[6,8] Amita Joshi,[5] Rituparna Das,[5] and Alfred J. Saah[5]

Endpoint	n	Number of Cases
HPV16/18-related CIN2+	2084	0
By time since day 1 of base study		
4 years or less	1930	0
>4 to 6 years	2083	0
>6 to 8 years	2037	0
>8 to 10 years	1914	0
>10 to 12 years	1333	0
>12 to 14 years	124	
By HPV type		
HPV16-related CIN2+	1787	0
HPV18-related CIN 2+	1981	0
By lesion type		
CIN 2	2084	0
CIN 3	2084	0
Adenocarcinoma in situ	2084	0
Cervical cancer	2084	0

Ten-year follow-up of human papillomavirus vaccine efficacy against the most stringent cervical neoplasia end-point—registry-based follow-up of *three cohorts from randomized trials*

BMJ Open 2017;7:e015867

Matti Lehtinen,[1,2] Camilla Lagheden,[2] Tapio Luostarinen,[2] Tiina Eriksson,[1] Dan Apter,[2] Katja Harjula,[1] Marjo Kuortti,[1] Kari Natunen,[1] Johanna Palmroth,[1] Tina Petäjä,[1] Eero Pukkala,[3] Mari Siitari-Mattila,[4] Frank Struyf,[5] Pekka Nieminen,[6] Jorma Paavonen,[6] Gary Dubin,[7] Joakim Dillner[2]

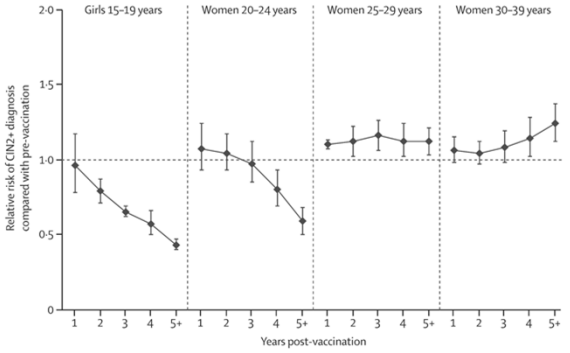
Finnish Cancer Registry-based follow-up of 98,561 person years of HPV-16/18 vaccinated and unvaccinated adolescent women

follow-up of 4.5 to 10 years post enrolment:

- unvaccinated cohort: 75 CIN3 and 4 invasive cervical cancers
- vaccinated women: 4 CIN3 and no cases of invasive cervical cancer

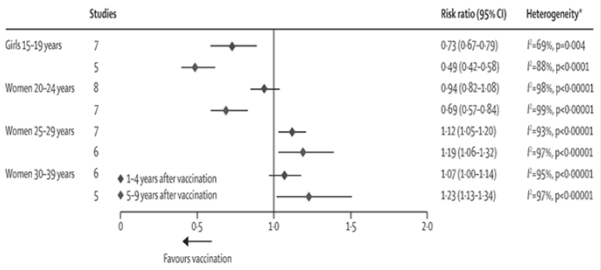
intention-to-treat VE against any CIN3+: 66% (95% CI 8-88%)

Changes in CIN2+ among screened girls and women during the first 7 years after the introduction of girls-only HPV vaccination, in countries with multi-cohort vaccination and high vaccination coverage



Drolet M et al. Lancet 2019;394:497-509.

Changes in CIN2+ among screened girls and women between the pre-vaccination and post-vaccination periods



Drolet M et al. Lancet 2019;394:497-509.

Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study

BMJ 2019;365:l1161

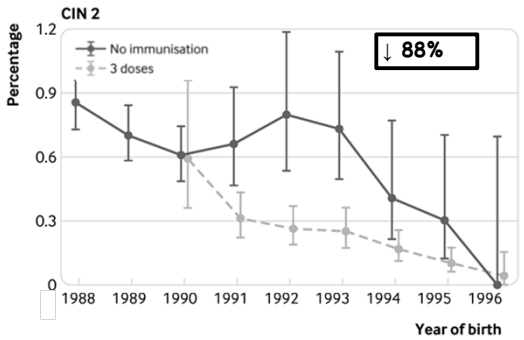
Tim Palmer,[1] Lynn Wallace,[2] Kevin G Pollock,[3,4] Kate Cuschieri,[5] Chris Robertson,[3,6,7] Kim Kavanagh,[7] Margaret Cruickshank[8]

retrospective population study, 1988-96

national vaccination and cervical screening programmes in Scotland

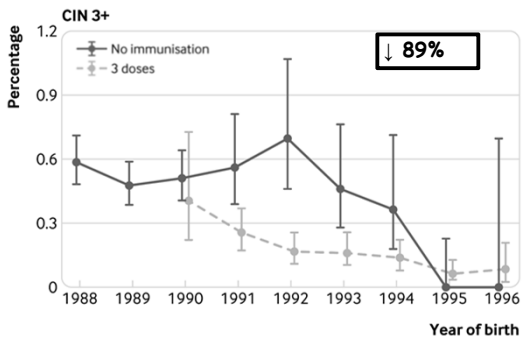
138,692 women

Histological abnormality (% of women screened) by year of birth and immunisation status; 1988-90=pre-immunisation programme cohort; 1991-94=catch-up cohort; 1995-96=routinely immunised cohort



Palmer T et al. BMJ 2019;365:l1161

Histological abnormality (% of women screened) by year of birth and immunisation status; 1988-90=pre-immunisation programme cohort; 1991-94=catch-up cohort; 1995-96=routinely immunised cohort

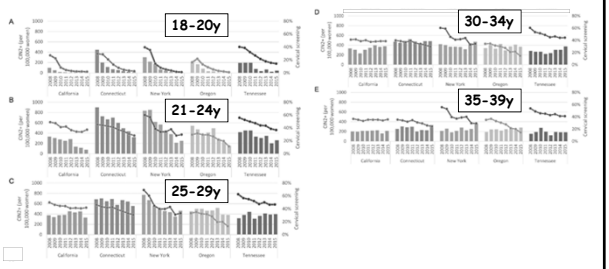


Palmer T et al. BMJ 2019;365:l1161

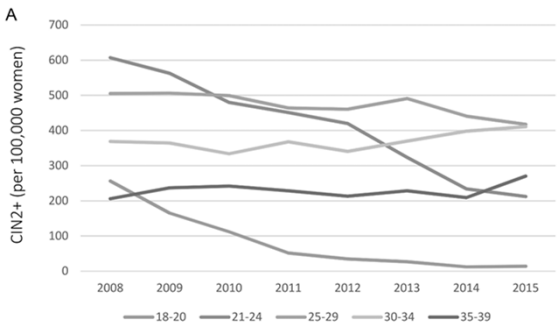
Trends in High-grade Cervical Lesions and Cervical Cancer Screening in 5 States, 2008–2015

Julia Warner Gargano,[1] Ina U. Park,[2] Marie R. Griffin,[3] Linda M. Niccolai,[4] Melissa Powell,[5] Nancy M. Bennett,[6] Michelle L. Johnson Jones,[1] Erin Whitney,[7] Manideepthi Pemmaraju,[3] Monica Brackney,[4] Nasreen Abdullah,[5] Mary Scahill,[8] Rebecca M. Dahl,[8] Angela A. Cleveland,[1] Elizabeth R. Unger,[9] and Lauri E. Markowitz[1]; HPV-IMPACT Working Group

Clin Infect Dis 2019;68:1282-91

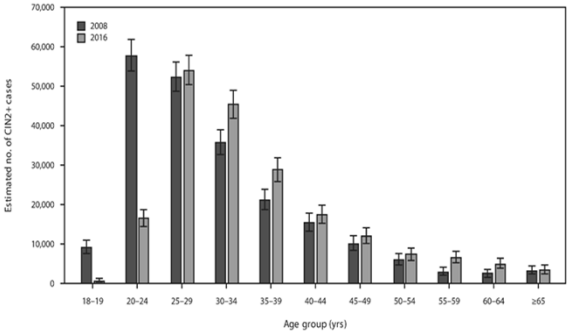


CIN2+ incidence per 100,000 women, US – 5 states, 2008-2015



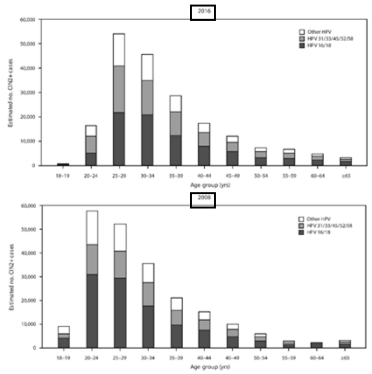
Gargano JW et al. Clin Infect Dis 2019;68:1282-91.

Estimated number of diagnosed CIN2+ cases, by age group — United States, 2008 and 2016



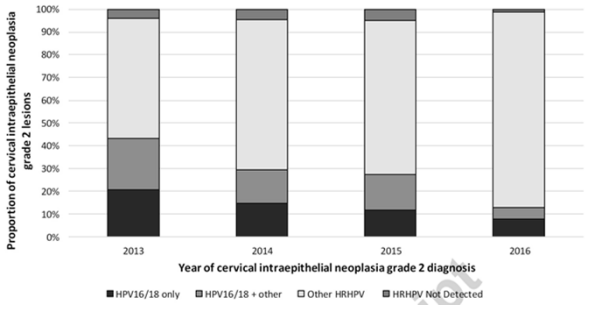
McClung NM, et al. MMWR Morb Mortal Wkly Rep 2019;68:337-43.

Estimated number of diagnosed CIN2+ cases, by human papillomavirus (HPV) type and age group — United States, 2016 and 2008

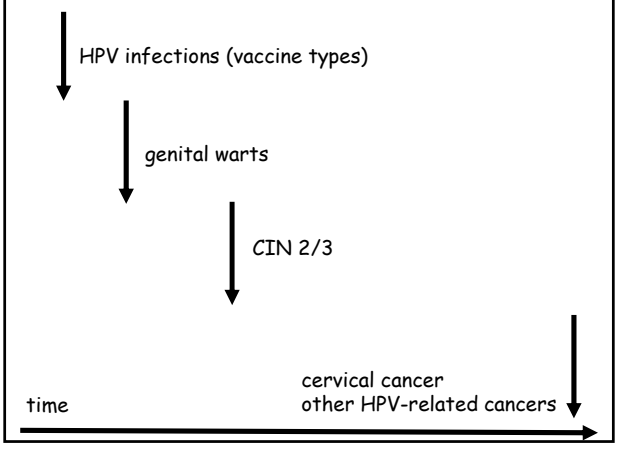


McClung NM, et al. MMWR Morb Mortal Wkly Rep 2019;68:337-43.

Changes in HPV genotypes associated with CIN2+ lesions in a cohort of young women, New Zealand, 2013-2016



Innes CR et al. Papillomavirus Res 2018; 77-82.



Vaccination protects against invasive HPV-associated cancers

Tapio Luostarinen[1,2], Dan Apter[3], Joakim Dillner[2], Tiina Eriksson[4], Katja Harjula[4], Kari Natunen[4], Jorma Paavonen[5], Eero Pukkala[1,4] and Matti Lehtinen[2,4]

[1] Finnish Cancer Registry, Helsinki, Finland
[2] Department of Laboratory Medicine, Karolinska Institute, Stockholm, Sweden
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[4] School of Health Sciences, University of Tampere, Tampere, Finland
[5] Department of Obstetrics and Gynecology, University of Helsinki, Helsinki, Finland

Int J Cancer 2018; 142: 2186–2187

Numbers and incidence rates (per 100,000 woman-years) of HPV-associated invasive cancers in cluster randomized cohorts of 9,529 14- to 17-year-old female vaccine (bHPV and qHPV) recipients and 17,838 non-HPV vaccinated, originally 14- to 19-year-old women. Passive follow-up using population-based Finnish Cancer Registry.

	HPV vaccinated women			Non-HPV vaccinated women		
Malignancy	Person years	*n*	Rate (95% CI)	Person years	*n*	Rate (95% CI)
Cervix cancer	65,656	0	–	124,245	8	6.4 (3.2, 13)
Vulva cancer	65,656	0	–	124,245	1	0.8 (0.1, 5.7)
Oropharyngeal cancer	65,656	0	–	124,245	1	0.8 (0.1, 5.7)
Other HPV cancers[1]	65,656	0	–	124,245	0	–
All HPV associated invasive cancers	65,656	0	–	124,245	10	8.0 (4.3, 15)

Scotland - Carcinoma in situ of the cervix uteri: ICD-10 D06

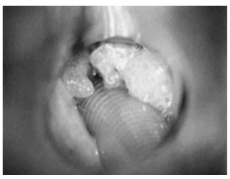
Numbers	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Under 5	-	-	-	-	-	-	-	-	-	-	-
5-9	-	-	-	-	-	-	-	-	-	-	-
10-14	-	-	-	1	-	-	-	-	-	-	-
15-19	1	-	-	-	1	-	-	-	-	-	-
20-24	8	1	11	4	7	13	11	11	8	4	4
25-29	23	34	25	34	26	33	24	38	39	43	9
30-34	39	38	39	37	43	37	37	58	52	47	47
35-39	42	44	36	43	30	39	32	53	47	36	43
40-44	34	41	46	41	36	28	49	47	44	44	32
45-49	24	30	29	44	35	29	34	41	36	43	33
50-54	21	25	27	20	27	26	33	37	28	17	30
55-59	15	21	29	26	24	17	22	19	25	30	21
60-64	13	17	12	22	22	22	14	13	22	25	15
65-69	26	18	21	14	13	20	16	19	17	15	14
70-74	13	19	14	16	18	13	16	15	17	14	11
75-79	17	12	19	16	17	12	11	10	18	14	8
80-84	10	4	12	10	12	7	13	15	15	7	3
85-89	3	8	7	5	6	7	3	11	9	1	4
90+	4	2	1	-	1	1	4	1	4	4	2
All Ages	293	314	328	333	318	304	319	388	381	344	276

https://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/Female-Genital-Organ/

HPV infections (vaccine types)

genital warts

CIN 2/3



laryngeal papillomas

time

A Prospective Study of the Incidence of Juvenile-Onset Recurrent Respiratory Papillomatosis After Implementation of a National HPV Vaccination Program

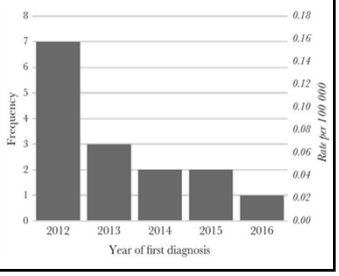
Daniel Novakovic,[1] Alan T. L. Cheng,[1,2] Yvonne Zurynski,[1,3] Robert Booy,[4] Paul J. Walker,[5] Robert Berkowitz,[6] Henley Harrison,[7] Robert Black,[8] Christopher Perry,[9] Shyan Vijayasekaran,[9] David Wabnitz,[10] Hannah Burns,[8] Sepehr N. Tabrizi,[11,12] Suzanne M. Garland,[11,12] Elizabeth Elliott,[1] and Julia M. L. Brotherton[13,14]

J Infect Dis 2018; 217: 208-212

national incidence of juvenile onset recurrent respiratory papillomatosis

15 incident cases

- all mothers not vaccinated
- 20% history of genital warts
- 13/15 born by vaginal delivery



Post-licencing real life safety data

2017, 92, 393–404 No 28

World Health Organization
Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

14 JULY 2017, 92th YEAR / 14 JUILLET 2017, 92e ANNÉE
No 28, 2017, 92, 393–404
http://www.who.int/wer

Global Advisory Committee on Vaccine Safety (GACVS):
- an independent expert clinical and scientific advisory body
- provides WHO with scientifically rigorous advice on vaccine safety issues

over 270 million doses of HPV vaccines have been distributed

first safety review in 2007, and subsequent in 2008, 2009, 2013, 2014 and 2015

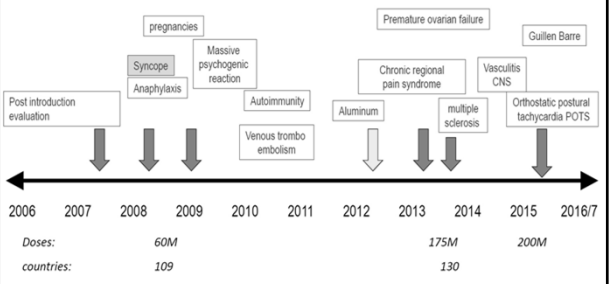
the risk of anaphylaxis characterized as app. 1.7 cases per million doses

syncope established as a common anxiety or stress related reaction to injection

no other adverse reactions identified - HPV vaccines are extremely safe

Reports of the Global Advisory Committee on Vaccination Safety (GACVS) & Strategic Advisory Group of Experts in immunization (SAGE) in relation to the HPV vaccine

World Health Organization



Quadrivalent HPV Vaccination and the Risk of Adverse Pregnancy Outcomes

N Engl J Med 2017;376:1223-33.

Nikolai M. Scheller, M.D., Björn Pasternak, M.D., Ph.D., Ditte Mølgaard-Nielsen, M.Sc., Henrik Svanström, Ph.D., and Anders Hviid, Dr.Med.Sci.

all pregnant women in Denmark (2006-2013), linked information on vaccination, adverse pregnancy outcomes, and potential confounders

HPV vaccine not associated with significantly higher risks for:

major birth defect :	1.19 (95% CI 0.90 to 1.58)
spontaneous abortion:	0.71 (95% CI, 0.45 to 1.14)
preterm birth:	1.15 (95% CI, 0.93 to 1.42)
low birth weight:	1.10 (95% CI, 0.85 to 1.43)
small size for gestational age:	0.86 (95% CI, 0.72 to 1.02)
stillbirth:	2.43 (95% CI, 0.45 to 13.21)

No increased risk of Guillain-Barré syndrome after human papilloma virus vaccine: A self-controlled case-series study in England

Vaccine 2017;35:1729-32

Nick Andrews [a,*], Julia Stowe [b], Elizabeth Miller [b]

[a] Statistics, Modelling and Economics Department, Public Health England, London NW9 5EQ, United Kingdom
[b] Immunisation and Blood Safety Department, Public Health England, 61 Colindale Avenue, London NW9 5EQ, United Kingdom

largest study to date to assess the risk of Guillain-Barré syndrome (GBS) following HPV vaccination

101 GBS episodes ascertained from a population given approximately 10.4 million HPV vaccine doses

no evidence of an increased risk of GBS following HPV vaccination (in the first 3, 6 and 12 months)

Postural Orthostatic Tachycardia Syndrome (POTS)
Complex Regional Pain Syndrome (CRPS)
Primary Ovarian Failure (POF)
Premature Ovarian Insufficiency (PIF)
Recurrent optic neuritis and neuromyelitis

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA)

Proposed diagnostic criteria of autoimmune/inflammatory syndrome induced by adjuvants (ASIA)

Major criteria
Previous exposure to an external stimulus (i.e. vaccine, adjuvant, silicone, nucleic acids, fragments of bacterial cell walls)
One of the following "typical" manifestations
Myalgia/myositis, muscle weakness
Arthralgia and/or arthritis
Chronic fatigue, non-refreshing sleep or sleep disturbances
Neurological manifestations (especially if associated with demyelination)
Memory loss and cognitive impairment
Fever
Dry mouth
Improvement of symptoms after the removal of the triggering agent
Typical biopsy of the involved organs
Minor criteria
Appearance of autoantibodies or autoantibodies directed against the suspected adjuvant
Other clinical manifestations (i.e. functional somatic syndromes)
Association with specific HLA haplotypes (i.e. HLA-DRB1, HLA-DQB1)
Development of autoimmune diseases
Diagnostic requirements:
Two major criteria
One major criteria + two minor criteria

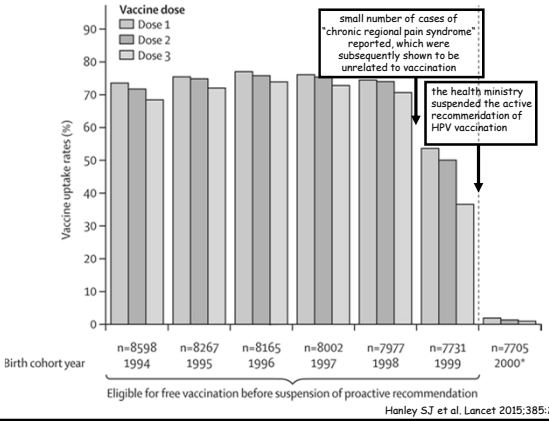
For the diagnosis of ASIA, at least two major or one major and two minor criteria must be met

Shoenfeld Y, Agmon-Levin N.
"ASIA" -autoimmune/inflammatory syndrome induced by adjuvants.
J Autoimmun 2011;36: 4-8

Influence of vaccine safety rumors on vaccination coverage

Japan	70% (2013)	→	0.6% (2015)
Denmark	90% (2012)	→	44% (2015)
Ireland	87% (2013)	→	49% (2016)
Columbia	88% (2012)	→	5% (2016)

Uptake of HPV vaccine by year of birth, females, Japan, 1994-2000



Hanley SJ et al. Lancet 2015;385:2571.

No association between HPV vaccine and reported post-vaccination symptoms in Japanese young women: Results of the Nagoya study

Sadao Suzuki*, Akihiro Hosono

Department of Public Health, Graduate School of Medical Sciences, Nagoya City University, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 466-8601, Japan

Papillomavirus Research 2018: 5: 96–103

ABSTRACT

Nagoya City introduced free HPV vaccination in 2010 and in April 2013 the Ministry of Health, Labour and Welfare included the HPV vaccine in the National Immunization Program. However, in June 2013, the Ministry suspended proactive recommendation of the vaccine after unconfirmed reports of adverse events. To investigate any potential association between the vaccine and reported symptoms, Nagoya City conducted a questionnaire-based survey.

Participants were 71,177 female residents of Nagoya City born between April 2, 1994 and April 1, 2001. The anonymous postal questionnaire investigated the onset of 24 symptoms (primary outcome), associated hospital visits, frequency, and influence on school attendance.

Totally, 29,846 residents responded. No significant increase in occurrence of any of the 24 reported post-HPV vaccination symptoms was found. The vaccine was associated with increased age-adjusted odds of hospital visits for "abnormal amount of menstrual bleeding" (OR: 1.43, 95% CI: 1.13–1.82), "irregular menstruation" (OR: 1.29, 95% CI: 1.12–1.49), "severe headaches" (OR: 1.19, 95% CI: 1.02–1.39), and chronic, persisting "abnormal amount of menstrual bleeding" (OR 1.41, 95% CI: 1.11–1.79). No symptoms significantly influenced school attendance and no accumulation of symptoms was observed.

The results suggest no causal association between the HPV vaccines and reported symptoms.

Bivalent Human Papillomavirus Vaccine Effectiveness in a Japanese Population: High Vaccine-Type–Specific Effectiveness and Evidence of Cross-Protection

Risa Kudo,[1,a] Manako Yamaguchi,[1,a] Masayuki Sekine,[1] Sosuke Adachi,[1] Yutaka Ueda,[2] Etsuko Miyagi,[3] Megumi Hara,[4] Sharon J. B. Hanley,[5] and Takayuki Enomoto[1]

[1]Department of Obstetrics and Gynecology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, [2]Departments of Obstetrics and Gynecology, Osaka University Graduate School of Medicine, Suita, [3]Department of Obstetrics and Gynecology, Yokohama City University School of Medicine, Yokohama, [4]Department of Preventive Medicine, Faculty of Medicine, Saga University, Saga, and [5]Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine, Sapporo, Japan

J Infect Dis 2019;219:382-90

Background. Proactive recommendations for human papillomavirus (HPV) vaccines in Japan have been suspended for 5 years because of safety concerns. While no scientific evidence exists to substantiate these concerns, one reason given for not reinstating recommendations is the lack of reliable vaccine effectiveness (VE) data in a Japanese population. This study reports the VE of the bivalent HPV vaccine in Japanese women aged 20–22 years.

Methods. During cervical screening between 2014 and 2016, women had Papanicolaou smears and HPV tests performed and provided data about their sexual history. Estimates of VE for vaccine-targeted HPV type 16 (HPV16) and 18 and cross-protection against other types were calculated.

Results. Overall, 2197 women were tested, and 1814 were included in the analysis. Of these, 1355 (74.6%) were vaccinated, and 1295 (95.5%) completed the 3-dose schedule. In women sexually naive at vaccination, the pooled VEs against HPV16 and 18 and for HPV31, 45, and 52 were 95.5% ($P < .01$) and 71.9% ($P < .01$), respectively. When adjusted for number of sex partners and birth year, pooled VEs were 93.9% ($P = .01$) and 67.7% ($P = .01$) for HPV16 and 18 and HPV31, 45, and 52, respectively.

Conclusions. The bivalent HPV vaccine is highly effective against HPV16 and 18. Furthermore, significant cross-protection against HPV31, 45, and 52 was demonstrated and sustained up to 6 years after vaccination. These findings should reassure politicians about the VE of bivalent HPV vaccine in a Japanese population.

History repeats itself in Japan: Failure to learn from rubella epidemic leads to failure to provide the HPV vaccine

Hum Vaccin Immunother 2017;13:1859-60

Yusuke Tanaka, Yutaka Ueda, Kiyoshi Yoshino, and Tadashi Kimura

Department of Obstetrics and Gynecology, Osaka University Graduate School of Medicine, Suita, Osaka, Japan

In 1989, a MMR vaccine, targeting all children aged 1 to 6 years, was introduced into the National Immunization Program (NIP).

In 1993, due to reports of serious aseptic meningitis following the MMR vaccination, the Japanese government withdraw its recommendation.

In 1995, the NIP revised its vaccination policy, to now strongly recommend, but not make mandatory, the rubella vaccine for both males and females.

There are susceptible pockets among female birth cohorts 1989–1993, with seropositive proportions of 78.3%.

Due directly to these gaps in 'herd' immunization resulting from politicized transitions in vaccination policy by the government, there were outbreaks of rubella with 17,050 cases and 45 cases of congenital rubella syndrome reported from 2012-2014.

Doctor wins 2017 John Maddox prize for countering HPV vaccine misinformation

Riko Muranaka awarded prize for efforts to explain jabs's safety amid scare campaigns which have seen Japanese vaccination rate fall from over 70% to 1%

Dr Riko Muranaka, who faced hostility and personal threats as she attempted to counter misinformation around the anti-cancer vaccine. Photograph: Kyoto University Photograph: Handout

A Japanese doctor who has stood up to a campaign of misinformation around a common anti-cancer vaccine has won a prestigious prize for championing evidence in the face of hostility and personal threats.

Riko Muranaka at Kyoto University was awarded the 2017 John Maddox prize on Thursday for her efforts to explain the safety of the human papilloma virus (HPV) vaccine amid strong opposition from anti-vaccine activists and a small group of academics.

Muranaka was praised by colleagues for her courage and leadership as she endured insults, litigation and attempts to undermine her professional status as the HPV vaccine came under attack in Japan. While the jab is used without fuss in many countries, in Japan and some other nations, fears raised by campaigners have hit vaccine uptake rates.

Anti-vaxxer wins libel case in Japan in blow for scientist

Court rules that critic of HPV vaccine did not fabricate his research

Riko Muranaka was ordered by a court to pay ¥3.3m (£30,000) in damages plus legal costs to the plaintiff, Shuichi Ikeda

Robin Harding in Tokyo 5 HOURS AGO

A prominent critic of the HPV vaccine has won a libel case in Japan, in a setback for scientists attempting to counter poorly founded claims that the procedure could have dangerous side effects.

Riko Muranaka, a doctor and journalist, was ordered by a court to pay ¥3.3m (£30,000) in damages plus legal costs to Shuichi Ikeda, former dean of the medical school at Shinshu University, for making false allegations claiming that Dr Ikeda fabricated his research.

The case has highlighted the unusually staunch opposition by activists in Japan to the use of the human papilloma virus (HPV) vaccine and is likely to have a chilling effect on scientists who respond to so-called "anti-vaxx" campaigners who say it is unsafe.

"This judgment turns an issue of science into an issue of libel and for doctors and scientists that is unacceptable," said Isamu Ishiwata, who chairs a group called Protecting The Lives We Can, which supports Dr Muranaka. "The contents of the judgement have nothing to do with the safety of the cervical cancer vaccine."

Controversy over the HPV vaccine, which protects against a sexually transmitted virus linked to almost all cases of cervical cancer, erupted in Japan in 2013 when a video released online claimed to show extreme neurological side effects of the jab. Japan's health ministry stopped recommending the injection and vaccination rates collapsed from more than 70 per cent to less than 1 per cent.

Doctors have predicted that the failure to vaccinate millions of young women in Japan could result in thousands of preventable cervical cancers. Japan's position has been heavily cited in other countries where the HPV vaccine has come under attack, such as Denmark and Ireland.

In 2016, Dr Ikeda appeared on television and claimed a link between the vaccine and the neurological symptoms. He later took Dr Muranaka to court after she wrote an article criticising his research. In the same year, Dr Muranaka was awarded the John Maddox prize for promoting evidence-based science in the face of adversity.

The libel case turned on the use of the word "fabricated" in Dr Muranaka's allegation that Dr Ikeda "fabricated" an experiment on a mouse. The court found that was not true; Dr Ikeda had indeed conducted the experiment.

The court ruling did not address the broader criticism that he publicly claimed a link between the HPV vaccination and neurological illness based on data from a single mouse, which Dr Muranaka claimed was insufficient evidence for Dr Ikeda's conclusion.

An internal investigation by Shinshu University cleared Dr Ikeda of fabrication but criticised him for presenting preliminary evidence from one mouse as a conclusive research result.

Japan's health ministry also criticised him in unusual terms, saying: "Dr Ikeda bears a large social responsibility for inviting public misunderstanding through his inappropriate announcement." Nonetheless, the ministry has declined to restart the HPV vaccination programme.

Meta-analyses of clinical trials covering tens of thousands of patients continue to show the HPV vaccine is safe. "Unfounded rumours about HPV vaccines continue to unnecessarily delay or impede the scaling up of vaccination, which is so urgently needed to prevent cervical cancer," said Elisabete Weiderpass, director of the International Agency for Research on Cancer, last month.

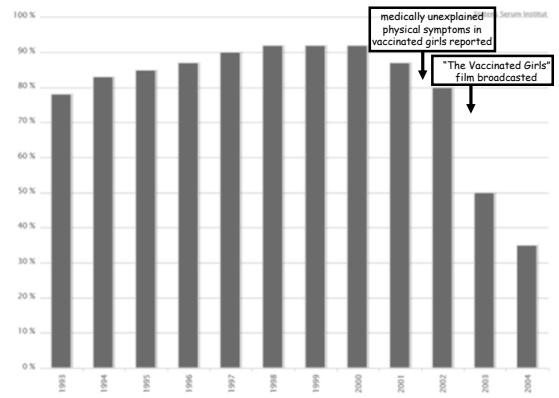
Dr Ikeda said he was pleased with the court ruling. "For a researcher, the word 'fabrication' is lethal," he said, according to Japanese media. "If 'fabrication' were attached to me I'd lose my standing to say anything at an academic conference."

Dr Muranaka said attacks on the HPV vaccine were fake news. "Women who decided not to vaccinate lost their chance to protect their life and health," she said. "The negative impact of Ikeda's message that the HPV vaccine caused damage to the brains of mice is enormous."

Influence of vaccine safety rumors on vaccination coverage

Japan	70% (2013)	→	0.6% (2015)
Denmark	90% (2012)	→	44% (2015)
Ireland	87% (2013)	→	49% (2016)
Columbia	88% (2012)	→	5% (2016)

Uptake of first HPV vaccine by year of birth, females, Denmark, 1993-2004



HPV-vaccination impact in Denmark: is the vaccine working?

Elsebeth Lynge[a], Malene Skorstengaard[b], Charlotte Lynderup Lübker[b] and Lise Thamsborg[b]

[a]Centre for Epidemiological Research, Nykøbing Falster Hospital, University of Copenhagen, Nykøbing Falster, Denmark; [b]Department of Public Health, University of Copenhagen, Copenhagen, Denmark

Exp Rev Vaccines 2018; in press

In 2012, a number of cases of postural orthostatic tachycardia syndrome (POTS) and similar syndromes in young women were reported and hypothesized to be associated with HPV-vaccination

Possible adverse effects were highlighted in a television documentary, and a negative attitude toward HPV vaccination disseminated on social media.

A dramatic decrease in HPV-vaccination coverage from 80–90% to 20–30%.

In 2015 the EMA reviewed the literature and found no evidence for a causal association between HPV-vaccination and POTS and related syndromes.

Studies in Denmark found girls reporting possible adverse effects to have been more frequent users of the health-care system than other girls even before the HPV vaccination indicating that factors other than the vaccination might have caused the syndromes.

HPV-vaccination impact in Denmark: is the vaccine working?

Elsebeth Lynge[a], Malene Skorstengaard[b], Charlotte Lynderup Lübker[b] and Lise Thamsborg[b]

[a]Centre for Epidemiological Research, Nykøbing Falster Hospital, University of Copenhagen, Nykøbing Falster, Denmark; [b]Department of Public Health, University of Copenhagen, Copenhagen, Denmark

Exp Rev Vaccines 2018; in press

Concerted effort StopHPV was initiated in spring 2017 by the Health Authorities, the Cancer Society, and the Medical Association to disseminate evidence on HPV-vaccination, including a website with answers to often-asked questions, YouTube film with women diagnosed with cervical cancer, and a Facebook group.

From the spring of 2018 boys are offered free vaccination.

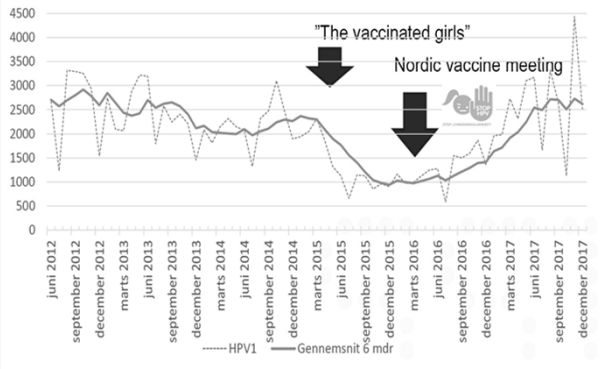
In June 2018 vaccination coverage back to 73%.

BUT:

Girls who could have been vaccinated at the age of 12 years were instead vaccinated at the age of 15–16 years, where more than one third of them are sexually active.

The initial, very good prospect from the start of HPV-vaccination in Denmark of reaching herd immunity was thus temporarily postponed for a 4–5 years' period before HPV-vaccination regained momentum.

Number of young women who initiate HPV vaccination per month in Denmark, June 2012 to December 2017



Courtesy of Palle Valentiner-Branth

Type 1 narcolepsy is not present in 29 HPV-vaccinated individuals with subjective sleep complaints

Dan Med J 2018;65:A5510

Eva Wiberg Torstensen[1], Louise Schouborg Brinth[2,3], Jesper Mehlsen[2], Birgitte Rahbek Kornum[1,4] & Poul Jørgen Jennum[1]

Evaluation for sleep disorders, including narcolepsy, in 29 HPV-vaccinated girls and women who were submitted for evaluation of narcolepsy.

All were evaluated by polysomnography and the Multiple Sleep Latency Test, and 18 individuals were also evaluated by measures of cerebrospinal fluid hypocretin-1 concentration.

None of the 29 girls and women showed signs of narcolepsy type 1.

Results do not suggest that an association exists between HPV vaccination and the development of narcolepsy type 1.

HPV vaccination and risk of chronic fatigue syndrome/myalgic encephalomyelitis: A nationwide register-based study from Norway

Berit Feiring [a,*], Ida Laake [a], Inger Johanne Bakken [b], Margrethe Greve-Isdahl [c], Vegard Bruun Wyller [d], Siri E. Håberg [e], Per Magnus [f], Lill Trogstad [a]

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[e] Division of Physical and Mental Health, Norwegian Institute of Public Health, PO Box 4404 Nydalen, 0403 Oslo, Norway
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Vaccine 2017;35:4203-12

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Keywords:
Human papillomavirus vaccine
Chronic fatigue syndrome
Myalgic encephalomyelitis
Vaccine safety
Vaccine uptake
Medical history

ABSTRACT

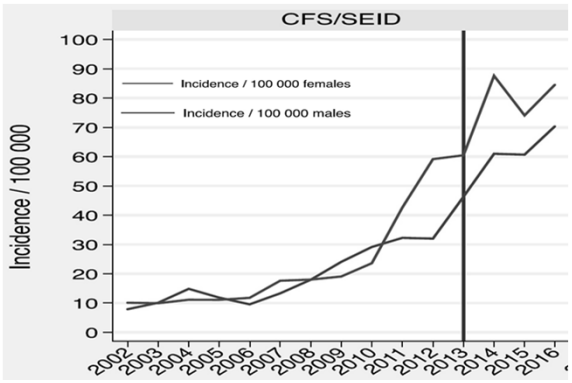
Background: Vaccination has been suggested to be involved in the aetiology of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME). HPV vaccine was introduced in the Norwegian Childhood Immunisation Programme and offered 12 year old girls from 2009. We studied the association between HPV vaccination and risk of CFS/ME and also assessed medical history in relation to both risk of CFS/ME and HPV vaccine uptake.

Methods: Individual data from national registries, including the Norwegian Population Registry, the Norwegian Patient Registry and the Norwegian Immunisation Registry were linked using the unique personal identification number. Yearly incidence rates of CFS/ME for 2009–2014 were calculated among the 824,133 boys and girls, aged 10–17 living in Norway during these 6 years. A total of 176,453 girls born 1997–2002 were eligible for HPV vaccination and included in further analyses. Hazard ratios (HRs) of CFS/ME were estimated using Cox regression. Risk differences (RDs) of vaccine uptake were estimated with binomial regression.

Results: A similar yearly increase in incidence rate of CFS/ME was observed among girls and boys, IRR = 1.15 (95% confidence interval (CI) 1.10–1.19) and 1.15 (95% CI 1.09–1.22), respectively. HPV vaccination was not associated with CFS/ME, HR = 0.86 (95% CI 0.69–1.08) for the entire follow-up period and 0.96 (95% CI 0.64–1.43) for the first two years after vaccination. The risk of CFS/ME increased with increasing number of previous hospital contacts, HR = 5.23 (95% CI 3.66–7.49) for 7 or more contacts as compared to no contacts. Girls with 7 or more hospital contacts were less likely to be vaccinated than girls with no previous hospital contacts, RD = −5.5% (95% CI −6.7% to −4.2%).

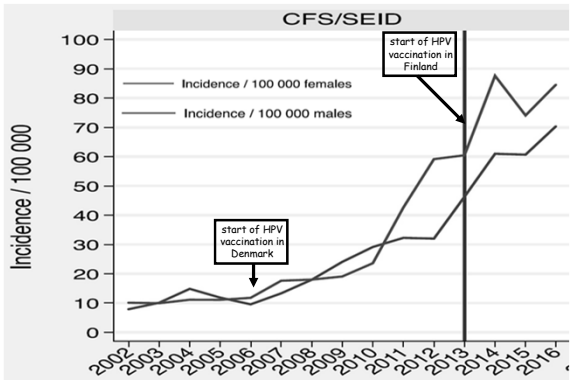
Conclusions: No indication of increased risk of CFS/ME following HPV vaccination was observed among girls in the first 6 birth cohorts offered HPV vaccine through the national immunisation programme in Norway.

Incidence rates per 100,000 person-years of Chronic Fatique Syndrome/Systemic Exertion Intolerance Disease (CFS/SEID) in children of 11–15 years, years 2002–2016, Finland



Skufca J et al. Vaccine 2018; 36: 5926-5933

Incidence rates per 100,000 person-years of Chronic Fatique Syndrome/Systemic Exertion Intolerance Disease (CFS/SEID) in children of 11–15 years, years 2002–2016, Finland



Skufca J et al. Vaccine 2018; 36: 5926-5933

SCIENTIFIC REPORTS

OPEN

Retraction: Murine hypothalamic destruction with vascular cell apoptosis subsequent to combined administration of human papilloma virus vaccine and pertussis toxin

Satoko Aratani, Hidetoshi Fujita, Yoshiyuki Kuroiwa, Chie Usui, Shumpei Yokota, Ikuro Nakamura, Kusuki Nishioka & Toshihiro Nakajima

Scientific Reports **6**: Article number: 36943; published online: 11 November 2016; updated: 11 May 2018

The Publisher is retracting this Article because the experimental approach does not support the objectives of the study. The study was designed to elucidate the maximum implication of human papilloma virus (HPV) vaccine (Gardasil) in the central nervous system. However, the co-administration of pertussis toxin with high-levels of HPV vaccine is not an appropriate approach to determine neurological damage from HPV vaccine alone. The Authors do not agree with the retraction.

Indian Journal of Medical Ethics Online First Published May 26, 2018

Indian J Med Ethics 2018;1-5

COMMENT

Increased incidence of cervical cancer in Sweden: Possible link with HPV vaccination

LARS ANDERSSON

Department of Physiology and Pharmacology, Karolinska Insitutet, SE-171 77 Solna, SWEDEN

The age-standardised incidence of invasive cervical cancer in Sweden has increased substantially in the last two years (20%) and there is a statistically significant increase for the entire period 2005-2015.

I discuss the possibility that HPV vaccination could play a role in the increase in the incidence of cervical cancer by causing instead of preventing cervical cancer disease in women previously exposed to HPV.

RETRACTION: Increased incidence of cervical cancer in Sweden: Possible link with HPV vaccination

EDITORS, *Indian Journal of Medical Ethics*

The comment "Increased incidence of cervical cancer in Sweden: Possible link with HPV vaccination" (DOI: 10.20529/IJME.2018.037) was published online in the *Indian Journal of Medical Ethics* on April 30, 2018 (1). The author gave his name and affiliation as Lars Andersson, department of Physiology and Pharmacology, Karolinska Institutet (KI), Sweden. On May 8, as soon as KI informed us that no such person worked there, we carried out a correction the next day and the institution's name was removed as affiliation (2).

On inquiry, the author informed us that he had used a pseudonym besides a false affiliation. He later made his identity known to *IJME*'s editor on the promise of strict confidentiality. On verification of his identity, the editor confirmed that (a) the author had the necessary qualifications, expertise and research experience on the subject of the article; and (b) the author did face a credible threat of harm, making it necessary not to be named publicly.

Further we reconfirmed the reviewers' conclusions: that the article used publicly available data with a simple statistical method; made a fair attempt to report a possible association of the increased incidence of carcinoma cervix with HPV vaccination; and suggested more research. We felt that the data and analysis could be scientifically appreciated and critiqued without reference to the author. Therefore, despite the author's unacceptable deception, the editors decided to retain the article having already made a correction to remove the false affiliation.

Following our decision, we received valuable advice from our editorial board and other well-wishers, emphasising that there should be zero tolerance towards the author's deception, irrespective of the content of the paper. While our assessment of the science of the article may be correct, we have concluded that tolerating the author's deception and retaining the article was an error of judgement. We express our deep gratitude to them and have accepted their advice.

Thus, this article is hereby retracted. We will provide a detailed account of this issue, with the nuances involved, in an editorial at a later date.

As editors, we are wary of the extreme ideological divide that views discussions on vaccines as either "pro" or "anti." In low and middle-income countries like India, where early HPV infection and incidence of carcinoma cervix are relatively high, scientific discussion and resolution of issues concerning the HPV vaccine is critical for women receiving it, and for policy making on its introduction in the universal immunisation programme. We hope that the hypothesis of possible harm of vaccinating women previously exposed to HPV is carefully explored in future studies.

Note: *Corrected on July 21, 2018.*

Short-Term Efficacy of CBD-Enriched Hemp Oil in Girls with Dysautonomic Syndrome after Human Papillomavirus Vaccination

Beniamino Palmieri MD[1,2], Carmen Laurino MSc[1,2] and Maria Vadalà MSc[1,2]
[1]Department of General Surgery and Surgical Specialties, University of Modena and Reggio Emilia Medical School, Surgical Clinic, Modena, Italy
[2]Network of the Second Opinion, Modena (MO), Italy

Isr Med Assoc J 2017;19:79-84

short-term effect of cannabidiol (CBD)-based treatments for relieving symptoms and improving the life quality in young girls with adverse drug effects following human papillomavirus (HPV) vaccine

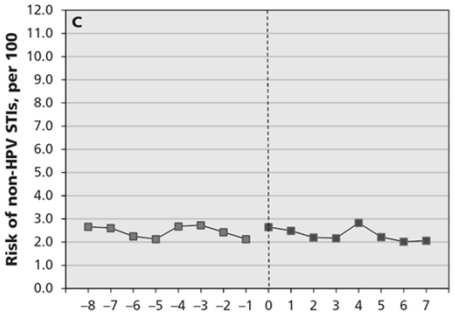
study demonstrated the safety and tolerability of CBD-rich hemp oil and the primary efficacy endpoint

randomized controlled trials are warranted to characterize the safety profile and efficacy

Effect of human papillomavirus (HPV) vaccination on clinical indicators of sexual behaviour among adolescent girls: the Ontario Grade 8 HPV Vaccine Cohort Study

CMAJ 2015;187:E74-81

Leah M. Smith MSc, Jay S. Kaufman PhD, Erin C. Strumpf PhD, Linda E. Lévesque PhD



Population-level sexual behaviours in adolescent girls before and after introduction of the human papillomavirus vaccine (2003–2013)

Gina S. Ogilvie MD DrPH, Felicia Phan MPH, Heather N. Pedersen MPH, Simon R. Dobson MD, Monika Naus MD MHSc, Elizabeth M. Saewyc PhD RN

CMAJ 2018;190:E1221-6

298,265 girls who self-identified as heterosexual

proportion of girls reporting ever having sexual intercourse decreased for 16%

self-report of sexual intercourse before age of 14 years decreased for 22%

reported substance use before intercourse decreased for 31 %

in the last 10 years sexual risk behaviours reported by adolescent girls either reduced or stayed the same

The Participation of HPV-Vaccinated Women in a National Cervical Screening Program: Population-Based Cohort Study

PLoS One 2015;10:e0134185.

Eva Herweijer[1], Adina L. Feldman[1,2], Alexander Ploner[1], Lisen Arnheim-Dahlström[1], Ingrid Uhnoo[3], Eva Netterlid[3,4,5], Joakim Dillner[1,6], Pär Sparén[1], Karin Sundström[6]*

a cohort of all women resident in Sweden, born 1977-1987 (N=629,703), and invited to cervical screening, was followed October 2006 - December 2012

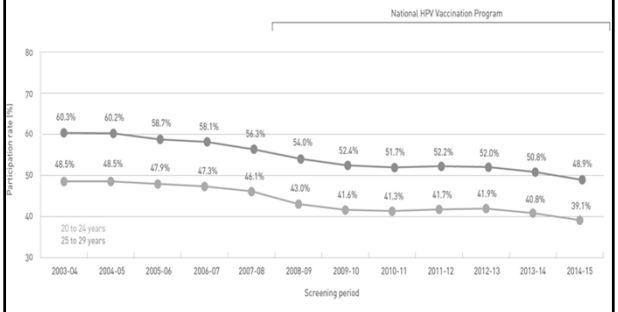
screening attendance after three years of follow-up was 86% in vaccinated women (N=4,897) and 75% in unvaccinated women (N=625,804)

the crude HR of screening attendance in vaccinated vs. unvaccinated women was 1.31 (95% CI 1.27-1.35) in the first screening round

in the second screening round, attendance was also higher in HPV-vaccinated women (crude HR=1.26, 95% CI 1.21-1.32; HR_{adj}=1.15, 95% CI 1.10-1.20)

HPV-vaccination is so far associated with equal or higher attendance to cervical screening in Sweden in a cohort of opportunistically vaccinated young women

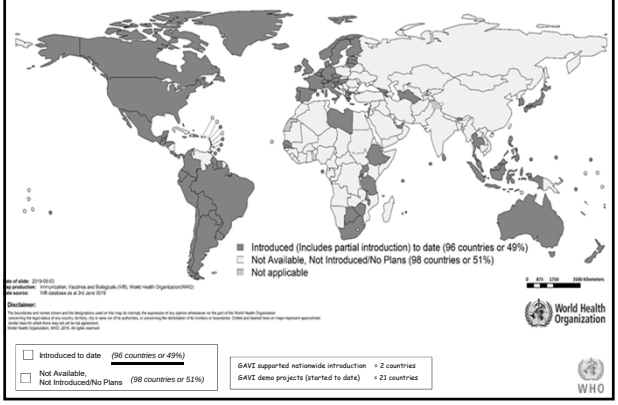
Estimated two year cervical screening rates for women aged 20 to 24 years and 25 to 29 years, 2003-2004 to 2014-2015, Victoria, Australia.

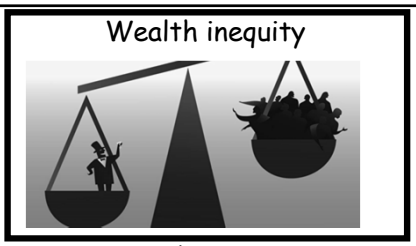


Victorian Cervical Cytology Registry Statistical Report 2015

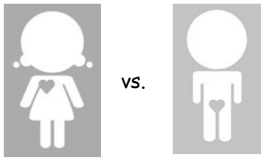
Implementation !
Implementation !
Implementation !

Countries with HPV vaccine in the national immunization programme (status June 2019)

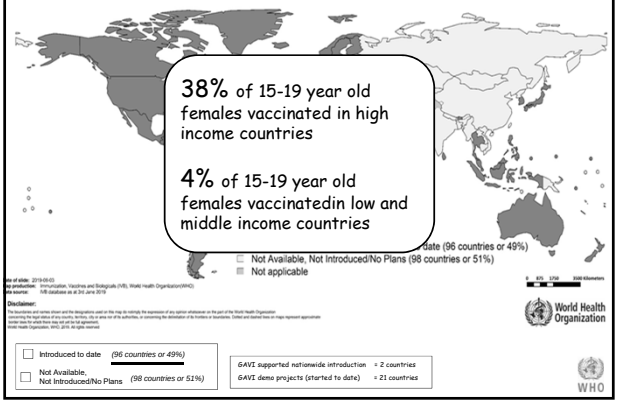




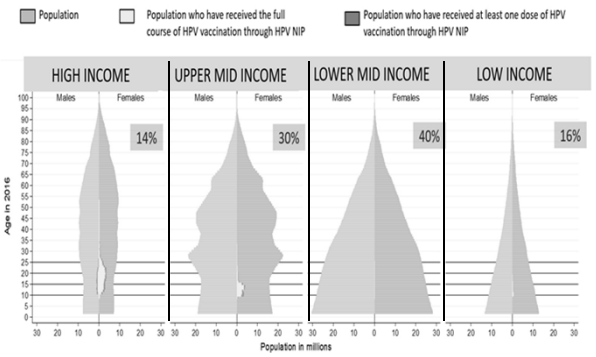
Gender inequity



Countries with HPV vaccine in the national immunization programme (status June 2019)



Population pyramids and the number of people vaccinated through national HPV vaccination programmes by income (by the end of 2016)



Courtesy of Laia Bruni, ICO, Barcelona

Human papillomavirus (HPV) vaccine coverage achievements in low and middle-income countries 2007–2016

Papillomavirus Research 2017;4:72-8.

Katherine E. Gallagher[a,b,*], Natasha Howard[c], Severin Kabakama[b], Sandra Mounier-Jack[c], Helen E.D. Burchett[c], D. Scott LaMontagne[d], Deborah Watson-Jones[a,b]

1.7 million girls reached and 1.4 million fully vaccinated

in 78% of low- and middle-income countries vaccine coverage above 80%

in 80% of high-income countries vaccine coverage less than 50%

Introduction of a National HPV vaccination program into Bhutan

Vaccine 2015;33:3726-30

Tandin Dorji[a], Ugyen Tshomo[b], Sangay Phuntsho[a], Tshewang Dorji Tamang[a], Tshokey Tshokey[c], Iacopo Baussano[d], Silvia Franceschi[d], Gary Clifford[d,*]

Dose/round (campaign month)	No. of girls immunized			% Coverage		
	12 years (N = 6706[#])	13–18 years (N = 41,698)	Total (N = 48,674[#])	12 years	13–18 years	Total
1 (May)	6666	38,183	44,849	99	92	92
2 (July)[*]	6733	36,962	43,695	100	89	90
3 (Nov)[**]	6679	37,184	43,863	100	89	90

more then 1,7 million girls immunized against HPV in South Africa 2014-2018 !!!

94.6% of schools reached and 86.6% of age-eligible learners vaccinated

no major adverse events following immunization detected

Wealth inequity

Gender inequity

vs.

Number of people vaccinated through HPV national vaccination programmes globally (2018)

86 million girls/women have received at least one-dose of HPV vaccine through national HPV vaccination programmes

14 million boys/men have received at least one-dose of HPV vaccine through national HPV vaccination programmes

Bruni L. et al. IPV Meeting 2018, unpublished data

Why to vaccinate males against HPV ?

inability of natural anti-HPV antibodies to prevent HPV reinfection in males

HPV vaccination is the only reliable method to ensure immune protection against new HPV infections and subsequent HPV-induced cancers in males

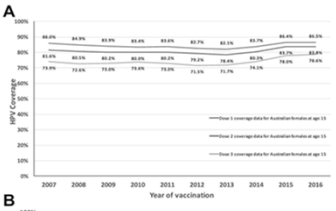
vaccination of males further increases protection of women against HPV-induced cancers by transmission interruption (herd protection)

Male HPV vaccination protects also against cervical cancer!

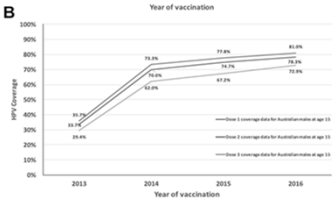
Gender-neutral vaccination

Country	Recommended	Publically Funded	Introduction	Coverage
Austria	X	X	2014	
Australia	X	X	2013	72.9% (2016)
Belgium	X			
Brazil	X	X	2016	
Canada	X	X	2013-2018	47.1% (2016)
Croatia	X	X	2017	
Czech Republic	X	X	2017	
Ireland	X			
Israel	X	X		
Italy	X	X	2017	
Norway	X			
Serbia	X	X	2017	
Sweden	X			
Switzerland	X	X	2016	
United States	X	X	2011	44.3% (2017)

Trend in HPV vaccine coverage at age 15 in Australia, 2013-2016



78.6%



72.9%

Brotherton and Bloem., Best Pract Res Clin Obstet Gynaecol 2017; in press.

National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2018

Tanja Y. Walker, MPH[1]; Laurie D. Elam-Evans, PhD[1]; David Yankey, PhD[1]; Lauri E. Markowitz, MD[2]; Charnetta L. Williams, MD[1]; Benjamin Fredua, MS[1,3]; James A. Singleton, PhD[1]; Shannon Stokley, DrPH[1]

TABLE 1. Estimated coverage with selected vaccines and doses among adolescents aged 13–17* years, by age at interview — National Immunization Survey-Teen (NIS-Teen), United States, 2018

	Age at interview (yrs), % (95% CI)†					Total	
	13	14	15	16	17	2018	2017
Vaccine	(n = 3,852)	(n = 3,875)	(n = 3,741)	(n = 3,751)	(n = 3,481)	(n = 18,700)	(n = 20,949)
Tdap§ ≥1 dose	87.1 (85.0–89.0)	87.7 (85.4–89.7)	89.7 (87.8–91.4)	89.0 (87.1–90.6)	91.0 (89.5–92.4)¶	88.9 (88.0–89.7)	88.7 (87.8–89.6)
MenACWY**							
≥1 dose	86.3 (84.2–88.1)	86.2 (84.0–88.1)	86.1 (83.7–88.2)	86.3 (84.0–88.3)	88.1 (86.3–89.6)	86.6 (85.6–87.5)††	85.1 (84.2–86.1)
≥2 doses§§	NA	NA	NA	NA	50.8 (47.7–53.8)	50.8 (47.7–53.8)††	44.3 (41.4–47.2)
HPV¶¶ vaccine							
All adolescents							
UTD***	39.9 (37.0–42.9)	50.3 (47.3–53.2)¶	54.0 (51.0–56.9)¶	54.5 (51.5–57.5)¶	57.5 (54.4–60.5)¶	51.1 (49.8–52.5)††	48.6 (47.3–49.9)
≥1 dose	62.6 (59.7–65.4)	66.9 (64.1–69.6)¶	69.7 (66.9–72.3)¶	71.2 (68.5–73.8)¶	70.1 (67.3–72.8)¶	68.1 (66.8–69.3)††	65.5 (64.3–66.7)
Females							
UTD	38.9 (35.0–42.9)	52.7 (48.5–56.8)¶	54.7 (50.4–59.0)¶	57.5 (53.3–61.6)¶	66.0 (61.8–70.1)¶	53.7 (51.8–55.6)	53.1 (51.2–55.0)
≥1 dose	61.1 (56.9–65.2)	68.6 (64.4–72.5)¶	70.7 (66.5–74.5)¶	73.5 (69.8–76.8)¶	76.3 (72.2–80.0)¶	69.9 (68.1–71.6)	68.6 (66.9–70.2)
Males							
UTD	40.9 (36.5–45.3)	47.7 (43.6–51.8)¶	53.2 (49.1–57.3)¶	51.8 (47.5–56.1)¶	50.0 (45.7–54.3)¶	48.7 (46.8–50.6)††	44.3 (42.6–46.0)
≥1 dose	64.0 (59.9–67.9)	65.1 (61.3–68.7)	68.7 (65.0–72.1)	69.2 (65.2–73.0)	64.7 (60.7–68.5)	66.3 (64.6–68.0)††	62.6 (60.9–64.2)

…

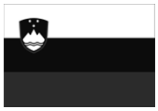
ECDC SCIENTIFIC ADVICE

Public consultation on draft guidance for introduction of HPV vaccines in EU countries: focus on 9-valent HPV vaccine and vaccination of boys and people living with HIV

Stockholm, 1 april 2019

The coverage for three/two doses of HPV quadrivalent/nonavalent vaccine in Slovenia

- school year 2009/2010 48.7 %
- school year 2010/2011 55.3 %
- school year 2011/2012 54.9 %
- school year 2012/2013 48.9 %
- school year 2013/2014 45.5 %
- school year 2014/2015 44.8 %
- school year 2015/2016 44.0 %
- school year 2016/2017 46.4 %
- school year 2017/2018 49.9 %



Odgovorne institucije in politika ne izražajo jasne podpore cepljenju

Zelo slaba kampanja za cepljenje (kampanja s figo v žepu)

Neodzivnost/neprimeren odziv na slabo precepljenost

"Feminizacija" cepiva

Medijski boj dveh proizvajalcev cepiv

Medijska diskreditacija vodilnih strokovnjakov v državi

Pomanjkljiv/prepozen program za zamudnice

Zahtevana privolitev staršev za cepljenje

Glasni nasprotniki cepljenja

Glasni nasprotniki obveznega cepljenja

Introduction of a National HPV vaccination program into Bhutan

Vaccine 2015;33:3726-30

Tandin Dorji[a], Ugyen Tshomo[b], Sangay Phuntsho[a], Tshewang Dorji Tamang[a], Tshokey Tshokey[c], Iacopo Baussano[d], Silvia Franceschi[d], Gary Clifford[d,*]

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2 (July)^	6733	36,962	43,695	100	89	90
3 (Nov)^^	6679	37,184	43,863	100	89	90

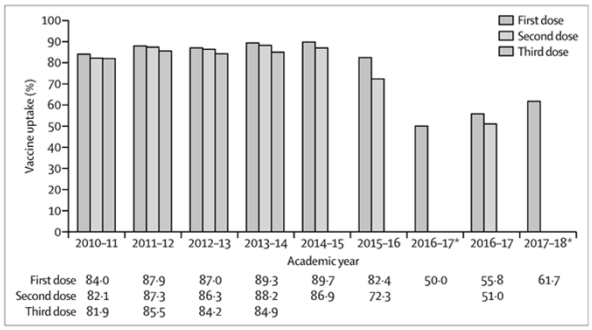
The HPV vaccination campaign was launched on 5 May 2010 by Her Majesty Ashi Kesang Choden Wangchuckattended by members of the royal family, government leaders, other dignitaries, representatives from the UN and other agencies, teachers and students.

more then 1,7 million girls immunized against HPV in South Africa 2014-2018 !!!

