

The logo features a magenta vertical bar above the word "VITAZ" in a bold, black, sans-serif font. The letters are closely spaced and have a modern, slightly rounded appearance.

VITAZ

STERK IN ZORG

24 OKTOBER 2024

HPV-TEST ALS PRIMAIRE SCREENING VOOR OPSPORING BAARMOEDERHALSKANKER

- START: 20.00 UUR, EINDE VOORZIEN OMSTREEKS 21.30 UUR.
- DIT SYMPOSIUM VINDT GELIJKTIJDIG PLAATS IN HET BIZNISHOTEL LOKEREN EN VIA MICROSOFT TEAMS.
- HET SYMPOSIUM WORDT OPGENOMEN VIA MICROSOFT TEAMS EN WORDT LATER ONLINE TER BESCHIKKING GESTELD.
- VOOR DE DEELNEMERS VIA TEAMS:
 - Gelieve uw microfoon en camera tijdens de presentaties af te sluiten.
 - U kunt steeds vragen stellen via de chatfunctie. Deze worden aan het einde van de presentaties verzameld en door de moderator, samen met de vragen uit de zaal voorgelegd aan de sprekers.
 - Accreditatie:
 - U