94.6% of schools reached and 86.6% of age-eligible learners vaccinated

no major adverse events following immunization detected

Rapid response to HPV vaccination crisis in Ireland



	2010–11	2011–12	2012–13	2013–14	2014–15	2015–16	2016–17*	2016–17	2017–18*
First dose	84·0	87·9	87·0	89·3	89·7	82·4	50·0	55·8	61·7
Second dose	82·1	87·3	86·3	88·2	86·9	72·3		51·0	
Third dose	81·9	85·5	84·2	84·9					

Corcoran B et al. Lancet 2018; 391:2103.

Simon Harris T.D.
Minister of Health

I am here to demonstrate my trust in HPV immunisation and how it protects women from developing cancer later in their lives.

We all know that the vaccine works and that it works very well.

No serious side effects in any country can be scientifically attributed to this vaccine.

Thanks to the HPV vaccine, Ireland's daughters, mothers, wives, sisters and loved ones can live long and fulfilling lives without living in fear of cervical cancer.

I, as Minister of Health continue to pledge my full support to the HPV vaccination program and the tremendous work carried out by many people sitting here in this room today.

IZJAVA O PRIVOLITVI

Spodaj podpisani _____, zakoniti zastopnik deklice:

Ime in priimek _____, rojene _____

SOGLAŠAM, da se deklico cepi proti okužbi s HPV.

Za varno cepljenje Vaše deklice proti HPV potrebujemo nekaj podatkov, zato Vas prosimo, da odgovorite na naslednja vprašanja:

Ali vaša deklica trenutno preboleva kakšno bolezen? Katero?	NE	DA	_____
Ali jemlje kakšna zdravila? Katera?	NE	DA	_____
Ali je imela kdaj hujšo alergijo na hrano? Na katero?	NE	DA	_____
Ali je imela kdaj hujšo alergijo na zdravila? Na katera?	NE	DA	_____
Ali je imela kdaj hujšo reakcijo po cepljenju? Po katerem?	NE	DA	_____
Ali nam želite še kaj sporočiti?	NE	DA	

Datum: Podpis zakonitega zastopnika:

The State of Vaccine Confidence 2016: Global Insights Through a 67-Country Survey

EBioMedicine 2016;12:295-301

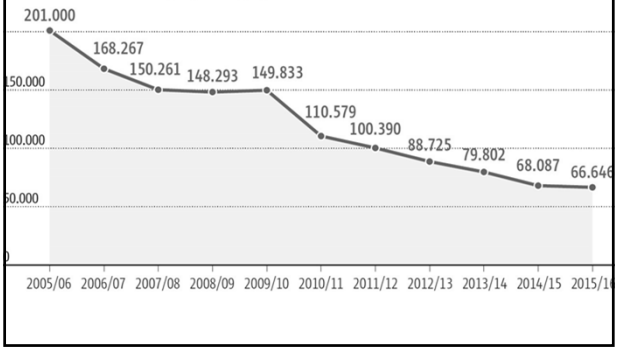
Heidi J. Larson, PhD [a,b,*,1], Alexandre de Figueiredo, MSc [c,1], Zhao Xiahong, BSc [d], William S. Schulz, MSc [a], Pierre Verger, PhD [e,f,g,h], Iain G. Johnston, PhD [i], Alex R. Cook, PhD [d,j], Nick S. Jones, PhD [c]

Slovenia?

Vaccines are important for children to have	= 64/67
Overall I think vaccines are safe	= 58/67
Overall I think vaccines are effective	= 53/67
Vaccines are compatible with my religious beliefs	= 64/67

Število cepljenih

prebivalcev Slovenije proti gripi



Seasonal influenza coverage in the EU for over-65s

Country	Year	65+ coverage
Austria	2014	20.3
Belgium	2013	58
Bulgaria	-	-
Croatia	-	-
Cyprus	-	-
Czech Republic	2014	15.5
Denmark	2016	40.8
Estonia	2016	2.8
Finland	2017	45.7
France	2016	49.8
Germany	2017	34.8
Greece	2014	48.9
Hungary	2016	19.9
Ireland	2017	53.5
Italy	2017	52
Latvia	2016	4.3
Lithuania	2016	22.6
Luxembourg	2016	38
Malta	-	-
Netherlands	2015	66.8
Poland	2014	50.9
Portugal	2015	50.1
Romania	-	-
Slovakia	2016	13.3
Slovenia	2016	9.8
Spain	2017	51.4
Sweden	2016	49.1
United Kingdom	2016	70.5

'No jab, no pay:' Australia cuts benefits for parents who don't vaccinate kids

By Naomi Ng, for CNN
Updated 1032 GMT (1732 HKT) April 13, 2015

Parents who refuse to vaccinate their children can lose up to $11,000 of welfare benefits a year under a new government policy.

"The choice made by families not to immunize their children is not supported by public policy or medical research nor should such action be supported by taxpayers in the form of child care payments," said Australian Prime Minister Tony Abbott.

Australian "constant reminder" policy

Australian parents who don't vaccinate will be fined as a 'constant reminder' they should

Sonja Haller | USA TODAY
Published 10:22 p.m. UTC Jul 10, 2018

Anti-vaxxer parents will be docked $20 USD from their family tax benefits every two weeks, announced Dan Tehan, Minister for Social Services.

"Immunization is the safest way to protect children from vaccine-preventable diseases," Tehan said.

"Parents who don't immunize their children are putting their own kids at risk as well as the children of other people."

Conclusions (i)

in the 12 years since its introduction, HPV vaccination has seen many positive developments: a reduced number of doses and more flexible schedules have reduced cost and facilitated program implementation

2vHPV, 4vHPV and 9vHPV vaccines are extremely safe, highly effective but underused (especially in males and only exceptionally used in HIV+ individuals)

as both genders are responsible for HPV transmission, both genders should get vaccinated to share the burden in reducing the risk of HPV-related disease, as well as have equal access to direct vaccine benefits

Conclusions (ii)

only gender-neutral vaccination will lead to control of HPV-related diseases in both women and men as well as maximizing prevention of cervical cancer

failure to implement gender-neutral, age-extended and global HPV vaccination looks like a missed public health opportunity

the magnitude of prevention potential of HPV-related cancers is currently not rivalled for any other neoplastic disease in humans

GIVE LOVE NOT HPV

We know HPV is causing cervical cancer

We have excellent HPV screening tests and HPV vaccines

We can envisage cervical cancer elimination

ipvs International Papillomavirus Society

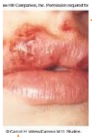
Impact and Safety of HPV vaccination in Scotland

Professor ME Cruickshank
Aberdeen Centre for Women's Health Research
University of Aberdeen, Aberdeen, UK

Scottish Cervical Cancer Prevention Programme (SCCPP)
funded by CSO

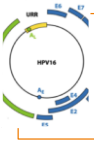
Human Papillomavirus

Rogoni-Stern 1842 reports relative risks of cervical cancer



Infectious cause of cancer?

HPV first seen under electron microscope 1942



Harald zur Hausen identified and attributed HPV to cervical cancer 1976

HPV vaccine 2006

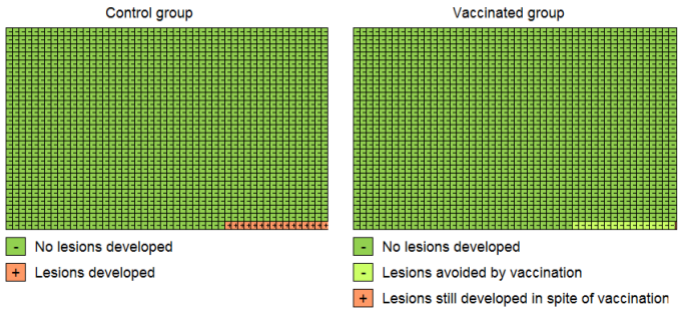
Successful vaccine programmes

- Clinically effective vaccine
- High Coverage/uptake rates

Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors (Review)

Arbyn M, Xu L, Simoens C, Martin-Hirsch PPL

Figure 8. Modified Cates plot: Number of cases of CIN2+ associated with HPV16/18 occurring in wom who were all hrHPV DNA negative at baseline. 16 out of 1000 non-vaccinated women developed the lesic (left) whereas fewer than one (0.2) out 1000 vaccinated women developed the lesion (right). Relative risk= ((95% CI: 0.01 to 0.05).



CIN associated with HPV16/18: high-certainty evidence that HPV vaccines lower risk of CIN2+ 99% (RR 0.01, 95% CI 0 - 0.05) and CIN3+ by 99% (RR 0.01, 95% CI 0.00 to 0.10).
Moderate certainty evidence for cervical glandular intraepithelial neoplasia (CGIN) is moderate: 90% reduction in risk of CGIN (RR 0.10, 95% CI 0.01 to 0.82).

Cochrane Library
Cochrane Database of Systematic Reviews

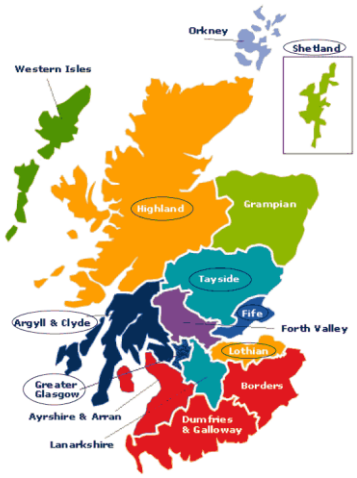
Prophylactic vaccination against human papillomaviruses to prevent cervical cancer and its precursors (Review)

Arbyn M, Xu L, Simoens C, Martin-Hirsch PPL

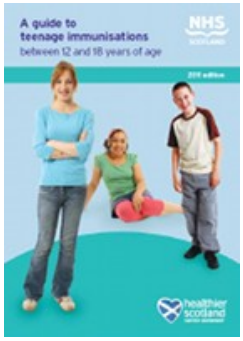
Safety:
The risk of serious adverse events was similar between those women who received HPV vaccine and those in the control arms (669 versus 656/10,000, RR 0.98 (0.92 to 1.05)
Few deaths and following investigation, none were considered to be attributable to the vaccine

What can be achieved in a public immunisation programme?

- Scottish surveillance on impact of HPV immunisation programme

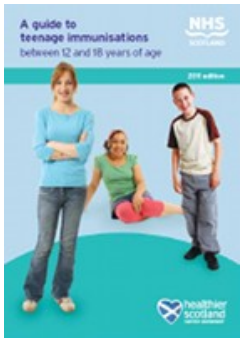


HPV Immunisation



- UK Programme
- School based
- Age 12-13 years
- Sept 2008
  - Bivalent vaccine HPV16/18
- 2012
  - Quadrivalent vaccine
  - HPV 16/18/6/11
- 2014 2 Dose regime

HPV Immunisation

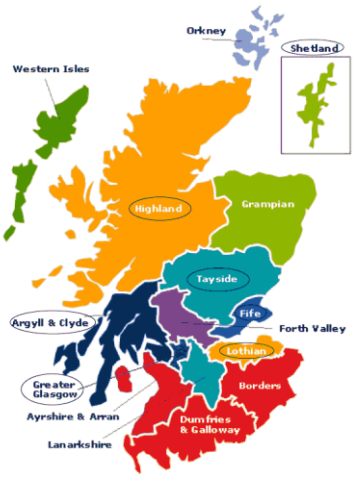


- Catch-up campaign 2008-2011
- Bivalent vaccine
- Girls up to 18 years (Born after 1 September 1990)
- 3 doses
- Uptake in catch-up 65% for 3 doses

National Health Service (NHS Scotland) and Scottish Cervical Screening

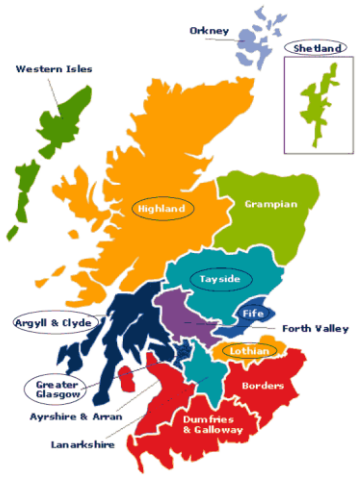
NHS SCOTLAND

- Organised call recall
- Age 20-60 years up to 2016
- 3 yearly LBC
- Free with national health service
- National Call-Recall System (SCCRS)
- National Colposcopy System (NCCIAS)

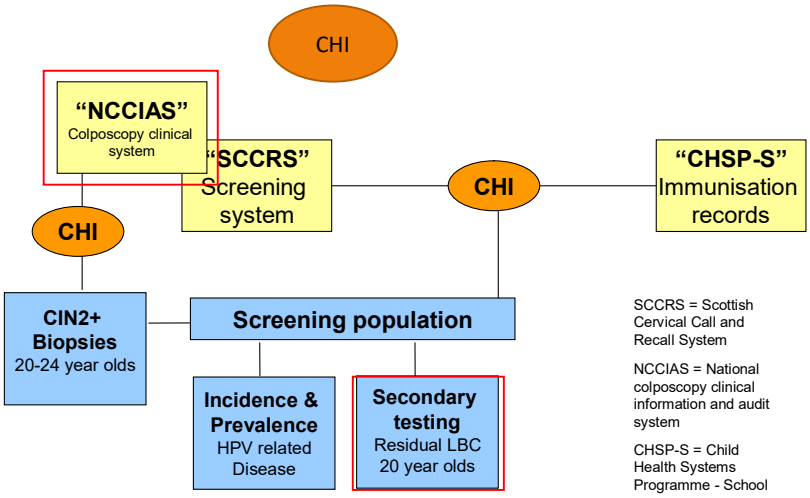


National Health Service (NHS Scotland) and Scottish Cervical Screening

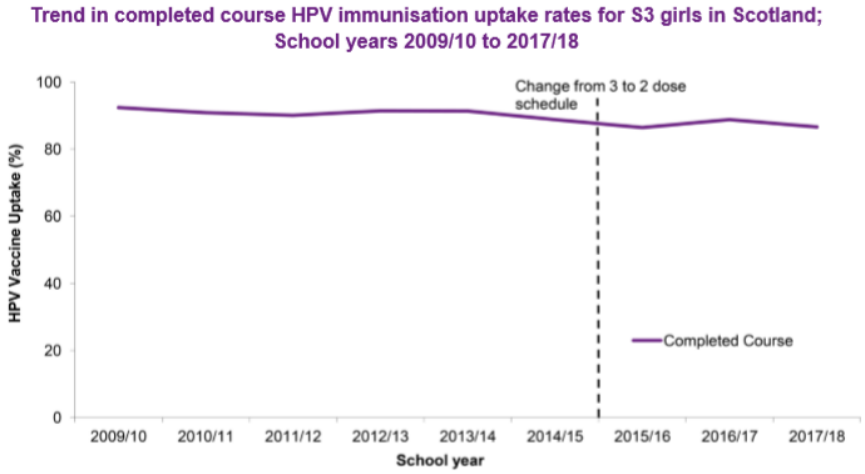
- Changed 2006 to age 25-65 years
- 3 yearly LBC up to 50
- 5 yearly after 50 years
- 71 % uptake



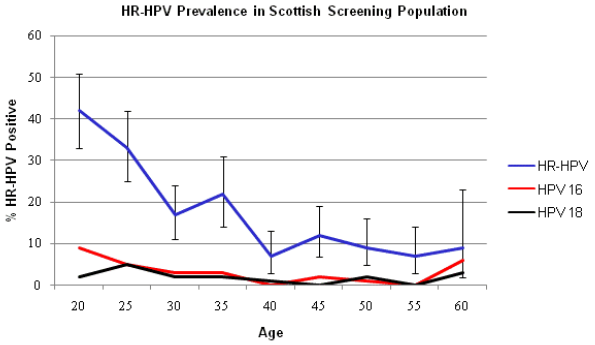
Data linkage ensures robust analyses



Vaccine uptake in 12/13 year old girls in Scotland



HPV is common in Scotland

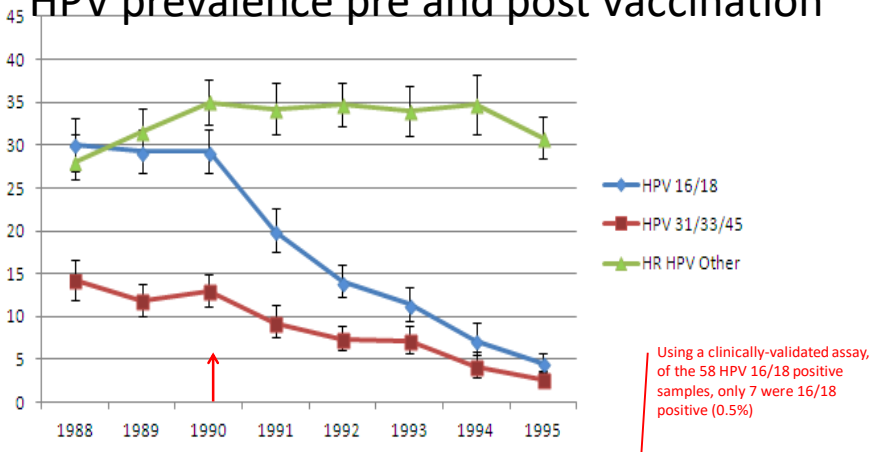


18% HR-HPV in women aged 20-60 attending for routine cervical screening

~280,000 infections in screen age women in Scotland.

	2007	2008	2009	2010	2011	2012	2013
CIN3	2,405	2,658	3,230	2,599	2,596	2,536	2,280
Cervical Cancer	293	314	328	332	317	304	309

HPV prevalence pre and post vaccination



Using a clinically-validated assay, of the 58 HPV 16/18 positive samples, only 7 were 16/18 positive (0.5%)

HPV 16/18 prevalence reduced from **30.0%** (26.9, 33.1%) **in 1988 cohort** to **4.5%** (3.5, 5.7%) **in the 1995 cohort**

HPV 31/33/45 prevalence reduced from **14.2%** (12-16.7%) **in the 1988 cohort** to **2.6%** (95% CI: 1.9-3.6%) **in the 1995 cohort**

Other HR-HPV - no significant changes

Kavanagh K, Pollock KG, Cuschieri K, Palmer T, Cameron RL, Bhatia R, Moore C, Cubie H, Cruickshank M, Robertson C. Lancet Infect Dis. 2017 Sep 28. pii: S1473-3099(17)30468-1

Treatments for CIN at colposcopy for women (age 20-21 years, by year of referral to colposcopy in Scotland

(Total number: 7013)

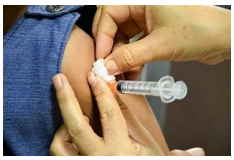
Treatment at colposcopy	2008-09	2009-10	2010-11	2011-12	2012-13	2013-14	Trend
Ablation (cold coagulation/ cryotherapy)	7.74% (104)	7.81% (112)	3.56% (44)	2.79% (35)	3.08% (29)	0.75% (6)	P < 0.01
Excison LLETZ/Cone/Type 3 excision)	15.92% (214)	11.65% (167)	11.72% (145)	12.44% (156)	8.92% (84)	6.98% (56)	P < 0.01
None	74.93% (1007)	79.78% (1144)	84.56% (1046)	83.01% (1041)	87.26% (822)	91.77% (736)	P < 0.01

Reduction in colposcopy workload and associated clinical activity following human papillomavirus (HPV) catch-up vaccination programme in Scotland: an ecological study

ME Cruickshank,[a] J Pan,[b] SC Cotton,[a] K Kavanagh,[b] C Robertson,[b,c] K Cuschieri,[d] H Cubie,[d] T Palmer,[e] KG Pollock[c]

BJOG An International Journal of Obstetrics and Gynaecology

HPV VACCINE SAFETY: Adverse Event from Immunisation (AEFI) monitoring



Two systems

- Passive: UK - MHRA – yellow card system
- Scotland – SMR01 system

'Pain at injection site'

Excellent safety profile

Scottish Government rapport is good

- AE queries from members of public dealt with promptly - TRUST

Adverse event monitoring of the human papillomavirus vaccines in Scotland. Cameron RL, Ahmed S, Pollock KG. Intern Med J. 2016 Apr;46(4):452-7.

INTERNAL MEDICINE JOURNAL

Adverse event monitoring of the human papillomavirus vaccines in Scotland

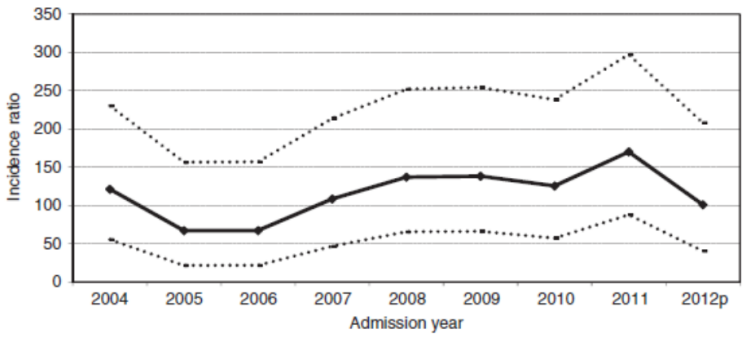
R. L. Cameron, S. Ahmed and K. G. J. Pollock

Vaccine Preventable Diseases, Health Protection Scotland, Glasgow, UK

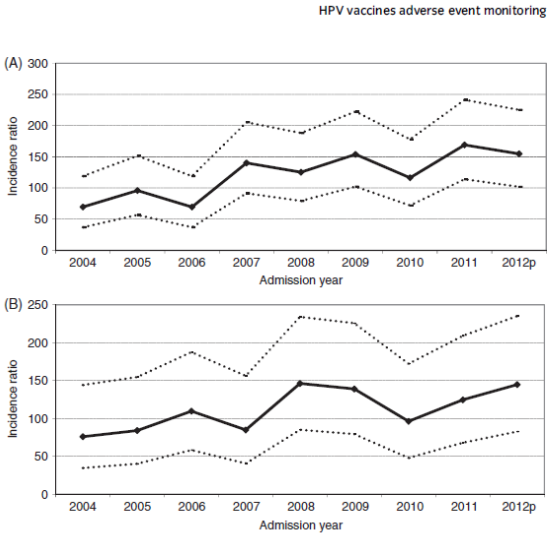
- Use SMR01 data – routinely collected data on diagnosis in secondary care
- ICD 10 coding
- Baseline calculated from 2003-2007
- Identified 60 conditions where concerns raised in relation to AEFI
  - Neurological
  - Autoimmune

54 conditions no change in incidence following introduction of the vaccine

* No ICD 10 code for POTS



Incidence ratio of Bell's Palsy in 12-18 year od girls. Observed incidence level did not increase over expected



A. Incidence ratio of coeliac disease in girls aged 12-18 years.
B. Incidence ratio of coeliac disease in boys aged 12-18 years.

Contents lists available at ScienceDirect
Vaccine
journal homepage: www.elsevier.com/locate/vaccine

The association of adverse events with bivalent human papilloma virus vaccination: A nationwide register-based cohort study in Finland

Jozica Skufca [a], Jukka Ollgren [a], Miia Artama [b,*], Esa Ruokokoski [a], Hanna Nohynek [a], Arto A. Palmu [b]

[a] Department of Health Security, Infectious Diseases Control and Vaccinations Unit, National Institute for Health and Welfare (THL), Helsinki, Finland
[b] Department of Public Health Solutions, Public Health Evaluation and Projection Unit, National Institute for Health and Welfare (THL), Tampere, Finland

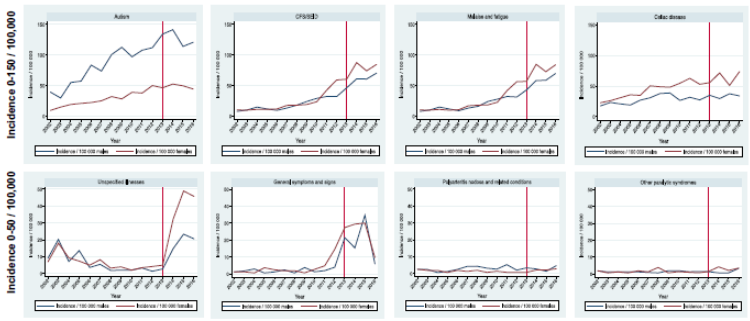


Fig. 1. Incidence rates per 100,000 person-years in females 11–15 years, Finland, 2002–2016. Outcomes (n = 8) with significant increases of the incidence rates in the post-vaccination period. Vertical line indicates year 2013 when HPV vaccination was introduced in the national vaccination programme in Finland.

RESEARCH

Prevalence of cervical disease at age 20 after immunisation with bivalent HPV vaccine at age 12-13 in Scotland: retrospective population study

Tim Palmer,[1] Lynn Wallace,[2] Kevin G Pollock,[3,4] Kate Cuschieri,[5] Chris Robertson,[3,6,7] Kim Kavanagh,[7] Margaret Cruickshank[8]

[1]Department of Pathology, University of Edinburgh, Edinburgh, UK
[2]Information Services Division, NHS Scotland, Glasgow, UK
[3]Health Protection Scotland, Glasgow, UK
[4]School of Health and Life Science, Glasgow Caledonian University, Glasgow, UK
[5]Scottish Human Papillomavirus

ABSTRACT

OBJECTIVE
To quantify the effect on cervical disease at age 20 years of immunisation with bivalent human papillomavirus (HPV) vaccine at age 12-13 years.

DESIGN
Retrospective population study, 1988-96.

SETTING
National vaccination and cervical screening

immunisation was associated with increasing vaccine effectiveness: 86% (75% to 92%) for CIN grade 3 or worse for women vaccinated at age 12-13 compared with 51% (28% to 66%) for women vaccinated at age 17. Evidence of herd protection against high grade cervical disease was found in unvaccinated girls in the 1995 and 1996 cohorts.

CONCLUSIONS
Routine vaccination of girls

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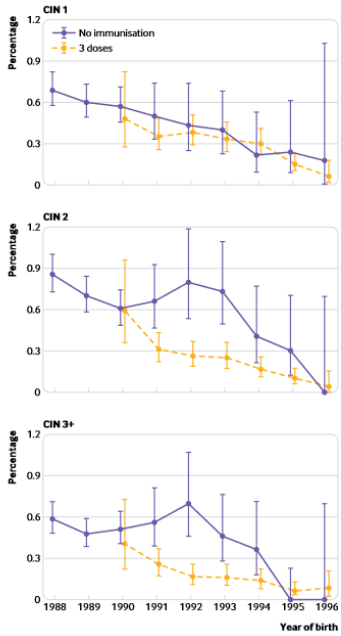
HPV vaccine linked to 'dramatic' drop in cervical disease

4 April 2019 Share

The routine vaccination of girls with the HPV vaccine in Scotland has led to a "dramatic" drop in cervical disease in later life, new research suggests.

Rates of CIN (% of women screened by year of birth and HPV vaccination status



Palmer T et al
BMJ 2019

1988-1994 cohorts: negative first smear

		Non immunised n (%)		Fully immunised n (%)		p value χ^2
Women neg initial cytology	93852	50776		43076		
No with samples at age 23-25 years	62482	36754 (72·4)		25728 (59.7*)		
Cytology	Negative	31631	86·1	23267	90·4	<0.0001
	Low grade	3987	10·8	2218	8·6	
	High grade	1136	3·1	243	1·0	
Histology	Negative	35387	96·27	25473	98.99	<0·0001
	HPV/CIN1	335	0·91	89	0·35	
	HG CIN	1021	2·78	166	0·65	
	Cancer	13	0·04	2	0·01	

Follow-up for 1988-1992 cohorts is 3 years, 1993 cohort is 2 years, and 1994 cohort is 1 year.

1988-1994 cohorts: abnormal first smear

		Non immunised n (%)		Fully immunised n (%)		p value χ^2
Women abnormal initial cytology	18386	11070		7316		
No with samples at age 23-25 years	11075	7721 (69.7)		3354 (45·8*)		
Cytology (% of women screened)	Negative	5788	74·9	2697	80·4	<0.0001
	Low grade	1573	20·4	600	17.9	
	High grade	360	4·7	57	1·7	
Histology (% of women screened)	Negative	7043	91·05	3220	95·81	<0·0001
	HPV/CIN1	238	3·08	63	1.87	
	HG CIN	452	5.84	78	2·32	
	Cancer	2	0·03	0	0	

Follow-up for 1988-1992 cohorts is 3 years, 1993 cohort is 2 years, and 1994 cohort is 1 year.

What has been in the impact in Scotland?

Reduction in HPV 16 and 18 and HPV 31, 33 and 45

Cross-protection at least 7.5 years long

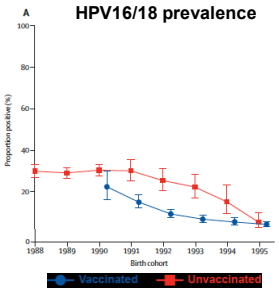
Evidence of herd protection vs. HPV 16, 18, 31, 33 and 45 in unvaccinated girls

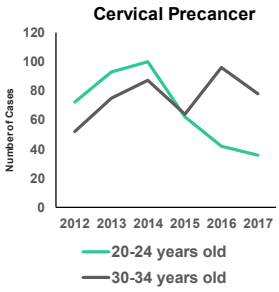
Vaccine associated with 88% and 94% reduction in CIN2 and 3+ at population level

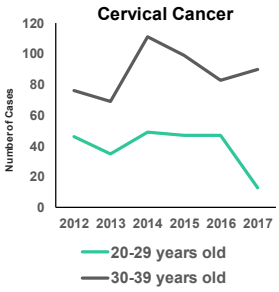
Biggest reduction in disease in more deprived women

Reduction in treatments performed at colposcopy

Impact of HPV vaccine on young women in Scotland: herd immunity and reductions in cervical precancer and cervical cancer







Kavanaugh et al, Lancet Infect Dis 17:1293-1302, 2017

From Scotland cancer statistics web site: https://www.isdscotland.org/Health-Topics/Cancer/Cancer-Statistics/Female-Genital-Organ/#cervix

Thank you

HPS
Kevin Pollock
Katy Sinka

Scottish Specialist Virology Centre
Kate Cuschieri
Heather Cubie
Catherine Moore

University of Aberdeen
Seonaidh Cotton
Ami Munro
Judith Wilson
Collette Gillespie

University of Strathclyde
Chris Robertson
Kim Kavanagh
Jiafeng Pan

University of Edinburgh
David Weller
Christine Campbell
Marie Gallagher

NHS Grampian
Louise Smart

NHS Lanarkshire
Sarah Liptrott
Val Harper

NHS Lothian
Camille Busby-Earle
Aliasdair Williams

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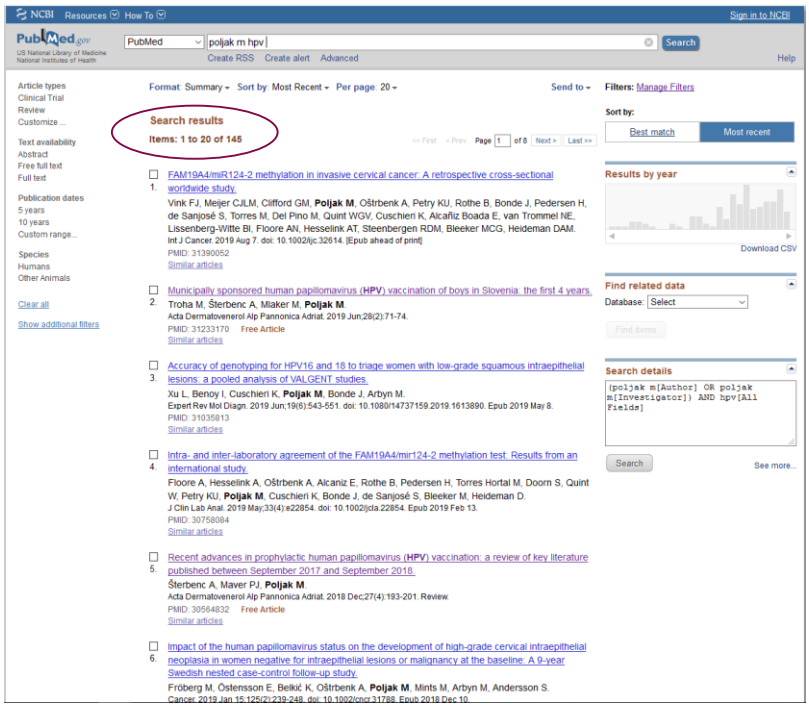
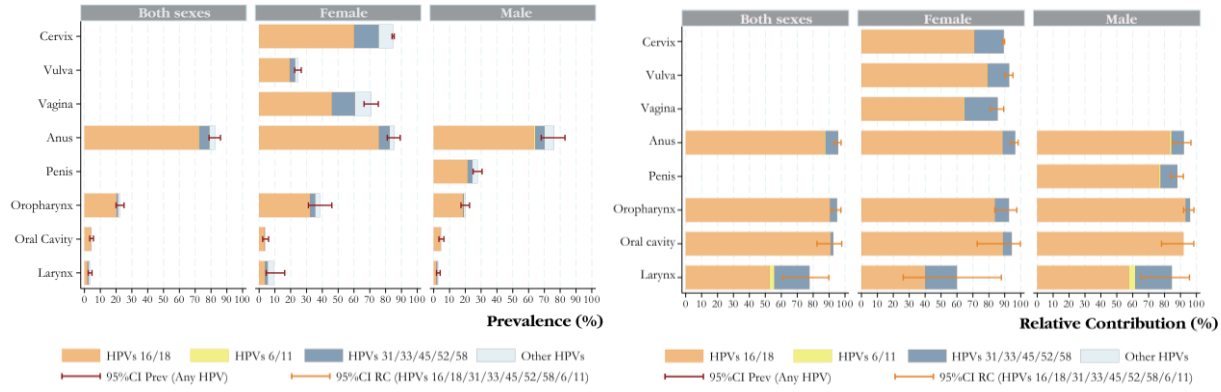
XXXIV Congresso Nazionale
della S.I.C.P.C.V.
25-26 September 2019

Cepiva proti HPV: pregled najpomembnejših objav v obdobju september 2018-september 2019

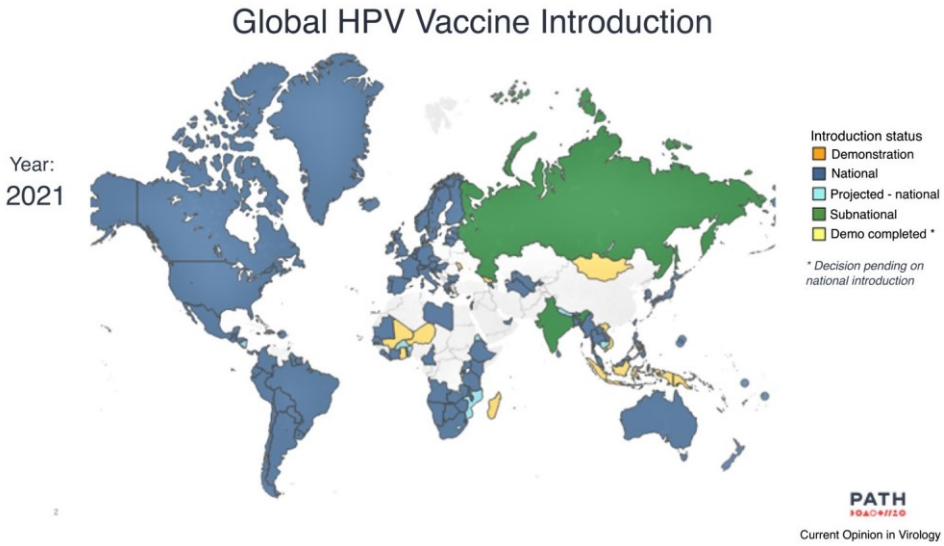
ASIST. DR. ANJA ŠTERBENC, DR. MED.
PROF. DR. MARIO POLJAK, DR. MED.
INŠTITUT ZA MIKROBIOLOGIJO IN IMUNOLOGIJO
MEDICINSKA FAKULTETA, UNIVERZA V LJUBLJANI



Breme s HPV povezanih rakov, ki jih povzročajo genotipi, vključeni v 9vHPV



De Sanjose S in sod., JNCI Cancer Spectrum. 2019;2:pky045.



Sanjose S, et al. Current Opinion in Virology 2019;39:16-22.

Priporočila in smernice

FDA News Release

FDA approves expanded use of Gardasil 9 to include individuals 27 through 45 years old

SHARE TWEET LINKEDIN PIN IT EMAIL PRINT

For Immediate Release October 5, 2018

- In a study in approximately **3,200 women 27 through 45 years of age**, followed for an average of 3.5 years, **Gardasil was 88 % effective** in the prevention of a combined endpoint of **persistent infection, genital warts, vulvar and vaginal precancerous lesions, cervical precancerous lesions, and cervical cancer** related to HPV types covered by the vaccine.
- The FDA's approval of Gardasil 9 in women 27 through 45 years of age is based on these results and new data on long term follow-up from this study.

Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices

Elissa Meites, MD[1]; Peter G. Szilagyi, MD[2]; Harrell W. Chesson, PhD[3]; Elizabeth R. Unger, PhD, MD[4]; José R. Romero, MD[5]; Lauri E. Markowitz, MD[1]

MMWR Morb Mortal Wkly Rep 2019;68:698–702

Recommendations

Children and adults aged 9 through 26 years. HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years. Catch-up HPV vaccination is recommended for all persons through age 26 years who are not adequately vaccinated.†

Adults aged >26 years. Catch-up HPV vaccination is not recommended for all adults aged >26 years. Instead, shared clinical decision-making regarding HPV vaccination is recommended for some adults aged 27 through 45 years who are not adequately vaccinated. (Box). HPV vaccines are not licensed for use in adults aged >45 years.

Human papillomavirus vaccination: The ESGO–EFC position paper of the European society of Gynaecologic Oncology and the European Federation for colposcopy

Eur J Cancer 2019;116:21-6

Elmar A. Joura [a,b], Maria Kyrgiou [c,d,*], Francisco X. Bosch [e,f,g], Vesna Kesic [h], Pekka Niemenen [i], Charles WE. Redman [j], Murat Gultekin [k]

ECDC SCIENTIFIC ADVICE

Public consultation on draft guidance for introduction of HPV vaccines in EU countries: focus on 9-valent HPV vaccine and vaccination of boys and people living with HIV

Stockholm, 1 april 2019

Izsledki, pridobljeni v kliničnih poizkusih

Efficacy and safety of prophylactic HPV vaccines. A Cochrane review of randomized trials

M. Arbyn & L. Xu

Expert Rev Vaccines 2018;17:1085-91

- All evaluated vaccines offered **excellent protection against cervical intraepithelial neoplasia of grade 2 or 3 (CIN2 or CIN3) and adenocarcinoma in situ** associated with HPV16/18 infection in young women who were not initially infected with hrHPV or HPV16/18. Vaccine efficacy was lower regardless of HPV DNA status.
- Vaccine efficacy was **lower in mid-adult women**.
- **No protection** against cervical precancer was found in **mid-adult women unselected by HPV DNA status** at enrollment.

HPV infections and cytologic abnormalities in vaccinated women 21–34 years of age: Results from the baseline phase of the Onclarity trial

Thomas C. Wright Jr [a,*], Valentin Parvu [b], Mark H. Stoler [c], Salma Kodsi [b], Karen Eckert [b], Karen Yanson [b], Charles K. Cooper [b]

Gynecologic Oncology 2019;153:259-65

- The impact of HPV vaccination was determined in a cervical cancer screening population from the USA-based, Onclarity Trial.
- HPV and cytology testing were determined in **14,153 women, 21–34 years**; and compared by vaccination status.
- The prevalence of **overall HPV, and genotypes 16, 18, 31, and 33/58** were significantly **lower in vaccinated women for each age group** (21-24 y, 25-29 y, 30-34 y) and all ages.
- Prevalence of **≥LSIL cytology** (for any HPV result), and **≥CIN2** (only for HPV 16+ or 18+ cases), was **lower in vaccinated women**.
- Data in this article suggest that **„catch-up" vaccination provides benefit** for adolescents and young adults.

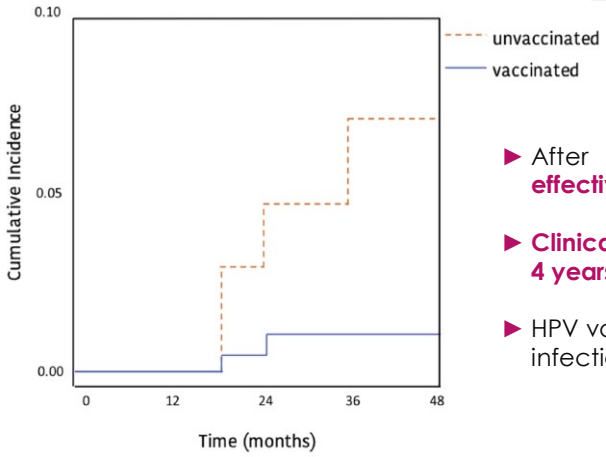
Nine-valent HPV vaccine efficacy against related diseases and definitive therapy: comparison with historic placebo population☆·☆☆

Anna R. Giuliano [a,*], Elmar A. Joura [b], Suzanne M. Garland [c,d,e], Warner K. Huh [f], Ole-Erik Iversen [g,h], Susanne K. Kjaer [i,j], Alex Ferenczy [k], Robert J. Kurman [l,m], Brigitte M. Ronnett [l,m], Mark H. Stoler [n], Oliver M. Bautista [o], Erin Moeller [o], Michael Ritter [o], Christine Shields [o], Alain Luxembourg [o]

Gynecol Oncology 2019;154:110-7

- The 9vHPV vaccine **prevents 98% of high-grade cervical dysplasia related** to the 9 HPV types covered by the vaccine.
- The 9vHPV vaccine **prevents 98% of cervical surgeries related to the 9 HPV types** covered by the vaccine.
- Vaccine **did not prevent diseases related to HPV types detected at baseline** but reduced diseases related to other HPV types.
- While early vaccination in HPV naïve persons is best, sexually active persons may benefit from catch-up vaccination programs.
- These data will be important to inform future public health vaccination recommendations.

SPERANZA project: Impact of vaccination on disease relapse after cervical conization



- After conization, HPV vaccine shows **80% clinical effectiveness in disease relapse prevention**.
- **Clinical benefits** of vaccination are demonstrated up to **4 years**.
- HPV vaccine has **no therapeutic effect** on prevalent HPV infection or disease.

Ghelardi A et al., Gynecol Oncol 2018;151:229-34.

Koliko odmerkov cepiva proti HPV in kdaj?

Two-dose recommendation for Human Papillomavirus vaccine can be extended up to 18 years – updated evidence from Indian follow-up cohort study

Papillomavirus Research 2019;7:75-81

Partha Basu[a,*], Richard Muwonge[a], Neerja Bhatla[b], Bhagwan M. Nene[c], Smita Joshi[d], Pulikottil O. Esmy[e], Usha Rani Reddy Poli[f], Geeta Joshi[g], Yogesh Verma[h], Eric Zomawia[i], Surendra S. Shastri[j], Sharmila Pimple[k], Devasena Anantharaman[l], Priya R. Prabhu[l], Sanjay Hingmire[c], Catherine Sauvaget[a], Eric Lucas[a], Michael Pawlita[m], Tarik Gheit[n], Kasturi Jayant[c], Sylla G. Malvi[c], Maqsood Siddiqi[o], Angelika Michel[m], Julia Butt[m], Subha Sankaran[l], Thiraviam Pillai Rameshwari Ammal Kannan[l], Rintu Varghese[l], Uma Divate[d], Martina Willhauck-Fleckenstein[m], Tim Waterboer[m], Martin Müller[m], Peter Sehr[p], Shachi Vashist[b], Gauravi Mishra[k], Radhika Jadhav[d], Ranjit Thorat[c], Massimo Tommasino[n], M. Radhakrishna Pillai[l], Rengaswamy Sankaranarayanan[q], for the Indian HPV vaccine study group

The protection offered by two doses of the quadrivalent HPV vaccine against incident and persistent infections in recepients at 15-18 years is comparable to that seen in 3-dose recipients at 15-18 years.

Effectiveness of varying number of doses and timing between doses of quadrivalent HPV vaccine against severe cervical lesions ☆

Christian Dehlendorff[a,1,*], Pär Sparén[b,1], Birgitte Baldur-Felskov[c], Eva Herweijer[b], Lisen Arnheim-Dahlström[b], Alexander Ploner[b], Ingrid Uhnoo[d], Susanne K. Kjaer[c,e]

Vaccine 2018;[Epub ahead of print]

Background: Based on immunogenicity studies, a 2 dose HPV vaccination-schedule was recently recommended for girls younger than 15 years. We aimed to investigate the effectiveness of quadrivalent HPV (qHPV) vaccination against CIN2 or worse (CIN2+), by age at vaccination, number of doses, and to test whether optimal timing of 2 doses of qHPV vaccine can confer the same level of protection as the originally recommended three dose-schedule.

Methods: A population-based cohort of all women aged 13–30 years, living in Denmark or Sweden during 2006–2013, was followed for qHPV vaccination status and first occurrence of CIN2+.

Results: The study cohort comprised 2,253,561 women, of which 33% were vaccinated during follow-up, and 1.7% were diagnosed with CIN2+. Vaccination at ages 13–16 and 17–19 was associated with a reduced risk of CIN2+ after 3 doses (IRR = 0.23, 95% CI 0.11–0.49, and IRR = 0.65, 95% CI 0.41–1.03, respectively), compared to being unvaccinated. After 1 and 2 doses there was a reduced risk, but not statistically significant. Women vaccinated ages 13–16 with 2 doses, where time between first and second dose was 5 months or longer showed no difference in risk compared to 3 doses.

Conclusions: Women vaccinated with 3 doses of qHPV showed a reduced risk of CIN2+ if they were vaccinated before age 20, with a further reduced risk if vaccinated before age 17. Vaccination with 2 doses, with the second dose 5 months or longer after the first dose, did not yield an increased risk of CIN2+, compared to 3 doses.

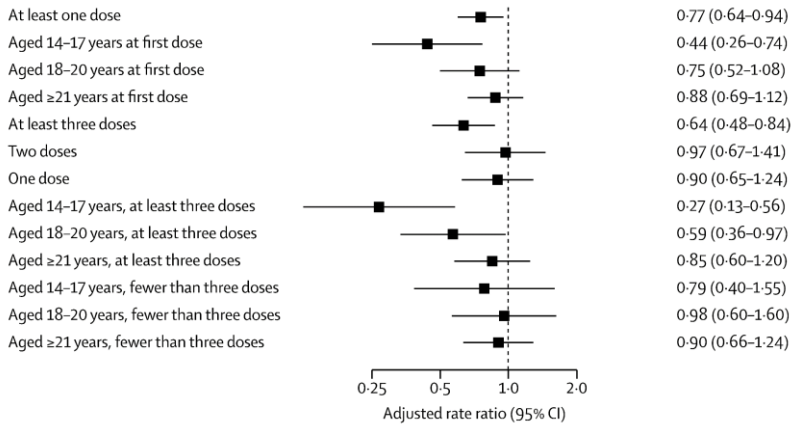
Antibody persistence after a single dose of quadrivalent HPV vaccine and the effect of a dose of nonavalent vaccine given 3-8 years later – an exploratory study

Vladimir Gilca[a,b], Chantal Sauvageau[a,b], Gitika Panicker[c], Gaston De Serres[a,b], Manale Ouakki[a], and Elizabeth R. Unger[c]

Hum Vaccin Immunother 2019;2:503-7

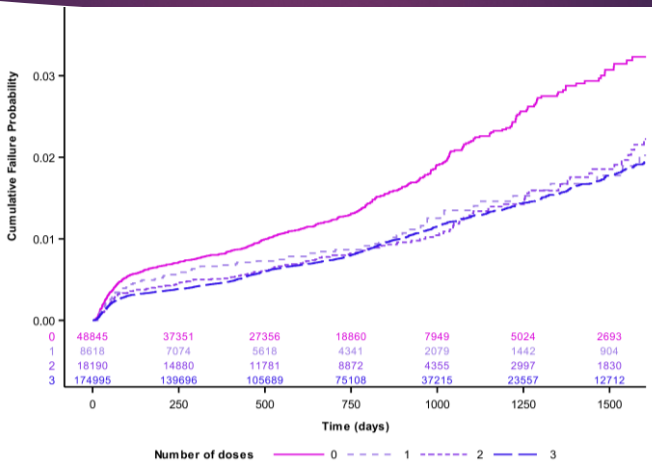
- Decision-making process regarding the 2-dose course completion in non-compliant vaccinees in jurisdictions which switched from 4vHPV to 9vHPV.
- Thirty-one girls aged 13–18 years participated in the study.
- **All participants were seropositive to 4 HPV types included in 4vHPV**.
- One month post-9vHPV administration **all 31 participants were seropositive to all 9 HPV types** with a 36.1 to 89.1-fold increase of GMTs.
- This schedule might be used in non-compliant vaccinees or when switching immunization programs from 4vHPV to 9vHPV.

Adjusted rate ratios and 95% CI for cervical intraepithelial neoplasia grade 3 or worse by HPV vaccination history



Silverberg MJ, et al. Lancet Child Adolesc Health 2018;2:707-14.

Cumulative failure probability plot for high grade cervical histopathology (CIN2/AIS+) among 250,648 screening women eligible for quadrivalent HPV vaccine at age 15 or under by final dose status



Brotherton JM in sod., Papillomavirus Research 2019; 8:100177.

Dose-related Effectiveness of Quadrivalent Human Papillomavirus Vaccine Against Cervical Intraepithelial Neoplasia: A Danish Nationwide Cohort Study

Freija Verdoodt,[1,©] Christian Dehlendorff,[2] and Susanne K. Kjaer[1,3]

Clin Infect Dis 2019;1-7

Background. A reduced, 2-dose schedule of human papillomavirus (HPV) vaccination has been endorsed for preadolescent women on the basis of immunogenicity data from randomized trials, and limited data suggest that even 1 dose may provide sufficient protection. Surveillance of the impact of <3 vaccine doses on clinical endpoints in the targeted age group is warranted.

Methods. We conducted a nationwide cohort study of all women aged 17–25 years, living in Denmark between 2006 and 2016. From nationwide registries, we extracted individual-level data on vaccination with the quadrivalent HPV (qHPV) vaccine at 16 years or younger, number of doses administered, diagnoses of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) or grade 3 or worse (CIN3+), and potential confounders. Using Poisson regression, we estimated incidence rate ratios (IRRs) with 95% confidence intervals (CIs) for CIN2+ and CIN3+, according to vaccination status.

Results. The cohort comprised 590 083 women, of which 215 309 (36%) women were vaccinated at ≤16 years, and among these, 40 742 (19%) received <3 vaccine doses. A total of 5561 women had a diagnosis of CIN3+. We found considerable vaccine effectiveness against CIN3+ after 1 (IRR, 0.38 [95% CI, .14–.98]), 2 (IRR, 0.38 [95% CI, .22–.66]), or 3 (IRR, 0.37 [95% CI, .30–.45]) vaccine doses, compared to unvaccinated women. Results were similar for CIN2+.

Conclusions. We find substantial effectiveness of qHPV vaccination against high-grade cervical precancerous lesions, among women vaccinated with 1, 2, or 3 doses at ≤16 years of age. One-dose vaccination appeared to provide similar protection as 3-dose vaccination.

Vaccine programme stakeholder perspectives on a hypothetical single-dose human papillomavirus (HPV) vaccine schedule in low and middle-income countries

Country	Date of national HPV vaccine intro[e]	Readiness and perceived advantages			Barriers			Information needs	
		Would support 1-dose	NITAG in place	Experience of off-label vaccine use	Community mobilisation needed[a]	HCW mobilisation needed[b]	Concerns over negative media	WHO recommendation required	Other country lessons on 1-dose
Ethiopia	2018[f]	Yes	Yes	No	Yes	Yes		Yes	Yes
Kenya	2019[f]	Yes	Yes	No	Yes	Yes	Yes	Yes	
Lesotho	2012–16	Yes	None (in development)	Under consideration					
Country Z	NA	Yes	Yes	No					
Nigeria	NA	Yes	Yes	No					
Senegal	2018[f]	Yes	Yes	No	Yes			Yes	
Uganda	2015-	Yes	Yes	No		Yes		Yes	
Zambia	2019[f]	Yes	Yes	Under consideration	Yes	Yes			
Zimbabwe	2018[f]	Yes	Yes	No[c]	Yes	Yes			
Lao PDR	2019[f]	Yes	Yes	No[c]	Yes			Yes	Yes
Nepal	NA	Yes	Yes	Under consideration				Yes	
Solomon Islands	2019[f]	Yes	None	Yes (current)				Yes	
Argentina	2011-	Yes	Yes	Yes (past)				No[d]	
Bolivia	2017-	Yes	Yes	Yes (past)				Yes[d]	
Brazil	2014-	Yes	Yes	Yes (past)					
Colombia	2012-	Yes	Yes	Yes (past)		Yes	Yes		Yes
Peru	2011-	Yes	Yes	Yes (past)			Yes	Yes	
Moldova	NA	Yes	Yes	No					

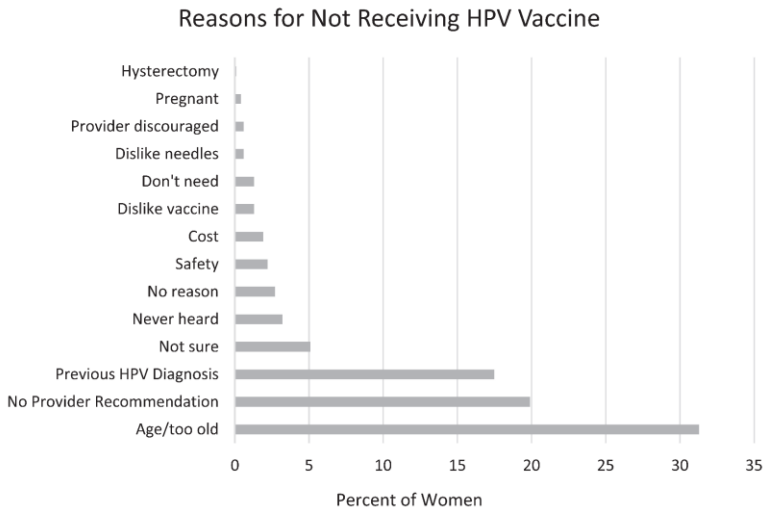
Gallagher K in sod., Papillomavirus Research 2018; 6:33-40.

Missed Opportunities for HPV Vaccination Among Vaccine-Eligible Women with High Grade Cervical Lesions

Savanah M. Russ *, Monica Brackney, James Meek, Linda M. Niccolai

Connecticut Emerging Infections Program, Yale School of Public Health, New Haven, CT, United States

Vaccine 2019;37:4262-7.



Should human papillomavirus vaccination target women over age 26, heterosexual men and men who have sex with men? A targeted literature review of cost-effectiveness

Nyi Nyi Soe[1], Jason J. Ong[2-4], Xiaomeng Ma[1], Christopher K Fairley[2-3], Phyu Mon Latt[6], Jun Jing[1], Feng Cheng[1*], Lei Zhang[1-3,5*]

Human Vaccines & Immunotherapeutics 2018

- 4/6 studies in **women over age 26 did not show cost-effectiveness**.
- 16/26 studies in **heterosexual men were cost-effective** - nonavalent vaccines, a low vaccine price, fewer required doses, and a long vaccine protection period were key drivers for cost-effectiveness.
- 4/4 studies on **MSM consistently reported cost-effectiveness**, particularly in MSM age <40 years and those who were HIV-positive.
- **Targeted HPV vaccination for MSM should be next priority in HPV** prevention after having established a solid girls vaccination programme.

A call for the introduction of gender neutral HPV vaccination to national immunisation programmes in Africa

Considering the **time it could take to fully implement programmes that would ensure herd immunity through female-only** HPV vaccination, we strongly **recommend gender-neutral HPV vaccination** for the prompt prevention of HPV-associated cancers.

Moreover, since **screening for HPV-associated cancers is largely unavailable to men** in Africa, vaccination represents the **single most important preventive measure** in this demographic.

Chido-Amajuoyi OG, et al. Lancet Glob Health 2019;7:e20-e21.

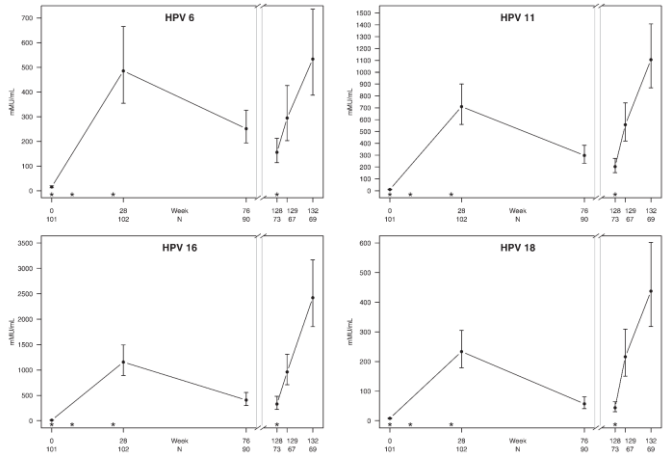
Cepljenje pri posameznikih z imunsko pomanjkljivostjo

A delayed dose of quadrivalent human papillomavirus vaccine demonstrates immune memory in HIV-1-infected men

Papillomavirus Res 2018;6:11-4.

G.B. Ellsworth[a], S.Y. Lensing[b], C.B. Ogilvie[c], J.Y. Lee[b], S.E. Goldstone[d], J.M. Berry-Lawhorn[e], N. Jay[e], E.A. Stier[f], J.S. Logan[g], M.H. Einstein[h,i], A. Saah[j], R.T. Mitsuyasu[k], D. Aboulafia[l,m], J.M. Palefsky[e], T.J. Wilkin[a,*]

Trend of geometric mean HPV titers by viral type over time including 95% CI



Human Papillomavirus Antibody Levels and Quadrivalent Vaccine Clinical Effectiveness in Perinatally Human Immunodeficiency Virus–infected and Exposed, Uninfected Youth

Clin Infect Dis 2019;pii:ciy1040

Anna-Barbara Moscicki,[1] Brad Karalius,[2] Katherine Tassiopoulos,[2] Tzy-Jyun Yao,[3] Denise L. Jacobson,[3] Kunjal Patel,[2] Murli Purswani,[4] and George R. Seage III[2]; for the Pediatric HIV/AIDS Cohort Study

Background. Persons who are infected with human immunodeficiency virus (HIV) are at high risk of human papillomavirus (HPV)-associated cancers. The objectives are to compare antibody titers to HPV 6, 11, 16, and 18 and rate of abnormal cytology between perinatally HIV-infected (PHIV) and perinatally HIV-exposed, uninfected (PHEU) youth.

Methods. This is a prospective observational cohort study of HPV4 vaccinated youth performed as part of the multicenter Pediatric HIV/AIDS Cohort Study Adolescent Master Protocol. Seroconversion and geometric mean titer (GMT) against HPV types 6, 11, 16, and 18 were calculated. Vaccine effectiveness included rates of abnormal cervical cytology and genital warts.

Results. Seroconversion to HPV 6, 11, 16, and 18 occurred in 83%, 84%, 90%, and 62% of 310 vaccinated PHIV youth compared to 94%, 96%, 99%, and 87% of 148 vaccinated PHEU youth, respectively ($P < .05$ for all comparisons). GMTs were lower in the PHIV vs PHEU within each category of HPV4 doses received. Higher GMTs were associated with younger age, lower HIV type 1 RNA viral load, and higher CD4% at first HPV4 vaccination, as well as shorter duration between last vaccine dose and antibody specimen. Abnormal cytology occurred in 33 of 56 PHIV and 1 of 7 PHEU sexually active vaccinated females, yielding incidence rates per 100 person-years of 15.0 (10.9 to 20.6) and 2.9 (0.4 to 22.3), respectively.

Conclusion. Antibody titers to HPV4 were lower for all serotypes in PHIV compared to PHEU youth. Protection against abnormal cytology was also diminished in sexually active PHIV females.

Quadrivalent HPV vaccine in HIV-1-infected early adolescent girls and boys in Kenya: Month 7 and 12 post vaccine immunogenicity and correlation with immune status

Vaccine 2018;36:7025-32

Nelly R. Mugo [a,b,c,*], Linda Eckert [d], Amalia S. Magaret [e,f,g], Anqi Cheng [g], Lawrence Mwaniki [c], Kenneth Ngure [b,h], Connie Celum [b,i,j], Jared M. Baeten [b,i,j], Denise A. Galloway [k], Dalton Wamalwa [l], Anna Wald [e,g,i,j]

- In an open-label trial among Kenyan, HIV-1-infected adolescents aged 9–14 years, we administered the quadrivalent HPV vaccine at 0, 2 and 6 months.
- 100 girls and 80 boys with a median age of 12 years.
- Seroconversion to HPV-18, 16, 11, 6 at month 7 occurred **in 93.3%, 98.3%, 97.2% and 99.6%** of vaccine recipients; similar rates have been reported in historical controls.

Long term follow up of persistence of immunity following quadrivalent Human Papillomavirus (HPV) vaccine in immunocompromised children

C. Raina MacIntyre [a], Peter J. Shaw [b], Fiona E. Mackie [c,d], Christina Boros [e], Helen Marshall [e], Holly Seale [f], Sean E. Kennedy [c,d], Aye Moa [a], Abrar Ahmad Chughtai [f], Mallory Trent [a,*], Edward V O'Loughlin [g], Michael Stormon [g]

Vaccine 2019;37:5630-6

Background: Human Papillomavirus (HPV) causes significant burden of HPV-related diseases, which are more prevalent in immunosuppressed compared to immunocompetent people. We conducted a multi-centre clinical trial to determine the immunogenicity and reactogenicity of HPV vaccine in immunocompromised children. Here we present the immunogenicity results 5 years post vaccination.

Methods: We followed up immunocompromised children (5–18 years) with a range of specified underlying conditions who were previously recruited from three Australian paediatric hospitals. Participants received three doses of quadrivalent HPV vaccine (Gardasil Quadrivalent HPV Types 6, 11, 16, 18) and were followed up between 2007 and 2016 (60 months post-vaccination). The immunogenicity primary outcome was seroconversion and geometric mean titres (GMT) of the quadrivalent HPV vaccine serotypes in the study.

Results: Of the 59 original participants, 37 were followed up at 60 months. The proportion of participants who seroconverted were: 86.5%, 89.2%, 89.2%, 91.9% by competitive Luminex immunoassay (cLIA) and 83.8%, 83.8%, 94.6%, 78.4% by total immunoglobulin G assays (IgG) for serotypes 6, 11, 16 and 18 respectively. GMT values ranged from 118 (95%CI: 79–177) for serotype 11, to 373 (95%CI: 215–649) for serotype 16 by cLIA. For IgG, serotype 16 had the highest GMT of 261 (95%CI: 143–477) and serotype 18 had the lowest value of 37 (95%CI: 21–68). All antibody titres were lower in females compared to males but the difference was not statistically significant except for serotype 16. No serious adverse event was reported during this follow-up period.

Conclusion: Our evidence, although limited by small numbers, is reassuring that a three dose schedule of HPV vaccine remains immunogenic in immunocompromised children to five years post vaccination. Large scale studies are required to determine long term protection in immunocompromised children.

Clinical trial registration: NCT02263703 (ClinicalTrials.gov).

Imunogenost cepiv proti HPV

Long-term Antibody Response to Human Papillomavirus Vaccines: Up to 12 Years of Follow-up in the Finnish Maternity Cohort

J Infect Dis 2019;219:582-9

Hanna Artemchuk,[1] Tiina Eriksson,[2] Mario Poljak,[3] Heljä-Marja Surcel,[4,5] Joakim Dillner,[1,6] Matti Lehtinen,[1,2] and Helena Faust[1]

[1]Department of Laboratory Medicine, Karolinska Institutet, Stockholm, Sweden; [2]University of Tampere, Finland; [3]Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Slovenia; [4]Faculty of Medicine, University of Oulu, and [5]European Science Infrastructure Services, Oulu, Finland; and [6]Clinical Pathology/Cytology, Karolinska University Laboratory, Karolinska University Hospital, Stockholm, Sweden

Background. Most cervical cancers are caused by vaccine-preventable infections with human papillomaviruses (HPV). The HPV prophylactic vaccines Gardasil and Cervarix have been widely used for >10 years and are reported to induce high antibody levels. A head-to-head comparison of the antibody responses induced by the 2 vaccines has been performed only up to 5 years.

Methods. Among 3300 Finnish females aged 16–17 years who got 1 of the 2 HPV vaccines in phase 3 licensure trials, virtually all consented to registry-based long-term follow-up. Linkage with the Finnish Maternity Cohort found that they donated >2500 serum samples up to 12 years later. Sera of 337 (38.6%) Gardasil and 730 (30.3%) Cervarix vaccine recipients were retrieved from the Finnish Maternity Cohort biobank and type-specific anti-HPV antibody levels were determined using in-house multiplexed heparin-HPV pseudovirion Luminex assay.

Results. Anti-HPV-16 and anti-HPV-18 antibody levels remained stable and above natural infection-related antibody levels for up to 12 years for most vaccine recipients. The median antibody levels were higher among Cervarix recipients 7–12 years post vaccination ($P < .0001$).

Conclusions. The stability of vaccine-induced antibody levels is in accordance with the high long-term protection reported previously. The differences in antibody levels induced by the 2 vaccines imply that continued follow-up to identify possible breakthrough cases and estimation of the minimal protective levels of serum antibodies is a research priority.

HPV-specific antibodies at the oral cavity up to 30 months after the start of vaccination with the quadrivalent HPV vaccine among mid-adult aged men ☆

Vaccine 2019;37:2864-9

Katherine H. Parker [a], Troy J. Kemp [a], Kimberly Isaacs-Soriano [b], Martha Abrahamsen [b], Yuanji Pan [a], Eduardo Lazcano-Ponce [c], Jorge Salmeron [c], Ligia A. Pinto [a,*], Anna R. Giuliano [b]

Background: HPV-16 and HPV-18 cause most oropharyngeal cancers, which are increasing in incidence among males. Although HPV vaccines are highly effective against a number of HPV-associated cancers, efficacy for oropharyngeal cancers has not yet been demonstrated. In addition, the level of antibodies required for protection against oral HPV infection is unknown.
Methods: 150 men ages 27–45 years from Tampa, FL, USA, and Cuernavaca, Mexico, received Gardasil at Day 1, Months 2, and 6. Then, sera and oral gargles were collected one month, 12 months, and 24 months after completion of the three doses (Month 7, 18 and 30 of the study) and tested for anti-HPV-16 and HPV-18 IgG antibody levels by a L1 VLP ELISA.
Results: All participants developed detectable serum anti-HPV-16 and anti-HPV-18 antibodies and most had detectable antibodies in oral gargles at Month 7 (HPV-16: 93.2%; HPV-18: 72.1%). By months 18 and 30, oral antibodies were detectable in a lower number of participants (HPV-16, 39.8% and 29.6%; HPV-18, 10.7% and 4.6% of individuals, respectively). Overall, oral HPV-16- and 18-specific antibody levels, normalized to total IgG at months 7, 18, and 30, correlated with serum levels (HPV-16, $R^2 = 0.93$; HPV-18, $R^2 = 0.91$).
Conclusions: Reduced detectability of oral and serum HPV-16 and HPV-18 antibodies was observed at months 18 and 30 after initiation of the quadrivalent vaccination. However, when detectable, serum and oral HPV-16 and HPV-18 antibody levels were strongly correlated.

Long-term Cross-reactivity Against Nonvaccine Human Papillomavirus Types 31 and 45 After 2- or 3-Dose Schedules of the AS04-Adjuvanted Human HPV-16/18 Vaccine

J Infect Dis 2019;219:1799-803

Nicolas Folschweiller,[1,©] Ulrich Behre,[2] Marc Dionne,[6] Paolo Durando,[10,11] Susanna Esposito,[12] Linda Ferguson,[7] Murdo Ferguson,[7] Peter Hillemanns,[3] Shelly A. McNeil,[8] Klaus Peters,[4] Brian Ramjattan,[9] Tino F. Schwarz,[5] Khuanchai Supparatpinyo,[13] Pemmaraju V. Suryakirian,[14] Michel Janssens,[1] Philippe Moris,[1] Annabelle Decreux,[1] Sylviane Poncelet,[1] and Frank Struyf[1]

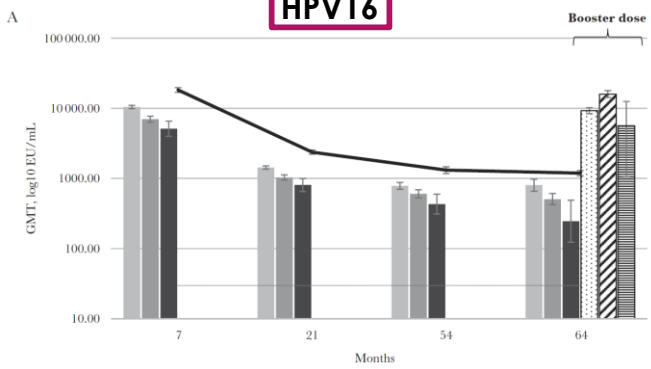
- Long-term cross-reactive immunogenicity against non-vaccine human papillomavirus (HPV) types 31 and 45 following 2 doses of AS04-adjuvanted HPV-16/18 vaccine in girls aged 9–14 years or following 3 doses in women aged 15–25 years, for up to 3 years (HPV-070 study) and up to 5 years (HPV-048 study) after the first vaccination.
- The antibody concentration was **similar in young girls as compared to women**. Specific **CD4+ T-cell and B-cell responses to HPV-31 and HPV-45 at month 36 were similar across groups**.

Persistence of Immunity When Using Different Human Papillomavirus Vaccination Schedules and Booster-Dose Effects 5 Years After Primary Vaccination

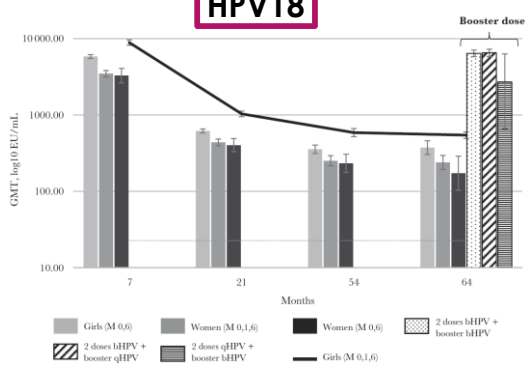
Eduardo Lazcano-Ponce,[1] Leticia Torres-Ibarra,[1] Aurelio Cruz-Valdez,[1] Jorge Salmerón,[1,2] Tonatiuh Barrientos-Gutiérrez,[1] Javier Prado-Galbarro,[1] Margaret Stanley,[3] Nubia Muñoz,[4] Rolando Herrero,[5] and Mauricio Hernández-Ávila[1]

J Infect Dis 2019;219:41-9

HPV16



HPV18



Nadomestitev cepilnih genotipov HPV?

Evidence for cross-protection but not type-replacement over the 11 years after human papillomavirus vaccine introduction

Hum Vaccin Immunother 2019; [Epub ahead of print]

Courtney Covert, Lili Ding, Darron Brown, Eduardo L. Franco, David I Bernstein & Jessica A. Kahn

- 1,540 women 13-26 years of age during the 11 years after HPV vaccine introduction.
- Prevalence of HPV types genetically related to HPV16 decreased significantly by 45.8%, **demonstrating evidence of cross-protection following 4vHPV vaccination**.
- Prevalence of HPV types genetically related to HPV18 did not change significantly (14.2% decrease).
- Prevalence of HPV types genetically unrelated to vaccine types did not change significantly (4.2% increase), demonstrating **no evidence of type replacement**.

Occurrence of human papillomavirus (HPV) type replacement by sexual risk-taking behaviour group: Post-hoc analysis of a community randomized clinical trial up to 9 years after vaccination (IV)

Int J Cancer 2019;145:785-96

Penelope Gray[1,2], Tapio Luostarinen[3], Simopekka Vänskä[4], Tiina Eriksson[1], Camilla Lagheden[2], Irene Man[5], Johanna Palmroth[1], Ville N. Pimenoff[6], Anna Söderlund-Strand[7], Joakim Dillner[2] and Matti Lehtinen[1,2]

The subpopulations with **increased sexual risk-taking behaviour** may be more facilitative of the preconditions for **HPV type replacement** occurrence after HPV vaccination induced ecological pressure. Among the originally HPV16/18 vaccinated 18-year-old females, the **HPV51** occurrence was consistently increased albeit in the originally non-HPV vaccinated the increase was statistically significant in the core-group with high sexual risk-taking behaviour only.

Spolno vedenje in HPV cepljenje

HPV vaccination has not increased sexual activity or accelerated sexual debut in a college-aged cohort of men and women

BMC Public Health 2019;19:821

Andrew F. Brouwer[1*†], Rachel L. Delinger[1†], Marisa C. Eisenberg[1], Lora P. Campredon[1], Heather M. Walline[2], Thomas E. Carey[2] and Rafael Meza[1]

No effect of human papillomavirus vaccination on sexual debut of school children

Dan Med J 2019;66:A5540

Rebekka O. Svarrer[1], Anna Lund Rasmussen[1], Finn Friis Lauszus[1] & Anne Hammer[1, 2]

Overall, no difference in the proportion of pupils with sexual debut or mean age at sexual debut was observed between HPV-vaccinated and unvaccinated adolescents in Denmark. However, **HPV-vaccinated adolescents were more likely to stop using a condom despite their higher STI awareness**.

Učinkovitost cepiva proti HPV v realnem življenju

Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis

Mélanie Drolet, Élodie Bénard, Norma Pérez, Marc Brisson, on behalf of the HPV Vaccination Impact Study Group

Lancet 2019;394:497-509

Cepljenje proti HPV

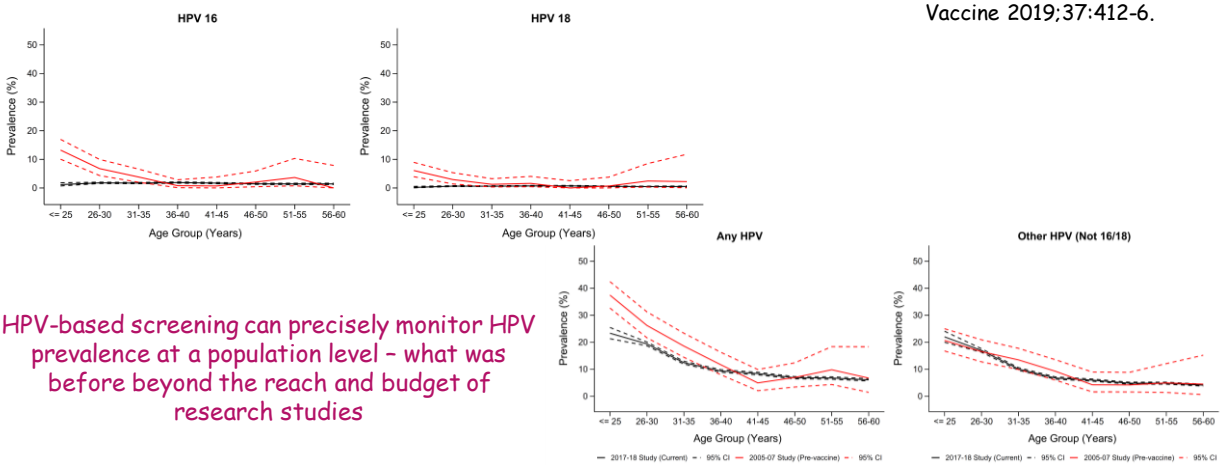
HPV okužbe (cepilni genotipi)

Čas

Age-specific HPV prevalence among 116,052 women in Australia's renewed cervical screening program: A new tool for monitoring vaccine impact

Julia ML. Brotherton [a,b,*], David Hawkes [c,d], Farhana Sultana [a,b], Michael J. Malloy [a,b], Dorothy A. Machalek [b,e,f], Megan A. Smith [g], Suzanne M. Garland [e,f,h], Marion Saville [c,h]

Vaccine 2019;37:412-6.

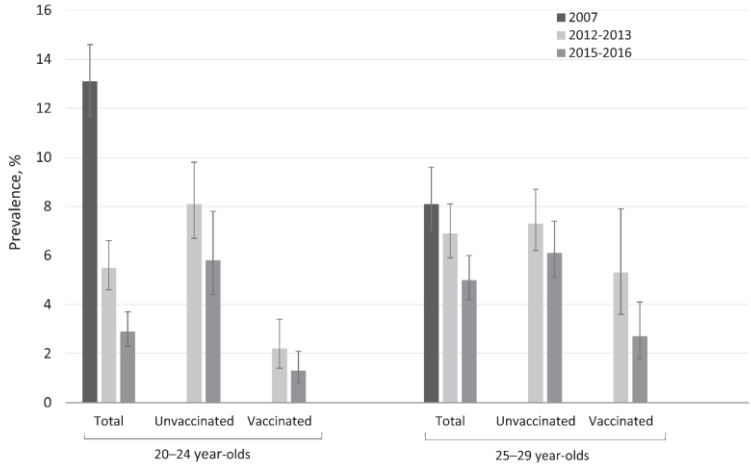


HPV-based screening can precisely monitor HPV prevalence at a population level – what was before beyond the reach and budget of research studies

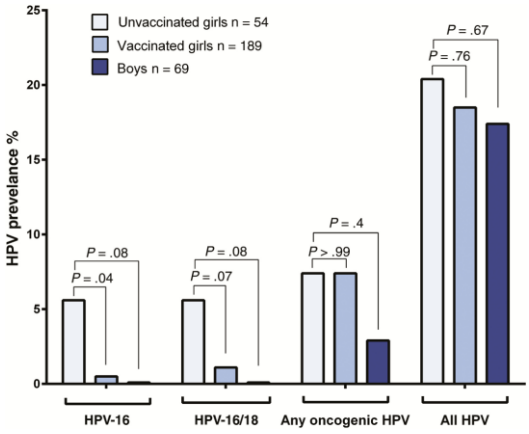
Declines in HPV vaccine type prevalence in women screened for cervical cancer in the United States: Evidence of direct and herd effects of vaccination

Lauri E. Markowitz [a,*], Allison L. Naleway [b], Rayleen M. Lewis [a,c], Bradley Crane [b], Troy D. Querec [d], Sheila Weinmann [b], Martin Steinau [d,1], Elizabeth R. Unger [d]

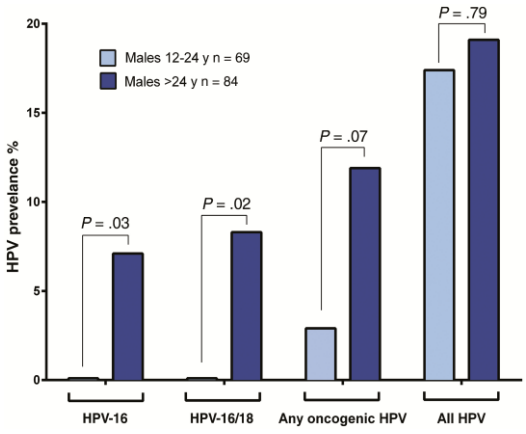
Vaccine 2019;37:3918-24



UK female-only vaccination program is associated with significant reductions in oropharyngeal HPV-16 infections

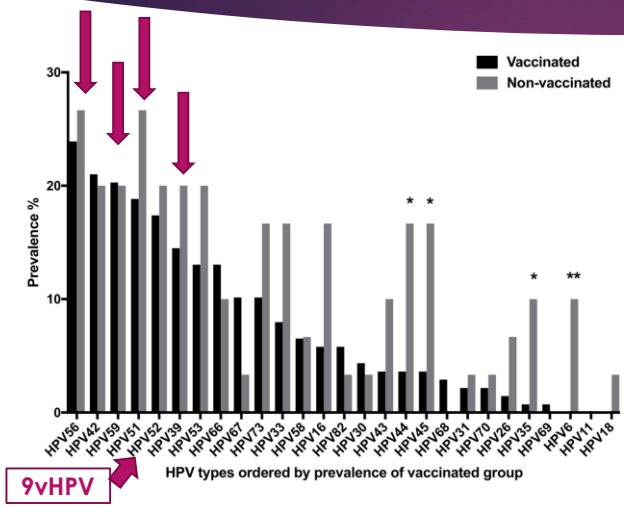


Potential herd immunity from female-only vaccination against oropharyngeal HPV infection in contemporaneously aged males



Mehanna H, et al. Clin Infect Dis 2018;ciy1081.

Changes in cervical HPV prevalence at a Youth Clinic in Stockholm, Sweden, a decade after the introduction of the HPV vaccine



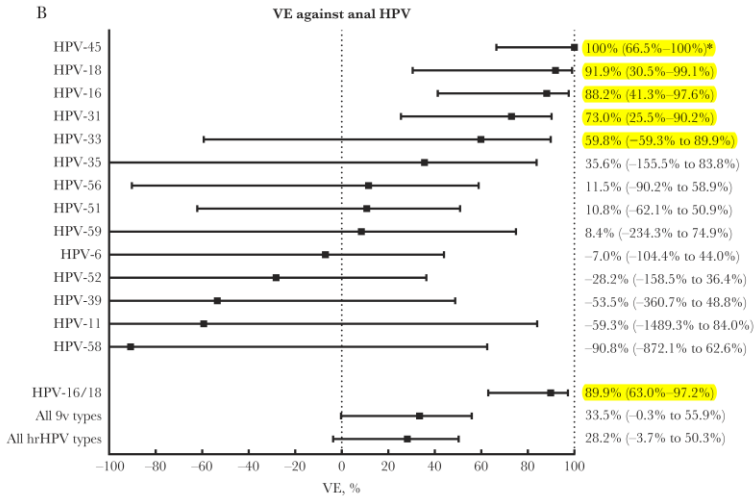
- HPV prevalence in 2017-2018 was high irrespective of vaccination status - 72.1% (all genotypes) and 65.1% (high risk HPVs)
- prevalence of **all 27 HPVs lower in vaccinated** (67.4 vs. 93.3%, p=0.003)
- prevalence of **all high-risk HPVs lower in vaccinated** (60.1 vs. 86.73%, p=0.006)
- prevalence of **4vHPVs lower in vaccinated** (5.8 vs. 26.7%, p=0.002)

Ährlund-Richter A in sod., Front Cell Infect Microbiol;2019;9:59.

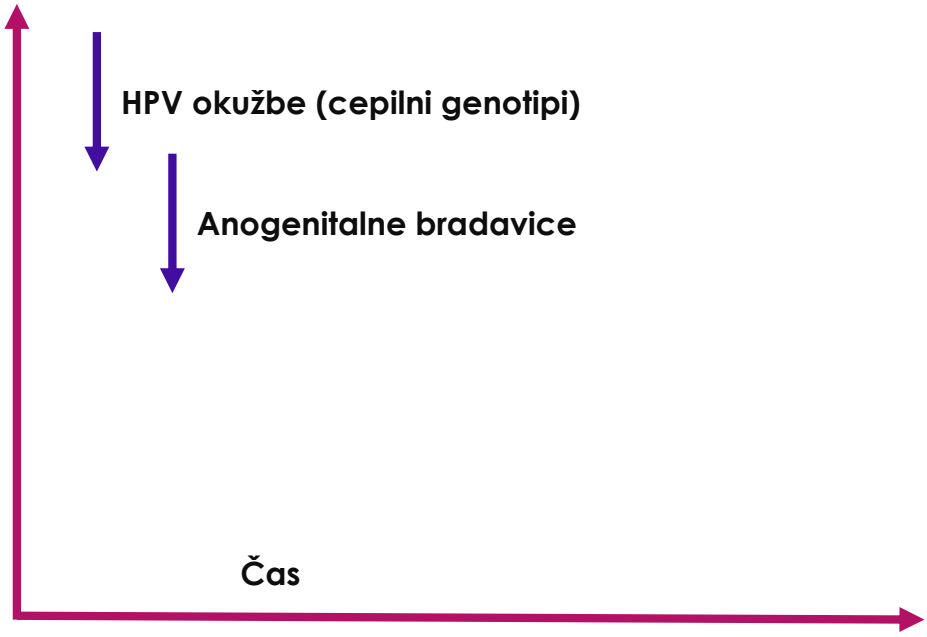
Bivalent Vaccine Effectiveness Against Anal Human Papillomavirus Positivity Among Female Sexually Transmitted Infection Clinic Visitors in the Netherlands

J Infect Dis 2019;1-6

Petra J. Woestenberg,[1,2] Audrey J. King,[1] Birgit H. B. van Benthem,[1] Suzan Leussink,[1] Marianne A. B. van der Sande,[3,4] Christian J. P. A. Hoebe[2,5] and Johannes A. Bogaards[1,6]; on behalf of the Medical Microbiological Laboratories and the Public Health Services[a]



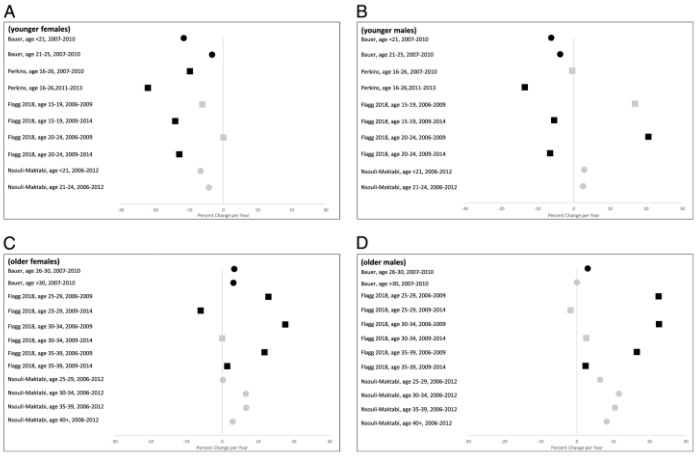
Cepljenje proti HPV



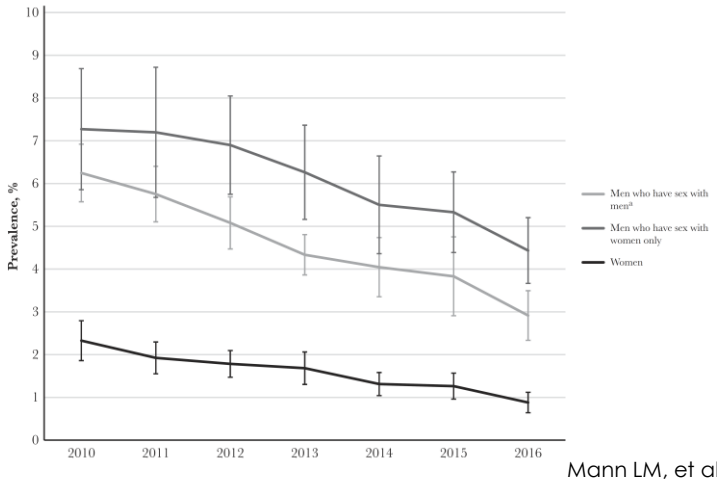
Human Papillomavirus Vaccination and Anogenital Warts: A Systematic Review of Impact and Effectiveness in the United States

Sex Transm Dis 2019;46:213-20

Anthony E. Yakely, BA[*], Lital Avni-Singer, BA[†], Carlos R. Oliveira, MD[‡], and Linda M. Niccolai, PhD[*]

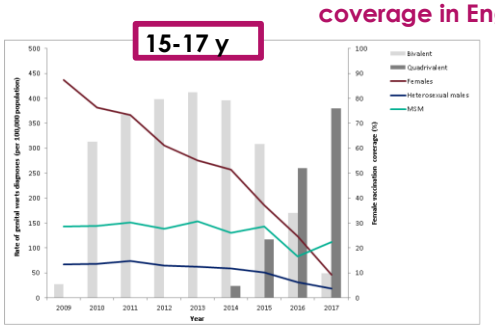


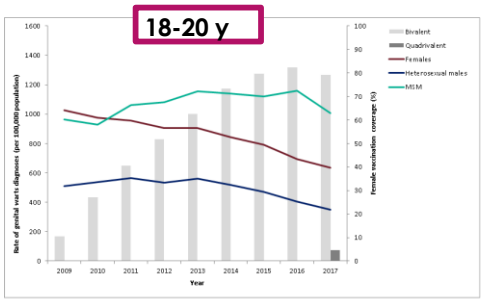
Annual anogenital wart prevalence among patients attending US Sexually Transmitted Disease Surveillance Network clinics, by patient type, 2010–2016

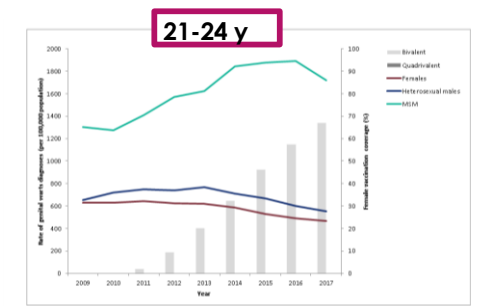


Mann LM, et al. J Infect Dis 2019;219:1389-97.

Rate of anogenital warts (AGWs) diagnoses and female HPV vaccination coverage in England 2009-2017

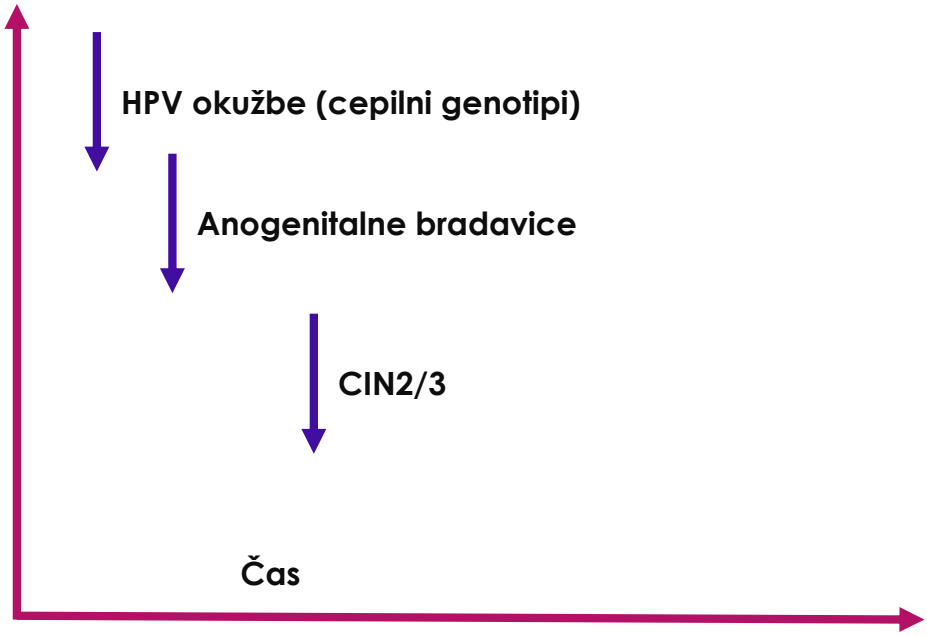






Cecchi M, et al. Epidemiology 2019;95:368-73.

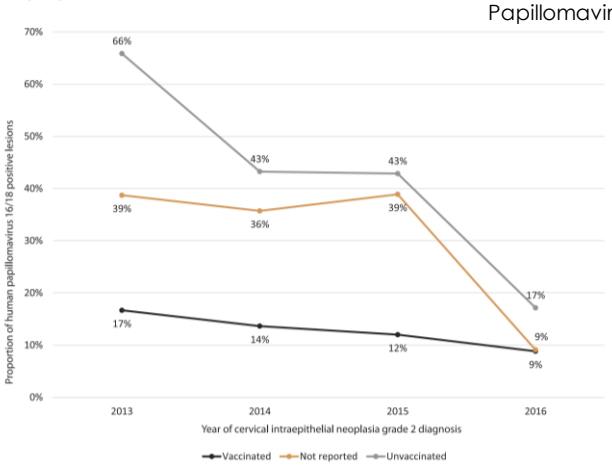
Cepljenje proti HPV



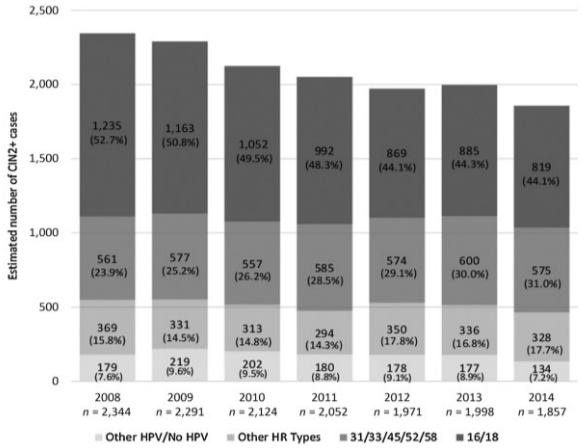
Changes in human papillomavirus genotypes associated with cervical intraepithelial neoplasia grade 2 lesions in a cohort of young women (2013–2016)

Carrie R. Innes[a,*], Peter H. Sykes[a,b], Dianne Harker[a], Jonathan A. Williman[c], Rachael A. Van der Griend[d], Martin Whitehead[d,e], Merilyn Hibma[f], Beverley A. Lawton[g], Peter Fitzgerald[h], Narena M. Dudley[i], Simone Petrich[j], Jim Faherty[k], Cecile Bergzoll[l], Lois Eva[m], Lynn Sadler[m], Bryony J. Simcock[a,b]

Papillomavirus Research 2018;6:77-82

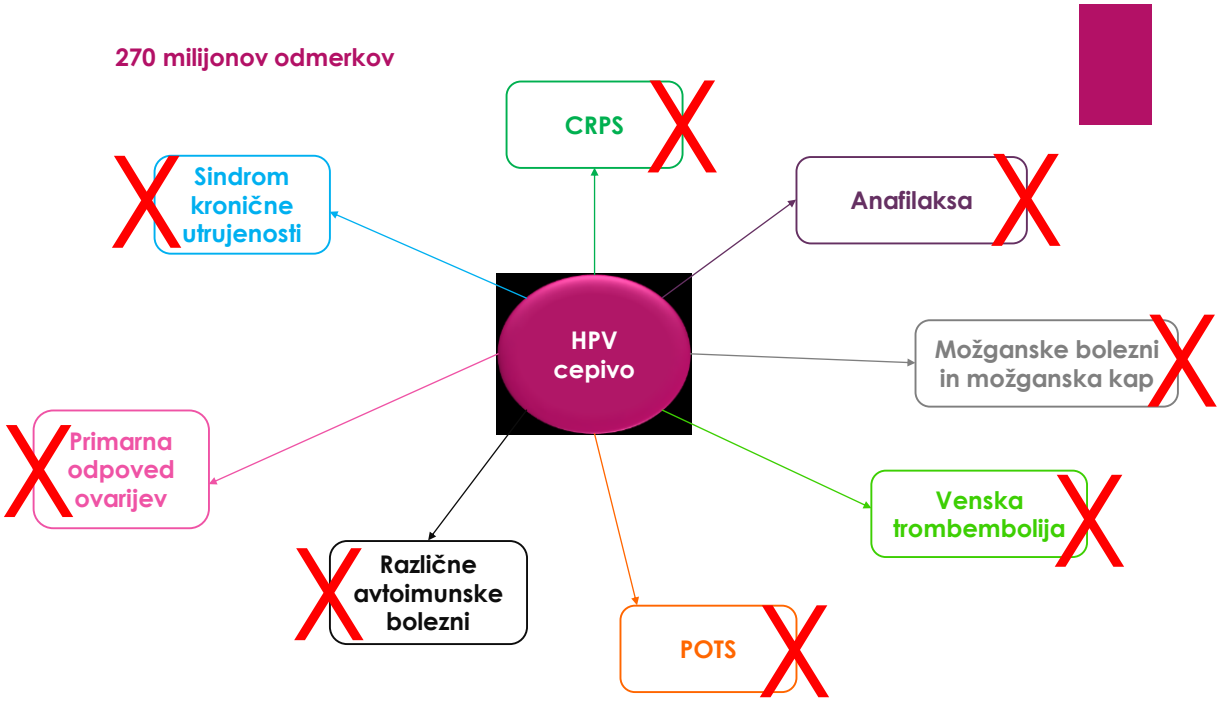


Declining trends in the proportion of HPV16/18-positive CIN2+ were observed among vaccinated (55.2%–33.3%, P < 0.001) and unvaccinated (51.0%–47.3%, P = 0.03) women



McClung NM, et al. Cancer Epidemiol Biomarkers Prev 2019;28:602-9.

Varnost cepiv proti HPV

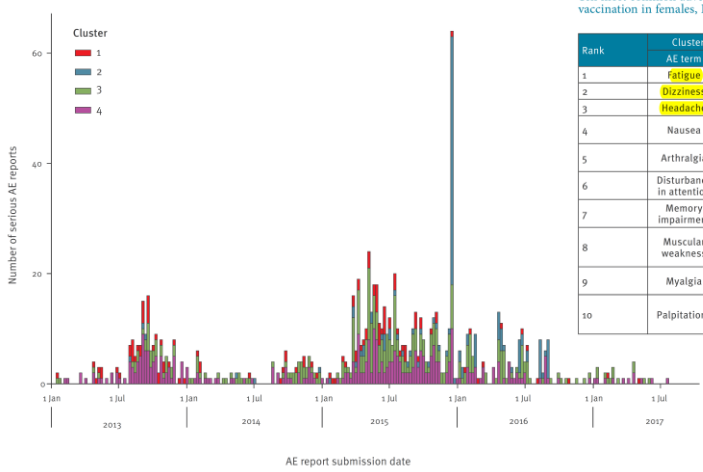


A cluster analysis of serious adverse event reports after human papillomavirus (HPV) vaccination in Danish girls and young women, September 2009 to August 2017

Daniel Ward[1], Nicklas Myrthue Thorsen[1], Morten Frisch[1,2], Palle Valentiner-Branth[3], Kåre Mølbak[3,4], Anders Hviid[1]

Euro Surveill 2019;24:pii=1800380

Submission dates of reports of serious adverse events to human papillomavirus vaccination in females, Denmark, January 2013–July 2017 (n = 919)



Ten most common adverse event (AE) terms within clusters of reports of serious AE following human papillomavirus vaccination in females, Denmark, 12 September 2009–17 July 2017 (n = 963)

Rank	Cluster 1 (120 reports)			Cluster 2 (130 reports)			Cluster 3 (329 reports)			Cluster 4 (384 reports)		
	AE term	n	%	AE term	n	%	AE term	n	%	AE term	n	%
1	Fatigue	114	95	Fatigue	120	92	Fatigue	294	89	Headache	142	37
2	Dizziness	113	94	Dizziness	118	91	Dizziness	248	75	Fatigue	126	33
3	Headache	107	89	Headache	111	85	Headache	242	74	Dizziness	104	27
4	Nausea	101	84	Cognitive disorder	102	78	Nausea	186	57	Syncope	71	18
5	Arthralgia	100	83	Abdominal pain	100	77	Arthralgia	149	45	Nausea	53	14
6	Disturbance in attention	99	83	Nausea	98	75	Disturbance in attention	143	43	Arthralgia	47	12
7	Memory impairment	88	73	Muscular weakness	94	72	Abdominal pain	118	36	Disturbance in attention	35	9
8	Muscular weakness	80	67	Palpitations	92	71	Syncope	110	33	Sensory disturbance (tied with 9)	34	9
9	Myalgia	75	63	Dysuria (tied with 10)	78	60	Muscular weakness	101	31	Abdominal pain (tied with 8)	34	9
10	Palpitations	73	61	Sleep disorder (tied with 9)	78	60	Myalgia/memory impairment[a]	100	30	Paraesthesia/ pain/migraine[a]	26	7

Safety of bivalent human papillomavirus vaccine in the US vaccine adverse event reporting system (VAERS), 2009–2017

Tiffany A. Suragh[1], Paige Lewis[1], Jorge Arana[1], Adamma Mba-Jonas[2], Rongxia Li[1], Brock Stewart[3], Tom T. Shimabukuro[1] and Maria Cano[1]

Br J Clin Pharmacol Infect Dis 2018;84:2928-32

AIMS

Human papillomavirus (HPV) vaccines prevent infection with oncogenic virus types. We analysed reports to the US Vaccine Adverse Event Reporting System (VAERS) of adverse events (AE) following bivalent HPV vaccine (2vHPV).

METHODS

We conducted descriptive analysis of 2vHPV reports, reviewed individual reports, calculated crude AE reporting rates and conducted empirical Bayesian data mining.

RESULTS

Of 241 2vHPV reports, 158 were in females, 64 in males (2vHPV is approved for females only) and 19 with unknown sex; 95.8% were classified as nonserious. Dizziness, headache, nausea and injection site reactions were the most common symptoms. Crude AE reporting rates were 33.3 reports per 100 000 doses distributed overall, and 1.4 per 100 000 for serious reports. Empirical Bayesian data mining identified disproportional reporting for three types of medical errors; assessment indicated findings that were probably driven by inadvertent 2vHPV use in males.

CONCLUSIONS

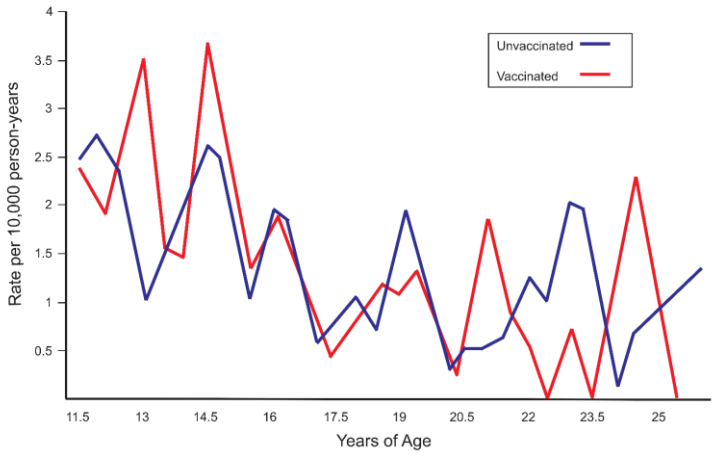
We did not identify any new or unexpected safety concerns in our review of 2vHPV reports to VAERS.

Long term risk of developing type 1 diabetes after HPV vaccination in males and females

Nicola P. Klein[a,*], Kristin Goddard[a], Edwin Lewis[a], Pat Ross[a], Julianne Gee[b], Frank DeStefano[b], Roger Baxter[a,1]

Vaccine 2019;37:1938-44

Diabetes mellitus type I incidence by age and HPV vaccination status after applying lag period and membership criteria



Human papillomavirus vaccination and the risk of autoimmune disorders: A systematic review and meta-analysis

Hai-yin Jiang [a,1], Yu-dan Shi [b,1], Xue Zhang [a], Li-ya Pan [a], Yi-rui Xie [a], Chun-ming Jiang [c], Min Deng [a], Bing Ruan [a,*]

Vaccine 2019;37:3031-9

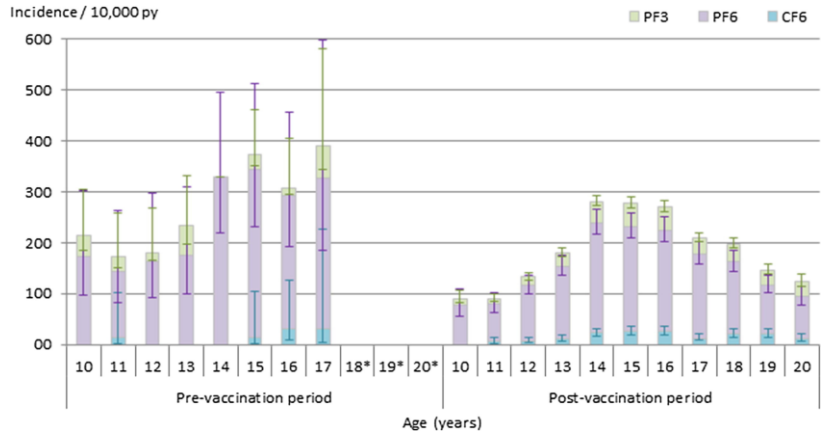
- A systematic review and meta-analysis to comprehensively evaluate the relationship between HPV vaccination and ADs risk.
- 20 studies involving more than **169,000 AD events** were included in our meta-analysis.
- Our results show that HPV vaccination **was not associated with an increased risk of subsequent ADs particularly among those with a prior ADs**.

No evidence found for an increased risk of long-term fatigue following human papillomavirus vaccination of adolescent girls

T.M. Schurink-van't Klooster [a,*], J.M. Kemmeren [a], N.A.T. van der Maas [a], E.M. van de Putte [b], M. ter Wolbeek [c], S.L. Nijhof [b], A.M. Vanrolleghem [d], J.A. van Vliet [a], M. Sturkenboom [e], H.E. de Melker [a]

Vaccine 2018;36:6796-802

Age distribution of certain and possible fatigue ≥ 6 months and 3–6 months in the pre- and post-vaccination period

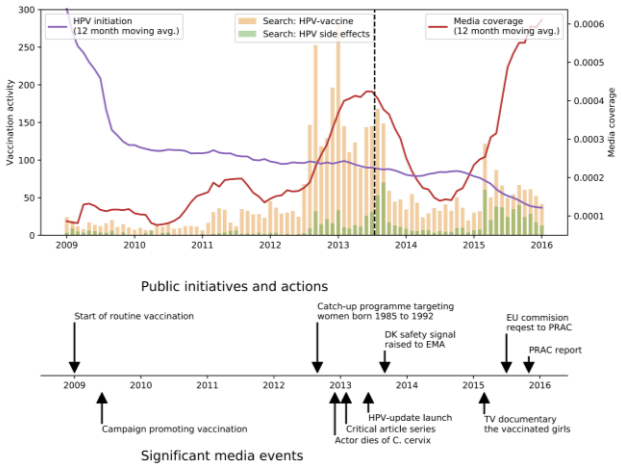


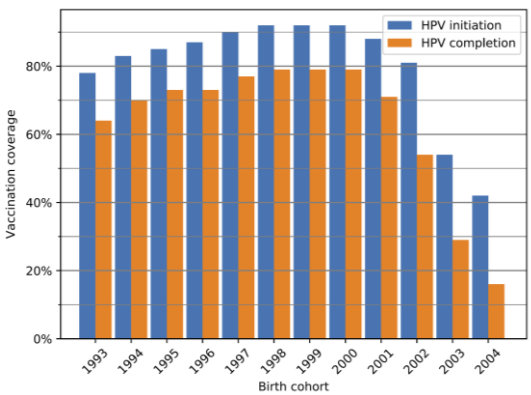
Vpliv medijev na precepljenost proti HPV

Decline in HPV-vaccination uptake in Denmark – the association between HPV-related media coverage and HPV-vaccination

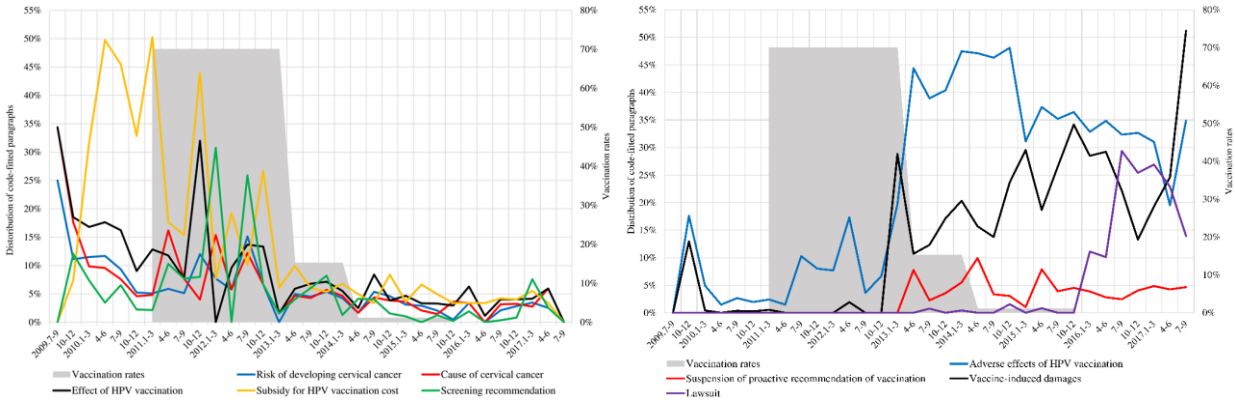
BMC Public Health 2018;18:1360

Camilla Hiul Suppli[1*], Niels Dalum Hansen[2], Mette Rasmussen[4], Palle Valentiner-Branth[1], Tyra Grove Krause[1] and Kåre Mølbak[3]





Newspaper coverage before and after the HPV crisis began in Japan



Okuhara T, et al. BMC Public Health 2019;19:770.

The failure of news coverage supportive of human papillomavirus vaccination: The investigation of the effects of online comments on female college students' vaccination intention

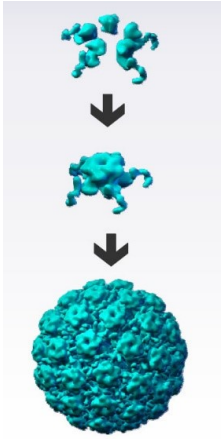
Vaccine 2019;[Epub ahead of print]

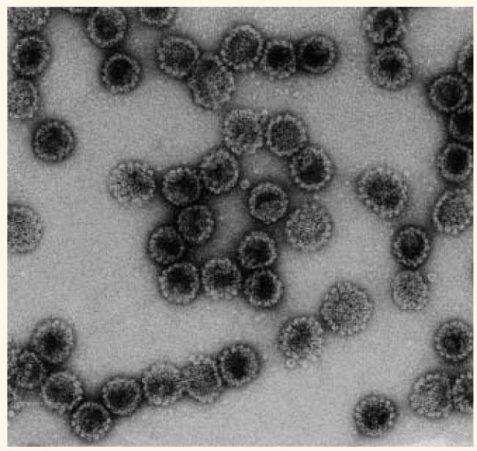
Wen Zhang [a], Qi Wang [b,c,*]

Razvoj novih profilaktičnih cepiv proti HPV

2vHPV, 4vHPV in 9vHPV

virusom podobi delci iz rekombinantnih virusnih beljakovin L1





L1 predstavlja najbolj imunogeno virusno beljakovino, ki v gostitelju izzove nastanek nevtralizirajočih protiteles, ki so značilna za posamezen genotip HPV

Cepiva proti HPV v kliničnih poizkusih

Vaccine	Phase	Clinical trials	Primary end-point
E. Coli-based HPV-16 and -18 L1 VLPs (Celcolin™)	III	NCT01735006	Subjects CIN 2–3 and/or VIN 2–3 and/or VaIN 2–3 associated with HPV -16 and/ or -18 cervical infection after vaccination
E. Coli-based HPV-6, -11 L1 VLPs (Gelcolin™)	I	NCT02405520	Measure adverse reactions and events of the vaccine
P. pastoris-based HPV-16, -18 VLPs	I	NCT01548118	Occurrence, intensity and relationship to vaccination of any solicited local or systemic reactions; occurrence, intensity and relationship to vaccination of any unsolicited symptom
H. polymorpha-based HPV -6, -11, -16 and -18 VLPs	I	NCT03085381	Systemic and local adverse events during the period of first dose vaccination to 30 days after last dose of vaccination

CIN: cervical intraepithelial neoplasia; HPV: Human Papilloma Virus; L1: Major capsid protein; VaIN: vaginal intraepithelial neoplasia; VIN: vulvar intraepithelial neoplasia; VLP: Virus-like particle.

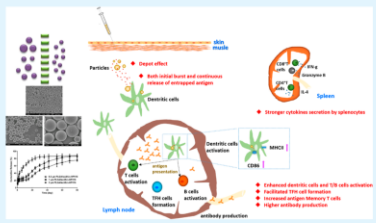
Barra F in sod., J Obstet Gynaecol 2019;39:1-10.

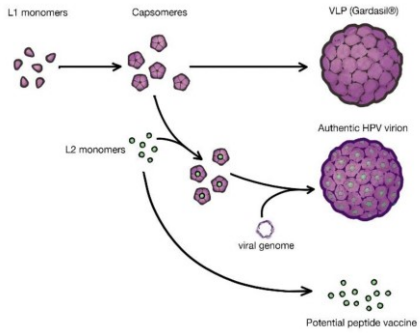
A Novel Human Papillomavirus 16 L1 Pentamer-Loaded Hybrid Particles Vaccine System: Influence of Size on Immune Responses

Chengcheng Jia,[†,‡,1] Tingyuan Yang,[†] Yongjiang Liu,[‡] Ali Zhu,[†] Fei Yin,[‡] Yajun Wang,[‡] Lan Xu,[‡] Yan Wang,[‡] Mei Yan,[‡] Qingman Cai,[§] Xiaoxu Liang,[§] Ruijun Ju,[§] Jianping Chen,[*,‡] and Lianyan Wang[*,†]

ABSTRACT: Cervical cancer remains the second-most prevalent female malignancy around the world, leading to a great majority of cancer-related mortality that occurs mainly in developing countries. Developing an effective and low-cost vaccine against human papillomavirus (HPV) infection, especially in medically underfunded areas, is urgent. Compared with vaccines based on HPV L1 viruslike particles (VLPs) in the market, recombinant HPV L1 pentamer expressed in *Escherichia coli* represents a promising and potentially cost-effective vaccine for preventing HPV infection. Hybrid particles comprising a polymer core and lipid shell have shown great potential compared to conventional aluminum salts adjuvant and is urgently needed for HPV L1 pentamer vaccines. It is well-reported that particle sizes are crucial in regulating immune responses. Nevertheless, reports on the relationship between the particulate size and the resultant immune response have been in conflict, and there is no answer to how the size of particles regulates specific immune response for HPV L1 pentamer-based candidate vaccines. Here, we fabricated HPV 16 L1 pentamer-loaded poly(D,L-lactide-*co*-glycolide) (PLGA)/lecithin hybrid particles with uniform sizes (0.3, 1, and 3 μm) and investigated the particle size effects on antigen release, activation of lymphocytes, dendritic cells (DCs) activation and maturation, follicular helper $CD4^+$ T (TFH) cells differentiation, and release of pro-inflammatory cytokines and chemokines. Compared with the other particle sizes, 1 μm particles induced more powerful antibody protection and yielded more persistent antibody responses, as well as more heightened anamnestic responses upon repeat vaccination. The superior immune responses might be attributed to sustainable antigen release and robust antigen uptake and transport and then further promoted a series of cascade reactions, including enhanced DCs maturation, increased lymphocytes activation, and augmented TFH cells differentiation in draining lymph nodes (DLNs). Here, a powerful and economical platform for HPV vaccine and a comprehensive understanding of particle size effect on immune responses for HPV L1 pentamer-based candidate vaccines are provided.

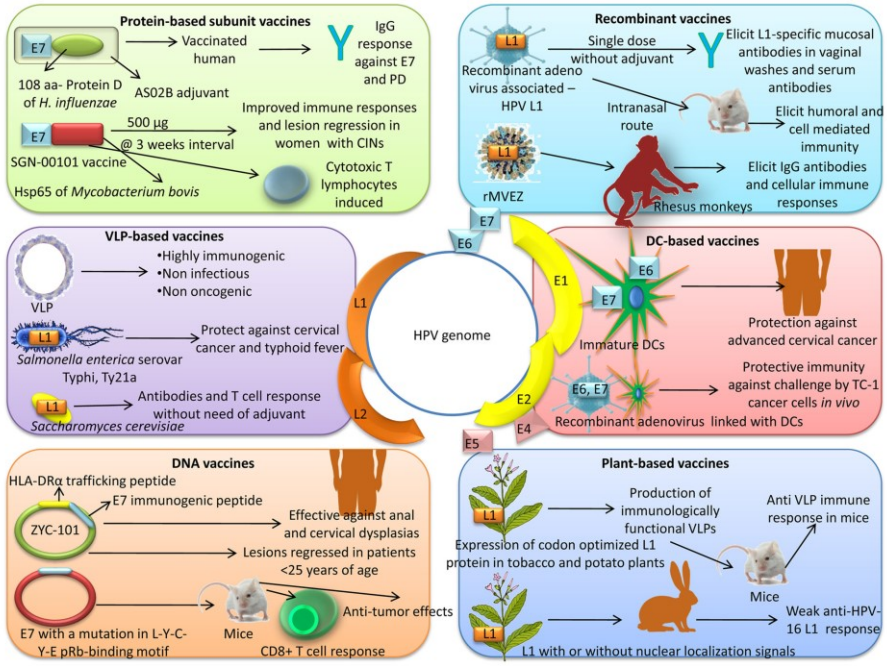
KEYWORDS: *human papillomavirus, pentamer, particle, size, adjuvant*





Yu MJ, JEMI-PEARLS. 2017;2:1-8.

Jia C in sod., ACS Appl Mater Interfaces. 2018;10:35745-59.

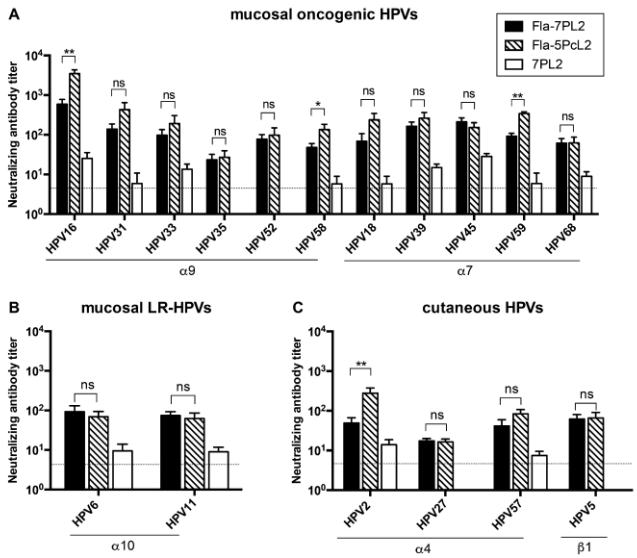


Dadar M in sod., Front Immunol. 2018;9:2478.

A rationally designed flagellin-L2 fusion protein induced serum and mucosal neutralizing antibodies against multiple HPV types

Ting Zhang [a], Xue Chen [a], Hongyang Liu [a], Qifeng Bao [a], Zhirong Wang [a], Guoyang Liao [b,*], Xuemei Xu [a,*]

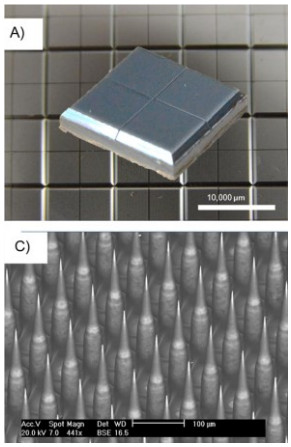
Vaccine 2019;37:4022-30

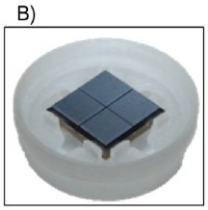


Immune response and reactogenicity of an unadjuvanted intradermally delivered human papillomavirus vaccine using a first generation Nanopatch™ in rhesus macaques: An exploratory, pre-clinical feasibility assessment

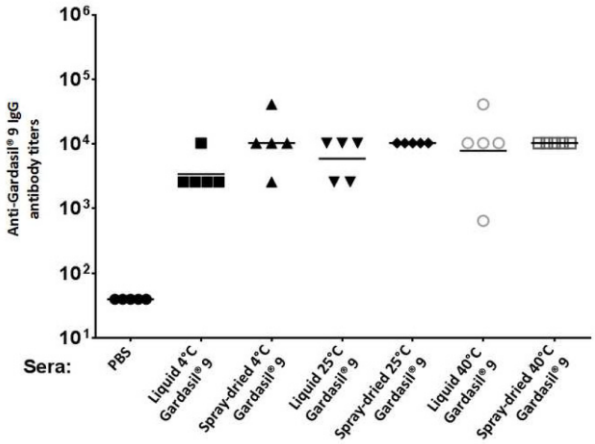
Vaccine 2019;2:100030.

Brian K. Meyer [a,*], Mark A.F. Kendall [b,c,1], Donna M. Williams [a], Andrew J. Bett [d], Sheri Dubey [d], Renee C. Gentzel [e], Danilo Casimiro [d,2], Angus Forster [c], Holly Corbett [b,3], Michael Crichton [b,c,4], S. Ben Baker [b,c,5], Robert K. Evans [a,6], Akhilesh Bhambhani [a]





Anti-Gardasil® 9 antibody titers in mice after immunization with Gardasil® 9 stored for 3 months at different temperatures



Kunda NK, et al. Hum Vaccin Immunother 2019;15:1995-2002.

A proof-of-concept study for the design of a VLP-based combinatorial HPV and placental malaria vaccine

Sci Rep 2019;9:5260

Christoph M. Janitzek[1,2], Julianne Peabody[3], Susan Thrane[1,2], Philip H. R. Carlsen[1,2], Thor G. Theander[1,2], Ali Salanti[1,2], Bryce Chackerian[3], Morten A. Nielsen[1,2] & Adam F. Sander[1,2]

In Africa, cervical cancer and placental malaria (PM) are a major public health concern. There is currently no available PM vaccine and the marketed Human Papillomavirus (HPV) vaccines are prohibitively expensive. The idea of a combinatorial HPV and PM vaccine is attractive because the target population for vaccination against both diseases, adolescent girls, would be overlapping in Sub-Saharan Africa. Here we demonstrate proof-of-concept for a combinatorial vaccine utilizing the AP205 capsid-based virus-like particle (VLP) designed to simultaneously display two clinically relevant antigens (the HPV RG1 epitope and the VAR2CSA PM antigen). Three distinct combinatorial VLPs were produced displaying one, two or five concatenated RG1 epitopes without obstructing the VLP's capacity to form. Co-display of VAR2CSA was achieved through a split-protein Tag/Catcher interaction without hampering the vaccine stability. Vaccination with the combinatorial vaccine(s) was able to reduce HPV infection *in vivo* and induce anti-VAR2CSA IgG antibodies, which inhibited binding between native VAR2CSA expressed on infected red blood cells and chondroitin sulfate A in an *in vitro* binding-inhibition assay. These results show that the Tag/Catcher AP205 VLP system can be exploited to make a combinatorial vaccine capable of eliciting antibodies with dual specificity.

Pristopi k izboljšanju precepljenosti proti HPV

Feasibility of a combined strategy of HPV vaccination and screening in Mexico: the FASTER-Tlalpan study experience

L León-Maldonado [a,b], A Cabral[c], B Brown [d], GW Ryan [e], A Maldonado[f], J Salmerón [b], B Allen-Leigh [f], and E Lazcano-Ponce [g] on behalf of the FASTER Study Group*

Hum Vaccin Immunother 2019;15:1986-94.

There has been a noticeable shift in discussions about cervical cancer, moving from prevention to elimination. Interventions such as FASTER, human papillomavirus (HPV) vaccination and HPV screening are innovative intervention strategies which can be utilized to begin a path to elimination. To explore the feasibility of the FASTER strategy, an evaluation was carried out in eight primary health-care centers within the Tlalpan Health-Jurisdiction of Mexico City between March 2017 and August 2018. A mixed methods approach was used to evaluate three components: infrastructure, patient acceptability, and health-care professionals' perceptions. This included checklists of requirements for the infrastructure rollout of FASTER and interviews with women and health-care professionals. Nearly all (93%) of the 3,474 women aged 25–45 years accepted HPV vaccination as part of a combined vaccination and screening program. The main reason for acceptance was prevention, while having doubts about the vaccine's benefits was the main reason for refusal. Most of the 24 health-care professionals had a positive opinion toward HPV vaccination and identified the need to increase dissemination, inform the population clearly and concisely and currently extend the age range for vaccination. The evaluation of eight primary health-care centers showed they had the necessary infrastructure for the development of a joint HPV prevention strategy, but many centers required improvements to become more efficient. Together these findings suggest that although HPV vaccine acceptance was high, there is the need to increase education and awareness among potential vaccine recipients and health-care professionals to implement the FASTER strategy.

Preclinical study of safety and immunogenicity of combined rubella and human papillomavirus vaccines: Towards enhancing vaccination uptake rates in developing countries

Asmaa Gohar[a], Nourtan F. Abdeltawab[b,*], Nahla Shehata[a], Magdy A. Amin[b]

Papillomavirus Res 2019;8:100172

Rubella vaccine was not part of national immunization programs (NIP) in several countries in the Middle East and North Africa (MENA), South-East Asia (SEA), and South Africa regions until the year 2000. Therefore, immunization coverage of females older than 20 years old in these countries has been the focus of national campaigns for rubella elimination in developing countries. Vaccines against human papillomavirus (HPV) are not part of NIPs in developing countries. To enhance the advantages of rubella-directed immunization campaigns and to increase HPV vaccine uptake in developing countries, this study aimed to test the stability, potency, efficacy and safety of a combined rubella and HPV vaccine. Female BALB/c mice were immunized subcutaneously with proposed combined HPV16/HPV18 VLP and rubella vaccine at weeks (W) 0, 3 then with HPV vaccine at W 7. Immunized mice developed antigen-specific antibodies against rubella and HPV significantly higher than mice immunized with rubella or HPV vaccine alone. The combined vaccine induced significantly higher splenocyte proliferation than control groups. In addition, pro-inflammatory cytokines IL-4, IL-6, IL-2, and IFNγ levels were significantly higher in mice immunized with the combined vaccine than control groups. Overall, the combined vaccine was safe and immunogenic offering antibody protection as well as eliciting a cellular immune response against rubella and HPV viruses in a single vaccine. This combined vaccine can be of great value to females above 20 years old in the SEA, MENA and South Africa regions offering coverage to rubella vaccine and a potential increase in HPV vaccine uptake rates after appropriate clinical testing.

Immunogenicity of a Quadrivalent Human Papillomavirus Vaccine When Co-Administered with Tetanus-Reduced Diphtheria-Acellular Pertussis and Quadrivalent Meningococcal Conjugate Vaccines in Healthy Adolescents: Results from a Randomized, Observer-Blind, Controlled Trial

Infect Dis Ther 2019;8:335-41

Yan Miao · Thembile Mzolo · Michele Pellegrini

- Impact of concomitant administration of a quadrivalent HPV (HPV4) and Tdap vaccine with a quadrivalent meningococcal CRM_{197}-conjugate vaccine (MenACWY-CRM)
- Healthy adolescents aged 11–18 years (801) were randomized to receive either HPV4 + Tdap + MenACWY or HPV4 + Tdap + Placebo and two additional doses of HPV4 at 2 and 6 months after the first dose.
- Seroconversion rates ranged between **98.0% (HPV-6) and 99.7% (HPV-11 and HPV-18)** in group HPV4 + Tdap + MenACWY and from **99.0% (HPV-11 and HPV-16) to 99.7% (HPV-6 and HPV-18)** in group HPV4 + Tdap + Placebo.

Implementing pharmacy-located HPV vaccination: Findings from pilot projects in five U.S. states.

William A. Calo, Parth D. Shah, Melissa B. Gilkey, Robin C. Vanderpool, Sarah Barden, William R. Doucette & Noel T. Brewer

Hum Vaccin Immunother 2019; [Epub ahead of print]

- 15 pharmacies in 5 states, 12 months → **13 doses** to adolescents and **3 doses** to age-eligible adults

HPV Vaccination in Correctional Care: Knowledge, Attitudes, and Barriers Among Incarcerated Women

Alia Moore, MD, MPH[1,2], Matthew Cox-Martin, PhD[3], Amanda F. Dempsey, MD, PhD, MPH[4], Katie Berenbaum Szanton, MD[5], and Ingrid A. Binswanger, MD, MPH[2,6]

J Correct Health Care. 2019;25:219-230

- Incarcerated women aged 18-26; **47/63 (75%)** who reported never receiving the HPV vaccine stated that they would be **somewhat or very likely to get the vaccine** during incarceration if it was offered

Interventions to increase uptake of the human papillomavirus vaccine in unvaccinated college students: A systematic literature review

Marie Barnard[a,*], Anna C. Cole[b], Lori Ward[c], Emily Gravlee[d], Mariah L. Cole[d], Caroline Compretta[e]

Prev Med Rep 2019;14:100884.

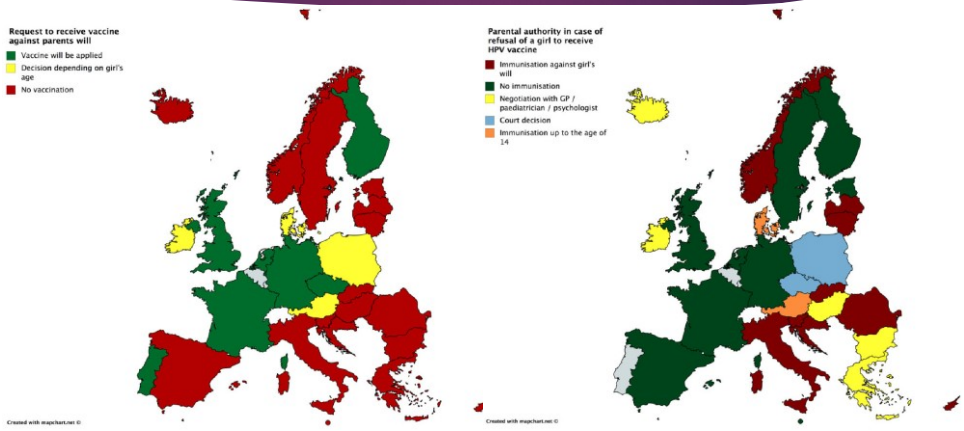
- Nine eligible for final qualitative review.
- A study exposing participants to a **narrative video about HPV vaccination** led by a combination of **peers and medical experts** produced the greatest difference in HPV vaccination initiation compared to a control group (21.8% vs 11.8%) of all the studies reviewed.
- **Few interventions resulted in substantial HPV vaccine uptake**.

Changes in comfort with skills required to recommend HPV vaccine among pediatric providers at baseline and after viewing a training video

Question	Proportion Reporting They Feel "Very Comfortable" With the Skill (Likert-Type Scale Score of 5)		
	Baseline (%)	Posttest (%)	*P*
1. Counseling about the rationale for routinely giving the HPV vaccine at age 11 to 12 years.	49.0	79.2	<.01
2. Counseling about the need to routinely vaccinate boys against HPV.	51.4	79.2	<.01
3. Addressing parental concerns about HPV being sexually transmitted, and the need to vaccinate prior to sexual debut.	51.0	77.1	<.01
4. Addressing parental concerns about the safety and side effects of the HPV vaccine.	39.6	78.1	<.01
5. Presenting the HPV vaccine as a cancer prevention vaccine.	74.0	87.5	.01
6. Facilitating completion of the 3-dose vaccine series once initiated.	49.9	68.8	<.01
7. Making a strong recommendation for HPV vaccine.	67.7	84.4	<.01
8. Discussing HPV vaccination again with a family who has previously declined it.	56.3	72.9	<.01

Kumar MM, et al. Clin Pediatr 2019;58:17-23.

Greater respect for children's autonomy tends to be associated with medium or high vaccination coverage rates and lower respect with lower rates

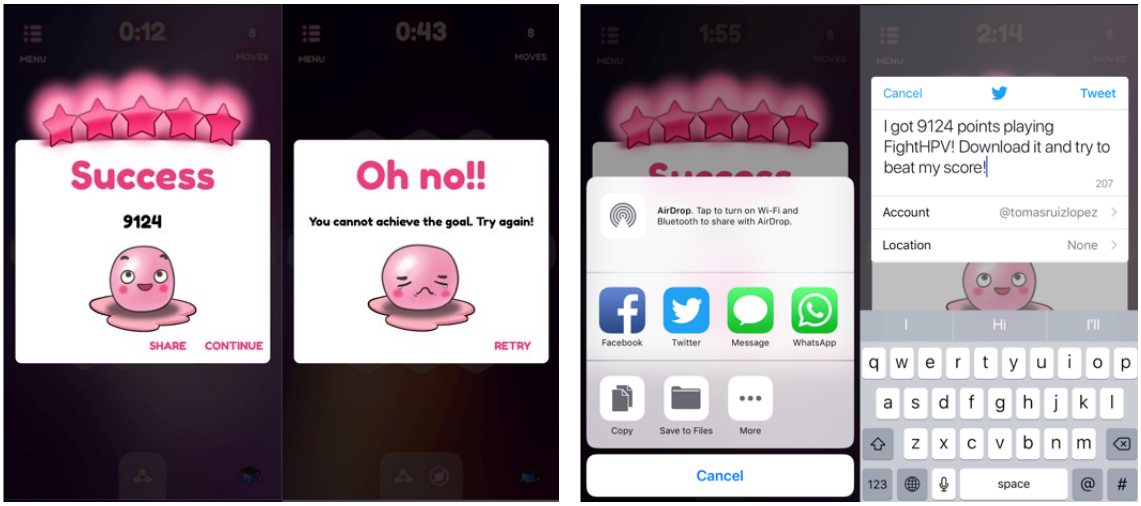


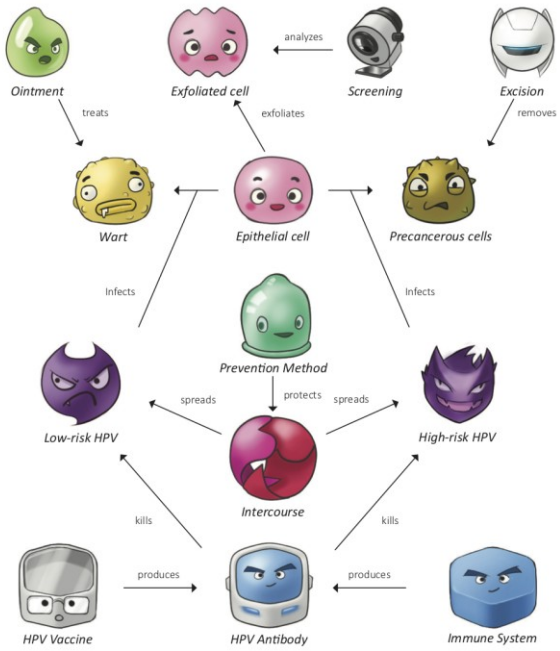
Martakis K, et al. J Child Health Care 2019; [Epub ahead of print].

FightHPV: Design and Evaluation of a Mobile Game to Raise Awareness About Human Papillomavirus and Nudge People to Take Action Against Cervical Cancer

JMIR Serious Games 2019;7:e8540.

Tomás Ruiz-López[1], MSc, PhD; Sagar Sen[2], MSc, PhD; Elisabeth Jakobsen[3], MSc; Ameli Tropé[3], MD, PhD; Philip E Castle[4], PhD; Bo Terning Hansen[1], PhD; Mari Nygård[1], MD, PhD





Ruiz-López T, et al. JMIR Serious Games 2019;7:e8540.

Using Facebook to reach adolescents for human papillomavirus (HPV) vaccination

Vaccine 2018;36:5955-61

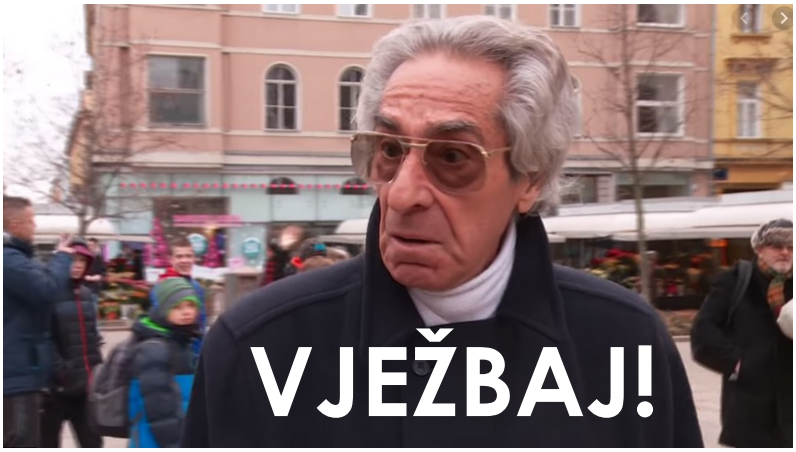
Salini Mohanty [a,c,*], Amy E. Leader [b], Emily Gibeau [c], Caroline Johnson [c]

- On average, each campaign reached **155,110 adolescents, engaged 2107 adolescents per advertising campaign, and accrued more than 3400 unique fans over the course of the project**.
- The campaign that **reached the greatest number of adolescents** was **Disease Risk**; it featured posts which explained HPV disease and how to reduce risk for HPV through preventions strategies.
- **Back to School was the least successful** in gaining fans of the 3forME page.
- **The Philadelphia campaign** was the most successful in gaining fans. This campaign had the lowest reach out of all six and had the second lowest average total engagement, but this campaign gained the highest number of likes (n = 1065) compared to any other campaign.
- Although adolescents were encouraged to sign-up for HPV immunization appointments through the Facebook page and website, **few chose to do so**.

The effect of exercise on local and systemic adverse reactions after vaccinations – Outcomes of two randomized controlled trials

V.Y. Lee [a,*], R. Booy [b,c], S.R. Skinner [c], J. Fong [d], K.M. Edwards [a]

Vaccine 2018;[Epub ahead of print]



Cepiva proti HPV v letu 2019

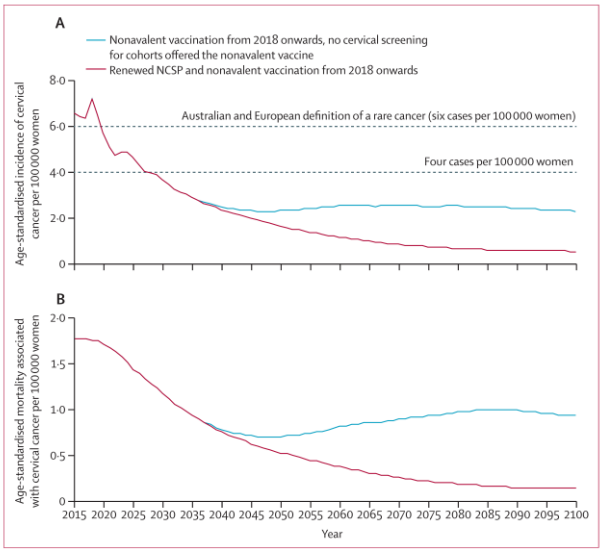
- UČINKOVITA
- VARNA
- PREMALO UPORABLJENA

Cepljenje proti HPV - prihodnost

The projected timeframe until cervical cancer elimination in Australia: a modelling study

Michaela T Hall, Kate T Simms, Jie-Bin Lew, Megan A Smith, Julia ML Brotherton, Marion Saville, Ian H Frazer, Karen Canfell

Lancet Public Health 2018;4:e19-e27



2020

age-standardised annual incidence of CCX will ↓ to fewer than **six new cases per 100 000 women**

2028

age-standardised annual incidence of CCX will ↓ to fewer than **four new cases per 100 000 women**

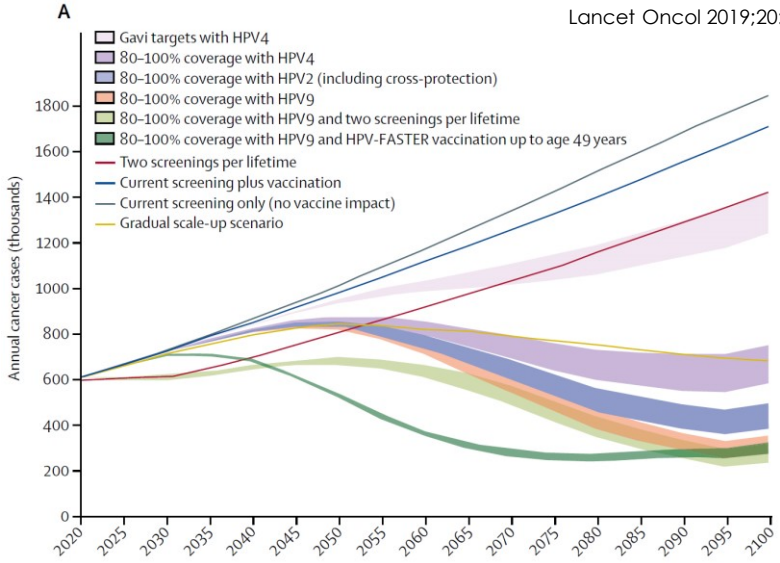
2066

age-standardised annual incidence of CCX will ↓ to fewer than **one new case per 100 000 women**

Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020–99: a modelling study

Kate T Simms, Julia Steinberg, Michael Caruana, Megan A Smith, Jie-Bin Lew, Isabelle Soerjomataram, Philip E Castle, Freddie Bray, Karen Canfell

Lancet Oncol 2019;20:394-407



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10 let programa cepljenja proti HPV v Sloveniji

Nadja Šinkovec, dr. med.
Dr. Veronika Učakar, dr. med.
Dr. Marta Grgič Vitek, dr. med.

Strokovno srečanje 10 let cepljenja proti HPV, Ljubljana, 3.9.2019

Cepljenje proti HPV v Sloveniji

- **2006** – V Sloveniji na voljo **štirivalentno cepivo** (do leta 2018);
- **2007** – V Slovenij na voljo **dvovalentno cepivo**;
- **2009/10** - Cepljenje proti HPV uvedeno v **Program cepljenja** v Sloveniji (za deklice v 6. razredu OŠ); Sprva se je za izvajanje programa uporabljalo 4-valentno cepivo po shemi 0, 2, 6 mesecev;
- **2014/2015** - **sprememba sheme cepljenja - dva odmerka** cepiva z vsaj 6-mesečnim presledkom;
- **2016** – V Sloveniji na voljo **devetvalentno cepivo**;
- Od **2016/17** se za izvajanje **programa cepljenja uporablja 9-valentno cepivo**.

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Program cepljenja proti HPV v Sloveniji

2. cepljenje in zaščita s specifičnimi imunoglobulini za učence, dijake in študente za šolsko leto 2019/20 ter druge mlade odrasle do dopolnjenega 26. leta starosti

2.1.6 Cepljenje proti okužbam s humanimi papilomavirusi (HPV)

- Cepljenje se izvaja ob sistematičnem pregledu pri deklicah, ki v šolskem letu 2019/20 obiskujejo 6. razred osnovne šole.
- Cepljenje se opravi tudi pri tistih, ki so obiskovale 6. razred v šolskem letu 2009/10 ali kasneje in še niso bile cepljene (zamudnice).
- Cepljenje se opravi s številom odmerkov glede na starost ob začetku cepljenja (za mlajše od 15 let sta dovolj dva odmerka s presledkom najmanj 6 mesecev, za starejše so potrebni 3 odmerki po shemi 0,2,6).

Cepljenje proti HPV, opredeljeno v točki 2.1.6, se plača iz sredstev OZZ.

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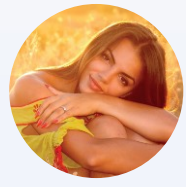
Cepljenje „zamudnic“ proti HPV

Zamudnice za cepljenje proti HPV so dekleta, ki so obiskovale 6. razred v šolskem letu 2009/10 ali kasneje in še niso bile cepljene proti HPV.

Če se dekle za cepljenje odloči **po 15. letu starosti, privolitev staršev ni potrebna.**

Izvajalci cepljenja proti HPV:
Vsa rutinska cepljenja praviloma opravljajo pediatri in šolski zdravniki (tudi študentski zdravniki), enako velja tudi za cepljenje zamudnikov/zamudnic, ki se lahko opravi ob prvem naslednjem sistematičnem pregledu ali po dogovoru z zdravnikom.
Cepijo lahko tudi drugi zdravniki.



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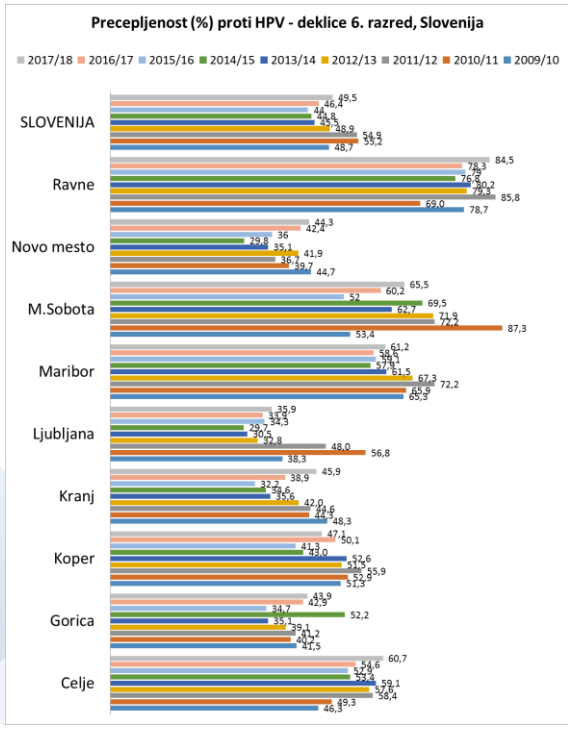
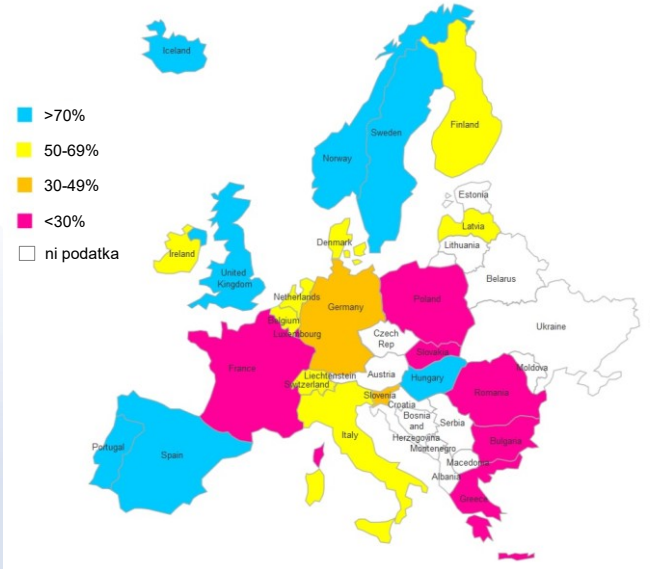
Precepljenost šestošolk proti HPV v Sloveniji, v obdobju 2009/10 - 2017/18



Precepljenost deklet proti HPV v Evropi

Delež cepljenih deklet proti HPV:

- >70 % (Madžarska, Islandija, Norveška, Portugalska, Španija, Švedska, VB),
- 50-69 % (Belgija, Danska, Finska, Irska, Italija, Latvija, Nizozemska, Švica),
- 30-49 % (Nemčija, Slovenija),
- <30 % (Bolgarija, Grčija, Francija, Luksemburg, Poljska, Romunija, Slovaška).

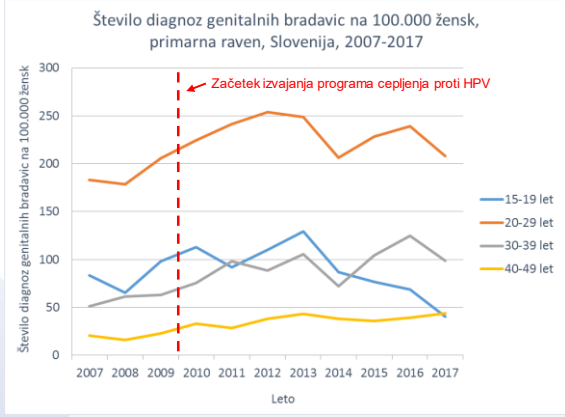


Vir: ECCMID, 2018

Uspešnost programa cepljenja proti HPV

Uspešnost programov v svetu se kaže kot:

- ↓ pogostosti okužb s HPV v populaciji mladih *(v Sloveniji nimamo vzpostavljenega rednega spremljanja)*
- ↓ pojavnosti genitalnih bradavic pri mladih ženskah in moških *(Slovenija - nakazuje se ↓ pojavnosti genitalnih bradavic pri mladih ženskah (graf))*
- ↓ pojavnosti predrakavih sprememb MV *(V Sloveniji je prva generacija deklet, vključenih v program cepljenja proti HPV, šele pričela s programom ZORA)*
- prvi podatki o uspešnosti cepljenja pri preprečevanju invazivnih s HPV povezanih rakov pri ženskah (Finska)



Vir: ZUBSTAT

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Varnost cepljenja proti HPV

- Do sedaj po svetu razdeljenih več kot 270 milijonov odmerkov teh cepiv (WHO, 2017).
- V Sloveniji je bilo v obdobju 2009 do 2018:
  - razdeljenih več kot **140.000 odmerkov** cepiva proti HPV;
  - v Register neželenih učinkov po cepljenju v tem obdobju prejeli **177 prijav neželenih učinkov** po cepljenju proti HPV.
- Neželeni učinki: najpogosteje lokalne reakcije na mestu cepljenja in zmerno povišana telesna temperatura, slabost, glavobol, utrujenost in omedlevica.

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Neželeni učinki po cepljenju proti HPV, 2009 – 2017, Slovenija

Leto	Razdeljeni odmerki cepiva proti HPV	Število prijav NU
2009	14.577	13
2010	20.530	31
2011	17.973	18
2012	15.371	32
2013	13.957	14
2014	11.047	23
2015	8.857	8
2016	10.709	9
2017	10.646	14
2018	17.699	15

- Skoraj vsako leto prijavljen kakšen resen NU (hospitalizacija zaradi omedlevice, glavobola, slabosti…, večinoma eno-dnevno opazovanje).
- O resnejših neželenih učinkih, kot so anafilaktična reakcija in šok niso poročali.
- Vsi NU so izzveneli v nekaj dneh brez posledic.

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Cepljenje dečkov proti HPV

- Preprečuje okužbe z genotipi HPV, ki lahko povzročijo raka zadnjika, penisa, ustnega dela žrela in genitalne bradavice.
- Posredno zaščiti ženske, ker cepljenje zmanjša možnost prenosa okužbe.

- V Sloveniji zaenkrat možno samoplačniško cepljenje od 9. leta dalje za dečke in moške.
- Letos maja poslan **predlog širitve nacionalnega programa cepljenja s cepljenjem proti okužbam s HPV za dečke** na Zdravstveni svet.
- Ko bo predlog potrjen s strani Zdravstvenega sveta in ko bodo zagotovljena finančna sredstva s strani ZZZS, bo tudi za dečke na voljo cepljenje proti HPV na stroške OZZ (tako kot pri deklicah).

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Cepljenje proti HPV – priporočila WHO, ECDC

WHO, 2017:

- Cepljenje proti HPV priporočeno predvsem za **deklice, stare med 9-14 let, ki so glavna ciljna skupina**.
- Visoka precepljenost deklic (>80 %) predstavlja dobro posredno zaščito tudi za dečke, razen določenih skupin (moški, ki imajo spolne odnose z moškimi).
- SZO priporoča cepljenje proti HPV **tudi za ostale ciljne skupine** (dekleta, stara 15 let in več, ter dečke), **vendar to ne sme vplivati na dobro izvajanje cepljenja pri primarni ciljni skupini**.

ECDC, 2019:

- **Univerzalno cepljenje obeh spolov** proti HPV zahteva **več resursov,** vendar pa najverjetneje zagotavlja **večji kolektivni učinek** programa pri nižji precepljenosti ciljne populacije. Univerzalna strategija bo lahko imela izrazitejši vpliv na zmanjšane prevalence in kroženja HPV v populaciji, s tem pa bodo **učinkoviteje zaščitene vse rizične skupine**.
- **Strategija cepljenja samo deklic** ob trenutnih cenah cepiva je verjetno **stroškovno učinkovitejša,** vendar s tem **ne ščiti dovolj moških, ki imajo spolne odnose z moškimi**. Ta strategija je tudi **manj pravična**, ker obema spoloma ne daje enake priložnosti za direktno zaščito pred okužbami s HPV in njihovimi posledicami in je bolj podvržena nenadnim nihanjem v precepljenosti.

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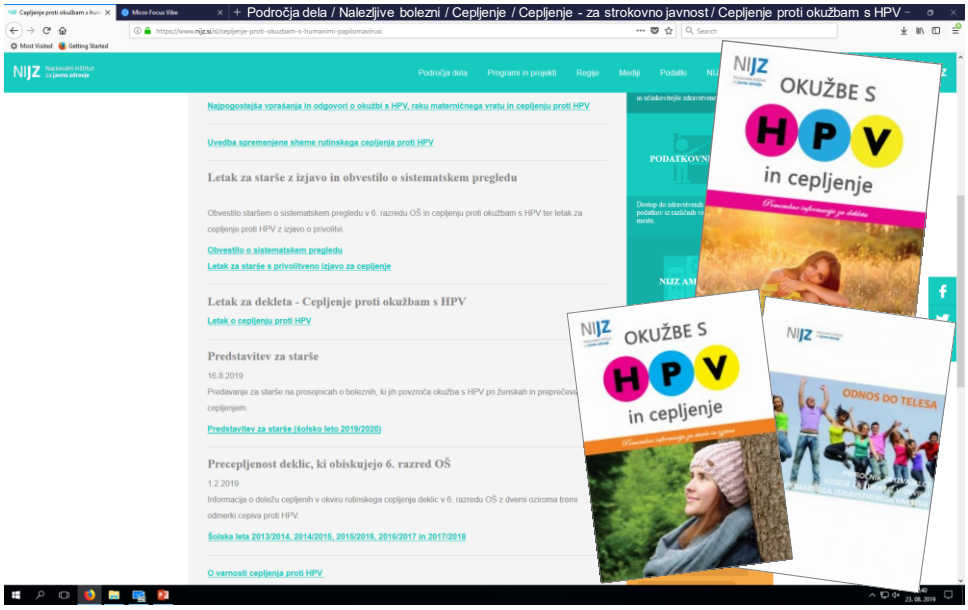
Cepljenje po spolu proti HPV v Evropi

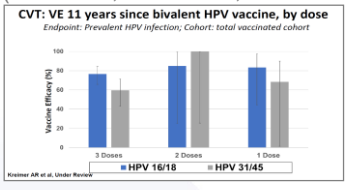
Vir: ECDC, Nacionalna priporočila

HPV gradiva na spletni strani NIJZ



Izzivi za prihodnost ?

- **Cepljenje z enim odmerkom cepiva**
  (Kostarika, PATRICIA, India HPV vaccine trial)



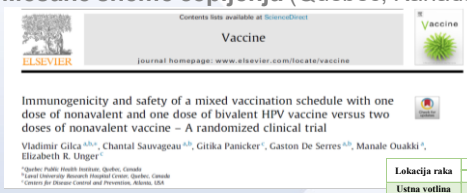
- India vaccine trial (17.596 cepljenih deklet z Gardasil-4, 1540 necepljenih kontrol; 4909 cepljenih z 1. dozo; 3416 cepljenih z 2. dozama po shemi 0,2; 4972 cepljenih z 2. dozama po shemi 0,6; 4330 cepljenih s 3. dozami po shemi 0,2,6; analiza po 7 letih):
  - incidence HPV okužb

	necepljene	3. doze	2. dozi 0,2	2. dozi 0,6	1. doza
HPV 16/18	10,8	1,3	2,2	0,9	1,5
HPV 31/33/45	13,7	5,8	3,7	5,2	6,7

  - med cepljenimi ni statističnih razlik glede na število prejetih odmerkov

Sankaranarayanan R et al, Vaccine 2018

- **Mešane sheme cepljenja** (Quebec, Kanada)



- **Cepljenje dečkov z dvovalentnim cepivom** (Norveška)

NIJZ Nacionalni inštitut za javno zdravje

Lokacija raka	Genotipi HPV klasificirani kot rakotvorni (IARC, 2018)	
	z zadostnimi dokazi	z omejenimi dokazi
Ustna votlina	HPV 16	HPV 18
Tonzile	HPV 16	---
Žrelo	HPV 16	---
Grlo	---	HPV 16
Anus	HPV 16	HPV 18, 33
Penis	HPV 16	HPV 18
Vulva	HPV 16	HPV 18, 33
Vagina	HPV 16	---
Materinčni vrat	HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59	HPV 26, 53, 66, 67, 68, 70, 73, 82

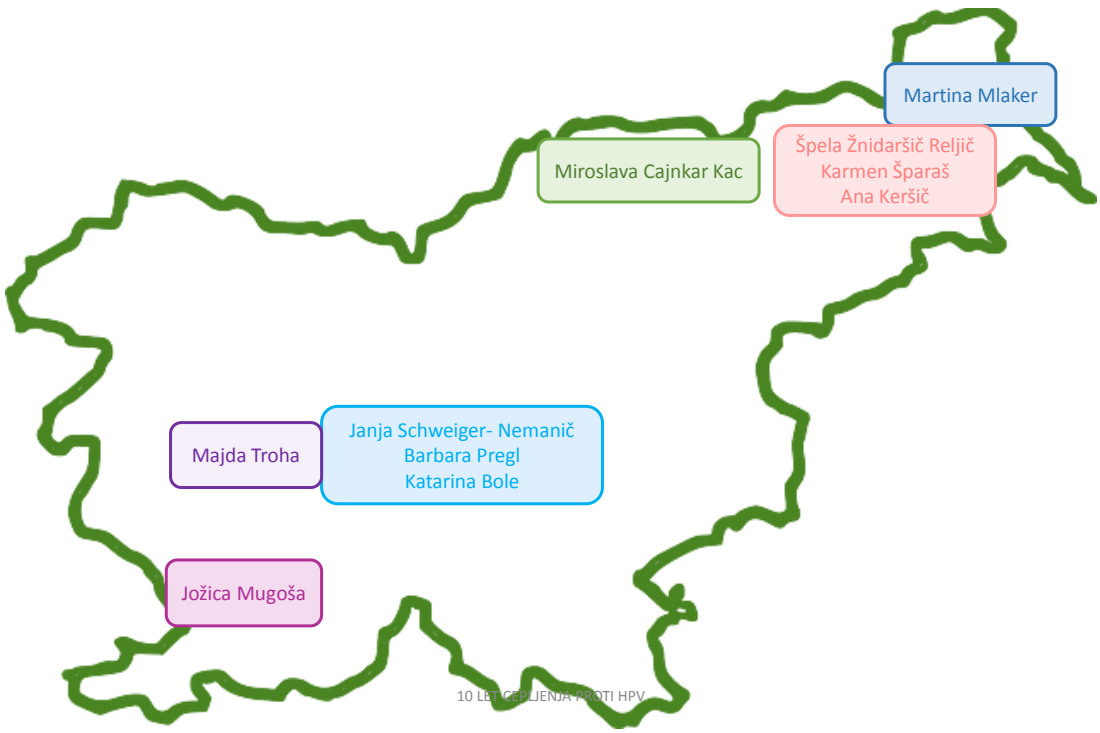
HVALA ZA POZORNOST!

H P V

NIJZ Nacionalni inštitut za javno zdravje

Slide


PRIMERI DOBRE PRAKSE
IZ RAZLIČNIH KRAJEV
SLOVENIJE


Martina Mlaker
Miroslava Cajnkar Kac
Špela Žnidaršič Reljič
Karmen Šparaš
Ana Keršič
Majda Troha
Janja Schweiger- Nemanič
Barbara Pregl
Katarina Bole
Jožica Mugoša

- **SEŽANA**
  - **prim. Jožica Mugoša, dr. med., spec. šol. med.**
- IDRIJA
  - **Majda Troha, dr.med., spec. šol. med.**
- **SLOVENJ GRADEC**
  - **Miroslava Cajnkar Kac, dr. med., spec. šol. med.**
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  - **Janja Schweiger – Nemanič, dr. med.**
  - **Barbara Pregl, dr. med., spec. druž. med.**
  - **Katarina Bole, štud. med.**

Prim. Jožica mugoša, dr. med. spec. šol. med.
UP. Šolski dispanzer Sežana

Hpv cepljenje -12 let

Prof.Vrščajeva in prof. Poljak pred 12 leti, obveščanje strokovne javnosti o cepljenju proti HPV

Šolski zdravniki, pridobivanje občinskih sredstev za cepivo in obveščanje staršev deklet za privolitev cepljenja
osebno: vse 4 kraške občine so odobrile denar za cepivo vsako leto, dokler je bilo samoplačniško, cepili 70-86 % deklet-6 generacij (8., 9. r. 7., 8.r. 6., 7.r. OŠ) z občinskim denarjem
za uspeh pripisujem kontaktu s starši na roditeljskih sestankih. -PREDAVANJA-razgovori, vprašalniki,pisna vprašanja…

V Komendi bodo proti HPV cepili na občinske stroške

LETO 2009 , po objavi v uradnem listu **prvo BREZPLAČNO NEOBVEZNO CEPLJENJE V SLOVENIJI- proti HPVE za deklice 6.r.**

NJIZ- dr. Vitkova aktivno sodeluje z IO SSSAM. –strategija in priprave na nov koledar cepljenja s cepljenjem šestošolk proti HPV .

Pripravljena zgoščenka s prezentacijo, za pomoč šolskim zdravnikom, pri predavanju staršem na roditeljskem sestanku v začetku šolskega leta

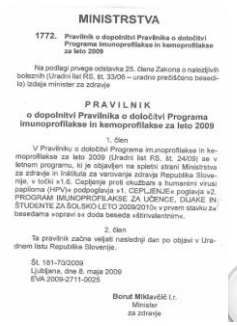
CD s kratkimi filmi ter letak - **privolitvena izjava** za podpis staršev s kratko obrazložitvijo.

PRVO STROKOVNO SREČANJE V MONSU. 2009 – CEPLJENJE PROTI HPV

Nadaljevali smo z istim načinom dela in imeli enake rezultate.

Predavanja za starše vseh učencev 6. razreda osnovne šole, ne samo deklic. Povedala sem, pokazala filme, razdelila strokovne brošure o **raku, nalezljivih boleznih in neprecenljivi zaščiti s cepljenjem.** Deklicam je razložila dispanzerska sestra, pokazala filme.

Uspeh**: kontakt s starši, graditev zaupanja, vzgled..**


MINISTRSTVA

1772. Pravilnik o dopolnitvi Pravilnika o določitvi Programa imunoprofilakse in kemoprofilakse za leto 2009

Na podlagi prvega odstavka 25. člena Zakona o nalezljivih boleznih (Uradni list RS, št. 33/06 – uradno prečiščeno besedilo) izdaja minister za zdravje

PRAVILNIK
o dopolnitvi Pravilnika o določitvi Programa imunoprofilakse in kemoprofilakse za leto 2009

1. člen

V Pravilniku o določitvi Programa imunoprofilakse in kemoprofilakse za leto 2009 (Uradni list RS, št. 24/09) se v letnem programu, ki je objavljen na spletni strani Ministrstva za zdravje in Inštituta za varovanje zdravja Republike Slovenije, v točki x1.6. Cepljenje proti okužbam s humanimi virusi papiloma (HPV)x podpoglavja x1. CEPLJENJE« poglavja x2. PROGRAMI IMUNOPROFILAKSE ZA UČENCE, DIJAKE IN ŠTUDENTE ZA ŠOLSKO LETO 2009/2010x v prvem stavku za besedama »opravi se« doda beseda »štirivalentnim«.

2. člen

Ta pravilnik začne veljati naslednji dan po objavi v Uradnem listu Republike Slovenije.

Št. 181-70/2009
Ljubljana, dne 8. maja 2009
EVA 2009-2711-0025

Borut Miklavčič l.r.
Minister
za zdravje

5

HVALA PROFESOR POLJAK ZA VAŠ PRISPEVEK IN PODPORO OD PRVEGA SREČANJA V MONSU VSE DO DANES

Hvala vsem za pozornost

- SEŽANA
  - prim. Jožica Mugoša, dr. med., spec. šol. med.
- IDRIJA
  - Majda Troha, dr.med., spec. šol. med.
- SLOVENJ GRADEC
  - Miroslava Cajnkar Kac, dr. med., spec. šol. med.
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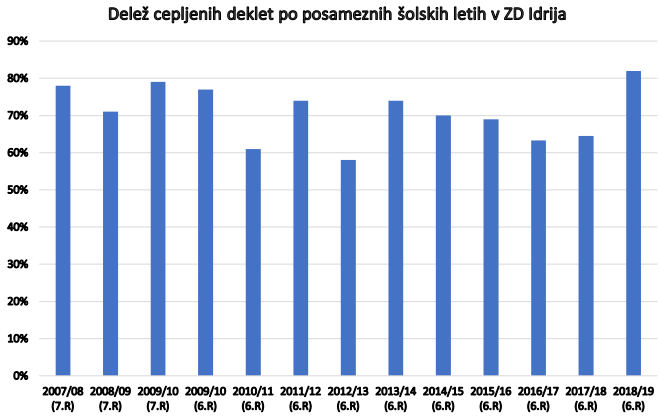
- LJUBLJANA
  - Janja Schweiger – Nemanič, dr. med.
  - Barbara Pregl, dr. med., spec. druž. med.
  - Katarina Bole, štud. med.

KAJ SMO NAREDILI V ZD IDRIJA

- 2007 – cepljenje deklet v 7. razredu OŠ (financirata občini Idrija in Cerkno)
- 2010 - vprašalnik za starše
- 2011 - vprašalnik za starše (Postojna, Slovenj Gradec, Idrija)
- 2014 - cepljenje dečkov v 6. razredu OŠ (financirata občini Idrija in Cerkno)
- 2016,2017 – vprašalnik o stališčih zdravstvenih delavcev in laikov do okužb s HPV

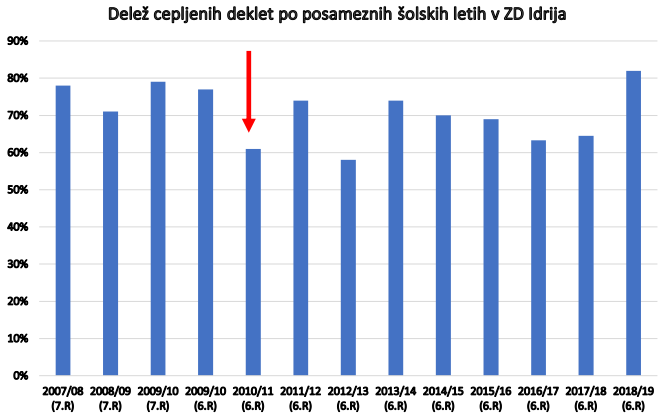
CEPLJENJE DEKLET

- Začetek leta 2007 (tri generacije deklet v 7. razredu)



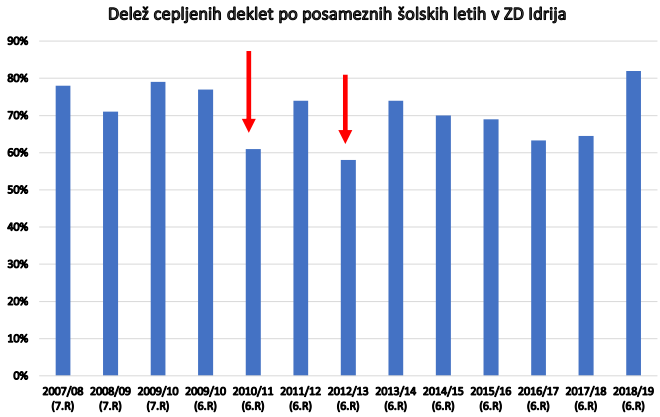
CEPLJENJE DEKLET

- Začetek leta 2017 (tri generacije deklet v 7. razredu)



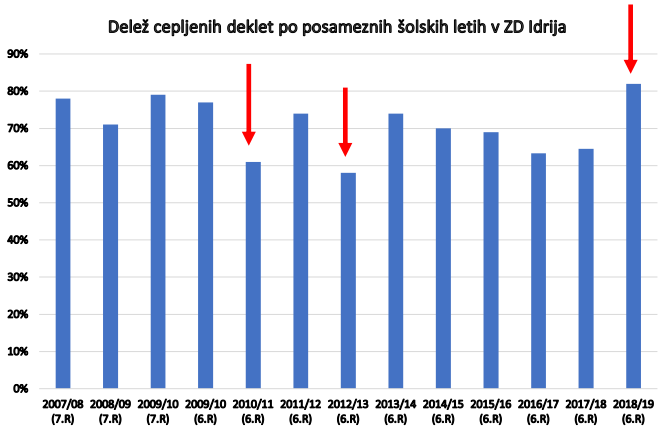
CEPLJENJE DEKLET

- Začetek leta 2017 (tri generacije deklet v 7. razredu)



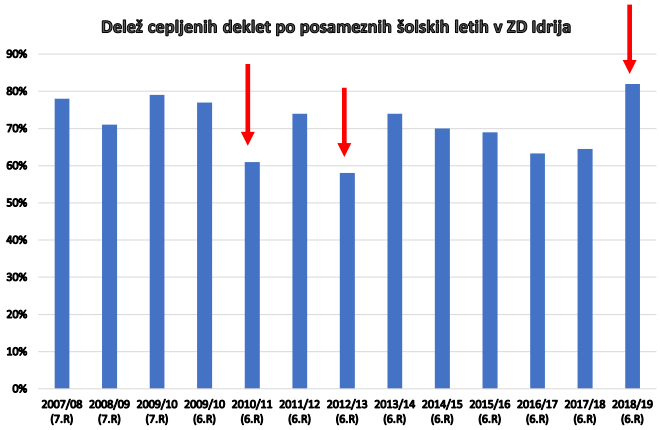
CEPLJENJE DEKLET

- Začetek leta 2017 (tri generacije deklet v 7. razredu)



CEPLJENJE DEKLET

- Začetek leta 2017 (tri generacije deklet v 7. razredu)



VPRAŠALNIK ZA STARŠE

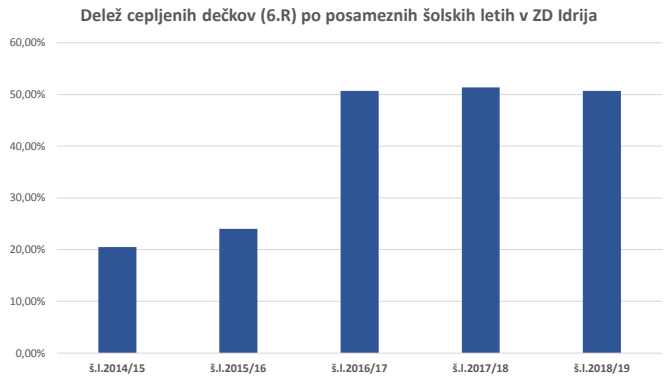
2010: Idrija, 2011: Slovenj Gradec, Postojna, Idrija

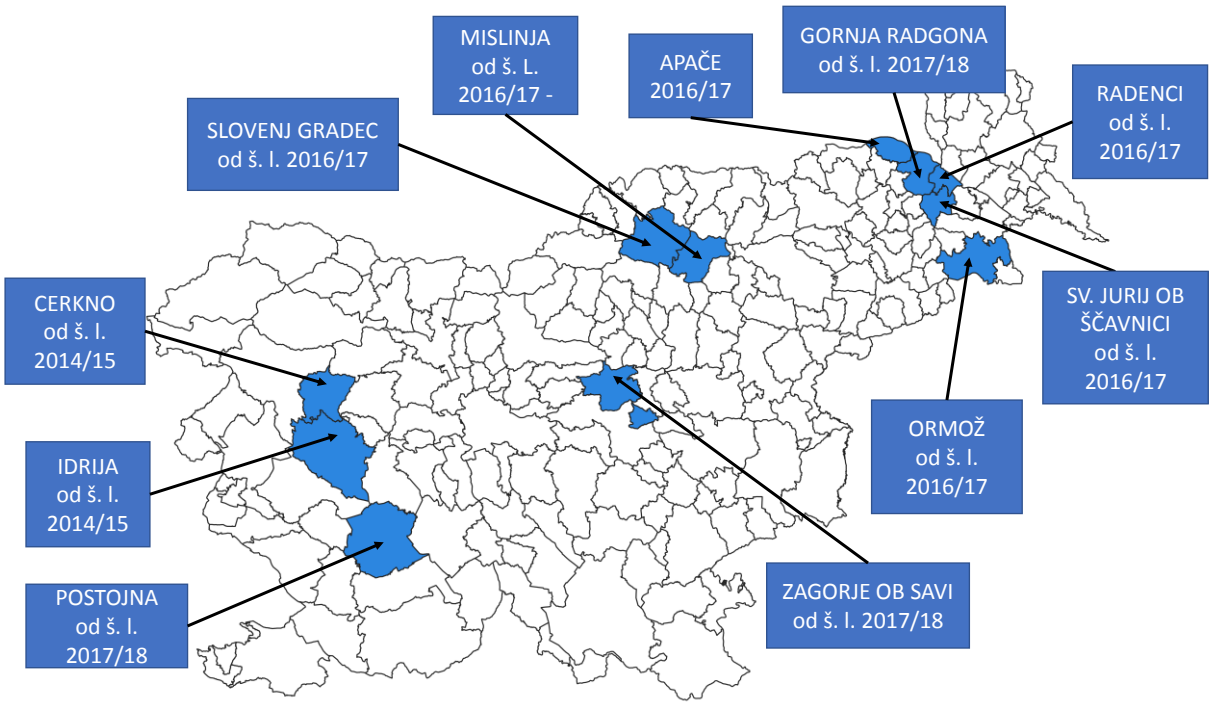
- Osveščanje o posledicah okužbe s HPV in cepljenju v obliki predavanja se mi zdi potrebno (92%)
- O cepljenju sem pred predavanjem imel(a) prepričanje, da je nepotrebno (24%), škodljivo (5%)
- Moje mnenje o cepljenju proti HPV se je po predavanju spremenilo (17%)
- Ali nam želite še kaj sporočiti?

Podpiram odločitev glede cepljenja deklet. Upam, da bo prišlo tudi do cepljenja fantov. Sama sem imela konizacijo pred 12 leti in iz svojih izkušenj vem, koliko stvari je lahko dekletom s cepljenjem prihranjenih.

CEPLJENJE DEČKOV

2014: EMA odobri uporabo qHPV za moške





VPRAŠALNIK O STALIŠČIH DO HPV OKUŽB IN CEPLJENJA MED ZDRAVSTVENIMI DELAVCI IN LAIKI

5 TRDITEV (DA, NE)

- ZDRAVSTVENI DELAVCI
  - Študentje/ke medicine (259)
  - Specialisti/ke šolske medicine, pediatri/nje (21)
  - Ginekologi (34)
- LAIKI
  - Starši šestošolcev/k (206)
  - Ženske v ginekoloških ambulantah (85)

REZULTATI VPRAŠALNIKA

- Strah pred neželenimi učinki, ki bi se lahko pokazali kasneje: ginekologi, študentje, laiki
- Pomen spletnih informacij pri odločitvi za cepljenje: ginekologi, študentje, laiki

Priporočilo zdravnika!

ČLANKA

Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2018;27:59-64
doi: 10.15570/actaapa.2018.14

Human papillomavirus (HPV) infection and vaccination: knowledge and attitudes among healthcare professionals and the general public in Slovenia

Majda Troha[1]✉, Anja Šterbenc[2], Martina Mlaker[3], Mario Poljak[2]

Acta Dermatovenerol APA

Acta Dermatovenerologica
Alpina, Pannonica et Adriatica

2019;28:71-74
doi: 10.15570/actaapa.2019.18

Municipally sponsored human papillomavirus (HPV) vaccination of boys in Slovenia: the first 4 years

Majda Troha[1]✉, Anja Šterbenc[2], Martina Mlaker[3], Mario Poljak[2]

ZAKLJUČEK

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  - **Barbara Pregl, dr. med., spec. druž. med.**
  - **Katarina Bole, štud. med.**

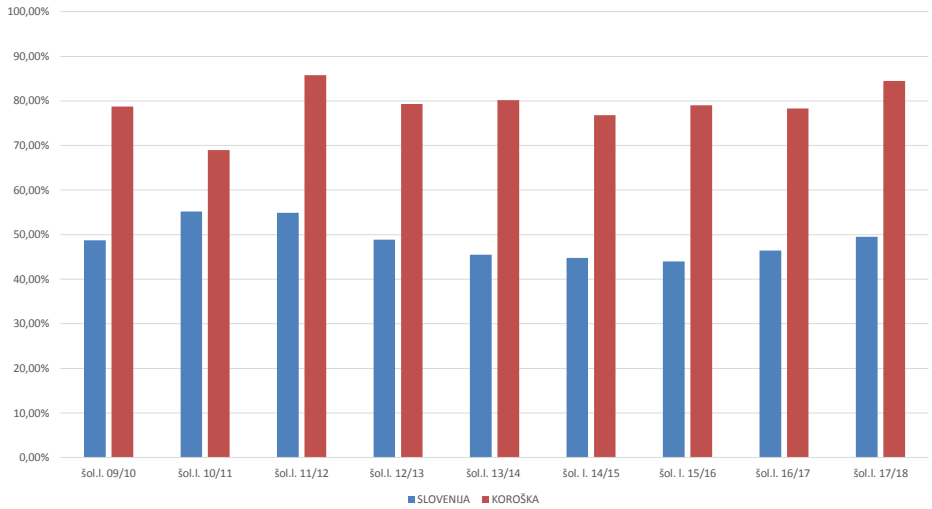
10 LET CEPLJENJA PROTI HPV

PRIMER DOBRE PRAKSE

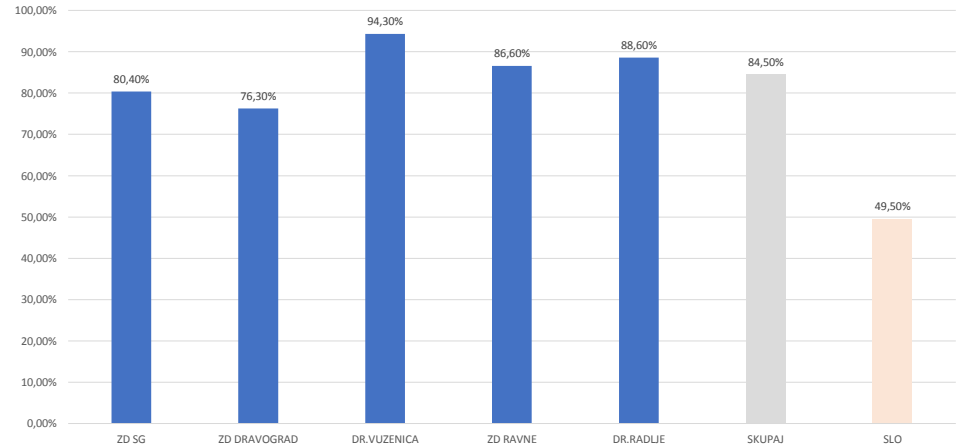
MIROSLAVA CANKAR KAC,
specialistka šolske medicine

Ljubljana, 3.9.2019

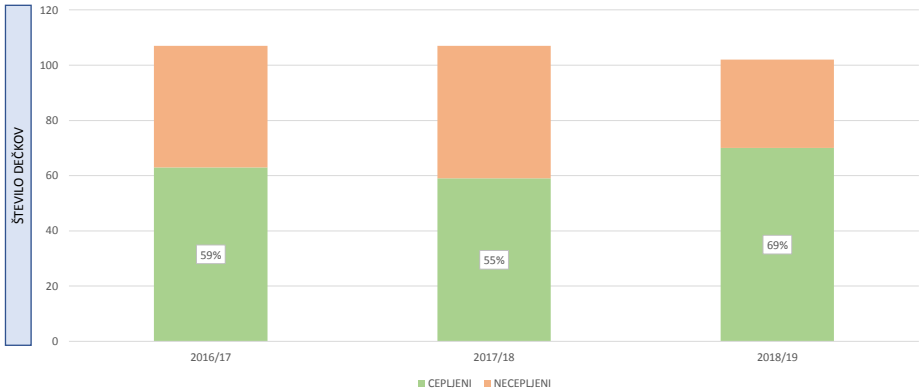
PRIMERJAVA SLOVENIJA - KOROŠKA



CEPLJENJE HPV DEKLICE PO KOROŠKIH OBČINAH 2017/2018



CEPLJENJE DEČKOV SLOVENJ GRADEC IN MISLINJA



KAKO USPEMO NA KOROŠKEM DOSEGATI 80% IN VEČ CEPLJENIH DEKLIC

- **ZAUPANJE deklic in staršev vsem članom tima, trdne vezi med stroko in starši,**
- **strokovno in objektivno PODAJANJE INFORMACIJ o okužbah s HPV in pomenu cepljenja za preprečevanje le-teh,**
- **DOSTOPNOST ZA INFORMACIJE (roditeljski sestanki, osebni pogovori v ambulantah, po telefonu, e-pošti...),**
- **starše poslušamo in se z njimi še posebej skrbno pogovarjamo, če dvomijo, ali jih je strah,**
- **TIMSKO delo,**
- **nenehno IZOBRAŽEVANJE zdravnikov in medicinskih sester na tem področju,**
- **Koroško društvo za boj proti raku,**
- **cepljenje dečkov.**

NAMESTO ZAKLJUČKA

- **Koroški človek je bil v delih Prežihovega Voranca vedno "trd", kajti tako je bilo življenje...**
- **A ko nekoga sprejme in mu zaupa, je ta predanost popolna...tudi še v današnjih dneh.**
- **In mogoče je prav v tem skrivnost tako velikega uspeha cepljenja pri nas.**

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10 LET CEPLJENJA PROTI HPV

Cepljenje proti HPV -naše izkušnje

Martina Mlaker, dr. med. spec. pediater
ZD Gornja Radgona

3. september 2019

Cepljenje proti HPV v OŠ dispanzerju Gornja Radgona

- v letu 2007
- pobuda s strani pediatrinje in ginekologinje iz ZD Gornja Radgona
- sprva samoplačniško za posameznice
- kasneje s sredstvi občin
- ciljna skupina: dekleta 8. in 9. razreda OŠ
- 4-valetno cepivo, trije odmerki
- v dveh letih cepljenje deklet od letnika **1992** do **1997**

Kako smo pristopili

- srečanje deklic in staršev s pediatrinjo ob prisotnosti predstavnikov šole nekaj dni pred cepljenjem
- zbiranje soglasij ob pomoči šole
- izvedba cepljenja v popoldanskem času/ob sistematskem pregledu v prostorih zdravstvenega doma

Precepljenost deklet (občinska sredstva)

- spodbudni rezultati, ki so odraz visoke angažiranosti pediatrov in lokalne skupnosti

leto rojstva	cepljene deklice	vse deklice	delež (%)
1992, 1993, 1994, 1995	229	293	78,2
1996, 1997	108	122	89,4

Šol. leto 2009/10 – vključitev cepljenja proti HPV v nacionalni program

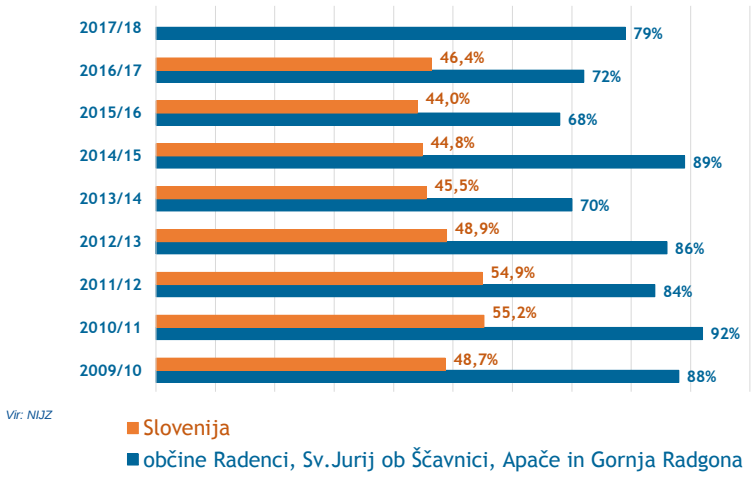
Naše izkušnje

- prva informacija o cepljenju za **6. razrede** na 1. skupnem roditeljskem sestanku vodstvo šole
- predavanje **pediatrinje** za starše in učence **6. razredov** ob prisotnosti **predstavnikov šole** tik pred samim cepljenjem (2. roditeljski sestanek)
- pisni material z informacijami o cepljenju; na spletnih straneh
- ime učenke na vsakem soglasju prednapisano
- zbiranje soglasij za cepljenje ob pomoči šole
- podpisana izjava se vloži v zdravstveni karton

Naše izkušnje

- izvedba cepljenja ob sistematskem pregledu / v popoldanskem času
- opozorilo: **ne cepi!**
- razgovor s starši, ki se niso odločili za cepljenje svojih hčera (individualno/na ponovnih sestankih), pisna gradiva staršem
- starši prihajajo do izbranih pediatrov
- individualna soglasja deklet (po 15. letu)
- slaba spodbuda s strani nekaterih ginekologov, družinskih zdravnikov in v večji meri zdravnikov drugih specialnosti

Precepljenost proti HPV v občinah Radenci, Sv.Jurij ob Ščavnici, Apače in Gornja Radgona in v Sloveniji



Vir: NIJZ

Cepljenje fantov 6. razredov

- pobuda s strani pediatrinje ob podpori celotnega pediatričnega tima
- v šol. letu 2016/17
- finančna podpora občin; sprva le 3 občine Radenci, Apače in Sv. Jurij ob Ščavnici
- v šol. letu 2017/18 tudi občina Gornja Radgona
- **9-valentno cepivo,** 2 odmerka v razmaku 6 mesecev
- boljša odzivnost deklet iz aktualne generacije nacionalnega programa
- boljša odzivnost deklet in fantov zamudnikov

Precepljenost fantov

Občina	Šol. leto 2016/17			Šol. leto 2017/18			Šol. Leto 2018/19		
	cepljeni	vsi	delež (%)	cepljeni	vsi	delež (%)	cepljeni	vsi	delež (%)
Radenci	13	19	68,4	10	25	40,0	11	21	52,4
Sv. Jurij ob Ščavnici	12	16	75,0	6	13	46,2	12	20	60,0
Apače	4	10	40,0	/	/	/	4	19	21,1
Gornja Radgona	/	/	/	11	31	35,5	15	31	48,4

Tudi odločitev za „ne-cepljenje“

je ODGOVORNOST !!

Lep pozdrav iz dežele ob Muri!

- SEŽANA
  - prim. Jožica Mugoša, dr. med., spec. šol. med.
- IDRIJA
  - Majda Troha, dr.med., spec. šol. med.
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  - Miroslava Cajnkar Kac, dr. med., spec. šol. med.
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  - Ana Keršič, štud. med.
- LJUBLJANA
  - Janja Schweiger – Nemanič, dr. med.
  - Barbara Pregl, dr. med., spec. druž. med.
  - Katarina Bole, štud. med.

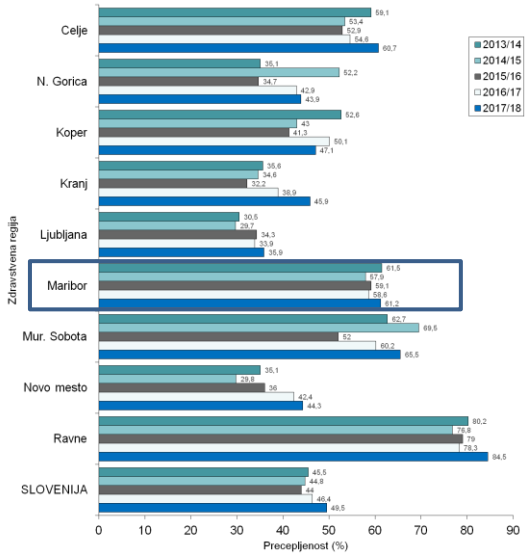
PRIMERI DOBRE PRAKSE CEPLJENJA PROTI OKUŽBAM S HPV V MARIBORU

ŠPELA ŽNIDARŠIČ RELJIČ, dr. med., spec. pediatrije
Zdravstveni dom dr. Adolfa Drolca Maribor

KARMEN ŠPARAŠ, dipl. m. s.
Srednja zdravstvena in kozmetična šola Maribor

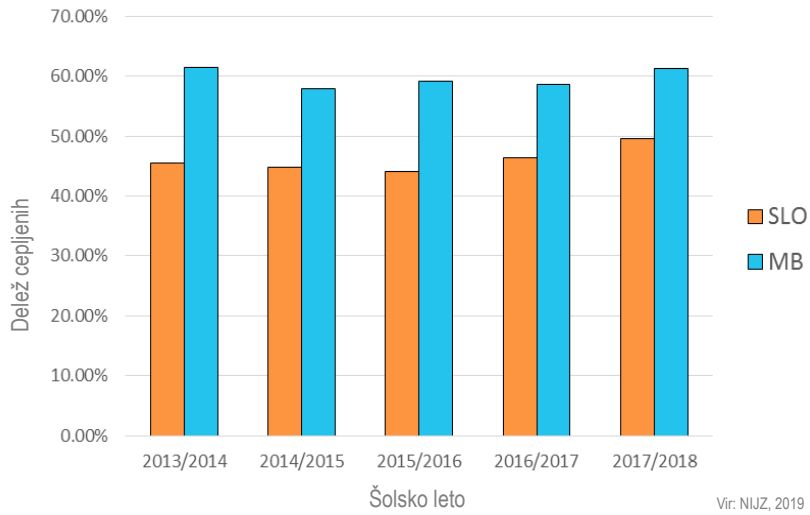
10 let cepljenja proti HPV, 3.9.2019 Ljubljana

DELEŽ ŠESTOŠOLK CEPLJENIH PROTI HPV V SLOVENIJI PO REGIJAH IN LETIH



Vir: NIJZ, 2019

DELEŽ ŠESTOŠOLK CEPLJENIH PROTI HPV V SLOVENIJI IN MARIBORU PO LETIH



Vir: NIJZ, 2019

SPODBUJANJE CEPLJENJA PROTI OKUŽBAM S HPV V MARIBORU

- **Ob sistematičnem pregledu v 3. razredu** OŠ **seznanjanje staršev** s cepljenjem proti HPV.

- **Individualno ozaveščanje** med preventivno in kurativno dejavnostjo: resnične zgodbe, lastne izkušnje in zgled.
- **Informativna gradiva**: zloženke, letaki za dekleta in starše, video posnetek, spletne strani NIJZ.

- **Komunikacija** z laično javnostjo preko klasičnih in digitalnih **medijev**.
- **Izobraževanja strokovne javnosti**: predavanja, delavnice.

- **Predavanja staršem** na šolah: zdravniki.
- **Predavanja mladostnikom**:
  - diplomirane medicinske sestre v šolah in ob sistematičnih pregledih,
  - Društvo študentov medicine Maribor: projekta Vakcinet ter Ljubezen in spolnost,
  - dijaki Srednje zdravstvene in kozmetične šole Maribor: projekt Procep.

PROCEP – PROJEKT V SREDNJI ZDRAVSTVENI IN KOZMETIČNI ŠOLI MARIBOR

- **Ustanovljen** v šolskem letu 2017/2018.

- **Namen delovanja**: ozaveščanje učencev, dijakov in bodočih zdravstvenih delavcev o pomenu cepljenja.

- **Način delovanja**: predavanja v vseh razredih SZKŠ MB in v nekaterih OŠ MB, zloženke, okrogle mize, stojnice, ankete.

- **Rezultati**: izboljšanje kulture cepljenja in večji delež cepljenih.

CEPLJENJE

- **najučinkovitejši način zaščite**
- ne zdravi že obstoječe okužbe
- zaščita traja **vsaj 10 let**
- cepijo se deklice in dečki
- cena za dečke je 69 €, za deklice 6.razreda OŠ in zamudnice je brezplačno

NEŽELENI UČINKI CEPLJENJA

- **enaki kot pri vsakem cepljenju** (rdečina, bolečina, oteklina, glavobol, utrujenost, povišana telesna temperatura, omedlevica…)
- **Vsi neželeni učinki se beležijo in dokumentirajo, da imajo nadzor nad cepivom!**

ZDRAVLJENJE OKUŽBE

- zdravijo se spremembe na koži (bradavice), predrakave in rakave spremembe
- redni ginekološki pregledi so zelo pomembni za zgodnje odkrivanje sprememb

NIJZ
Scan me
Scan me

Zloženka je nastala v okviru šolskega projekta Procep.

Zloženko je pod mentorstvom gospe Karmen Šparaš in gospe Eve Črešnar Dvornik pripravila dijakinja SZKŠ Urška Spevan.

SREDNJA ZDRAVSTVENA IN KOZMETIČNA ŠOLA MARIBOR
ŠOLA ZA ŽIVLJENJE

Cepljenje proti HPV

PROCEP

ZAŠČITI SEBE IN DRUGE

GENOTIPI HPV

- nizkorizični
- srednjerizični
- visokorizični

HPV 16 ⟶ najpogostejši visokorizični HPV v Sloveniji

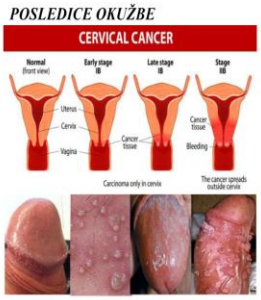
PRENOS OKUŽBE

- s telesnimi stiki s kožo ali sluznico
- spolno prenosljiva ⟶ širi se pri vseh oblikah spolnih odnosov (oralni, analni, vaginalni spolni odnos)
- okužba najpogostejša pri osebah starih 15-25 let

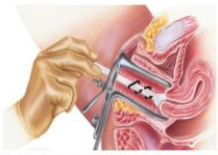
POSLEDICE OKUŽBE

- predrakave spremembe in rak materničnega vratu
- genitalne bradavice (kondilomi)
- papilomi grla
- rak zunanjega spolovila
- rak nožnice, penisa, zadnjika, ust in grla

POSLEDICE OKUŽBE



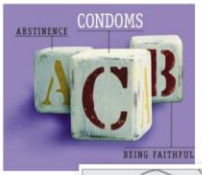
- lahko brez simptomov in znakov
- spremembe na maternični vratu odkrijemo le z mikroskopskim pregledom celic, odvzetih pri brisu materničnega vratu (BMV)



Ker običajno nimajo težav, večina sploh ne ve, da so okuženi in prenašalci HPV.

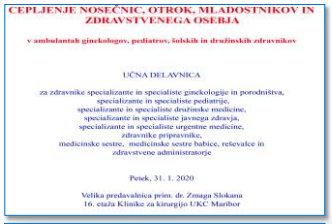
PREVENTIVA

- načela varne spolnosti/načela ABC:
  - ✓ **A = abstinenca spolnih kontaktov** (mladi naj s spolnostjo začnejo čim kasneje)
  - ✓ **B = bodi zvest** (večje število spolnih partnerjev ⟶ večja možnost okužbe s HPV)
  - ✓ **C = kondom** (niti dosledna raba kondoma ne ščiti popolnoma pred okužbo s HPV)



IZZIVI ZA IZBOLJŠANJE DELEŽA CEPLJENIH PROTI OKUŽBAM S HPV

- Umestitev cepljenja proti okužbam s HPV **za dečke v Program cepljenja.**
- **Preprečevanje zamujenih priložnosti:** vabila na cepljenje, manj lažnih kontraindikacij za cepljenje.
- **Izobraževanja zdravstvenega osebja**: strokovna srečanja, učne delavnice, spletna izobraževanja.
- **Promocija cepljenja** na družbenih omrežjih, spletnih straneh, z letaki, v klasičnih medijih.
- Umestitev vsebin o okužbah s HPV in zaščiti v **redna izobraževanja in izbirne vsebine učencev OŠ** ter **dijakov in študentov zdravstvenih strok**.


CEPLJENJE NOSEČNIC, OTROK, MLADOSTNIKOV IN ZDRAVSTVENEGA OSEBJA

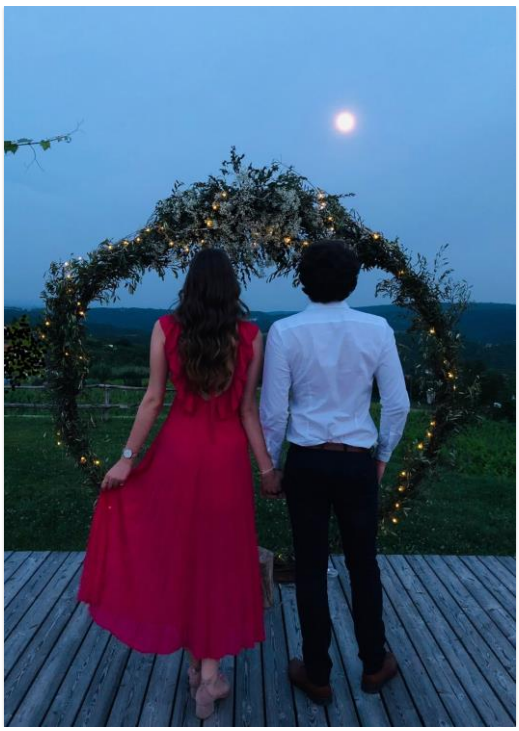
v ambulantah ginekologov, pediatrov, šolskih in družinskih zdravnikov

UČNA DELAVNICA

za zdravnike specializante in specialiste ginekologije in porodništva, specializante in specialiste pediatrije, specializante in specialiste družinske medicine, specializante in specialiste javnega zdravja, specializante in specialiste urgentne medicine, zdravnike pripravnike, medicinske sestre, medicinske sestre babice, referalce in zdravstvene administratorje

Petek, 31. 1. 2020

Velika predavalnica prim. dr. Zmaga Slokanu
16. etaža Klinike za kirurgijo UKC Maribor



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  - **Katarina Bole, štud. med.**

10 LET CEPLJENJA PROTI HPV

Primeri dobre prakse:

PRIZADEVANJA PROJEKTA VAKCINET

Predstavitev: Ana Keršič, 5. letnik MF UM

LJUBLJANA, SEPTEMBER 2019

O projektu …

- Ustanovitev decembra 2017
- DŠMM
- Vizija: *"Ozaveščanje širše javnosti o pomenu cepljenja in odstranitvi predsodkov o nevarnosti cepiv in cepljenja"*
- Metode dela:
  - *Predavanja za srednješolce, (bodoče) starše, študente*
  - *Akcije, kongresi*
  - *Facebook*

O projektu …

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O projektu …

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  - *Facebook*

O projektu …

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- Metode dela:
  - *Predavanja za srednješolce, (bodoče) starše, študente*
  - *Akcije, kongresi*
  - *Facebook*

CEPLJENJE PROTI OKUŽBAM HPV

- Predavanja o HPV za starše šestošolcev osnovnih šol
- Predavanja o cepljenju za dijake, predavanja za bodoče starše

CEPLJENJE PROTI OKUŽBAM HPV

- Organizacija skupinskega cepljenja članov projekta

- Organizacija skupinskega cepljenja najbolj aktivnih članov društva (študentov MF UM)

CEPLJENJE PROTI OKUŽBAM HPV

- Objavljanje infografik na socialnih omrežjih Facebook in Instagram

- Delitev aktualnih prispevkov, študij, ipd.

Kontakti:

Facebook: @Vakcinet

Instagram: @projekt_vakcinet

Email: vakcinet@medicinec.si

Hvala za pozornost ☺

- SEŽANA
  - prim. Jožica Mugoša, dr. med., spec. šol. med.
- IDRIJA
  - **Majda Troha, dr.med., spec. šol. med.**
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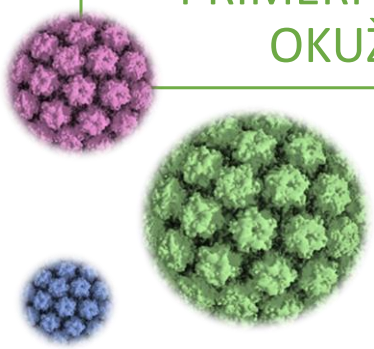
  - **Katarina Bole, štud. med.**

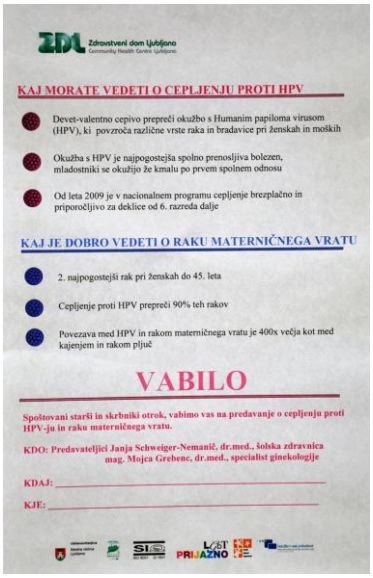
PRIMERI DOBRE PRAKSE CEPLJENJA PROTI OKUŽBAM S HPV V ZD LJUBLJANA



JANJA SCHWEIGER-NEMANIČ dr. med, šolska zdravnica

ZLOŽENKA ZA STARŠE – KAJ MORATE VEDETI O HPV

1. HPV je **najpogostejša SPO**
2. **ABC** varne spolnosti
3. cepimo deklice v **6. razredu OŠ z Gardasilom 9**, z 2 dozama po shemi 0-6 mesecev
4. **po 15. letu** cepimo s 3 dozami, po shemi 0-2-6 mesecev in se same odločajo za cepljenje
5. ZAMUDNICE so vse deklice **rojene l. 1998** in kasneje
6. Cepljenje priporočamo tudi po 26.letu
7. **Cepijo** šolski zdravniki, zdravniki v študentskih ambulantah, ginekologi in zdravniki družinske medicine
8. vsak dan se lahko cepijo dekleta in fantje od 10. do 12. ure na **Ginekološki kliniki v Ljubljani**, cena cepiva je 55 EUR plus strošek aplikacije cepiva
9. Cepljenje NE izključuje rednih obiskov pri ginekologu in odziva na vabilo na redne presejalne preglede programa ZORA
10. Na redne ginekološke preglede nujno prinesti cepilno knjižico


Zdravstveni dom Ljubljana
Community Health Centre Ljubljana

KAJ MORATE VEDETI O CEPLJENJU PROTI HPV

- Devet-valentno cepivo prepreči okužbo s Humanim papiloma virusom (HPV), ki povzroča različne vrste raka in bradavice pri ženskah in moških
- Okužba s HPV je najpogostejša spolno prenosljiva bolezen, mladostniki se okužijo že kmalu po prvem spolnem odnosu
- Od leta 2009 je v nacionalnem programu cepljenje brezplačno in priporočljivo za deklice od 6. razreda dalje

KAJ JE DOBRO VEDETI O RAKU MATERNIČNEGA VRATU

- 2. najpogostejši rak pri ženskah do 45. leta
- Cepljenje proti HPV prepreči 90% teh rakov
- Povezava med HPV in rakom maternicnega vratu je 400x večja kot med kajenjem in rakom pljuč

VABILO

Spoštovani starši in skrbniki otrok, vabimo vas na predavanje o cepljenju proti HPV-ju in raku maternicnega vratu.

KDO: Predavateljici Janja Schweiger-Nemanič, dr.med., šolska zdravnica mag. Mojca Grebenc, dr.med., specialist ginekologije

KDAJ: _____

KJE: _____

PRIJAZNO

10 LET CEPLJENJA PROTI HPV, MONS 2019

KOMUNIKACIJA V OSNOVNI ŠOLI

ŠOLSKI ZDRAVNIK
primarna preventiva

68%

GINEKOLOG
sekundarna preventiva in bolezen

STARŠI

MEDICINSKE SESTRE
Zdravstvena vzgoja I. In II. steber

UČENCI/DIJAKI

KOMUNIKACIJA V SREDNJI ŠOLI

ŠTUDENTJE MEDICINE 58%

SREDNJEŠOLCI

10 LET CEPLJENJA PROTI HPV, MONS 2019

68

- SEŽANA
  - prim. Jožica Mugoša, dr. med., spec. šol. med.
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10 LET CEPLJENJA PROTI HPV

CEPILNI DAN PROTI HPV v ZD za študente

BARBARA PREGL, dr. med., spec. druž. med.

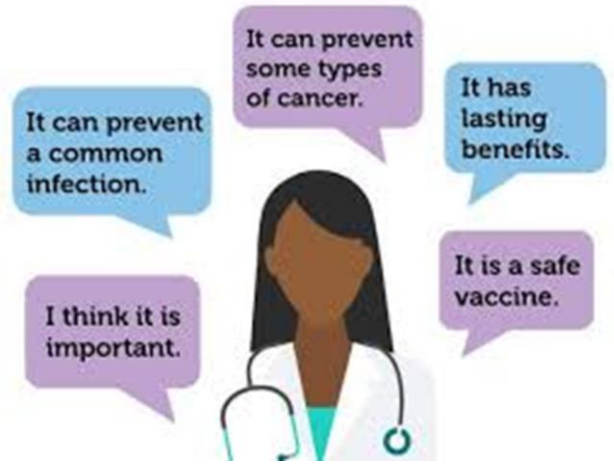
Zdravstveni dom za študente Univerze v Ljubljani
www.zdstudenti.si

STATISTIKA CEPLJENJA PROTI HPV do leta 2018

LETO	2014	2015	2016	2017	2018
ŠTEVILO CEPLJENIH	2 4V: 2	27 4V:27	66 4V: 63 9V: 3	89 4V: 11 9V: 78	176 zamudnice: 138 samoplačniki: 38

PROBLEM

- KAKO PRIDOBITI ČIMVEČ MLADIH ZA CEPLJENJE PROTI HPV???



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www.zdstudenti.si

PROMOCIJA CEPILNEGA DNE

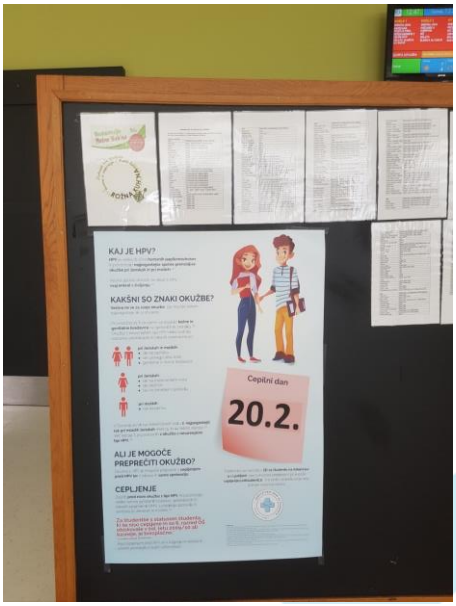
OBVESTILO NA INTERNETNI STRANI www.zdstudenti.si:

Sreda, 17.4.2019 je cepilni dan proti humanim papiloma virusom (HPV)

V Zdravstvenem domu za študente se bomo v sredo, 17. aprila 2019, od 10. do 16. ure ponovno posvetili preventivi proti HPV okužbam. Na brezplačno cepljenje vabimo študentke zamudnice (rojene leta 1998 ali mlajše, ki še niso bile cepljene) in samoplačniško cepljenje vse ostale ženske in moške, ki se želijo zaščititi pred okužbo s HPV. Cena samoplačniškega cepljenja je 70 eur na odmerek.

NOV EMAIL NASLOV:
cepljenje@zdstudenti.si

PLAKATI



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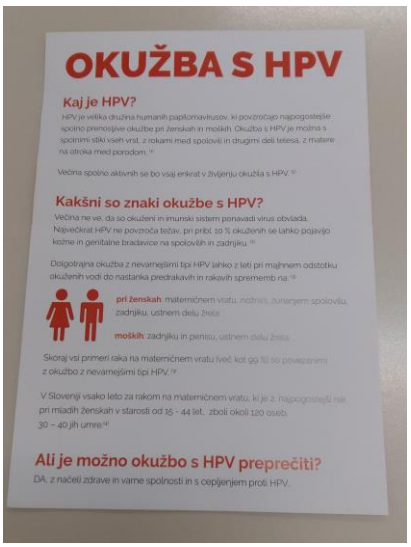
www.zdstudenti.si

LETAK, CEPILNI KARTONČEK



ČLANKI V REVIJAH

www.abczdravja.si — ABCzdravja 37

ABC

A Letno za posledicami okužbe s HPV pri nas umre od 40 do 50 žensk.

B Okužba je najpogostejša med mladimi med 20. in 25. letom.

C Studentje, zapomnite si datum cepljenja: 17. april!

Študente pozivajo k pravočasnemu cepljenju proti HPV

V Sloveniji v zadnjih letih za rakom na materničnem vratu zboli 120 žensk na leto, od tega jih 40 do 50 umre. Več kot 99 % teh rakov je povezanih z okužbo z nevarnejšimi tipi HPV. Pri približno 1000 ženskah letno odkrijejo nove primere predrakavih sprememb materničnega vratu visoke stopnje, ki potrebujejo kirurško zdravljenje. Rak materničnega vratu je tako drugi najpogostejši rak med mladimi ženskami v starosti 15–44 let, ki so velikokrat še v rodnem obdobju ali imajo doma majhne otroke.

Avtorica: **Maja Korošak**

Mojca Miholič, dr. med., spec. druž. med., strokovna vodja Zdravstvenega doma za študente Univerze v Ljubljani, zato apelira na mlade, da se pravočasno cepijo. »V nasprotju z ženskami za moške ni preventivnih presejalnih pregledov za bolezni, ki jih povzročajo HPV. Edini način preprečevanja okužb tako za moške kot ženske je cepljenje proti HPV, zato v Zdravstvenem domu za študente ... bila leta 2009 v šestem razredu osnovne šole in se takrat niso cepile. Brezplačno cepljenje torej zajame študentke prvih in drugih letnikov fakultete.«

Slabša imunost pri moških

Kot še pove dr. Miholič, si želijo doseči čim večjo precepljenost. »Najbolje bi bilo, če bi bili cepljeni pred prvim spolnim stikom. Prej so mladi cepljeni, manj težav bo v tej populaciji v zvezi z boleznimi HPV. Prav tako je zaželeno, da sta cepljena oba spola. Za zdaj pa so moški neprivilegirani.« Zakaj je pomembno, da se cepijo tudi fantje? »Breme bolezni zaradi okužbe s HPV je pri moških veliko. Slaba imunost moških po naravni okužbi jih naredi še posebej ranljive. Moški imajo genetsko slabšo naravno imunost po okužbi s HPV, kar pomeni, da prej zbolijo, če se okužijo, kakor ženske. Za njih pa ne obstajajo preventivni programi, kakor sta pri ženskah Zora ali Dora. Pomembna je tudi »čredna imunost«: moškim določeno zaščito predstavlja dobra precepljenost žensk, a je tudi povsem odvisna od te.« Za katerimi bole... HPV. »Napadena je predvsem koža na meji s sluznico. Možen je prenos z okuženimi predmeti (brisače, na stranišču) in z okužene matere s kondilomi na novorojenčka med porodom. Ko se na primer moški na stranišču okuži z virusom HPV in se z rokami dotakne spolovila partnerice, jo s tem okuži,« pojasnjuje dr. Miholič.

HPV največkrat ne povzročajo težav in okužena oseba nevede prenaša virus na druge osebe. Manj nevarni tipi HPV lahko povzročijo nastanek trdovratnih in ponavljajočih se genitalnih bradavic (kondilomov) na vulvi, vhodu v nožnico, na koži presredka, na penisu, v zadnjični odprtini in okoli nje. V ustih in žrelu povzročijo virusi HPV nastanek papilomov, lahko se pojavi hripavost in pri dojenčkih težave z dihanjem. Nevarnejši tipi HPV so krivi za dolgotrajnejšo okužbo in predrakave in rakave spremembe na anogenitalnem področju, glavi ter vratu pri obeh spolih.

OKUŽBE S HPV
SE LAHKO NALEZEŠ ŽE S TESNIM STIKOM

BIGSTOCK

O POMEMBNOSTI PREVENTIVE PROTI HUMANIM PAPILOMAVIRUSNIM (HPV) OKUŽBAM SO FEBRUARJA LETOS OZAVEŠČALI TUDI V ZDRAVSTVENEM DOMU ZA ŠTUDENTE NA AŠKERČEVI CESTI V LJUBLJANI. NA BREZPLAČNO CEPLJENJE SO POVABILI ŠTUDENTKE ZAMUDNICE (ROJENE 1998 ALI MLAJŠE, KI ŠE NISO BILE CEPLJENE) IN SAMOPLAČNIŠKO VSE DRUGE ŽENSKE IN MOŠKE, KI SO SE ŽELELI ZAŠČITITI PRED OKUŽBO S HPV.

dr. Mojca Miholič, dr. med. spec. spl. med.

Akcija je potekala pod vodstvom zdravnic, specialistk družinske medicine, iz Zdravstvenega doma za študente Univerze v Ljubljani, in sicer: **dr. Mojce Miholič** in **dr. Barbare Pregl** z drugimi sodelavkami (s sestrami in z zdravnicami). Zanimalo nas je, kako je takšen dan, poimenujmo ga »1. cepilni dan proti HPV za študente«, potekal in kakšen je bil odziv.

»Danes je bil prvi cepilni dan za HPV, nad odzivom pa smo prijetno presenečeni,« je za uvod povedala zdravnica Mojca Miholič, strokovna vodja Zdravstvenega doma za študente Univerze v Ljubljani. »Naslednje cepljenje bomo organizirali 17. aprila, ko bomo drugič cepili zamudnice in samoplačnice, ki so se danes odločile za cepljenje. Na cepljenje proti HPV je danes prišlo tudi kar nekaj moških študentov. Načrtujemo pa že tudi cepljenje v začetku naslednjega študijskega leta, v začetku oktobra 2019«. Pojasnila je razliko med termini, ki se v povezavi s cepljenjem proti HPV pogosto pojavljajo: prvo cepljenje, zamudniki, samoplačniki. »Obvezno zdravstveno zavarovanje krije cepljenje proti HPV deklетom v 6. razredu osnovne šole. Termin zamudnice se je pojavil 2011. leta, ko so začeli postopoma vključevati možnost cepljenja zamudnic, 2015 pa so med zamudnice vključili vsa dekleta rojena leta 1998 in pozneje, ki v 6. razredu oz. v šolskem letu 2009/10 niso bila cepljena, velja pa do 26. leta starosti,« pojasni zdravnica.

NAČELA VARNE SPOLNOSTI ABC (ODLOŽITEV SPOLNIH ODNOSOV-ABSTINENCA, UPORABA KONDOMA, ZVESTOBA-BE FAITHFULL) KOT PREVENTIVA PROTI VSEM SPB.

PRECEPITI DEKLETA, PREDEN POSTANEJO SPOLNO AKTIVNA

»Spolno aktivnost v osnovni šoli oziroma pogovarjanje o njej nekateri razumejo, kot da je to nekaj prezgodnjega in nekaj, kar se še ne tiče osnovnošolcev, predvsem gledano z vidika staršev, vendar pogosto to ni tako. Radi bi prosvetlili prav mlajša dekleta in fante. S programom bi radi dosegli precepljenost deklet, preden postanejo spolno

10 | REVIJA ZA MOJE ZDRAVJE

ZAKAJ CEPLJENJE PROTI HPV

Zdravstveni dom za študente Univerze v Ljubljani poziva k cepljenju proti humanim papilomavirusom (HPV), 17. aprila od 10. do 16. ure na brezplačno cepljenje študentk zamudnic (rojene 1998 ali mlajše, ki še niso bile cepljene) in samoplačniško vse druge ženske in moške, ki se želijo zaščititi pred okužbo s HPV.

Kako se okužba prenaša

S HPV, najpogostejšo spolno prenosljivo boleznijo, se vsaj enkrat v življenju okuži večina spolno aktivnih. Največkrat so okužbe prehodne narave in ne povzročajo težav, lahko pa vodijo v nastanek genitalnih bradavic. Trajna okužba z nevarnejšimi tipi HPV pri majhnem odstotku okuženih lahko povzroči tudi predrakave in rakave spremembe materničnega vratu (RMV), zunanjega spolovila in zadnjika ter ustno-žrelnega prostora pri obeh spolih. Okužba s humanimi papilomavirusi (HPV) se prenaša s tesnimi stiki s kožo ali sluznico okužene osebe. Najpogosteje se okužba prenaša pri vseh vrstah spolnih stikov, med ljubkovanjem, z okuženimi prsti rok med različnimi deli telesa, kjer tudi dosledna uporaba kondoma ne zaščiti popolnoma pred okužbo s HPV.

Bolezen narašča

Mojca Miholič, dr. med., spec. druž. med., strokovna vodja Zdravstvenega doma za študente Univerze v Ljubljani opozarja na pravočasno zaščito mladih: »V Sloveniji v zadnjih letih povprečno zboli za rakom na materničnem vratu 120 žensk na leto, od tega jih 40 do 50 umre. Več kot 99 odstotkih jih je povezanih z okužbo z nevarnejšimi tipi HPV. Pri približno tisoč ženskah letno odkrijejo nove primere predrakavih sprememb materničnega vratu visoke stopnje, ki potrebujejo kirurško zdravljenje. Rak materničnega vratu je tako drugi najpogostejši rak med mladimi ženskami v starosti 15–44 let, ki so velikokrat še v rodnem obdobju ali imajo doma majhne otroke.« Breme zaradi bolezni, povezanih s HPV, je veliko in narašča.

Zdravstveni dom za študente Univerze v Ljubljani
www.zdstudenti.si

NOVINARSKA KONFERENCA Z OKROGLO MIZO NA TEMO HPV IN POMEMBNOSTI CEPLJENJA, maj 2019

SODELOVANJE Z DŠMS – PROJEKT VIRUS

DOPIS IZ ZDŠ ŠTUDENTSKIM ORGANIZACIJAM IN MEDIJEM

SPOROČILO ZA JAVNOST

ZD za študente Univerze v Ljubljani poziva k cepljenju proti humanim papilomavirusom (HPV)

V ZD za študente bo 17. aprila že 2. cepilni dan, na katerem se lahko mladi cepijo proti virusu HPV

Ljubljana, 8. april 2019 – **S HPV, najpogostejšo spolno prenosljivo boleznijo, se vsaj enkrat v življenju okuži večina spolno aktivnih. Največkrat so okužbe prehodne narave in ne povzročajo težav, lahko pa vodijo v nastanek genitalnih bradavic. Trajna okužba z nevarnejšimi tipi HPV pri majhnem odstotku okuženih lahko povzroči tudi predrakave in rakave spremembe materničnega vratu (RMV), zunanjega spolovila in zadnjika ter ustno-žrelnega prostora pri obeh spolih. Poleg preventivnih pregledov s presejanjem za RMV pri ženskah (ZORA) je v Sloveniji na voljo tudi cepljenje proti HPV za dekleta in fante. Cepljenje je brezplačno za deklice v 6. razredih OŠ in zamudnice, rojene leta 1998 ali kasneje, ki kot šestošolke po začetku cepilnega programa leta 2009 niso bile cepljene, samoplačniško pa za ostale ženske in moške. Cepljenje proti HPV se lahko po predhodnem naročanju opravi tudi v Zdravstvenem domu za študente Univerze v Ljubljani.**

Okužba s humanimi papilomavirusi (HPV) se prenaša s tesnimi stiki s kožo ali sluznico okužene osebe. Najpogosteje se okužba prenaša pri vseh vrstah spolnih stikov, med ljubkovanjem, z okuženimi prsti rok med različnimi deli telesa, kjer tudi dosledna uporaba kondoma ne zaščiti popolnoma pred okužbo s HPV. Možen je prenos z okuženimi predmeti (brisače, na stranišču) in z okužene matere s kondilomi na novorojenčka med porodom. Okužba je najpogostejša med mladimi v starosti med 20. in 25. leti. HPV največkrat ne povzroča težav in okužena oseba nevede prenaša virus na druge osebe. Manj nevarni tipi HPV lahko povzročijo nastanek trdovratnih in ponavljajočih se genitalnih bradavic (kondilomov) na vulvi, vhodu v nožnico, na koži presredka, na penisu, v in okoli zadnjične odprtine. V ustih in žrelu povzročijo virusi HPV nastanek papilomov, lahko se pojavi hripavost in pri dojenčkih težave z dihanjem. Nevarnejši tipi HPV so krivi za dolgotrajnejšo okužbo in predrakave in rakave spremembe na anogenitalnem področju, glavi ter vratu pri obeh spolih. Breme zaradi bolezni, povezanih s HPV, je veliko in naraščа.

Mojca Miholič, dr. med., spec. druž. med., strokovna vodja Zdravstvenega doma za študente Univerze v Ljubljani zato opozarja na pravočasno zaščito mladih: *»V Sloveniji v zadnjih letih povprečno zboli za rakom na metrničnem vratu 120 žensk na leto, od tega jih 40 do 50 umre. Več kot 99 % jih je povezanih z okužbo z nevarnejšimi tipi HPV. Pri približno 1000 ženskah letno odkrijejo nove primere predrakavih sprememb materničnega vratu visoke stopnje, ki*

POTEK CEPILNEGA DNE

1 ali 2 MEDICINSKI SESTRI

ZDRAVNICA

1 MEDICINSKA SESTRA

Zdravstveni dom za študente Univerze v Ljubljani
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CEPILNI DAN

	DEKLETA						SKUPAJ DEKLETA	FANTJE			SKUPAJ FANTJE	SKUPAJ
	ZAMUDNICE			SAMOPLAČNICE								
	1.doza	2.doza	3.doza	1.doza	2.doza	3.doza		1.doza	2.doza	3.doza		
20.2. 2019	59	1	0	33	11	1	105	5	8	0	13	118
17.4. 2019	58	46	0	36	20	0	160	3	4	0	7	167

Zdravstveni dom za študente Univerze v Ljubljani

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STATISTIKA CEPLJENJA PROTI HPV do leta 2019

	2014	2015	2016	2017	2018	2019 (do junija)	SKUPAJ
ŠTEVILO CEPLJENIH	2 4V: 2	27 4V:27	66 4V: 63 9V: 3	89 4V: 11 9V: 78	176 zamudnice: 138 samoplačniki: 38	597 zamudnice: 349 samoplačniki: 248	957

ŠTEVILO ZAKLJUČENIH CEPLJENJ (prejete vse 3 doze): 119 (skupno 357 doz)

Zdravstveni dom za študente Univerze v Ljubljani

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NASLEDNJI CEPILNI DAN BO OKTOBRA 2019.

CEPIMO VSAK PETEK DOPOLDAN.

SPREMLJATE NAŠO INTERNETNO STRAN.

VPRAŠAJTE NA cepljenje@zdstudenti.si.

- SEŽANA
  - prim. Jožica Mugoša, dr. med., spec. šol. med.
- IDRIJA
  - Majda Troha, dr.med., spec. šol. med.
- SLOVENJ GRADEC
  - Miroslava Cajnkar Kac, dr. med., spec. šol. med.
- GORNJA RADGONA
  - Martina Mlaker, dr. med., spec. ped.
- MARIBOR
  - Špela Žnidaršič Reljič., dr. med., spec. ped. in Karmen Šparaš, dipl. m. s.
  - Ana Keršič, štud. med.
- **LJUBLJANA**
  - Janja Schweiger – Nemanič, dr. med.
  - Barbara Pregl, dr. med., spec. druž. med.
  - **Katarina Bole, štud. med.**

10 LET CEPLJENJA PROTI HPV

PROJEKT VIRUS delavnice volne in zdrave spolnosti

društvo študentov medicine slovenije

Projekt.virus@slomsic.org

- Izobraževanja, VP MF:
  - Kongres „Od A do HPV“
  - Varna spolnost za študente: „Med rjuhami“
- Javne akcije osveščanja
  - Teden boja proti RMV
  - Evropski teden boja proti raku
- Pojavljanje v medijih
  - Radio študent
  - Okrogla miza: novinarska konferenca GUD VAJB

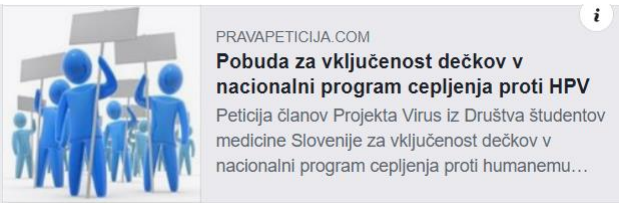
Socialna omrežja

- FB: Projekt VIRUS
- Instagram: projektvirus

- Infografike,
- pogosto zastavljena vprašanja,
- nova dognanja in aktualne novice na povezanih področjih,
- Zgledi vlečejo: fotoreportaže iz cepljenj članov
- Novo: Spletni nabiralnik za anonimna vpr.

Izredni dogodki

- EPSA SU: predavanje in javna akcija v Portorožu
- Peticija za vključitev dečkov v nacionalni program cepljenja proti HPV



GENITALNE BRADAVICE

Andreja Murnik Rauh

Dermatovenerološka klinika

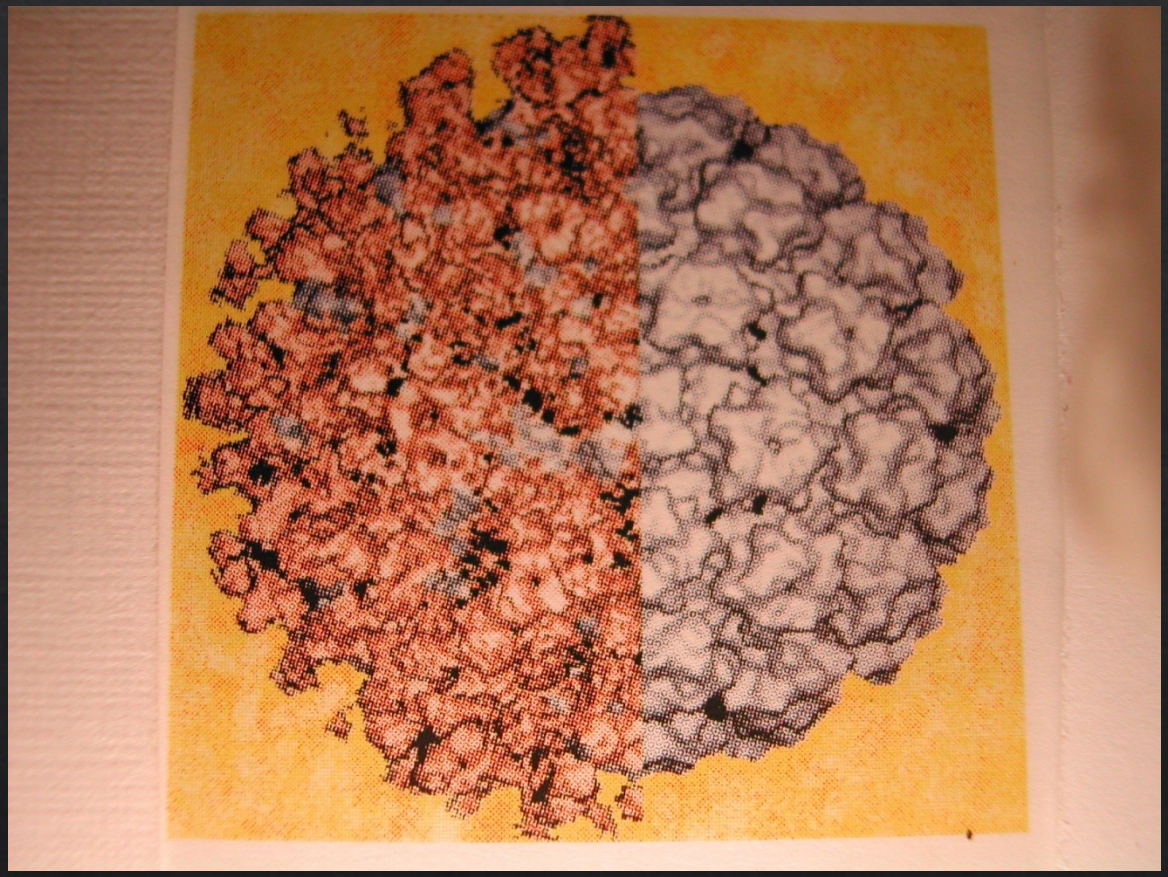
Univerzitetni klinični center Ljubljana

ETIOLOGIJA

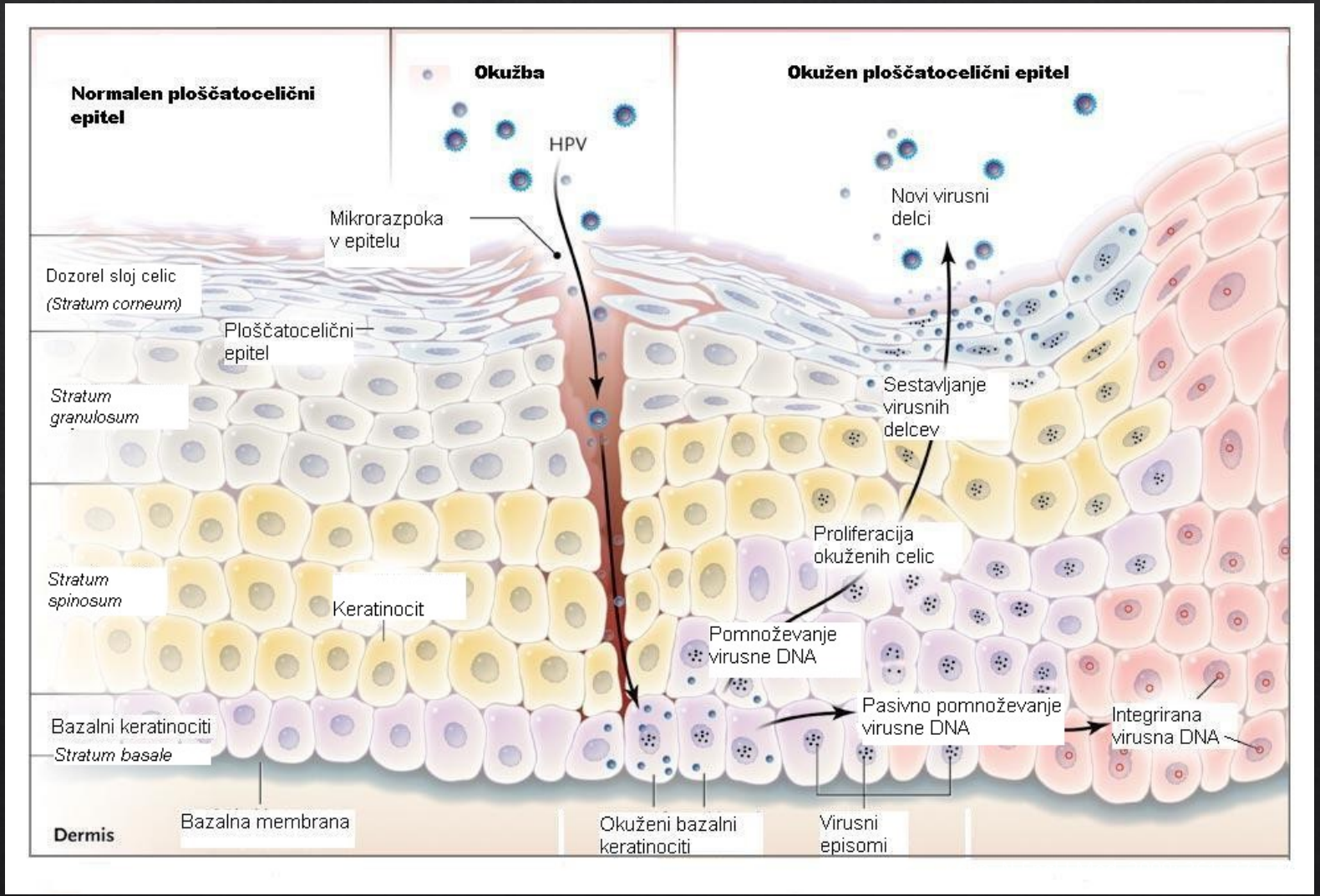
- 250 različnih genotipov HPV
- 150 dokončno opredeljenih – 40 se jih prenaša s spolnimi stiki
- HPV delimo na več skupin
- Sluznične – anogenitalne glede na rakotvorni potencial:
  - ***Nizkorizični***
  - ***Visokorizični***
  - ***Verjetno visokorizični***
  - ***Genotipi z nejasnim rakotvornim potencialom***

- Okužba z visokorizičnimi genotipi HPV je povezana z intraepitelijsko neoplazijo najvišje stopnje in malignimi ploščatoceličnimi tumorji.
- Okužba z nizkorizičnimi genotipi HPV je povezana z razvojem benignih novotvorb - genitalnih bradavic.

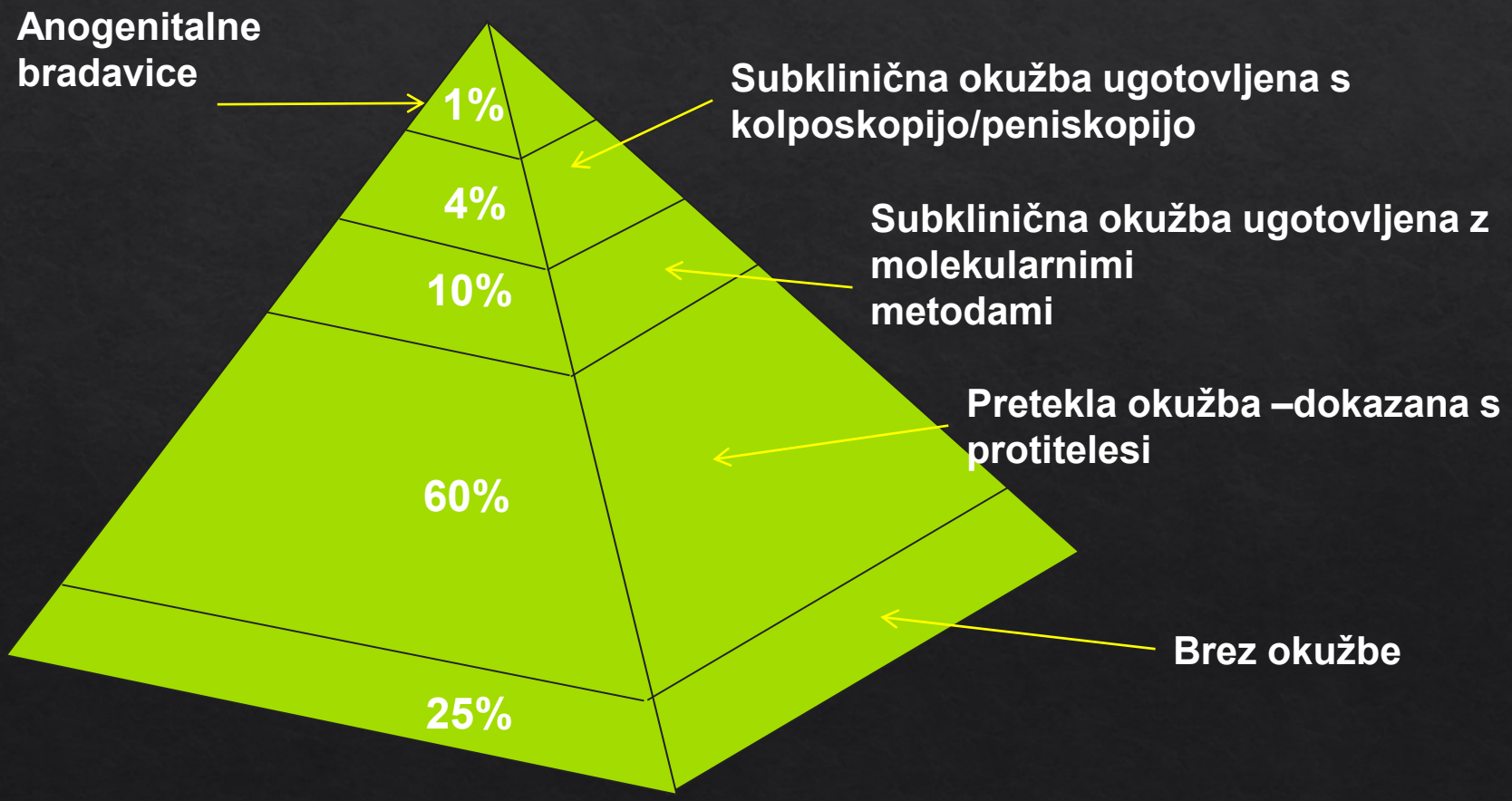
HUMANI VIRUS PAPILOMA (HPV)



Potek okužbe s HPV



GENITALNA OKUŽBA S HPV



EPIDEMIOLOGIJA

- Najpogostejša benigna novotvorba v anogenitalnem področju.
- Okužba z genotipom HPV-6 in HPV-11 v več kot 95%.
- 60% spolno aktivnega prebivalstva okuženega s HPV, le 1% ima AGB.
- Večina okužb s HPV poteka brez simptomov in ostaja neprepoznana.
- Mlajši odrasli v obdobju največje spolne aktivnosti (20.-40. let), pri obeh spolih.
- Pri večini okužba izzveni sama od sebe, pri 10% trajna.
- AGB se po uspešnem zdravljenju lahko ponovijo v 30 ali več %.
- Ne vemo ali gre pri ponovitvi AGB za novo okužbo s HPV ali ponoven nastanek spodbudijo že prisotni HPV.
- HPV se nahaja v dlačnih mešičkih okrog spolovila in zadnjika.
- Incidenca AGB narašča.

NAČIN PRENOSA

- spolni stiki (analni, vaginalni, oralni)
- ob porodu v okuženem porodnem kanalu
- s prsti rok
- zelo redko z brisačami, oblačili

75% možnost okužbe pri spolnem stiku z osebo z AGB

Kondom pred okužbo s HPV ne zaščiti povsem!

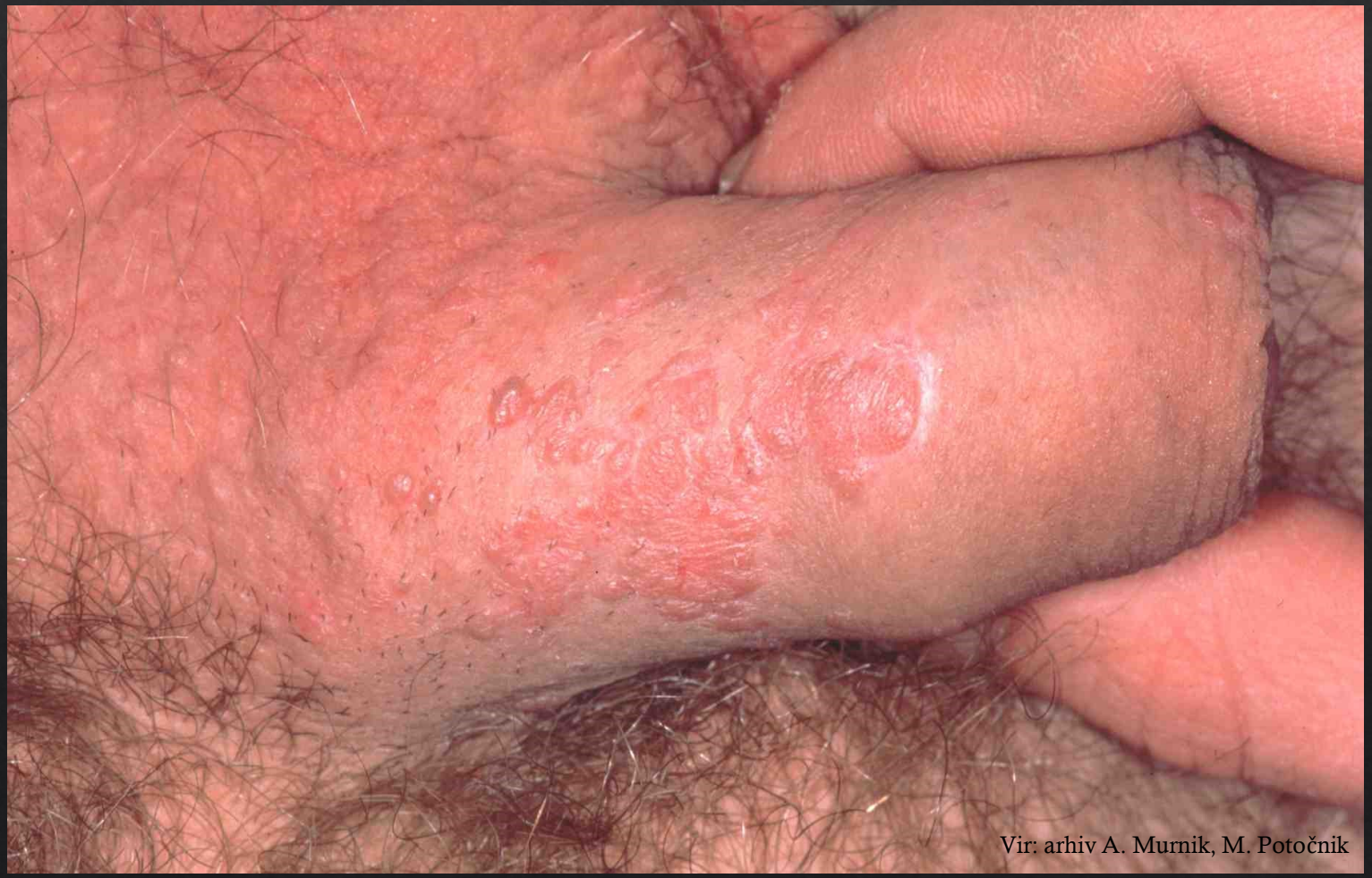
KLINIČNA SLIKA 1/2

- Inkubacijska doba različna.
- Pri večini okuženih se AGB sploh ne pojavijo.
- Začetni dogodek je poškodba penisa ali vulve in vstop virusa v celice kože ali sluznice.
- Klinične vrste AGB:
  - klasični ostri kondilomi *(condylomata acuminata)*
  - ploščati kondilomi *(condylomata plana)*
  - gigantski kondilomi *(condylomata gigantea* ali Buschke-Löwensteinovi kondilomi).

KLINIČNA SLIKA 2/2

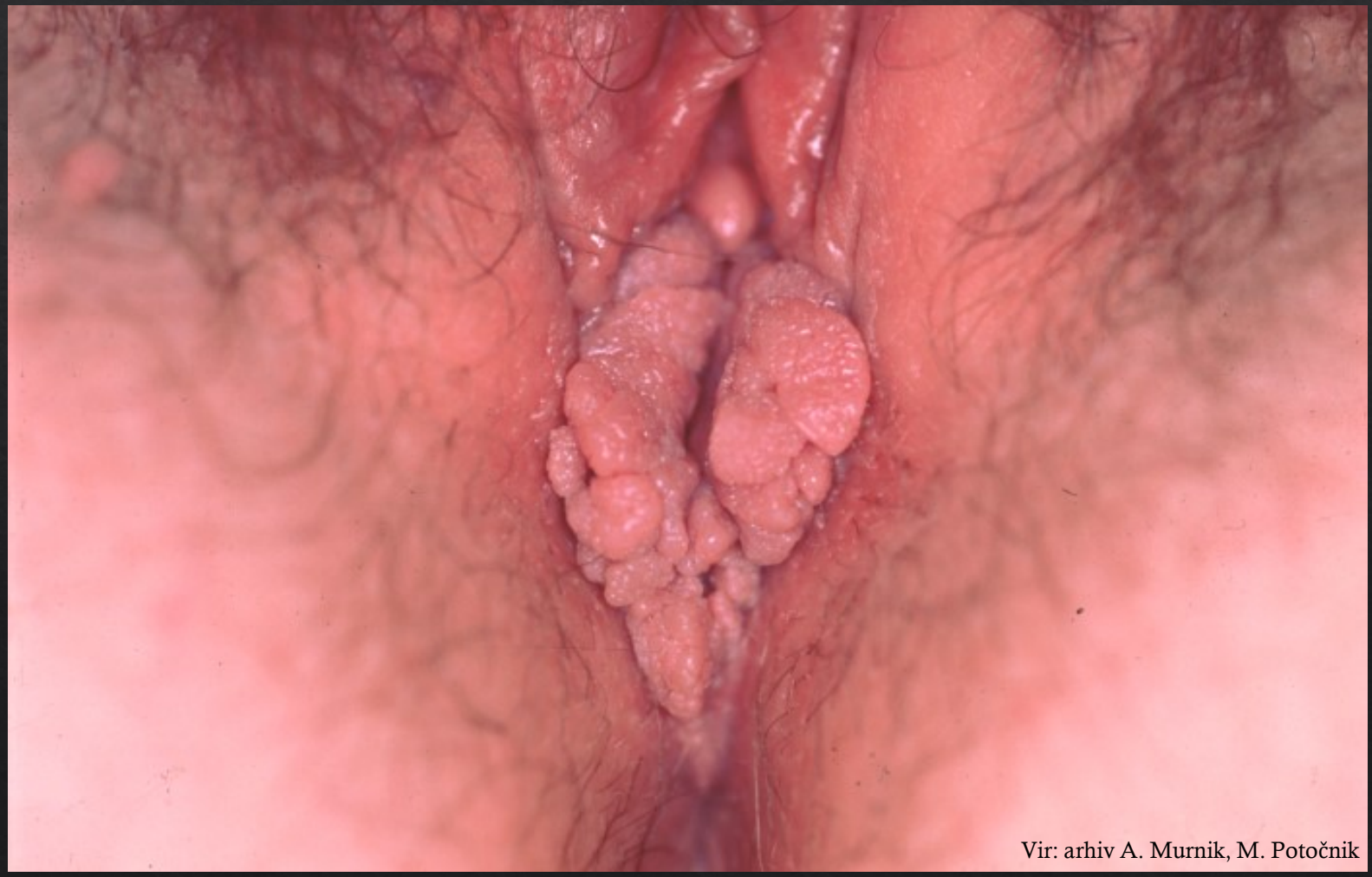
- Najprej za bucikino glavico velike, belkaste, rožnate, lahko ploščate papule.
- Papilomatozne, cvetačaste bradavičaste tvorbe, ki se lahko združijo v plošče.
- Lahko prekrijejo celotno zunanje spolovilo.
- Ne srbijo in ne bolijo.
- V kožnih gubah se zaradi pritiska lahko sploščijo (petelinja roža), macerirajo, rosijo, zaudarjajo, lahko tudi odmrejo.
- V sečnici lahko povzročajo krvavitve, izcedke, zmanjšan curek urina.
- Pri analnih odnosih - proktolog (eventuelna maligna alteracija).

GENITALNE BRADAVICE



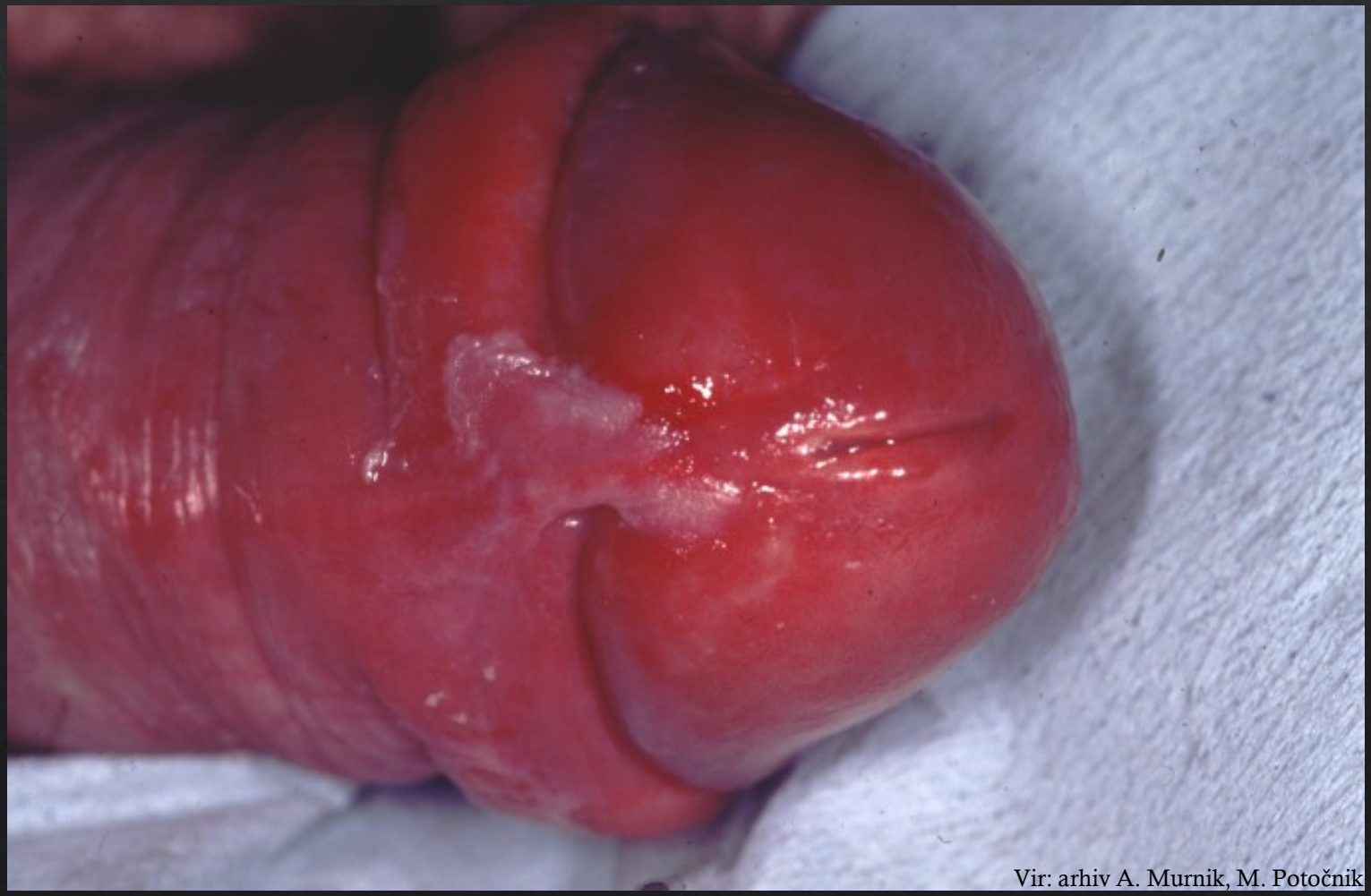
Vir: arhiv A. Murnik, M. Potočnik

GENITALNE BRADAVICE



Vir: arhiv A. Murnik, M. Potočnik

GENITALNE BRADAVICE



Vir: arhiv A. Murnik, M. Potočnik

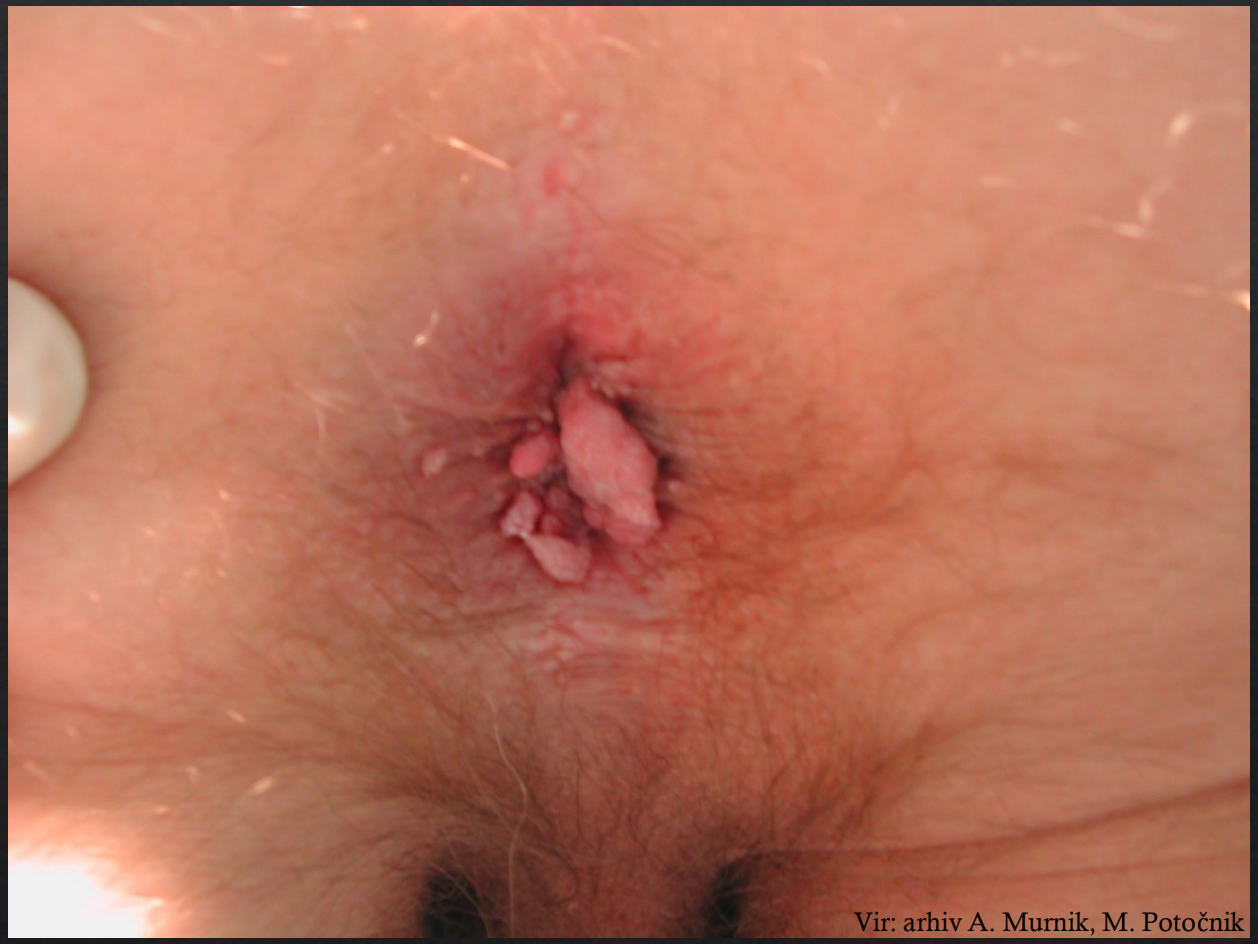
GENITALNE BRADAVICE

Vir: arhiv A. Murnik, M. Potočnik

GENITALNE BRADAVICE

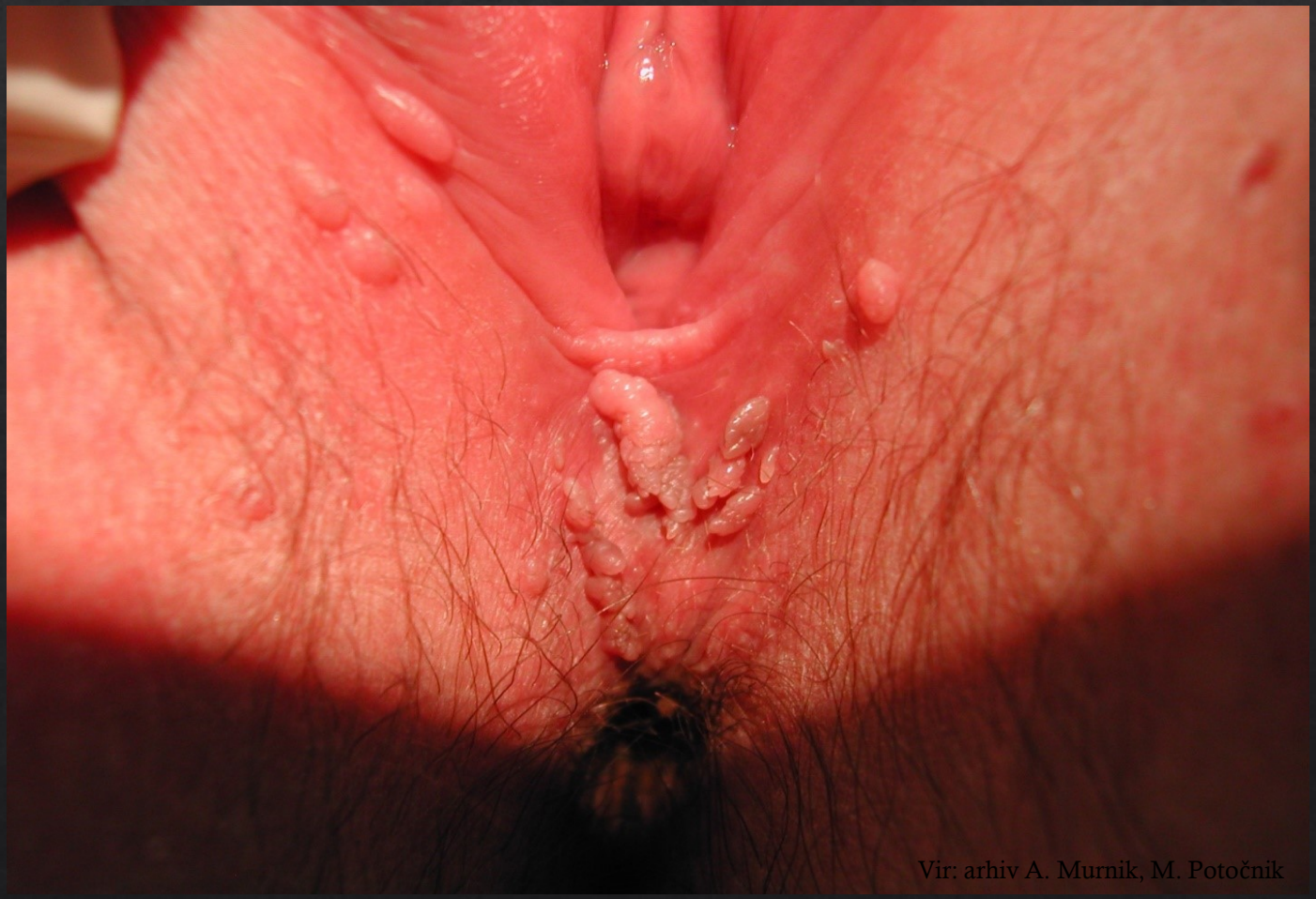
Vir: arhiv A. Murnik

ANALNE BRADAVICE



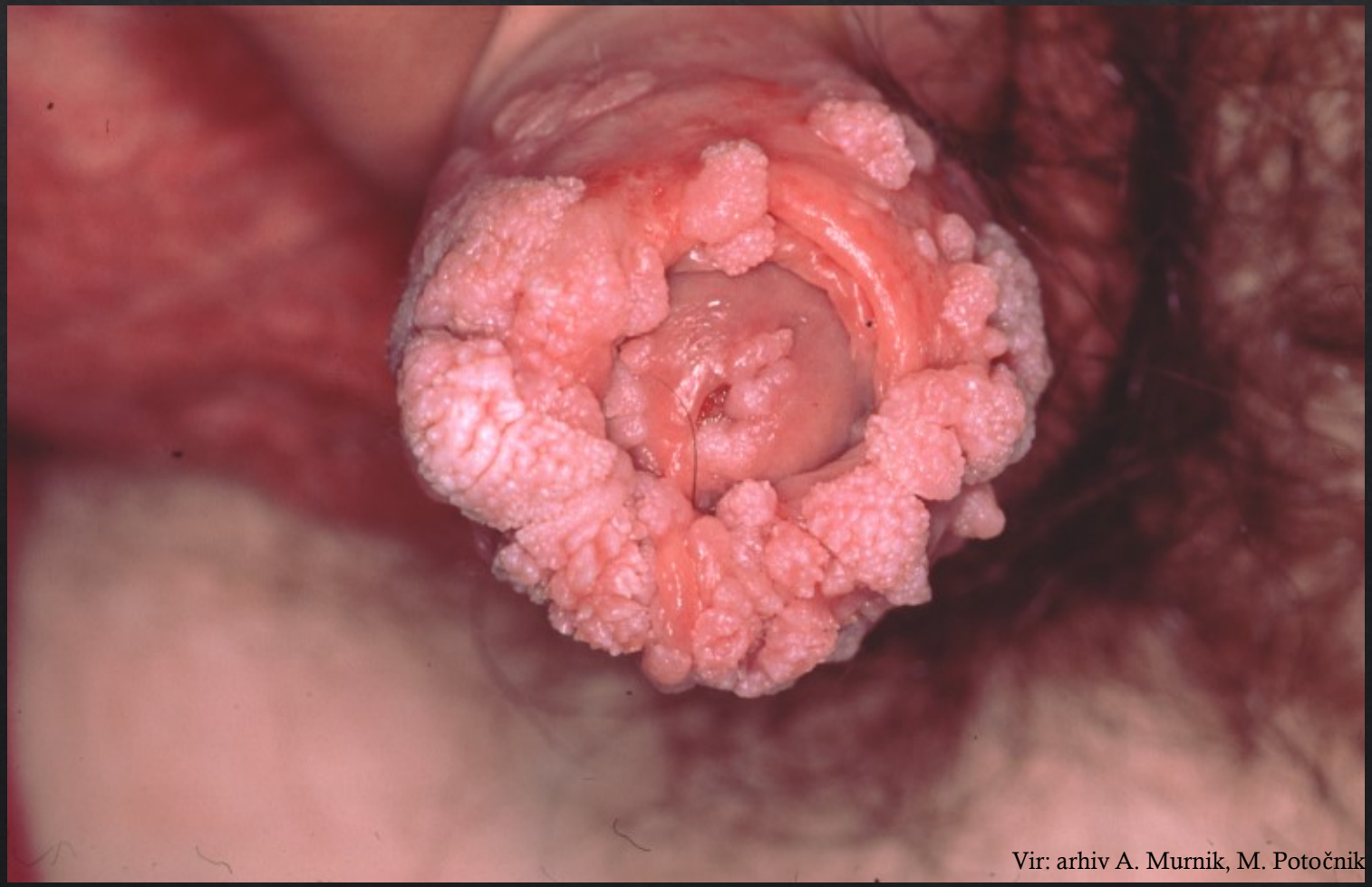
Vir: arhiv A. Murnik, M. Potočnik

GENITALNE BRADAVICE



Vir: arhiv A. Murnik, M. Potočnik

GENITALNE BRADAVICE

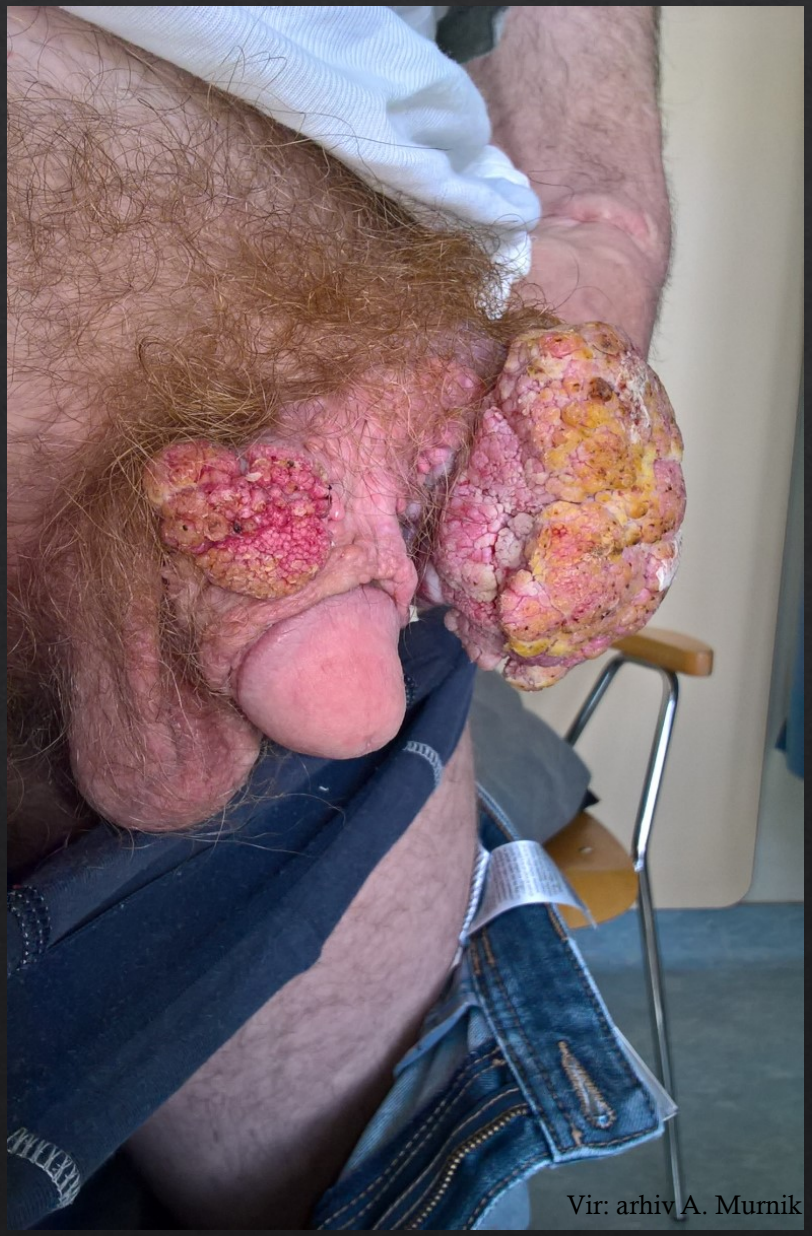


Vir: arhiv A. Murnik, M. Potočnik

GENITALNE BRADAVICE (Buschke Lowenstein)

Vir: arhiv A. Murnik

GENITALNE BRADAVICE Buschke Lowenstein



Vir: arhiv A. Murnik

DEJAVNIKI TVEGANJA

- Število spolnih partnerjev.
- Zgodnji spolni odnosi.
- AGB pri spolnih partnerjih.
- Neuporaba kondoma.

DIAGNOSTIKA

- Značilna klinična slika.
- Histološka preiskava redko, le ob sumu na rakavo spremembo.
- Genotipizacija ne sodi v rutinsko diagnostiko.

ZDRAVLJENJE 1/4

- Protivirusnega zdravila ni.
- Strogo odsvetujemo britje.
- Ni enotno določenih smernic, dogovor med bolnikom in zdravnikom.
- Tekoči dušik, imikvimod, podofilotoksin, elektrokavter, laser, ekskohleacija, ekscizija,….
- Izbira zdravljenja odvisna od morfologije, razširjenosti sprememb, lokacije.
- Profilaktično cepljenje v zgodnji odrasli dobi pred prvimi spolnimi odnosi (9 valentno cepivo proti HPV 6, 11, 16, 18, 31, 33, 45, 52, 58).
- Kondom pred okužbo s HPV ne zaščiti povsem.
- Po zdravljenju se lahko ponovijo v 30 ali več %.
- Ne vemo ali gre za novo okužbo ali ponoven nastanek spodbudijo že prisotni HPV.
- Velika psihična obremenitev.

ZDRAVLJENJE 2/4

- Bolnik izvaja sam:
  - podofilotoksin,
  - imikvimod.

- Izvaja zdravnik:
  - krioterapija s tekočim dušikom,
  - kirurško zdravljenje – ekscizija,
  - ekskohleacija,
  - elektrokirurgija,
  - laser,
  - triklorocetna kislina.

ZDRAVLJENJE 3/4

Podofilotoksin

- prečiščen izvleček rastlin Podophyllum hexandrum Royle ali P. peltatum
- zavira mitoze, povzroča nekrozo AGB
- 0,5% raztopina v etanolu in 0,15% krema
- 2x na dan 3 dni v tednu, 4 dnevi premora
- Lahko ponovimo 4-6 X ne več kot 10cm^2
- Nezaželen učinek: prehodna pekočina (50-65%), napetost, rdečina in/ali erozije,…

Imikvimod

- 5% krema (Aldara)
- Modifikator imunskega odgovora s spodbujanjem lokalnega nastajanja interferonov alfa in gama ter imunskih celic (vključno s celicami CD4+T)
- Sledi zmanjšanje AGB po velikosti in številu in zmanjšanje HPV DNK
- 3-krat na teden na AGB čez noč
- Zjutraj prizadeti predel umijemo z vodo (na koži ne več kot 8 ur)
- Dokler AGB ne izginejo (največ 16 tednov)
- Nezaželeni učinki: blaga ali zmerna rdečina, erozije, edem,…

ZDRAVLJENJE 4/4

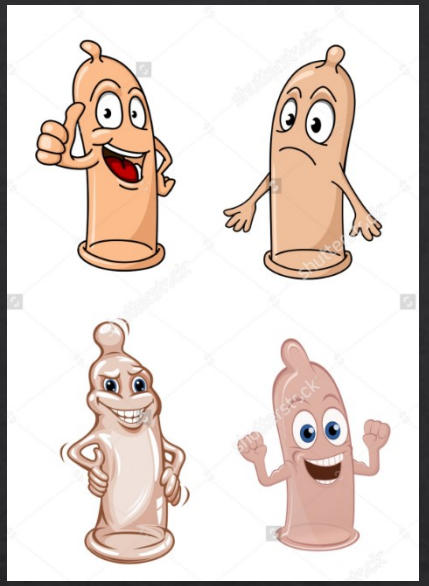
Zamrzovanje (krioterapija)

- S tekočim dušikom
- Epidermalna in dermalna nekroza in tromboza dermalnega žilja
- Posebni aplikatorji ali paličice z vato
- Preprosta in ekonomična metoda
- Učinkovito, potrebne ponovitve
- Nezaželeni učinki: hipopigmentacije, zelo redko brazgotine

Kirurško zdravljenje

- Lahko je primarno zdravljenje
- V lokalni anesteziji
- Ponovitev AGB na izrezanem predelu ali poleg njega v 20–30 %
- Nezaželeni učinek: brazgotine

PREPREČEVANJE



- Monogamija
- Kondom?
  - HPV se nahaja in prenaša s predelov in na predele, ki jih kondom ne pokriva.
  - Uporaba lubrikantov pri analnih odnosih zmanjša trenje in poškodbe sluznice
  - Kondom zaščiti pred drugimi povzročitelji SPO
- Cepljenje

HVALA ZA VAŠO POZORNOST

Zora
Državni program zgodnjega odkrivanja predrakavih sprememb materničnega vratu

Eliminacija raka materničnega vratu – vloga programa ZORA

Urška Ivanuš
Mojca Florjančič
Državni program ZORA
Onkološki inštitut Ljubljana, Zaloška 2, 1000 Ljubljana

Kontakt: mflorjancic@onko-i.si

Strokovno srečanje Sekcije za šolsko, študentsko in adolescentno mladino
Ljubljana, MONS, 3. 9. 2019

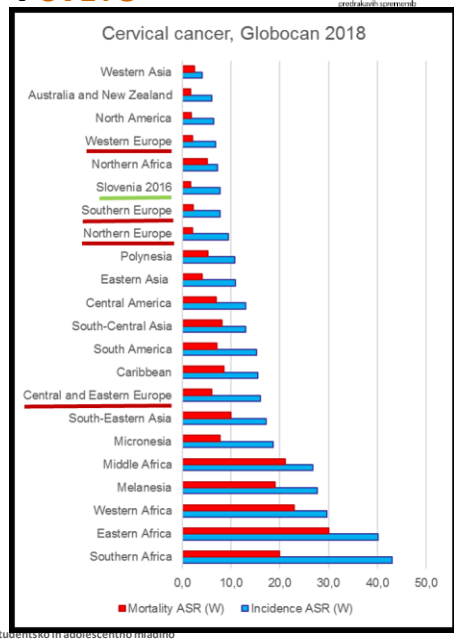
Incidenca in umrljivost za RMV v SVETU

(starostno standardizirana stopnja - svet)

Zora
Državni program zgodnjega odkrivanja predrakavih sprememb

- **četrti najpogostejši rak na svetu** pri ženskah in sedmi pri obeh spolih (≈ 500.000 novih primerov/leto).
- okrog 85% novih primerov je iz **manj razvitih** področij, kjer predstavlja skoraj 12% vseh rakov pri ženskah.

  Razlike v:
  - prevalenci okužb s HPV
  - dostopnosti presejanja za RMV (ki zmanjša incidenco RMV do 80 %)
  - dostopnosti cepiva proti HPV in precepljenosti
- Tudi **v Evropi so velike razlike** med državami; incidenca je največja v srednji in vzhodni Evropi.



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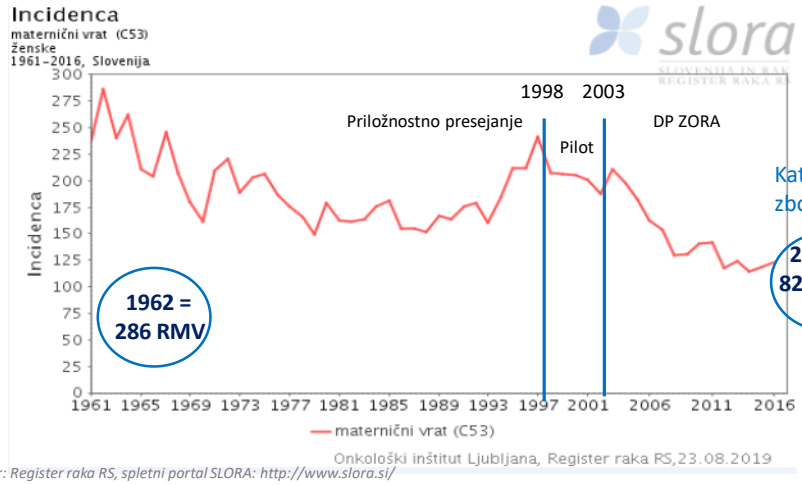
Ljubljana, MONS, 3. 9. 2019

Breme RMV v Sloveniji - INCIDENCA



Vir: Register raka RS, spletni portal SLORA: http://www.slora.si/

Po uvedbi programa ZORA leta 2003 se je INCIDENCA RMV PREPOLOVILA

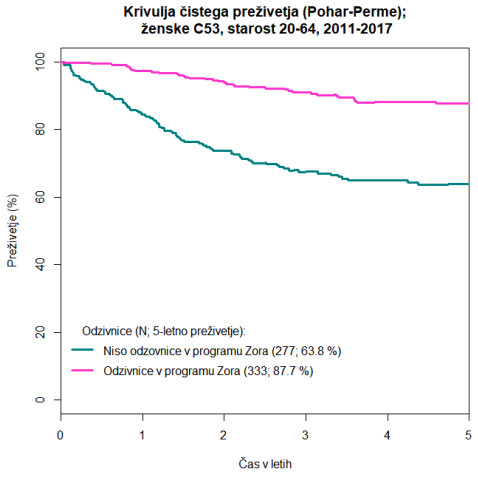
Katere ženske zbolevajo in umirajo zaradi RMV?

Ženske, ki se ne udeležujejo presejanja

- V tej manjši skupini (20-30 % vseh žensk) vznikne okoli 60 % vseh novih primerov RMV
- Pri njih je rak v 80 % odkrit v napredovalem stadiju, zato je preživetje slabše.

Ženske, ki se udeležujejo presejanja

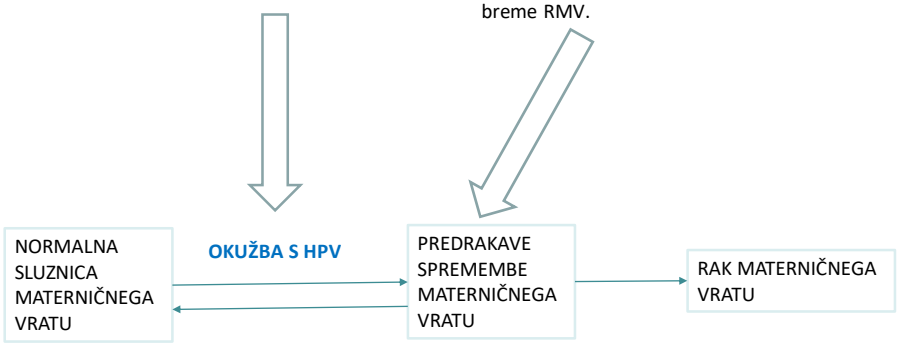
- V tej večji skupini (okoli 70-80 % vseh žensk) vznikne okoli 40 % vseh RMV.
- Pri njih je rak odkrit praviloma v omejenem stadiju, zato je preživetje boljše.



Vir: Podatkov Registra ZORA in RRRS

Sinergija delovanja cepljenja proti HPV in presejanja proti raku materničnega vratu

- S **cepljenjem** manjšamo breme okužb s HPV in posledično breme predrakavih sprememb ter RMV.
- S **presejanjem** odkrivamo in zdravimo predrakave spremembe materničnega vratu in s tem posledično zmanjšujemo breme RMV.



Svetovna zdravstvena organizacija: Poziv k eliminaciji raka materničnega vratu

https://www.who.int/cancer/cervical-cancer/cervical-cancer-elimination-strategy

Poziv k eliminaciji RMV kot javnozdravstvenega problema (SZO, maj 2018):

- s cepljenjem proti HPV
- organiziranim presejanjem za RMV in
- učinkovitim zdravljenjem

Cilji 90-70-90:

- 90 % deklet popolno cepljenih proti HPV do 15. leta starosti
- 70 % žensk presejanih v organiziranem presejalnem programu v starosti 35 in 40 let
- 90 % žensk s patološkimi spremembami materničnega vratu pravilno zdravljenih

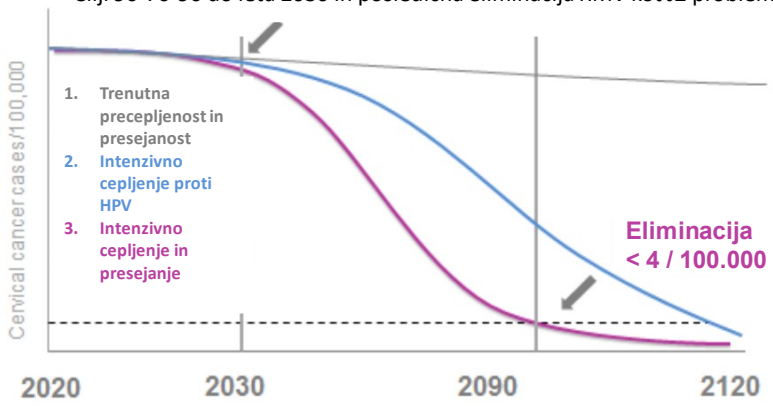
Eliminacija RMV kot JZ problema bo dosežena, ko bo breme RMV v populaciji manjše kot 4/100.000 žensk.

Za ohranjanje eliminacije bolezni bo nujno še naprej izvajati preventivne ukrepe – cepljenje proti HPV in presejanje za raka materničnega vratu!

Svetovna zdravstvena organizacija: Poziv k eliminaciji raka materničnega vratu

https://www.who.int/cancer/cervical-cancer/cervical-cancer-elimination-strategy

Cilji 90-70-90 do leta 2030 in posledična eliminacija RMV kot JZ problema



NIJZ Nacionalni inštitut za javno zdravje

REPUBLIKA SLOVENIJA
MINISTRSTVO ZA ZDRAVJE

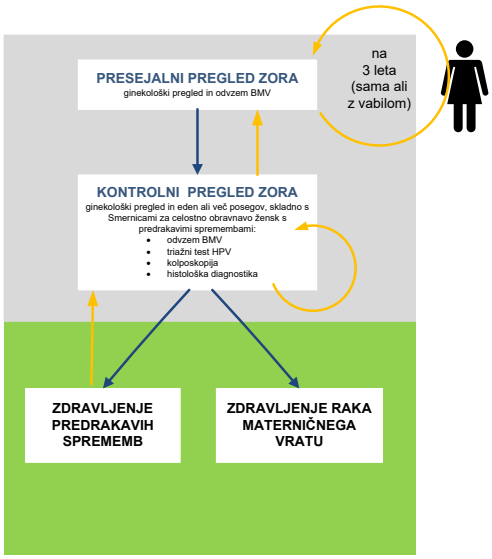
Novinarska konferenca ob 13. Evropskem tednu preprečevanja raka materničnega vratu

https://zora.onko-i.si/novice/novica/novinarska-konferenca-ob-13-evropskem-tednu-preprecevanja-raka-maternicnega-vratu

Program ZORA

- Organiziran, populacijski presejalni program za zgodnje odkrivanje predrakavih in rakavih sprememb maternicnega vratu
- Ciljna skupina: ženske, **20–64 let**
- Presejalni test: **bris maternicnega vratu za citološki pregled**
- Presejalni interval: **3-letni**

- Sedež: OIL
- Sodelujoče ustanove: ginekološke ambulante, laboratoriji (citološki, patološki, HPV), NIJZ, OIL
- Centralni presejalni register ZORA
- Zakonska podlaga
- Mehanizmi za zagotavljanje in nadzor kakovosti storitev

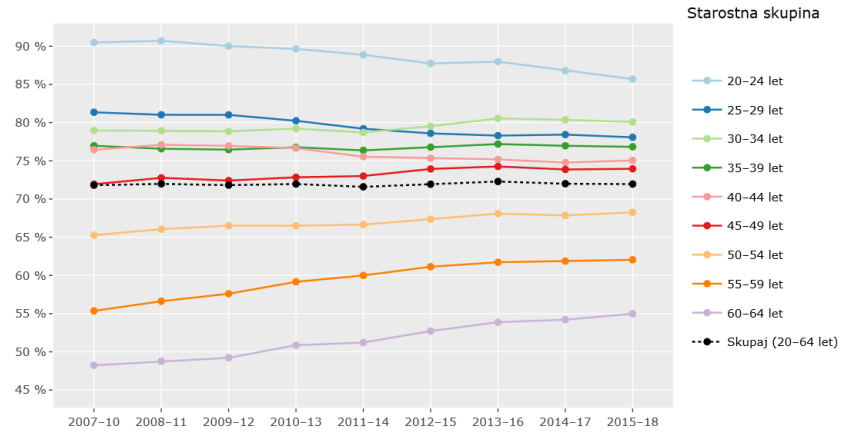


Cilji in kazalniki DP ZORA

- doseči 70 % 3-letno pregledanost žensk ciljne populacije
- odkriti in zdraviti že predrakave spremembe oz. raka v nižjem stadiju
- zmanjšati breme raka v Sloveniji

- odstotek žensk v ciljni skupini, ki so pregledane po smernicah programa (pregledanost)
- število novih bolnic v določenem letu, preračunano na 100.000 prebivalk (incidenčna stopnja RMV)
- umrljivost zaradi RMV
- razmerje med številom novo odkritih predrakavih in rakavih sprememb na leto

3-letna pregledanost po starostnih skupinah



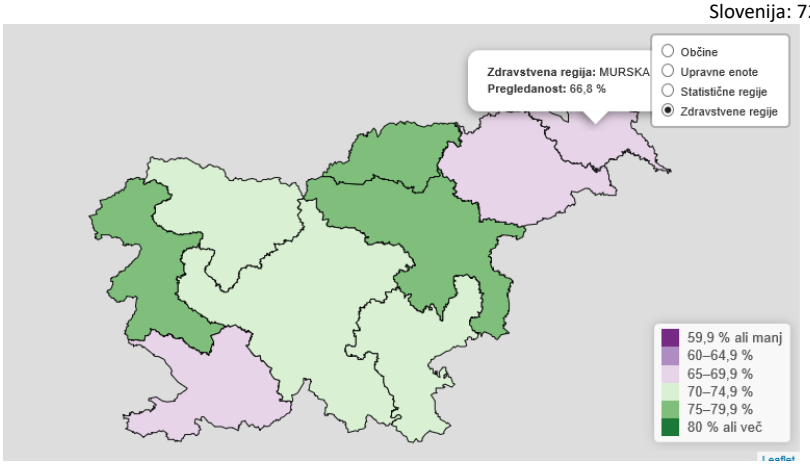
Slovenija: 72,0 %

Vir: Register ZORA

3-letna pregledanost po zdravstvenih regijah

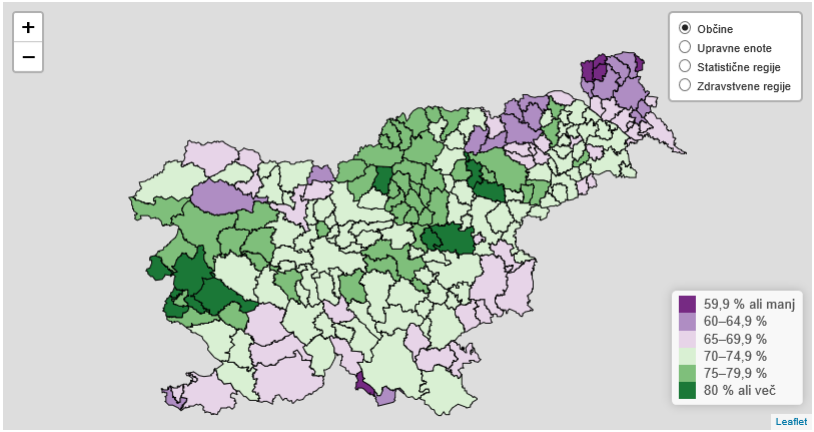
NG: 79,7 %
MS: 66,8 %

Slovenija: 72,0 %



Vir: Register ZORA

3-letna pregledanost po občinah



MAX: Hrastnik (82,4 %), Slovenske Konjice (81,3 %), Brda (81,3 %)
MIN: Hodoš (51,8 %), Osilnica (52,4 %), Kuzma 58,1%)

Vir: Register ZORA

Slovenija: 72,0 %

Podatki Registra ZORA

- BMV: > 4.710.000 → Citopatološki laboratoriji: 9 (19)
- HISTO: > 133.000 (od 2004) → Histopatološki oddelki: 11
- HPV: > 100.000 (od 2010) → Molekularna laboratorija: 2

Vir: Register ZORA

Strokovne smernice in priporočila za ginekologe

Navodila za laboratorije

Napotnici za BMV in ttHPV


Register organiziranega odkrivanja raka materničnega vratu ZORA

Osebni podatki preiskovanke
Priimek in ime .... EMŠO
Naslov (ulica, hišna številka, kraj, poštna številka) ....
Naročnik preiskave ....

Mesto odvzema	1	Ektocerviks	2	Endocerviks	6	Ekto + Endo	3	Vagina	4	Vulva	5	Drugo
Razlog odvzema	1	ZORA	2	Preventiva	3	Kurativa	4	Kontrolni pregled			5	Drugo

Klinična diagnoza in opombe:
MKB

Menstruacijski ciklus		HNZ		Zadnji test HPV (hc2)	
Zadnja menstruacija		Normalna kolposkopija		Leto zadnjega testa HPV (hc2)	
Hormonska kontracepcija		Atipična kolposkopija		Zadnji citološki izvid	
Maternični vložek		Biopsija		Leto zadnjega citološkega izvida	

Številka preparata	Zdravnik	Datum odvzema	Številka arhiva

Naziv/žig laboratorija — **CITOLOŠKI IZVID** — **KLASIFIKACIJA PO BETHESDI** — **Datum sprejema**

KAKOVOST BRISA
11 Bris uporaben
12 Bris neuporaben

BRIS PATOLOŠKI
C PATOLOŠKE SPREMEMBE
Ploščate celice
20 APC-N Atipične ploščate celice, neopredeljene
21 APC-VS Atipične ploščate celice, ni mogoče izključiti PIL visoke stopnje
22 PIL-NS PIL nizke stopnje (blago diskariotične celice)
23 PIL-VS PIL visoke stopnje (zmerno/hudo diskariotične celice)
24 P-CA Ploščatocelični karcinom
Žlezne celice
25 AŽC-N Atipične žlezne celice, neopredeljene
26 AŽC-VN Atipične žlezne celice, verjetno neoplastične
27 AIS Endocervikalni adenokarcinom in situ
28 A-CA Adenokarcinom

ONKOLOŠKI INŠTITUT LJUBLJANA 2011


NAPOTNICA ZA TRIAŽNI TEST HPV

Pošiljatelj .... Št. protokola ....
Plačnik ....
Priimek in ime
Datum rojstva EMŠO
Bivališče .... Poštna št.
Št. KZZ ....

Datum in izvid zadnjega triažnega testa HPV ....

INDIKACIJA ZA TRIAŽNI TEST HPV – triaža na klinični poti:

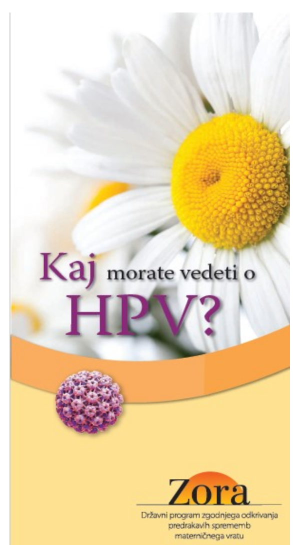
- ☐ **APC-N** (atipične ploščate celice, neopredeljene)
- ☐ **AŽC-N** (atipične žlezne celice, neopredeljene)
- ☐ **PIL-NS ≥ 35 let** (PIL nizke stopnje pri ženski stari 35 let in več)
- ☐ **CIN 1**
- ☐ **CIN – po zdravljenju**

Datum odvzema — Žig, številka in podpis zdravnika

Ponatis prepovedan. — ONKOLOŠKI INŠTITUT LJUBLJANA 2011

Strokovno srečanje Sekcije za šolsko, študentsko in adolescentno mladino
Ljubljana, MONS, 3. 9. 2019

Informativni materiali za ženske



Strokovno srečanje Sekcije za šolsko, študentsko in adolescentno mladino
Ljubljana, MONS, 3. 9. 2019

Informativni materiali za ženske

Izobraževanja za strokovno in laično javnost

- 9. izobraževalni dan programa ZORA:
  - **12. november 2019, Brdo pri Kranju – VABLJENI!**
- Delavnice za citopatologe in patologe
- Delavnice za ginekologe in medicinske sestre
- Šola za presejalce
- Promocija programa na različnih dogodkih
- Objavljanje novosti in obvestil na spletni strani programa
  - https://zora.onko-i.si/

Izzivi, ki nas čakajo

- Prenova IS DP ZORA
- Katera presejalna metoda v bodočnosti?
- Prva cepljena generacija deklet že vstopa v program ZORA
- Kako obravnavati cepljena dekleta (manjše tveganje za okužbo s HPV in za predrakav/rakave spremembe)?

Presejalna politika za cepljene in necepljene deklice zaenkrat ostaja enaka!

Zaključek

Zoprna misel,
O, kako dolgo že.....
Res to nočna mora je,
A glej, **ZORA** reši vse!

Okužbe s HPV pri mladih ženskah

Ljubljana, 3.9.2019

Doc. dr. NINA JANČAR, dr. med., KO za reprodukcijo. GK, UKC Ljubljana

Humani papilomavirusi – HPV

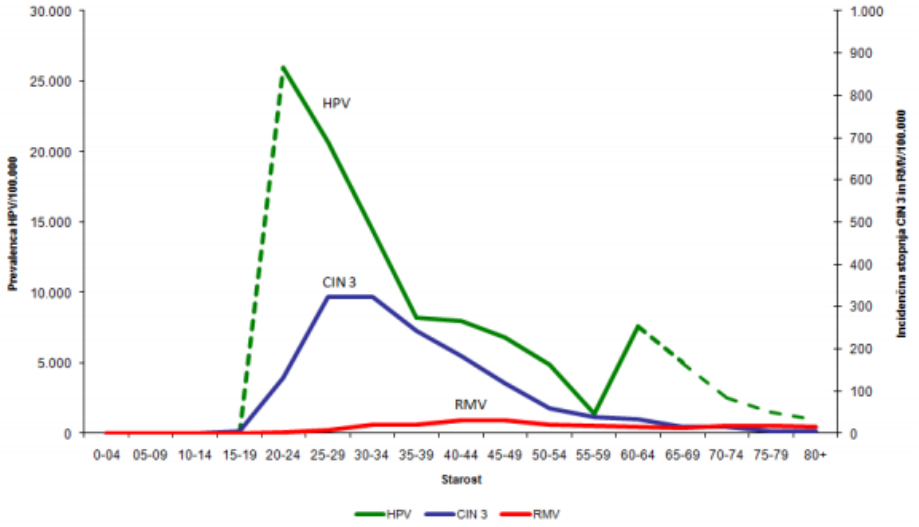
- Najpogostejša virusna SPO
- Poznamo > 200 genotipov
- Visokorizični genotipi (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68) povzročajo predrakave spremembe in raka materničnega vratu, nožnice, vulve, zadnjika, penisa, žrela in ustne votline.
- Nizkorizični genotipi (predvsem 6 in 11) povzročajo genitalne bradavice.

Okužbe s HPV

- Prve okužbe že kmalu po začetku spolnega življenja.
- Največja pojavnost v starostni skupini 20 – 25 let.
- Večina okužb izzveni samih po 12 – 24 mesecih.
- Okoli 10 % pa jih vztraja.
- V starosti **20 – 25 let** je v Sloveniji v vsakem trenutku s HPV okužena **vsaka 4.** ženska; s starostjo se prevalenca okužb s HPV manjša, veča pa se incidenca CIN in RMV.

Ljubljana, september 2019

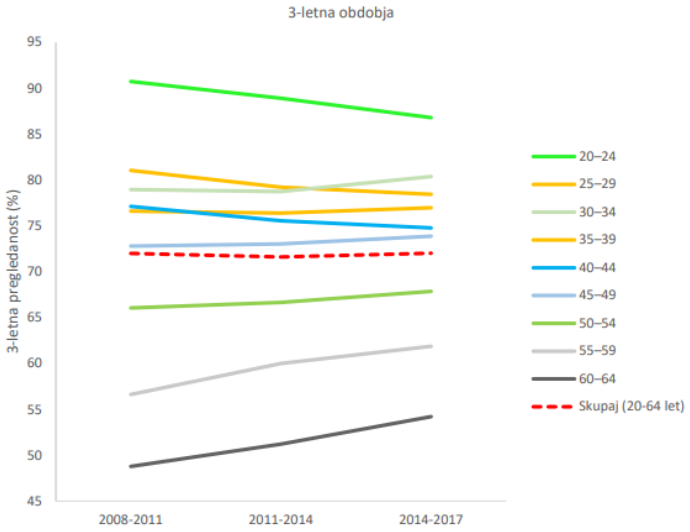
Prevalenca okužb s HPV in incidenca sprememb MV glede na starost



Začetek presejanja za RMV

- V večini evropskih držav se presejanje za RMV prične **med 25. in 30. letom** starosti žensk.
- V Sloveniji pa se presejanje za RMV v DP ZORA prične **že pri 20. letu** starosti žensk.

Pregledanost žensk v programu ZORA



Vpliv zgodnjega presejanja

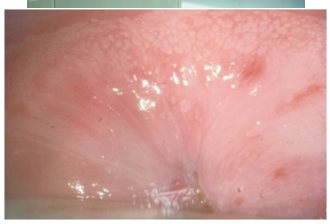
- 1. odvzem BMV pri starosti **20. let** (**Priporočila DP ZORA**)

Dejansko stanje:

- V gin. amb. pride najstnica, ki že ima spolne odnose; ginekolog odvzame **prvi PAP bris že pred 20. letom starosti.**
- **Zakaj je to problem?**
  - Ker je okužba s HPV v tej starosti zelo pogosta, obstaja možnost, da jih zaradi ponavljajočih patoloških brisov MV **začnemo (pre)zgodaj zdraviti.**
  - Zdravljenje je **pogosto prekomerno!**

Nizkorizične spremembe maternične vratu – PIL-NS (CIN 1)

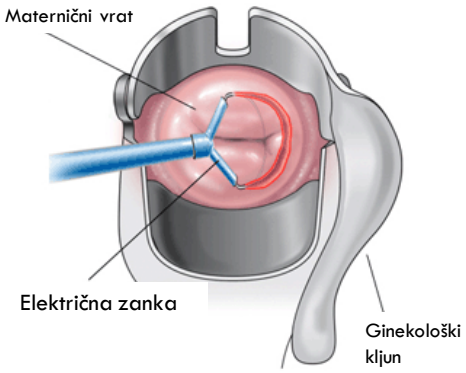
- Večina žensk je mladih,
- ≈60% jih spontano izzveni v 1 letu,
- ≈90% v treh letih,
- ≈10% vztraja ali napreduje.
- **Pogosti pregledi pri ginekologu zaradi spremljanja – STRES…**



Spremembe PIL-NS

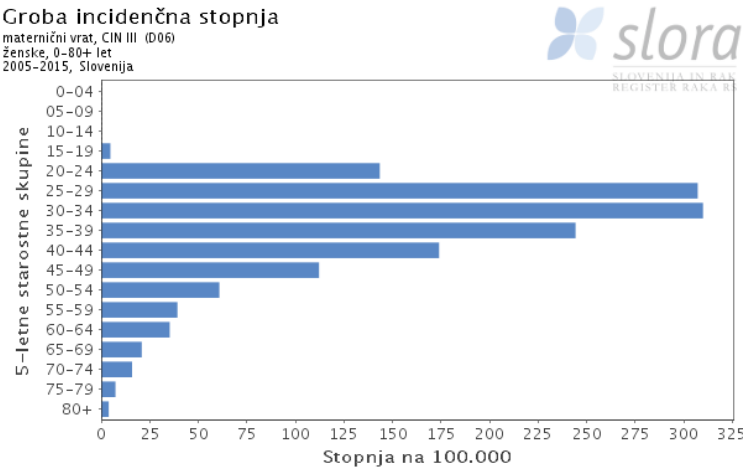
- Smernice za obravnavo teh sprememb: SPREMLJANJE!
- Spremljanje vključuje kolposkopijo, PAP bris in HPV test / 12 mesecev.
- Zdravimo LE, če vztrajajo 2 leti, ali če napredujejo v hujšo obliko.
- Vedno zdravimo z destrukcijskimi tehnikami: laserska vaporizacija, elektrokoagulacija, krioterapija. Nikoli ne izrezujemo teh sprememb!

Visokorizične spremembe materničnega vratu – PIL-VS (CIN 2, 3)



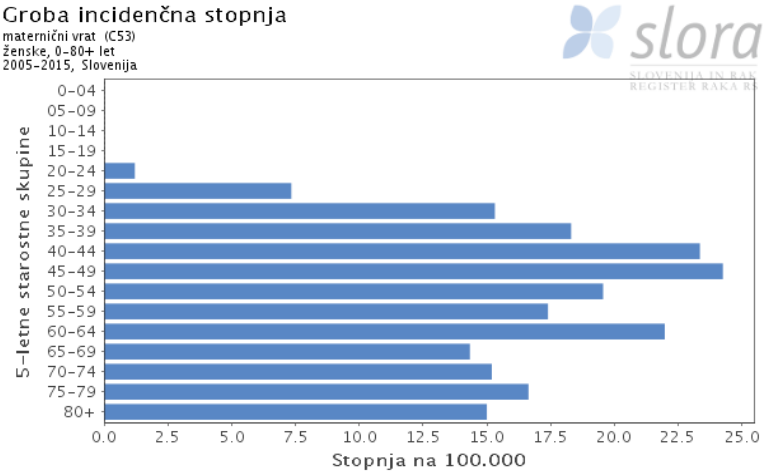
- Posledica dolgotrajnejše okužbe z VR-HPV.
- Redkeje spontano izginejo.
- Nezdravljene lahko napredujejo v RMV.
- Zdravimo z izrezanjem dela MV.
- Pri nuliparah in CIN 2 destrukcija lezije.

Dolgotrajna okužba s HPV



Ljubljana, september 2019

Rak materničnega vratu



Ljubljana, september 2019

Ekscizijski posegi (histopatologija Ginekološke klinike UKC Lj, 2014 in 2015)

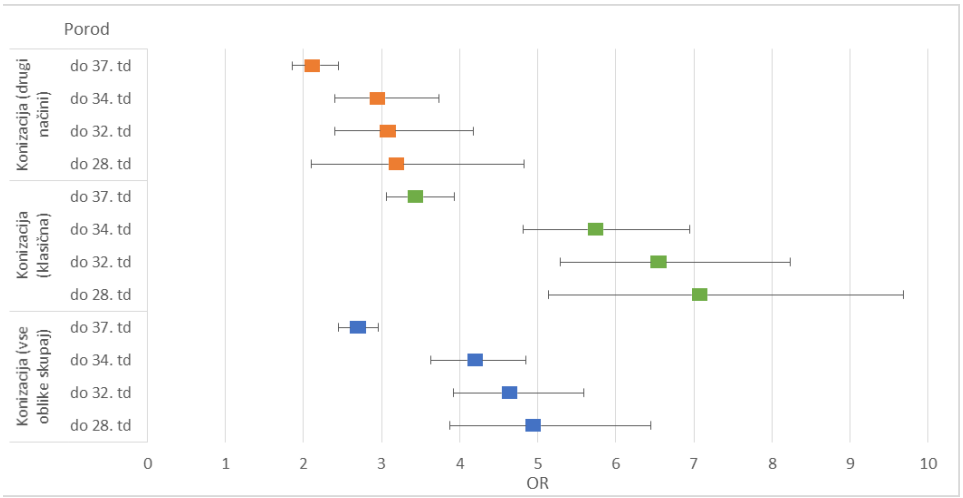
Starost ženske / diagnoza	Število posegov	Delež (N = 1268)
≤ 25 let	122	10 %
≤ 30 let	325	25 %
≤ 35 let	587	46 %
≤ 42 let	861	68 %
Brez displazije, vnetje, PIL-NS	363	28 %

Posegi pri ženskah starih ≤ 30 let

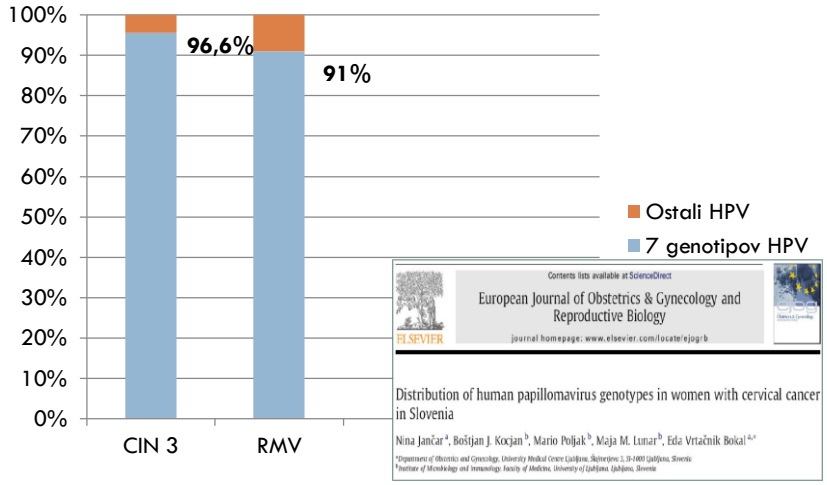
Histološka diagnoza izrezanega tkiva	Število posegov	Delež
Brez displazije	56	17,2 %
CIN 1	23	7,1 %
CIN 2	71	21,8 %
CIN 3	169	52 %
RMV	6	1,8 %
Vse	325	100 %

24,3 % žensk, starih 30 let ali manj, smo preveč agresivno zdravili !

Razmerje obetov (OR) za prezgodnji porod po posegu na maternični vratu (Slo 2003-2012) 192.730 porodov enojčkov; 4.579 porodnic po posegu zaradi CIN



Spremembe MV, ki jih povzroča 7 VR genotipov, vsebovanih v 9-val. cepivu



Okužba s HPV in nosečnost

- Okužba maternične vratu s HPV nima nobenega vpliva na plod.
- Zdravljenje PIL-VS lahko varno odložimo za 3-4 mesece po porodu (potrebno vodenje v kolposkopski ambulanti).
- Genitalne bradavice – možen prenos na novorojenčka med porodom – rekurentna respiratorna papilomatoza (lahko zapora dihalne poti).

Okužba s HPV in nosečnost

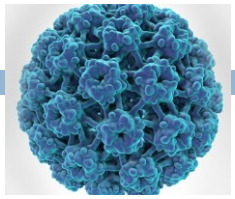
- UKREPANJE: v nosečnosti lahko zdravimo genitalne bradavice z lasersko vaporizacijo, krioterapijo ali izrezanjem.
- Če je več genitalnih bradavic v vagini ali na introitusu je to indikacija za porod s CARSKIM REZOM.

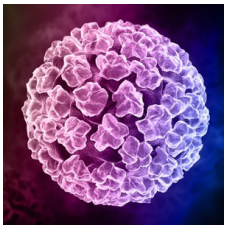
Zaključki

- Delež porodnic z anamnezo posegov na maternični vratu ob porodu naraščа (boljše presejanje, staranje porodnic).
- Z doslednim izvajanjem cepljenja proti HPV bi lahko preprečili skoraj vse te posege.
- Upoštevanje strokovnih smernic in spremljanje PIL-NS.
- Skrbna izbira ustreznega načina zdravljenja, predvsem pri ženskah, ki še niso rodile.

Novo cepilno mesto:

- Od decembra 2018 cepimo proti HPV tudi na Ginekološki kliniki UKC Ljubljana, Specialistične ambulante Leonišče.
- Cepljenje je samoplačniško, za ženske izven programa cepljenja (starejše od 22 let) in za dečke ter moške od 9. leta starosti dalje.





ANALNI HPV- PATOLOGIJA

Boštjan Mlakar

Zasebna klinika ZDRAV SPLET
Maribor, Ljubljana

ANALNA HPV OKUŽBA SODI MED NAJPOGOSTEJŠE SPO

V naši raziskavi, ki je zajemala tako simptomatske kot nesimptomatske MSM, ki so obiskali proktološki ambulanti ZDRAV SPLET v LJ in MB smo z analnim brisom dokazali enega ali več HPV pri 75% HIV negativnih in 95% HIV pozitivnih MSM (1).

1. Milošević M, Poljak M, Mlakar B. Anal HPV infection in Slovenian men who have sex with men. Central European Journal of Medicine 2010; 5: 698-703)

ANALNI SEKS JE DEL NORMALNE SPOLNE PRAKSE MED HETEROSEKSUALNIMI PARI

The National Health Statistics Report from 2006 to 2010 (Sexual Behavior, Sexual Attraction, and Sexual Identity in the United States: Data from the 2006–2010 National Survey of Family Growth) included information on the prevalence of anal sex practices acquired from in person interviews with 22,682 males and females aged 15–44 in the US.

They found that "37% of women and 45% of men ever had anal sex with an opposite-sex partner."

TUDI V SLOVENIJI HETEROSEKSUALNI PARI ANALNO SEKSAJO VEČ KOT SI MISLIMO

Slovenian study in 2008 found that more than 20% of females and more than 30% of men practice anal sex. (1)

1. Bernik I, Klavs B. Spolno življenje v Sloveniji. Zbirka Dialogi, XII.letnik, 2011

KAKO SEM „STAKNIL“ ANALNO HPV OKUŽBO, ČE PA NISEM ANALNO SEKSAL/A?

a) Britje, depilacija analne regije
b) Vneta in nadražena koža analne regije
c) Spontan prenos HPV zaradi bližine introitusa vagine
d) Samokužba ob umivanju, brisanju
e) Tudi radoveden prst, ki se „igra“ okoli ritke in „pobegne“ vanjo je analni seks….

ANALNA HPV OKUŽBA JE:

a) večinoma asimptomatska in izveni sponatno,
b) samo 1 do 2% okuženih ima klinično evidentne anogenitalne kondilome.

(Brown TJ, Angela YM, Tyring SK. An overview of sexually transmitted diseases. Part II. St.Louis : Mosby, Journal of the American Academy of Dermatology, 1999: 661-77)

Prekanceroze (MB. Bowen) in analni karcinomi povzročeni z visokorizičnimi HPV so zelo redki.

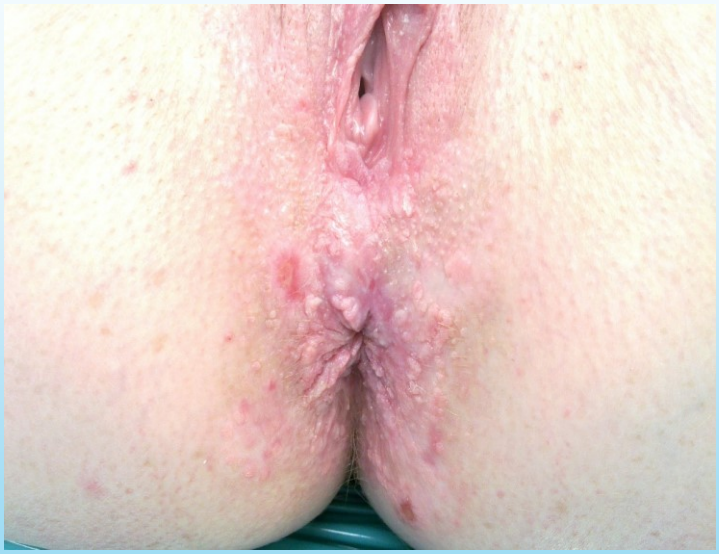
KONDILOMI

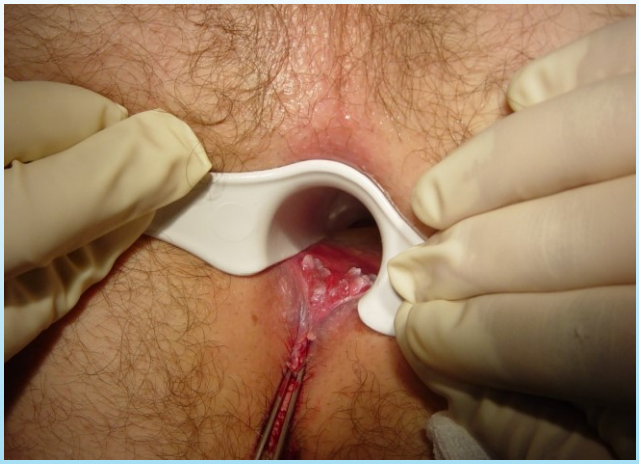
a) Pri osebi, ki ima kondilome kjerkoli v anogenitalni regiji je potrebno opraviti temeljit pregled celotnega spolovila, anusa in analnega kanala, vključno s proktoskopijo.

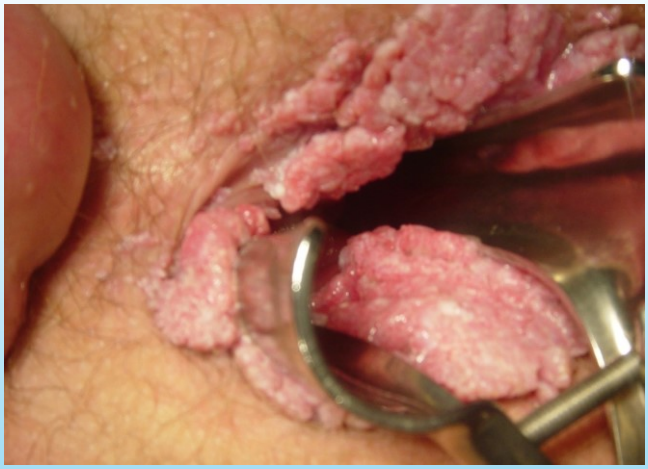
b) Pri ženski je potrebno opraviti tudi ginekološki pregled in odvzeti bris maternične vratu.

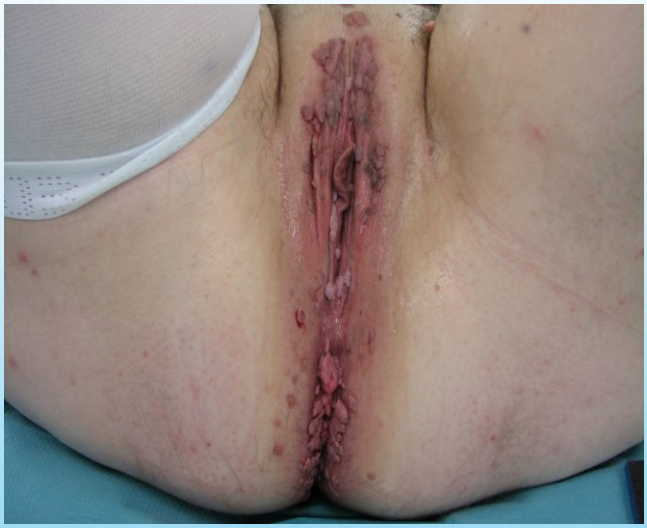
c) Pri moških moramo razpreti tudi meatus sečnice, saj se lahko spremembe skrivajo tudi znotraj sečnice in ga po potrebi napotiti k urologu.

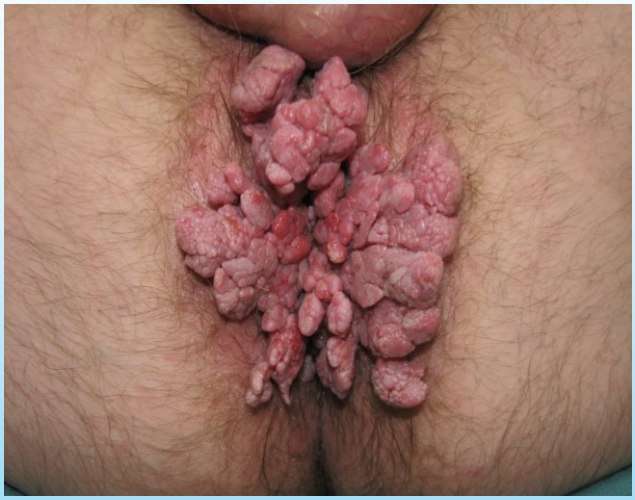
d) V primeru hripavosti je osebo potrebno napotiti tudi k otorinolaringologu. Pogledati je potrebno tudi ustno votlino.











BREZ REKTALNEGA PREGLEDA IN PROKTOSKOPIJE NE GRE…

Samo 6% simptomatskih MSM je imelo kondilome omejene le na zunanjost zadnjika, 84% je imelo kondilome istočasno zunaj in znotraj zadnjikovega kanala, 10% pa izključno znotraj analnega kanala.

(Sohn N , Robiloti JG Jr. The gay bowel syndrome: a rewiew of colonic and rectal conditions in 200 male homosexuals. The American Journal of Gastroenterology 1977; 67: 478-84.)

Intraanalne kondilome je vsekakor potrebno poslati na histološko preiskavo, saj smo ugotovili displazijo pri 23% pacientov z intraanalnimi kondilomi.

(Mlakar B. Proctoscopy should be mandatory in men that have sex with men with external anogenital warts. Acta Dermatovenerologica Alpina, Pannonica et Adriatica 2009; 18: 7-11.)

ZDRAVLJENJE

a) Prilagodimo obsežnosti obolenja in mestu nahajanja kondilomov,
b) Krioterapija,
c) Elektrokoagulacija,
d) Ekscizija (histologija),
e) Imunomodulator celično posredovane imunosti (imiquimod),
f) Condylox (podofyllotoxin).

SPODBUJANJE NARAVNE ODPORNOSTI KOT DOPOLNILO KLASIČNEGA ZDRAVLJENJA

Oralno uživanje propolisa in Ehinaceje se je izkazalo kot učinkovito pri zmanjševanju virusnih bradavic (1, 2).

1. Zedan H et al. Propolis as an alternative treatment for cutaneous warts. Int J Dermatol, 2009; 48(11):1246-9.

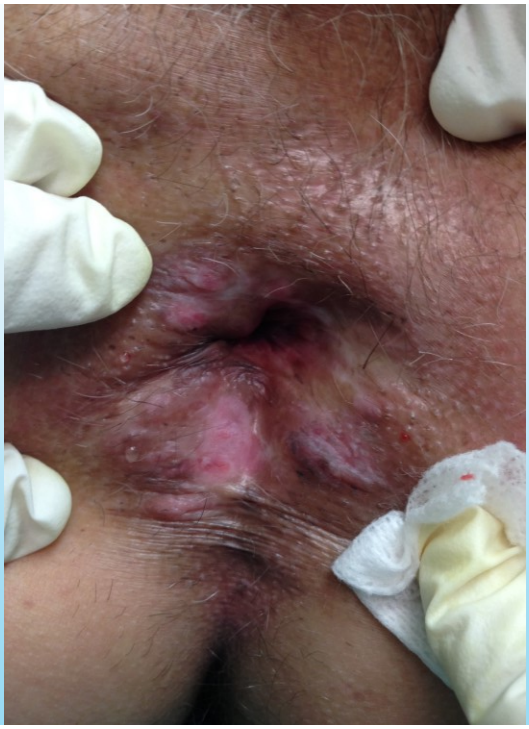
2. Cassano N et al. Oral supplementation with nutraceutical containing Echonacea, methionine and antioxidant/immunostimulating compounds in patients with cutaneous viral warts. G. Ital. Dermatol Venerol, 2011; 146(3): 191-5.

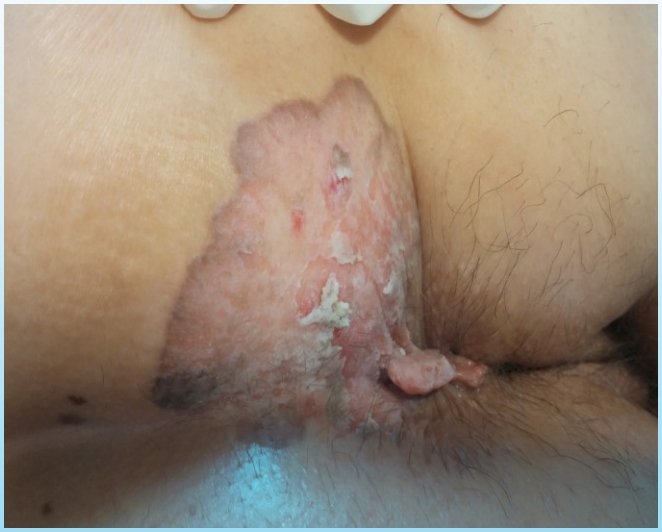
MORBUS BOWEN

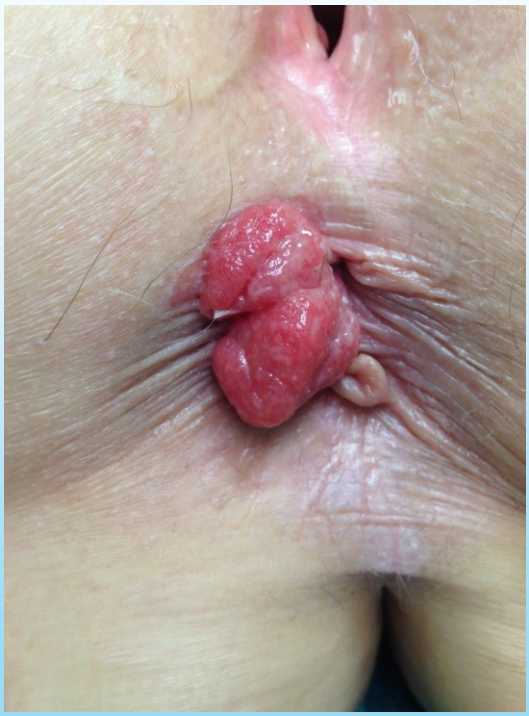
a) je intraepitelijska oblika ploščatoceličnega karcinoma,
b) najpogosteje sta povzročitelja HPV 16 in 18,
c) pogosti simptomi in znaki so srbečica, pekoč občutek in občasna krvavitev, lahko pa poteka tudi popolnoma asimptomatsko in je naključna najdba ob pregledu.

Zdravljenje je odvisno od lokacije, števila lezij, velikosti spremembe, terapevtskih izkušenj z metodo in razpoložljivosti metode, kozmetičnega učinka in pacientovih želja ter pacientovega zdravstvenega statusa.

(Neubert T, Lehmann P. Bowen's disease – a review of newer treatment options. Therapeutics and clinical risk management 2008; 4: 1085-95.)







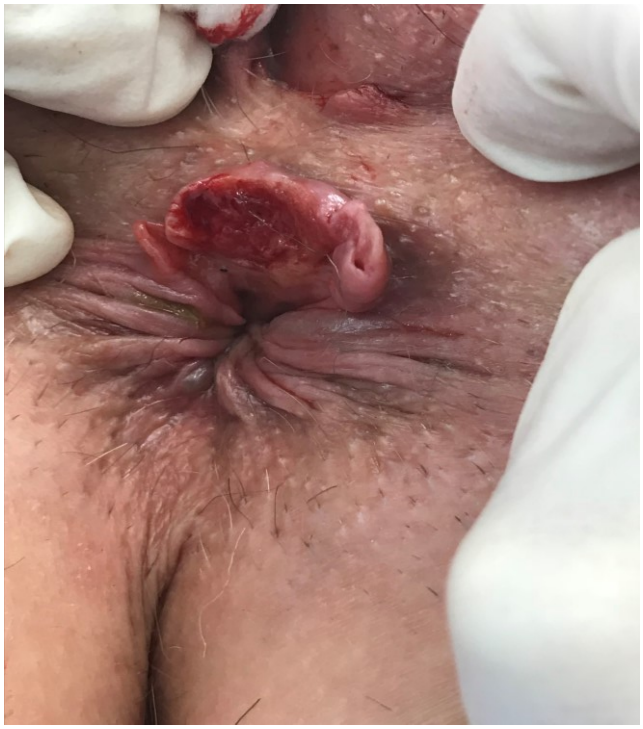
PLOŠČATOCELIČEN KARCINOM ANUSA

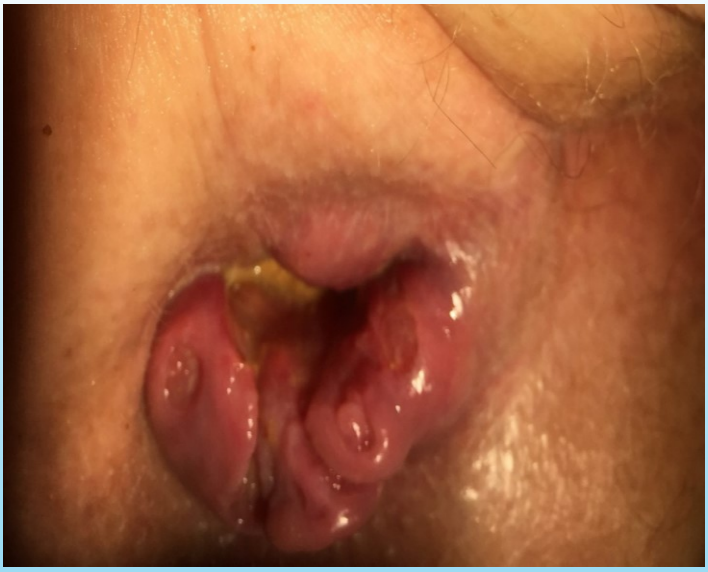
Pomembni dejavniki tveganja so tvegano spolno življenje, okužba z visokorizičnim HPV, predvsem s sevoma 16 in 18 ter okužba s HIV ter Crohnova bolezen.

(Oblak I et al. Smernice za obravnavo bolnikov s skvamoznoceličnim karcinomom analnega kanala in kože perianalno. Onkologija 2013; 2: 105-8.)

(Salati SA, Al Kadi A. Anal cancer - a review. International Journal of Health Sciences 2012; 6: 206-30.)

Pričakuje se porast analnega karcinoma pri HIV pozitivnih MSM, zato smo tudi v Sloveniji pričeli testno izvajati analno citologijo pri določeni skupini teh pacientov.





ZAKLJUČKI

a) Zmanjšanje obolevnosti za kondilomi in/ali predrakavimi in rakavimi spremembami v anogenitalni regiji bomo najverjetneje dosegli v prihodnosti s spodbujanem cepljenja proti najpogostejšim HPV.

b) Zavedati se moramo, da tudi dosledna uporaba kondoma ne more popolnoma preprečiti HPV okužbe, saj se virus nahaja tudi izven področja, ki ga kondom prekrije.

c) Proktoskopija je potrebna pri vseh, ki imajo zunanje kondilome v anogenitalni regiji.

d) Vsem, ki prakticirajo receptivne analne spolne odnose svetujem preventivni proktološki pregled na 2 do 3 leta.

e) Spodbujanje naravne odpornosti in zdravega življenskega sloga.

HPV okužbe v področju glave in vratu

Aleš Grošelj
Klinika za otorinolaringologijo in cervikofacialno kirurgijo
UKC Ljubljana

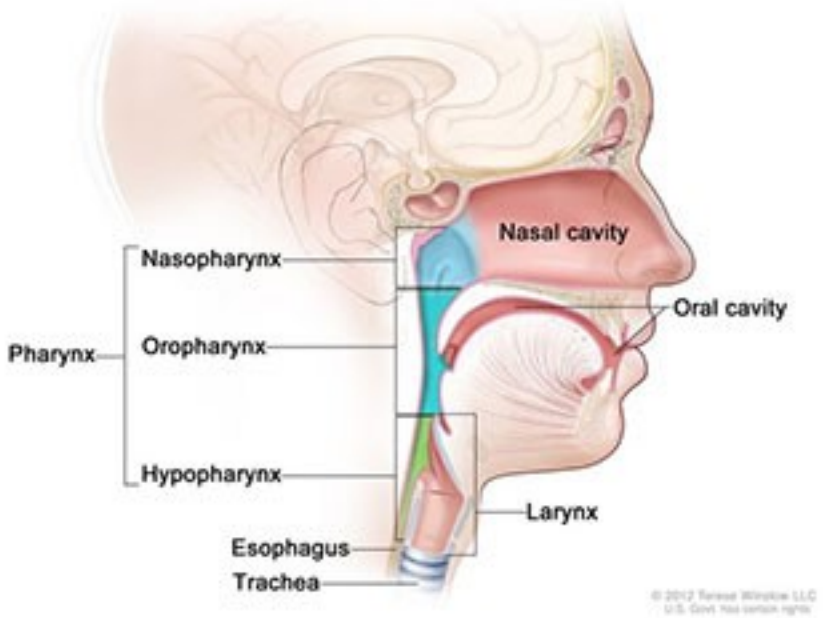
Rak glave in vratu

- Letna incidenca:

v svetu: 650.000 (6. najpogostejši rak)

v Sloveniji: 400-450

- ustna votlina, 34%
- ustni del žrela, 20-25%
- grlo, 20-25%
- spodnji del žrela, 10-15%



Etiologija

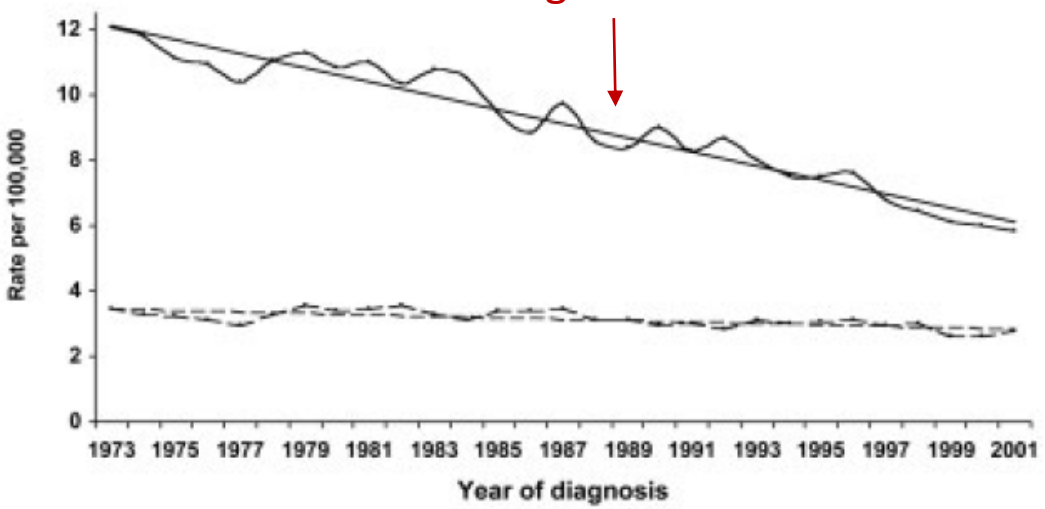
TOBAK in ALKOHOL sta še vedno najpomembnejša vzročna dejavnika

Incidenca med kadilci 6x (do 20x) višja kot med nekadilci
Tveganje za nov malignom 5x višje med aktivnimi kadilci

ALKOHOL = manj močan kancerogen kot tobak,
skupaj delujeta sinergistično

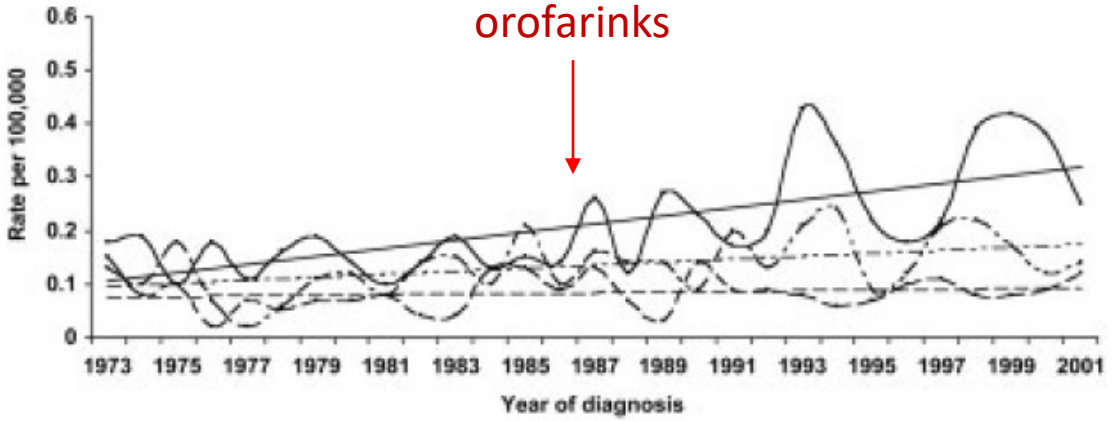
Epidemiologija

Rak glave in vratu



A
—— Men: PC = -52; APC = -2.4; $P < 0.001$
– – –Women: PC = -20; APC = -0.7; $P < 0.001$

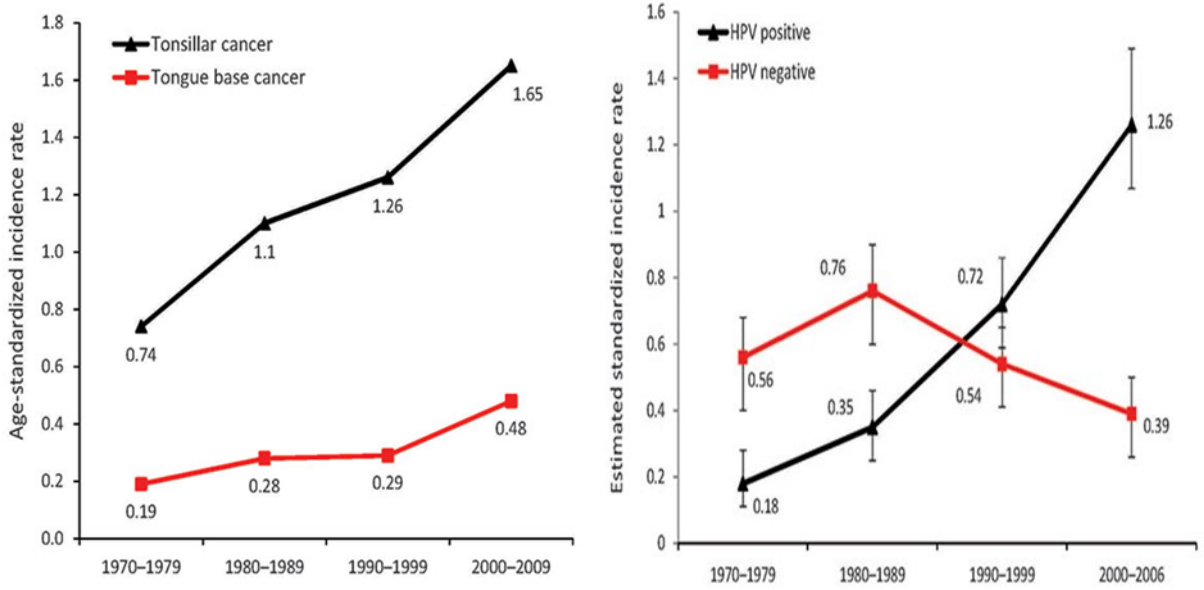
orofarinks

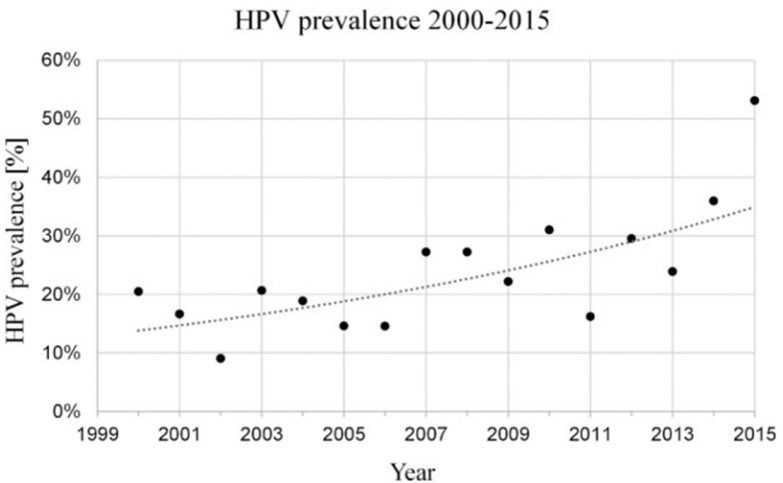


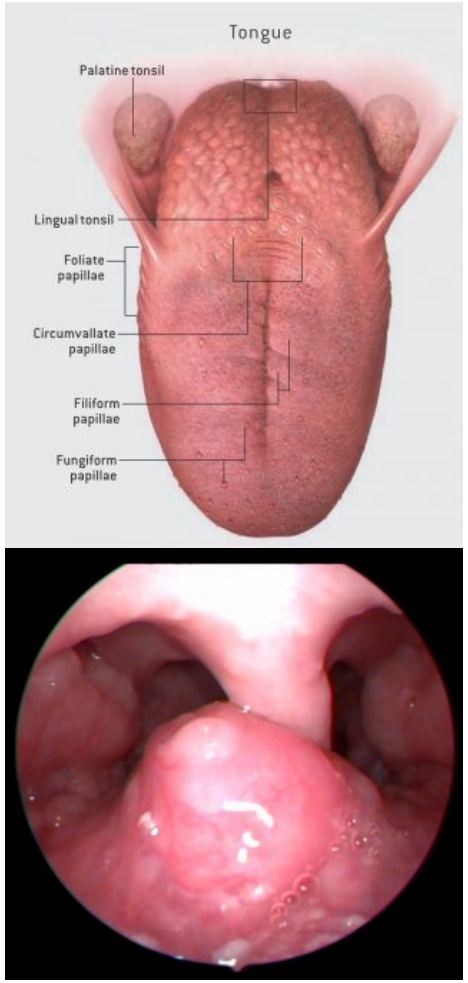
B
——Tonsil: PC = +41; APC = +3.9; $P < 0.001$
– – – –Base of tongue: PC = +8.6; APC = +1.73; $P = 0.04$
– – – Other pharynx: PC = -21; APC = 0.24; $P = 0.7$

Shiboski et al , Cancer 2005

Predilekcijska mesta za HPV rak orofarinksa







International Agency for Research on Cancer

World Health Organization

Group 1 agent	Cancers for which there is sufficient evidence in humans	Other sites with limited evidence in humans	Established mechanistic events
Epstein–Barr virus (EBV)	Nasopharyngeal carcinoma, Burkitt's lymphoma, immune-suppression-related non-Hodgkin lymphoma, extranodal NK/T-cell lymphoma (nasal type), Hodgkin's lymphoma	Gastric carcinoma,* lympho-epithelioma-like carcinoma*	Cell proliferation, inhibition of apoptosis, genomic instability, cell migration
Hepatitis B virus (HBV)	Hepatocellular carcinoma	Cholangiocarcinoma,* non-Hodgkin lymphoma*	Inflammation, liver cirrhosis, chronic hepatitis
Hepatitis C virus (HCV)	Hepatocellular carcinoma, non-Hodgkin lymphoma*	Cholangiocarcinoma*	Inflammation, liver cirrhosis, liver fibrosis
Kaposi's sarcoma herpes virus (KSHV)	Kaposi's sarcoma,* primary effusion lymphoma*	multicentric Castleman's disease*	Cell proliferation, inhibition of apoptosis, genomic instability, cell migration
Human immunodeficiency	Kaposi's sarcoma, non-Hodgkin lymphoma, Hodgkin's	Cancer of the vulva,* vagina,* penis,* non-	Immunosuppression (indirect action)
			on, genomic instability, inhibition of response, anti-apoptotic activity
			on and transformation of T cells
	associated lymphoid tissue (MALT) gastric lymphoma*		, oxidative stress, altered cellular turn-over and gene expression, methylation, mutation
Clonorchis sinensis	Cholangiocarcinoma*	..	..
Opisthorchis viverrini	Cholangiocarcinoma	..	Inflammation, oxidative stress, cell proliferation
Schistosoma haematobium	Urinary bladder cancer	..	Inflammation, oxidative stress

*Newly identified link between virus and cancer. †For other types, see table 2.

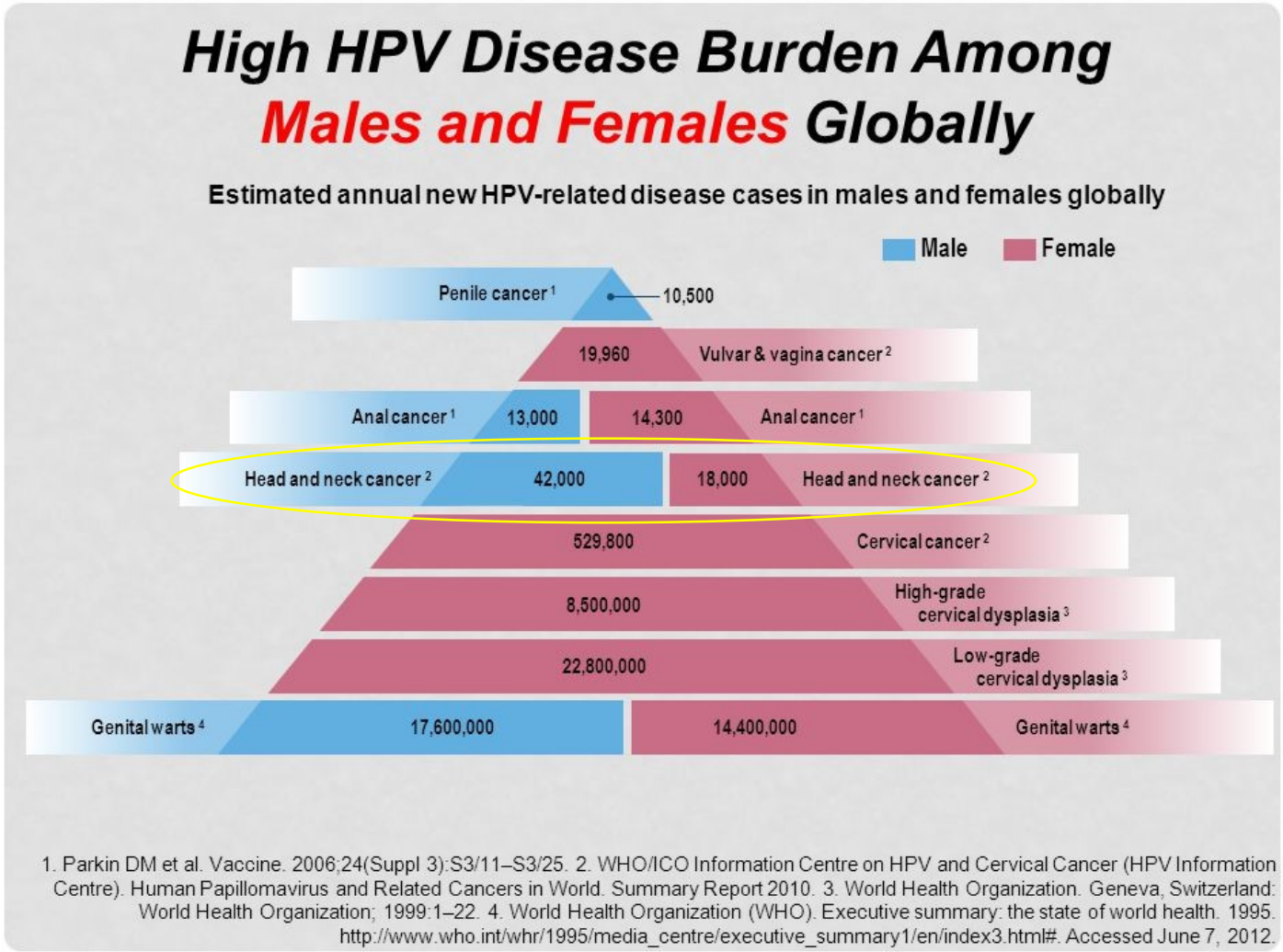
Table 1: **Biological agents assessed by the IARC Monograph Working Group**

HPV-16

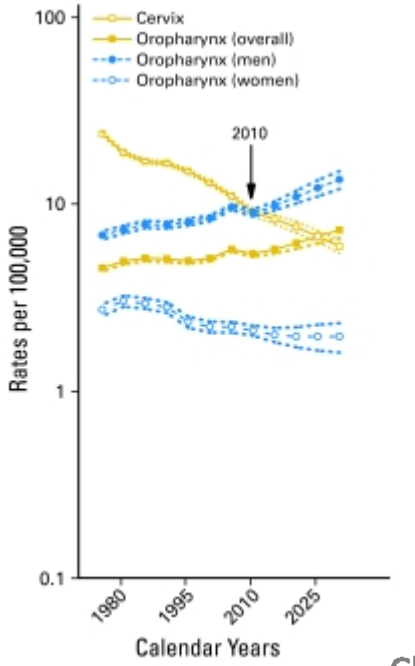
Rak maternične vratu, anogenitalnega predela, rak ustne votline, ustnega žrela (nebnici)

Rak grla

de Martel, Lancet 2012



V ZDA naj bi bila letna incidenca HPV raka orofarinksa višja od raka maternične vratu do l.2020



Chaturvedi, J Clin Oncol 2011

V letu 2015 je bilo v ZDA 11,788 prijavljenih
rakov maternične vratu
in 18,917 primerov PC raka orofarinksa - 15,479 (82%) moških
in 3,438 (18%) žensk.

Slovenija

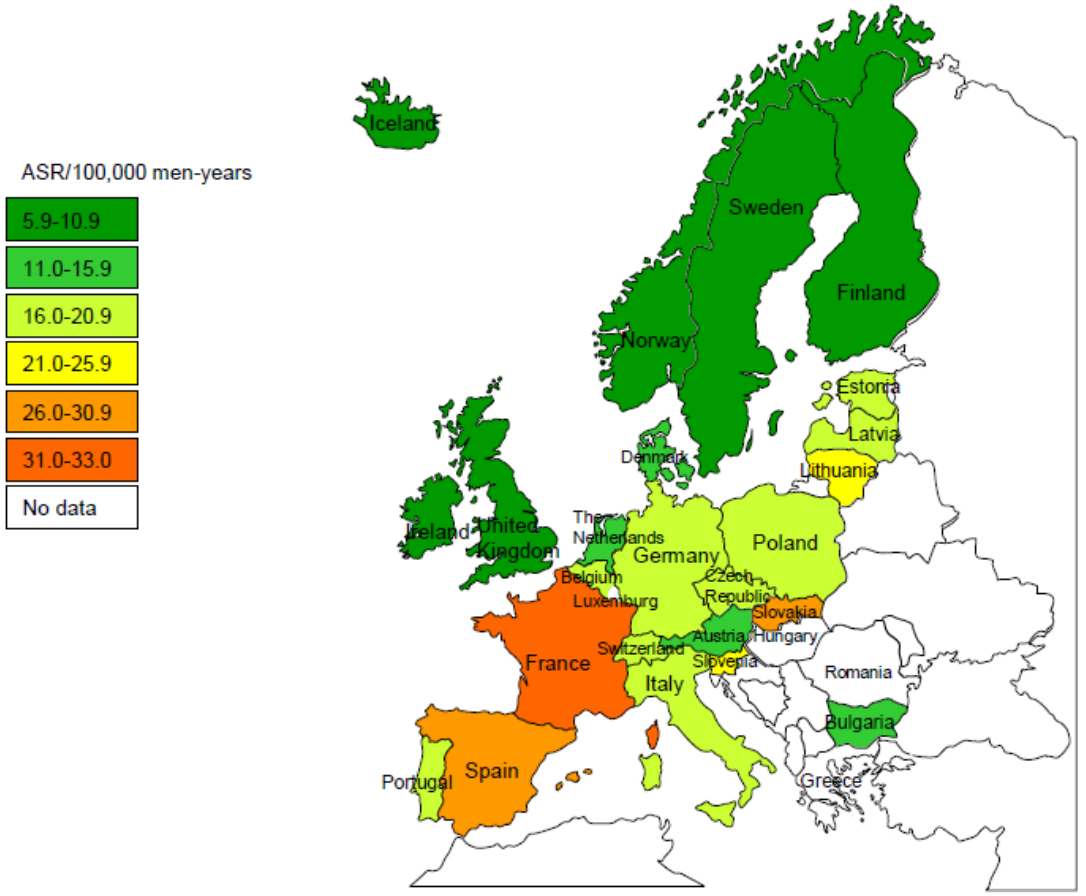
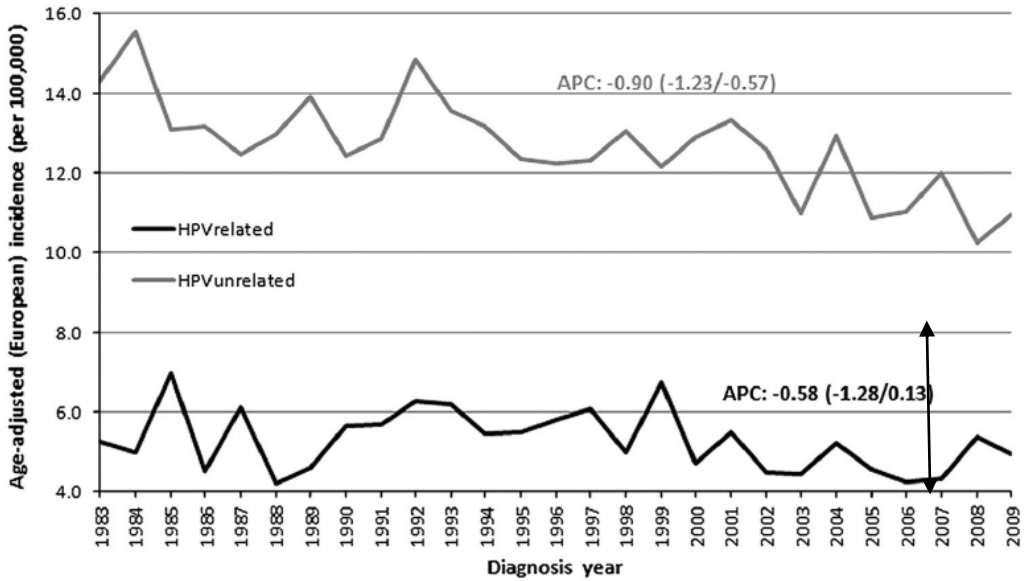


Figure 2 Age-standardised incidence rate (ASR) of a subset of head and neck cancers irrespective of human papillomavirus status.

Hartwig, BMJ 2012



Strojan, Eur Arch Otorhinolaryngol 2014

HPV rak orofarinka je spolno prenosljiva bolezen

Table 2. Associations of Oropharyngeal Cancer with Sexual Behaviors.*

Sexual Behavior	Patients with Oropharyngeal Cancer (N=100)	Control Patients (N=200)	Adjusted Odds Ratio (95% CI)†	
			All Patients	HPV-16+ Patients‡
	number (percent)			
Lifetime no. of vaginal-sex partners				
0–5	31 (31)	108 (54)	1.0	1.0
6–25	41 (41)	63 (32)	2.2 (1.2–4.0)	2.7 (1.4–5.5)
≥26	28 (28)	29 (14)	3.1 (1.5–6.5)§	4.2 (1.8–9.4)¶
Lifetime no. of oral-sex partners				
0	12 (12)	38 (19)	1.0	1.0
1–5	46 (46)	110 (55)	1.9 (0.8–4.5)	3.8 (1.0–14.0)
≥6	42 (42)	52 (26)	3.4 (1.3–8.8)	8.6 (2.2–34.0)**

Ženske partnerice bolnikov
s potrjenim HPV rakom enaka prevalenca
kot splošna populacija

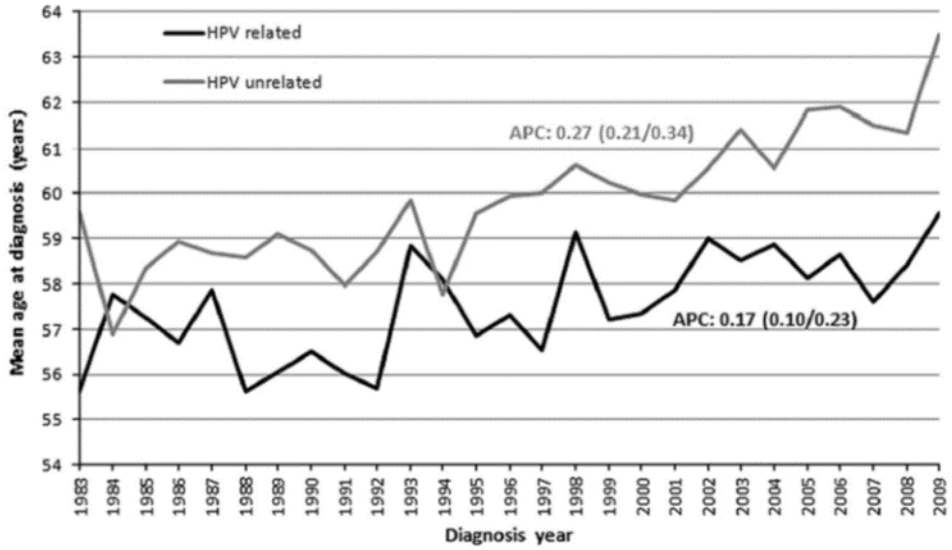
D´Souza, NEJM 2007

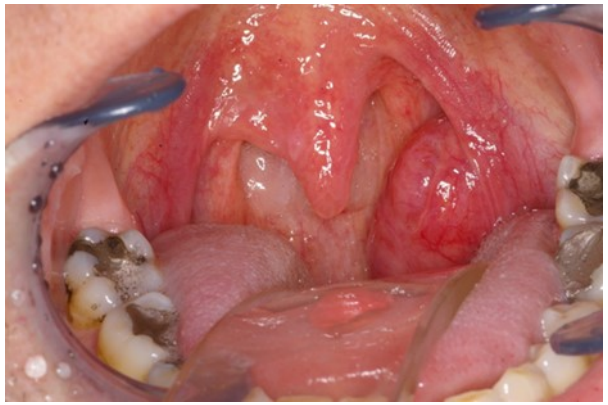
HPV rak orofarinksa ima drugačen potek

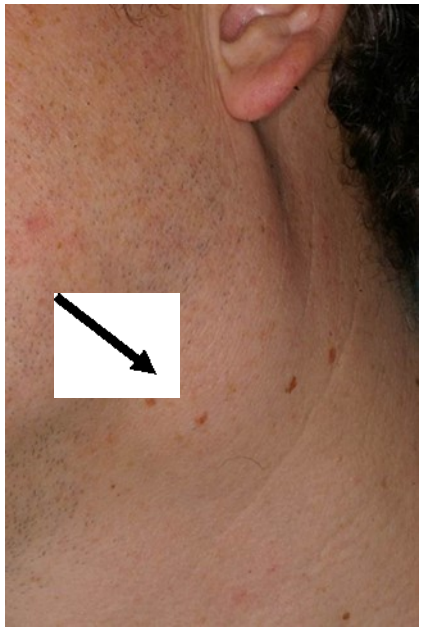
Značilnost	HPV negativni HNSCC	HPV pozitivni HNSCC
Incidenca	PADA	NARAŠČA
Etiologija	KAJENJE ALKOHOL	ORALNI SPOLNI ODNOSI
Starost	STAREJŠI	MLAJŠI
Spol	MOŠKI 3:1	MOŠKI 3:1
Polje kancerizacije	DA	NEZNANO
P53 mutacije	POGOSTO	REDKO
Predilekcijsko mesto	NI	OROFARINKS (TONZILE)
Prognoza	SLABŠA	BOLJŠA
		Leemans, Nature Reviews 2011

Klinična slika

- Moški
- Mlajši
- Višji socio-ekonomski status
- Več spolnih stikov
- Dober performance status
- Majhen primarni tumor (T1/2)
- Napredovala metastatska bolezen
- cistične metastaze
- nekadilci







Spremenjena TNM klasifikacija – HPV raki orofarinksa so obravnavni kot samostojna bolezen

-Bolniki s HPV rak orofarinksa imajo bolj napredovalo nodalno bolezen, vendar boljšo prognozo kot HPV neg. raki

-Preglednejša zasnova kliničnih raziskav zdravljenja HPV- in HPV+ rakov orofarinksa

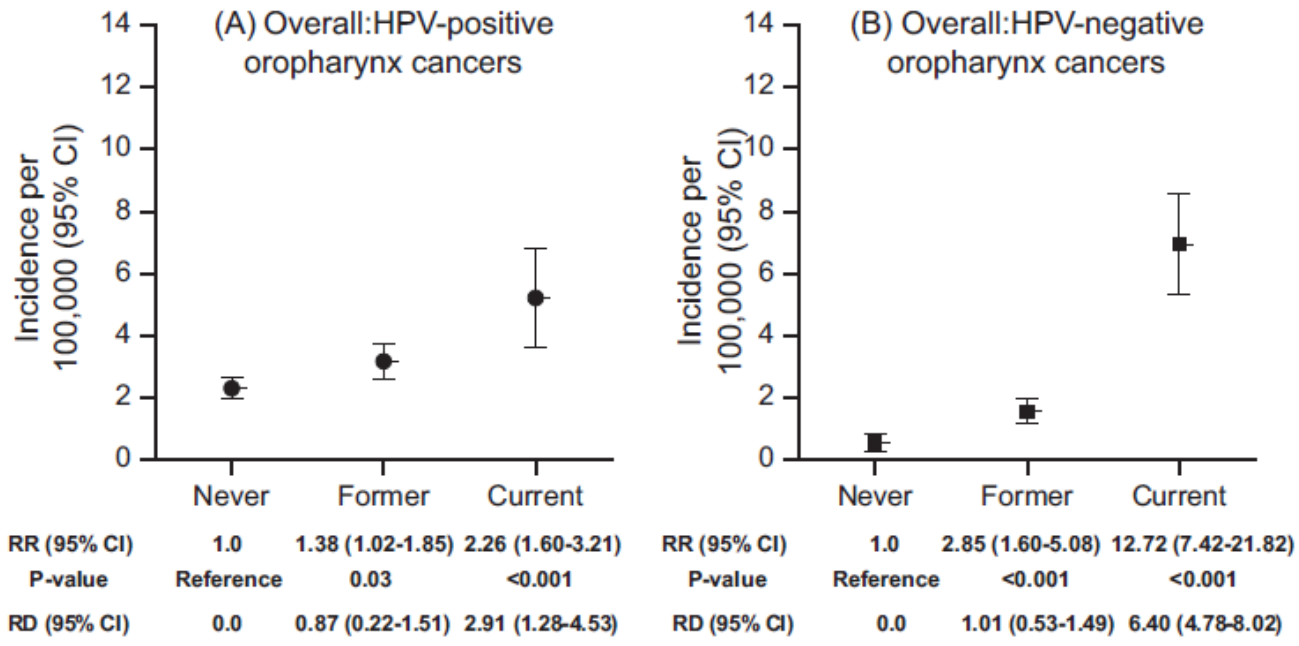
-Lažje oblikovanje smernic za zdravljenje obeh vrst rakov

Table 3. The 8th edition N classification for non-viral related head and neck cancer and stage grouping for viral and non-viral unknown primary – cervical nodes

	N category for non-viral CUP and HNC		
N	Clinical N classification	Pathologic N classification	
N1	Single ipsilateral LN, ≤3 cm, no ENE	Single ipsilateral LN, ≤3 cm, no ENE	
N2a	Single ipsilateral LN, 3–6 cm, no ENE	Single ipsilateral LN, ≤3 cm, with ENE[a], single ipsilateral LN, 3–6 cm, no ENE	
N2b	Multiple ipsilateral LNs, ≤6 cm, no ENE	Multiple ipsilateral LNs, ≤6 cm, no ENE	
N2c	Bilateral or contralateral LNs, ≤6 cm, no ENE	Bilateral or contralateral LNs, ≤6 cm, no ENE	
N3a	Any LN >6 cm, no ENE	Any LN >6 cm, no ENE	
N3b	Any LN with clinical ENE[a]	A single LN >3 cm with pathologic ENE[b] Any multiple ipsilateral/bilateral/contralateral LN(s) with ENE	
Stage grouping for viral and non-viral-related CUP			
Stage	HPV+/p16+ CUP	EBV+ CUP	Non-viral related CUP
Stage I	T0_N1_M0	Not applicable	Not applicable
Stage II	T0_N2_M0	T0_N1_M0	Not applicable
Stage III	T0_N3_M0	T0_N2_M0	T0_N1_M0
Stage IV	Clinical: T0_N1–3_M1 Pathological: T0_N1–2_M1	IVA: T0_N3_M0 IVB: T0_N1–3_M1	IVA: T0_N2_M0 IVB: T0_N3_M0 IVC: T0_N1–3_M1

HNC head and neck cancer, *LN* lymph node, *ENE* extranodal extension, *CUP* cervical nodal metastasis with unknown primary
[a]Clinical ENE refers to unambiguous clinical/radiological evidence of gross ENE, such as dermal involvement or soft tissue invasion with deep fixation/tethering to underlying muscle or adjacent structures or clinical signs of nerve involvement
[b]Pathologic ENE could be further recorded as ENEmi: microscopic ENE ≤ 0.2 cm beyond nodal capsule; ENEma: major ENE > 0.2 cm beyond nodal capsule; soft tissue deposit within lymphatic drainage without identifiable LN would be recorded as pN+ and ENE+

Delež kadilcev tudi med HPV raki orofarinksa



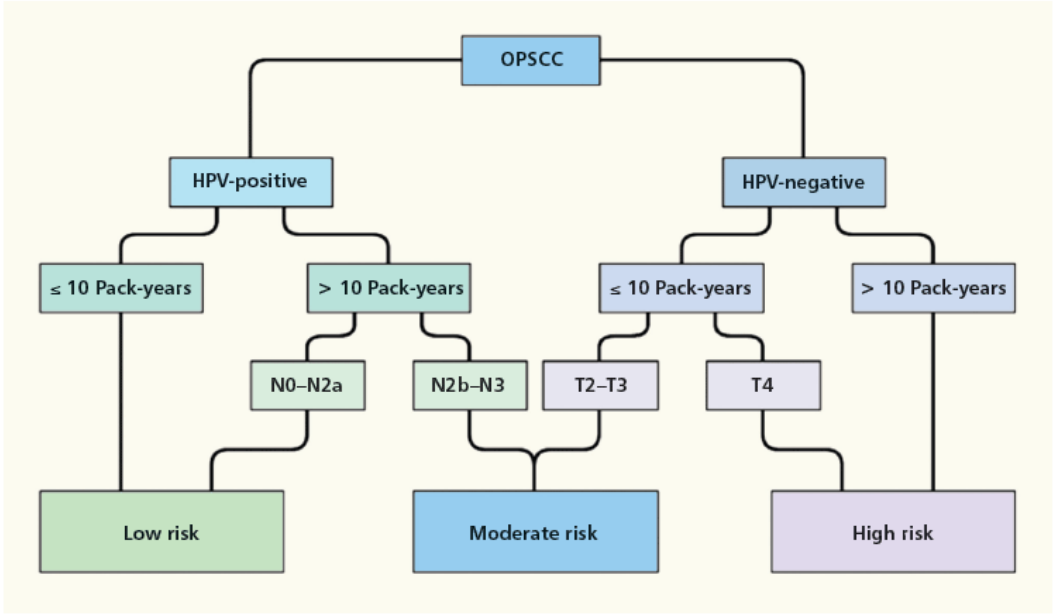
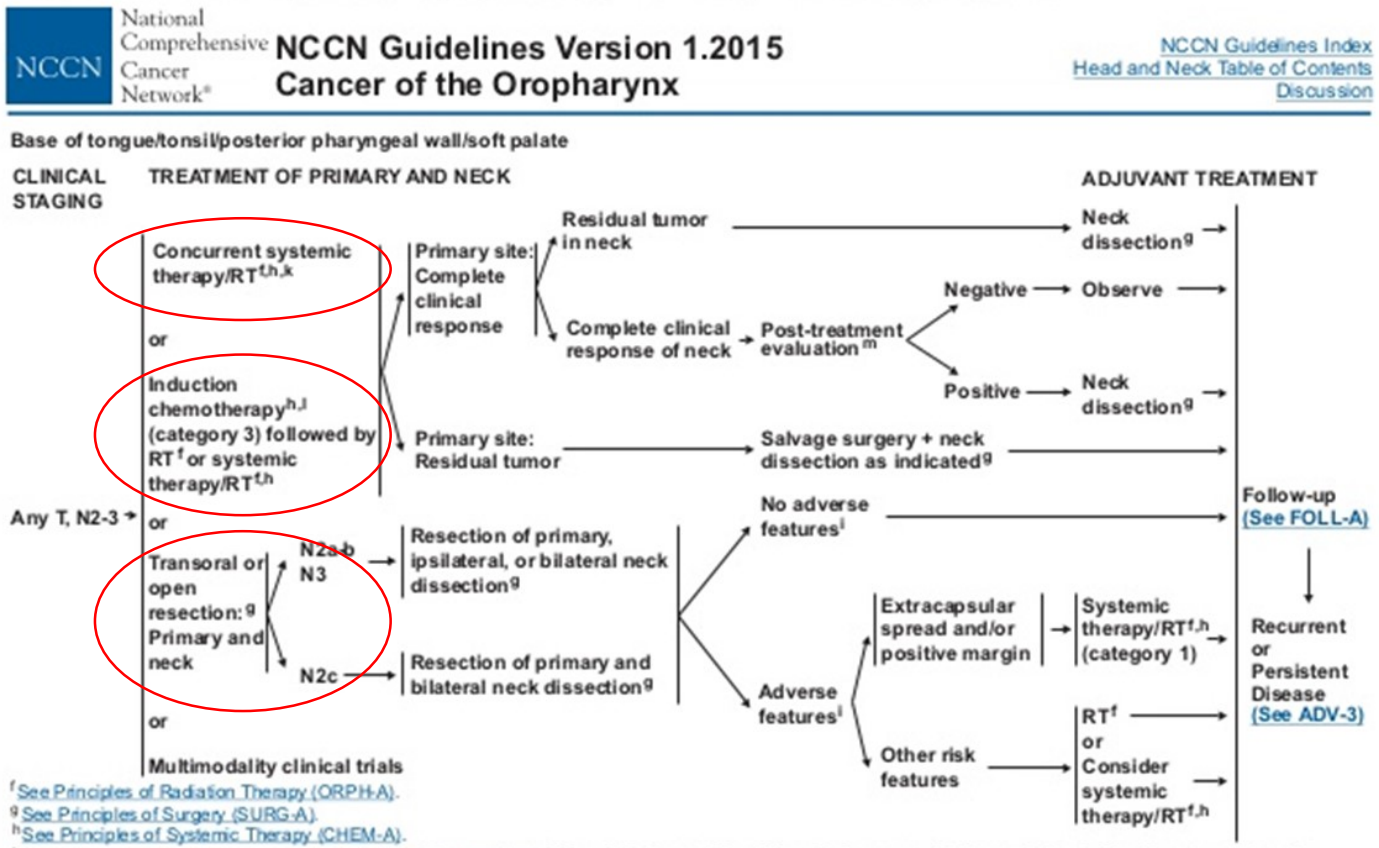


Figure 3. Risk Stratification for Oropharyngeal Squamous Cell Carcinoma (OPSCC)—In a large retrospective analysis of the impact of HPV on outcomes in OPSCC, patients were divided into risk-of-death categories (low, moderate, and high) based on their HPV status, tumor burden, and tobacco use. HPV = human papillomavirus; Adapted from Ang et al. N Engl J Med. 2010.[34]

Chaturvedi, Oral Oncology 2016

Zdravljenje HPV pozitivnega raka orofarinksa



Dileme zdravljenja HPV pozitivnega raka orofarinksa

Table 1 De-intensification trials for the treatment of HPV-positive OPC

Trial	Phase	No.	Treatment
Chemotherapy de-intensification			
RTOG 1016 (NCT01302834)	III	987	High-dose cisplatin IV with accelerated IMRT *versus* cetuximab IV
De-escalate (NCT01874171)	III	334	Cetuximab *versus* high-dosage cisplatin with concurrent radiotherapy
TROG 12.01 (NCT01855451)	III	200	Cetuximab *versus* weekly cisplatin with concurrent radiotherapy
Radiotherapy de-intensification			
NRG-HN002 (NCT02254278)	III	295	IMRT (60 Gy) with cisplatin IV *versus* IMRT alone
LCCC 1120 (NCT01530997)	III	43	IMRT (54–60 Gy) with concurrent cisplatin IV
The Quarterback Trial (NCT01706939)	III	24	IMRT (56 Gy) with weekly carboplatin *versus* RT (70 Gy) with carboplatin
NCT02281955	III	60	IMRT (60 Gy) with weekly cetuximab, carboplatin, paclitaxel, or carboplatin
NCT02908477	III	214	IMRT (30 or 36 Gy) plus docetaxel *versus* RT (60 Gy) with weekly cisplatin
Surgery/adjuvant de-intensification			
ADEPT (NCT01687413)	III	41	Surgery followed by IMRT (36 Gy) + weekly docetaxel
MC1273 (NCT01932697)	II	81	Surgery followed by IMRT (36 Gy) + weekly docetaxel
ECOG-E3311 (NCT01898494)	II	377	TORS alone *versus* TORS with either low dose IMRT, standard IMRT, or standard IMRT with cisplatin IV
PATHOS (NCT02215265)	II/III	242	TORS alone *versus* TORS with RT (60 Gy), PORT (50 Gy), or RT (60 Gy) with cisplatin IV

Gy gray, *IMRT* intensity-modulated radiotherapy, *IV* intravenous, *N* number of patients currently enrolled, *RT* radiotherapy, *TORS* transoral robotic surgery

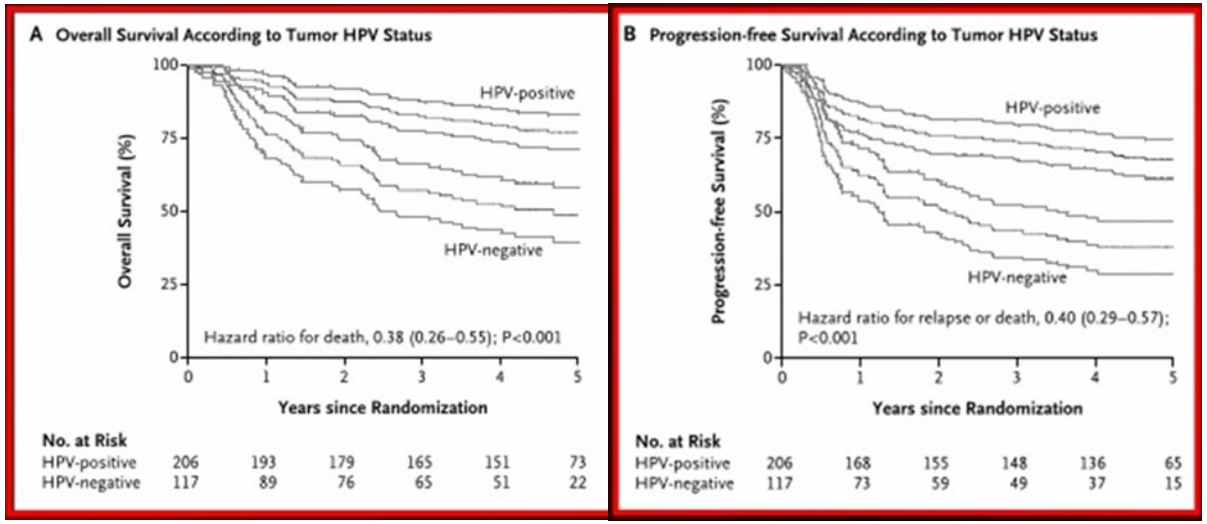
Fung, Cancer Metastasis rev, 2017

HPV rak orofarinksa ima dobro prognozo

- Boljši odgovor na RT/KT
  (preživetje 82 % vs. 57 %)
- Boljša prognoza tudi po krg zdravljenju

- Zaradi nodalnega statusa so HPV + raki
večinoma napredovali stadij,
vendar je 3-letno preživetje več kot 80 %

- Ekstrakapsularno širjenje in perinevralna
invazija imata manjši vpliv kot pri p16- rakih.



Ang, NEMJ 2010

HPV rak ustne votline

- Hipoteza kroničnega parodontitisa – izpostavljenost bazalnih epitelijskih celic =
  - večje virusno breme
  - višje tveganje za prenos
  - višje tveganje za pojav raka (4x)
- Višji delež okuženih s HPV, vendar brez onkogenske aktivnosti (ekspresija E6/E7)
- Velik lokalen vpliv tobaka/alkohola – drugačne poti karcinogeneze
- Izhod zdravljenja med HPV pozitivnimi in negativnimi raki ustne votline - ni razlik
- Rezultati raziskav na maternični vratu: maligna transformacija se zgodi v populaciji celic z unikatnim profilom ekspresije genov – podobni profili tudi v ustni votlini?

Candotto *ORAL & implantology*, 2017

V Sloveniji HPV okužba do l. 2009 ni imela vpliva na rast incidence raka glave in vratu

Zaradi generacijsko pogojenih sprememb je pričakovati rast incidence

HPV povezanega raka glave in vratu.

'No jab, no pay:' Australia cuts benefits for parents who don't vaccinate kids

By Naomi Ng, for CNN
Updated 1032 GMT (1732 HKT) April 13, 2015

Parents who refuse to vaccinate their children can lose up to $11,000 of welfare benefits a year under a new government policy.

Susan Close, South Australia's Minister for Education and Child Development:

"I'm not particularly interested in hearing an argument that isn't based in science."

Strokovno srečanje Sekcije za šolsko, študentsko in adolescentno medicino

10 let cepljenja proti HPV

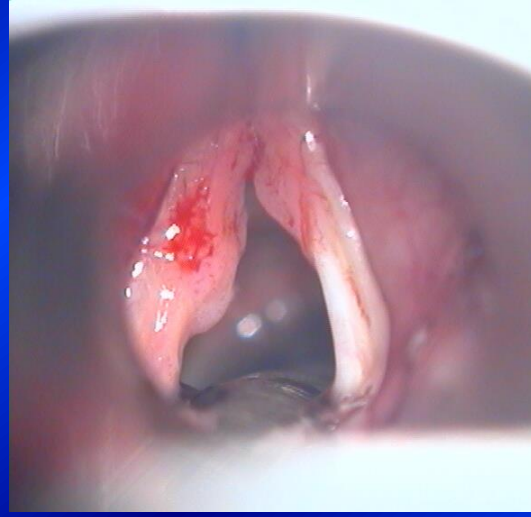
Recidivantna respiratorna papilomatoza

Irena Hočevar Boltežar

Klinika za ORL in CFK, Ljubljana

Medicnska fakulteta UL

Klasifikacija

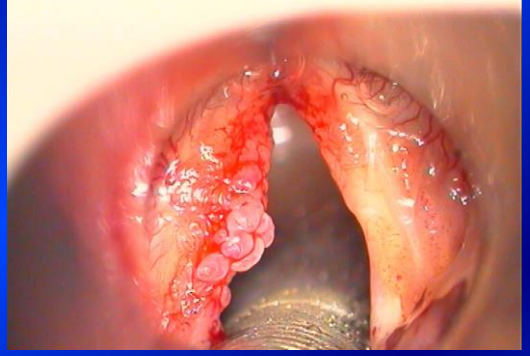


- glede na starost ob pojavu RRP:
  juvenilna in odrasla oblika
  meja 12, 15, 16, 18 let ???

- glede na potek bolezni:
  neagresivna in agresivna oblika (>10 krg.ali >3 krg/leto ali zgodaj v subglotis)

(Lindeberg, 1986; Richardson, 2017; Doyle, 1994)

Epidemiologija



- incidenca: ZDA 1,7 - 4,3 / 100.000 otrok
  1,8 / 100.000 odraslih

juvenilna oblika: 0,17 - 1,34 na 100.000; M = Ž
odrasla oblika: 0,54 na 100.000 ; M > Ž

- dva starostna vrha: <5let in 20-30 let (Cohn, 1991)
  tretji starostni vrh: 64 let
  najpogosteje – v srednjih letih

(Cohn, 1991; Derkay 1995; Derkay in Darrow 2006; San Giorgi, 2016)

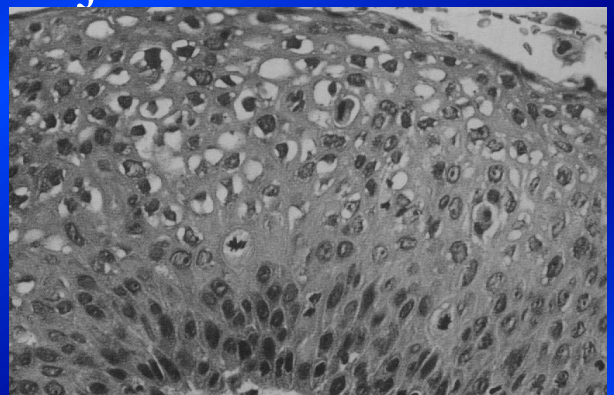
Povzročitelj

- HPV virus (DNA virus)
- preko 210 genotipov HPV virusa
- najpogostejša tipa 6 in 11 (90 % RRP), manj pogosta tipa 16 in 18

- vstopno mesto: bazalne celice epitelija poškodovane sluznice
- razmnoževanje virusa: zgornje plasti epitelija

- hiperplazija bazalnih celic, koilociti
-

(Gallaghar, 2008; Cubie, 2013)

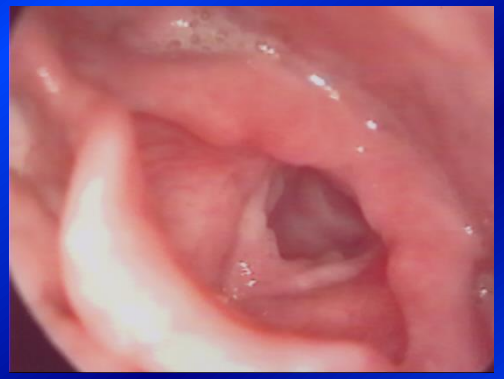


Način prenosa

- intrauterina okužba (Derkey , 1995)
- ob rojstvu: pri prehodu skozi porodni kanal (prvorojenec, vaginalni porod, najstniška mati) (Kashima, 1992)
- 45% otrok iz revnih družin (Leunig, 2007)

- kasneje v življenju inhalatorno ali s spolnimi kontakti (več partnerjev, oralni seks, pogostejši genitalni papilomi) (Wiatrak, 2003; Goon, 2008)
- latentna okužba od rojstva, sprožilni dejavniki

(Wiatrak, 2003; Derkay in Darrow, 2006; Leunig, 2007 Goon, 2008)

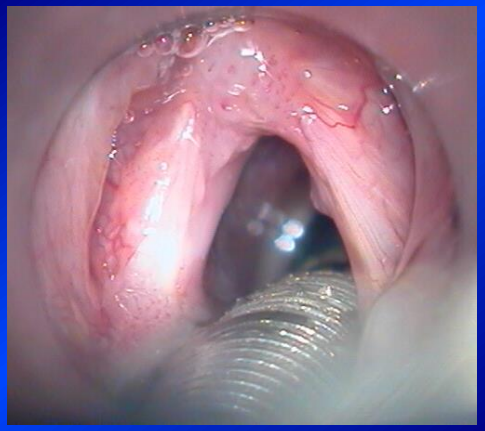


Odgovor gostitelja

- prisotnost HPV11 v 5-25% pri zdravih

  19-23% pri drugih benignih lezijah grla

(Orth, 1978; Lack, 1980; Rihkanen. 1994; Aaltonen 2002)



Defekt v imunskem sistemu gostitelja:

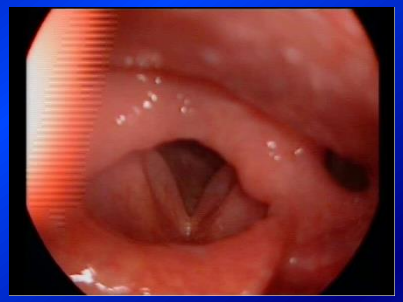
- ni razlike v nivoju Ig G
- motnja T-celic
- spremenjeno CD4/CD8 razmerje
- okvara limfocitnega odgovora na mitogeno stimulacijo
- manjša funkcija NK celic

(Bonagura, 2010; Lucs, 2012; Gall, 2013; DeVoti, 2014; Carifi 2015)

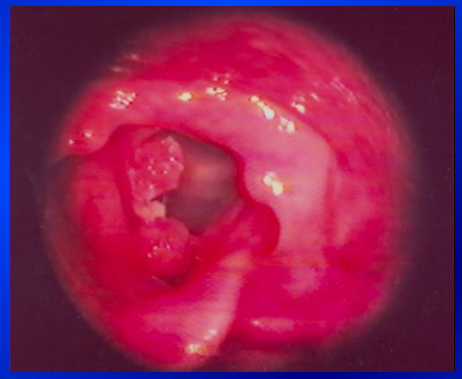
Odgovor gostitelja

- T-limfocitni koinhibitorni receptor in njegov ligand programirane smrti 1 (PD-1) >>> lokalno imunosupresivno okolje >>> imunski sistem zataji >>> rast papilomov (Ahn, 2018)

- Odrasli bolniki : laringofaringealni refluks (40% pepsin)
  sočasna okužba s HSV 2 (45% HSV 2)
  imunosupresivni učinek
  >>> sproži rast papilomov
  (Formanek, 2017)



Klinični potek



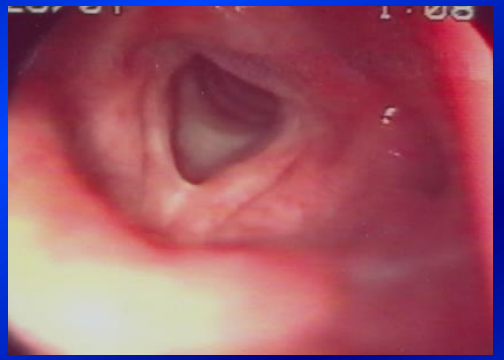
- Bolezenski znaki: hripavost, kronični kašelj, zaostanek v rasti in razvoju pri otroku, šibek jok, ponavljajoče se pljučnice, težave pri dihanju, stridor, cianoza, zadušitev

- multiple, eksofitične lezije v grlu
- najpogostejša lokacija: glasilki, ventrikularni gubi, subglotis, laringealna stran poklopca

- možen razsoj v spodnja dihala (0,8-4,4% pri otrocih, 7-12% pri odraslih) – zelo slaba prognoza

(Wiatrak, 2003; derkay in Darrow, 2006; Goon, 2008)

Klinični potek



- agresivna oblika 17% otrok, 19% odraslih
- spontana ozdravitev – zelo redka
- počasnejša rast papilomov po puberteti ?

- brazgotine v grlu, sinehija v sprednji komisuri, stenoza grla (pomen GER)

- maligna alteracija 3-7% (tip 16 in 18, razširitev na spodnja dihala, predhodno obsevanje, kajenje, odrasli)
- smrt zaradi zadušitve ali malignoma

(Wiatrak, 2003; Derkay in Darrow, 2006; Goon, 2008, Di Giorgi, 2016)

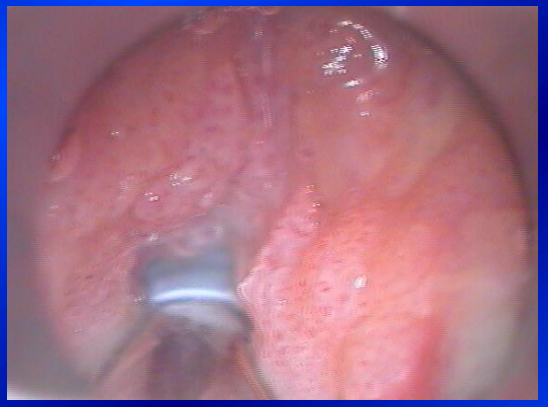
Klinični potek

Rizični dejavniki za agresivno obliko bolezni

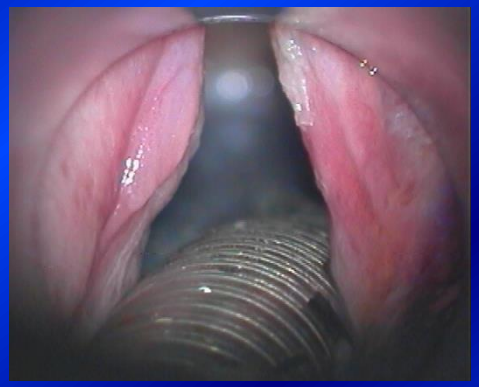
(različne ocene resnosti bolezni: razširjenost po mestih, nujnost krg. posega, stridor, hripavost)

- HPV tip 11
- rojstvo s carskim rezom
- v nosečnosti genitalna papilomatoza matere
- starost < 3 leta (4 leta)
- gastroezofagealni refluks
- soinfekcija z drugimi virusi (HSV2)

(Lindeberg, 1986; Doyle, 1994; Derkay in Darrow, 2006; Stern, 2007; Gallaghar, 2008; Pou, 1995)



Klinični potek



Rizični dejavniki za agresivno obliko bolezni -molekularni nivo:

- višja bazalna aktivnost 2',5'-oligoadenilat sintetaze
- ekspresijske spremembe v E6/E7 regiji
- HLA sistem
- polimorfizem v TAP 1 (transporter associated with antigen presentation 1)

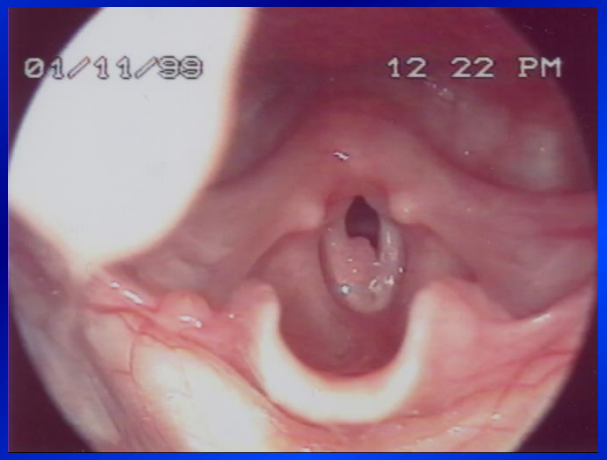
- NE: količina virusov, stopnja proliferacija (%Ki-67+celic)

(Bonagura, 2010; DeVoti, 2014;

Naši bolniki

1979-2018: 203 bolnikov (140 M, 63 Ž)

- juvenilna oblika 37 bolnikov (M= Ž)
  povp. starost ob pojavu 5,6 leta
  agresivna bolezen 21 (56,8%)



- odrasla oblika 166 bolnikov (M>Ž)
  povp. starost ob pojavu 43,7 leta
  agresivna bolezen 14 (8,4%)

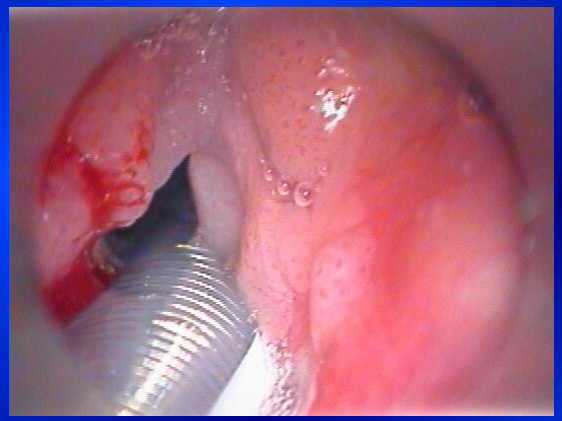
- kirurško zdravljenje (mikrokirurška ekscizija, CO2 laser, mikrodebrider)
- adjuvantno zdravljenje (cidofovir, valaciklovir, indol-3-karbinol, PPI, cepljenje)

Načini zdravljenja

Opuščeni načini zdravljenja:

- UZ, kriokirurgija, sukcijska diatermija
- obsevanje
- steroidi, estrogen, limfokini, levamisol
- podofilin, antibiotiki
- cepljenje z avtovakcino

(Derkay, 1995; Derkay in Darrow, 2006; Goon, 2008)



Načini zdravljenja

Kirurško zdravljenje

- mikrokirurgija, ekscizija z submukozno infiltracijo f.r.
- *CO2 laser* (evaporacija na nivoju epitelija)
- 585-nm pulsed dye laser (fleksibilni)
- KTP laser (fleksibilni)
- argon-plazma koagulacija
- *laringealni mikrodebrider (shaver)*
- traheotomija (otroci 11-60%)

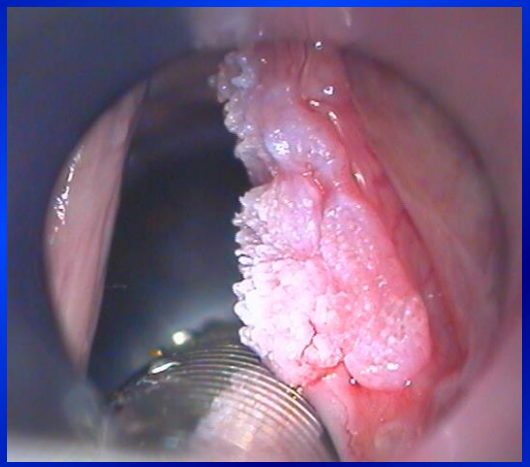
- jet-ventilacija, delo v apnei namesto z laserskimi tubusi

(Derkay in Darrow, 2006; Goon, 2008; di Giorgi, 2016; Tran, 2018)

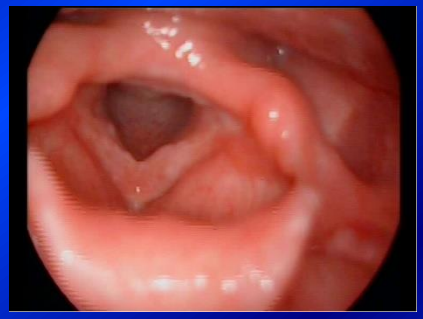
Načini zdravljenja

Adjuvantno zdravljenje: 10-21%(> 4 krg./leto, hitra rast z dihalno stisko, oddaljena razširitev)

- interferon
- protivirusna zdravila (aciklovir, valaciklovir, ribavirin, !*cidofovir)*
- indol-3-karbinol
- fotodinamična terapija
- inhibitorji protonske črpalke
- (Derkay in Darrow, 2006; Goon, 200; Carifi, 2015)



Načini zdravljenja



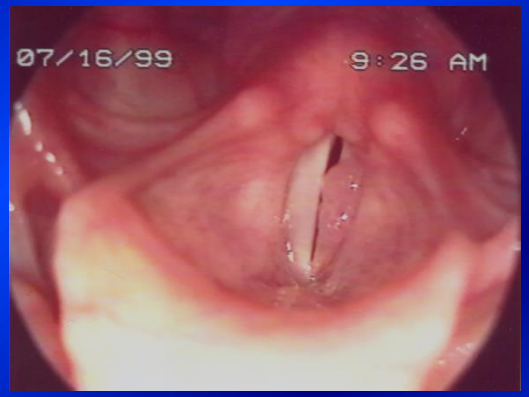
Adjuvantno zdravljenje – agresivna oblika bolezni

- inhibitorji ciklooksigenaze 2 - celecoxib
- inhibitor EGFR (gefitinib)
- monoklonalno protitelo proti vaskularnemu endotelnemu rastnemu faktorju (VEGF) - bevacizumab
- anti-PD1 protitelesa -avelumab

- cepljenje – preventivno, kurativno

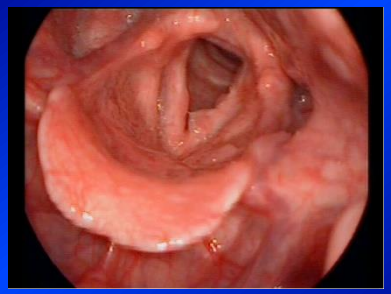
(Derkay, 2018; Mikamo, 2019; Ivancic, 2018)

Adjuvantno zdravljenje



Alfa interferon

- modulira imunski odgovor
- popoln uspeh (CR) 30-50%, delni uspeh (PR) 20-42%
- boljši uspeh pri HPV tipa 6 (64%) kot 11 (14%)
- precej stranskih pojavov, indiciran le pri agresivni obliki
- “rebound “ efekt po prekinitvi v 50%
- opisano tudi lokalno injiciranje
- (Kashima, 1988: Goon, 2008)



Adjuvantno zdravljenje

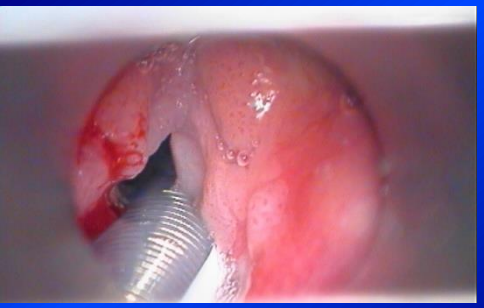
Aciklovir, valaciklovir

- inhibira podvajanje DNA pri HSV
- teoretična osnova: HSV pomaga pri HPV podvojevanju >>inhibicija HSV upočasni rast HPV
- sočasna okužba pri 50% bolnikov s papilomatozo grla
- popoln uspeh pri 2/3 bolnikov (majhne serije)
- valaciklovir manj stranskih učinkov

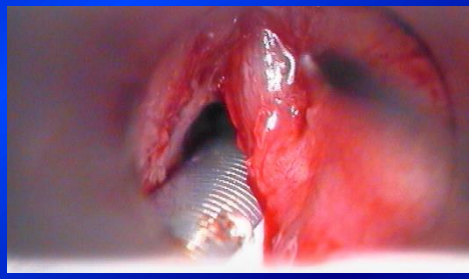
(Kiroğlu, 1994)

Naše izkušnje: aciklovir 9 bolnikov - CR 5, PR 3, NR 1

valaciklovir 11 bolnikov – CR 3, PR 5, NR 3



Adjuvantno zdravljenje



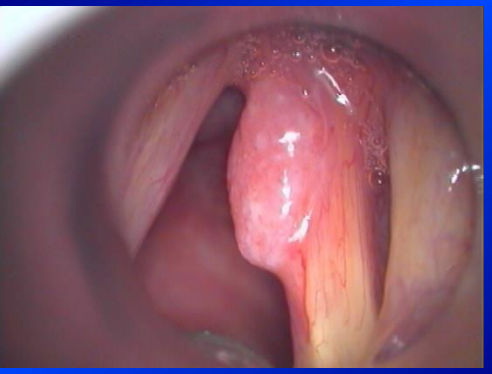
Cidofovir

- selektivno inhibira DNA polimerazo
- lokalno injiciranje po krg. odstranitvi mase
- tudi ambulantno transoralno, redko sistemsko
- CR pri 50-60% bolnikov, PC pa pri 35% bolnikov (podaljša čas med operacijami, malo brazgotin)

  skoraj ni stranskih učinkov, serumski nivo pri lokalni aplikaciji zelo nizek, ni pogostejše displazije, raka

- ireverzibilna atrofija, nekroza, fibroza tiroaritenoidne mišice pri visoki koncentraciji (psi)
- podgane – mamarni karcinom

(Jackowska, 2018)



Adjuvantno zdravljenje

Indol -3-karbinol

- inhibira hidroksilacijo estradiola v 16 alfa-hidroksisteron
- zmanjšuje papilomatozno rast v celičnih kulturah
- CR in PR v 75%
- stranski učinek ob dolgotrajni terapiji – osteopenija

Naše izkušnje: 6 otrok – 2 CP, 3 PR, 1 NR

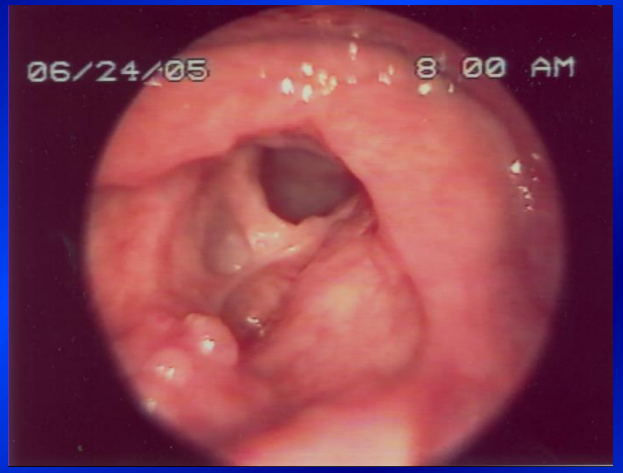
Kiroğlu in sod. 1994; Rosen in sod. 1998; Wiatrak 2003; Derkay in Darrow 2006; Hočevar-Boltežar in sod. 2011; Hočevar-Boltežar in sod. 2014

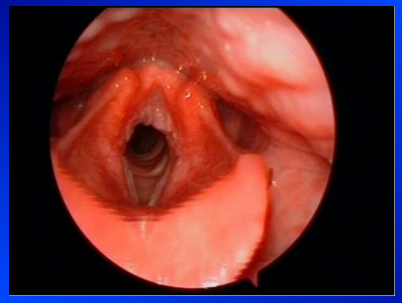
Adjuvantno zdravljenje

Fotodinamična terapija

- prenos energije na snov, ki se koncentrira v papilomih (dihematoporfirin, mezo-tetra hidroksifenil klorin)
- fotoaktivacija argonski barvni laser
- podaljša intervale med krg. posegi
- stranski učinki na koži pri izpostavljenosti dnevni svetlobi

(Derky, 2006, Goon, 2008)





Adjuvantno zdravljenje

Inhibitorji protonske črpalke (IPP)

- GER oz. LPR aktivira latentno okužbo, pospešuje brazgotinjenje po krg. odstranitvi
- korelacija med izboljšanjem papilomatoze in jemanjem IPP ter opustitvijo IPP in poslabšanjem bolezni
- 15 % bolnikov s papilomatozo grla dobiva redno IPP
- pepsin v tkivu papilomov pri 40% bolnikov

(Derkay, 2006)

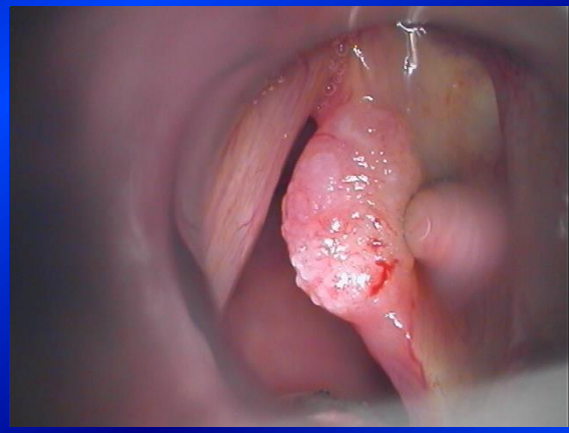
Naše izkušnje: 14/50 foniatričnih bolnikov ima znake LPR, vsi IPP, vsi podaljšanje intervalom med krg. posegi

Adjuvantno zdravljenje

Selektivni COX-2 inhibitorji (celecoxib)

- signali preko EGFR in PI-3 kinaze
- papilomi – povečana koncentracija ciklooksigenaze-2 (COX-2)
- celecoxib – supresija rasti papilomov, indukcija apoptoze
- možnost uporabe nesteroidni protivnetnih zdravil – COX inhibitorjev za zdravljenje papilomatoze grla

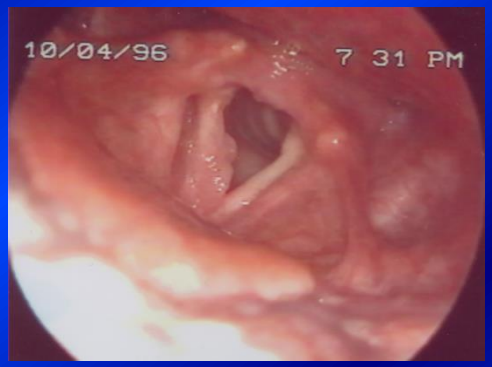
(Wu, 2005; Limsukon, 2009)



Adjuvantno zdravljenje

Monoklonalno protitelo proti vaskularnemu endotelnemu rastnemu faktorju (VEGF) - bevacizumab

- zmanjšuje angiogenezo
- lokalno injiciranje – PR
- sistemska uporaba – pri odpornosti na drugo zdravljenje
  - ciklusi na 6 tedno (sicer recidiv)
  - stranski učinki (ledvice, hipertenzija, tromboza)



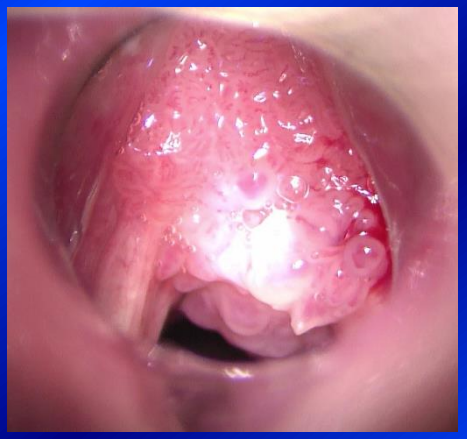
(Zur, 2017, Best, 2017)

Adjuvantno zdravljenje

Inhibitor T- imfocitnega receptorskega liganda programirane smrti – PD-1 -penbrolizumab

- PD-1 povzroča zmanjšan lokalni imunski odgovor
- povečana infiltracija papilomov z PD-1 T limfociti in povečana ekspresija PD-1
- uspešna th solidnih tumorjevz inhibitorji PD-1
- študije na RRP, močno razširjene oblike

(Pai, 2018)

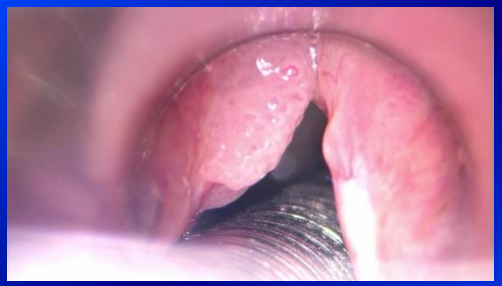


Adjuvantno zdravljenje

Cepljenje

- cepivo za mumps lokalno po krg. odstranitvi papilomov
- nejasen mehanizem učinka – vpliv na imunski odgovor?
- remisija pri 9/11 (82%), 29/38 (76%) po 1-26 injekcijah, follow-up 2-19 let

- HspE7: rekombinanto spajanje Hsp65 Mycobacterium bovis BCG in E7 proteina iz HPV 16 , lokalno po krg.
- signifikantno znižanje števila krg. pri otrocih

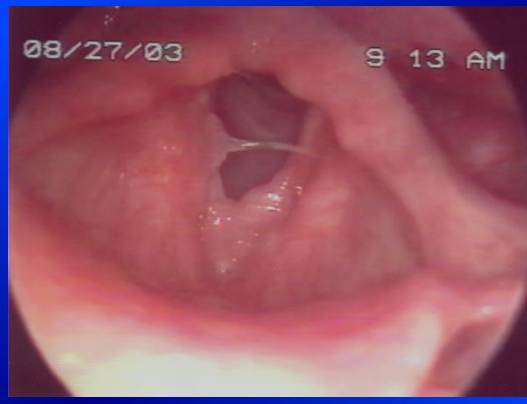


Adjuvantno zdravljenje

- HPV cepljenje, dekleta 11-26 let, 70 držav, nekatere M in Ž (11)
  štirivalentno cepivo tudi proti HPV 6 in 11
  vpliv na B-celični in T-celični imunski sistem

- Preventiva: zmanjšanje incidence RRP v Avstraliji - cepljenih (80%Ž, 75%M) (Novakovic, 2017)

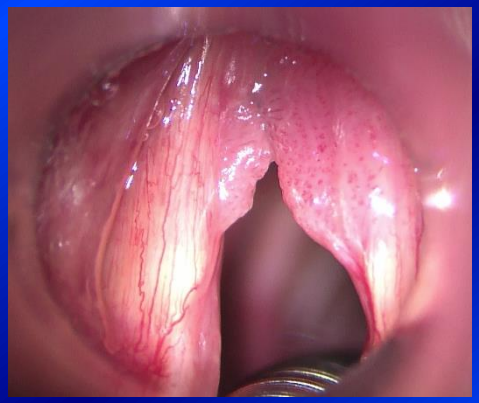
- Terapevtsko HPV cepljenje
  - uporaba zgodnjih virusnih proteinov E6 in E7 - ideja



Adjuvantno zdravljenje

- Cepljenje s 4-valentnim HPV L1 cepivom za zdravljenje RRP:
  - posamezni case-reporti
  - manjše serije
  - serokonverzija oziroma porast protiteles
  - povečan interval med operacijami, manjše število operacij (Derkay, 2018)

Naše izkušnje: 11 pacientov, sledenje do 52 mes.
podaljšanje intervalov, manjše št. op/leto
1 CR, 10 PR (Hočevar Boltežar, 2014)



Hvala za pozornost!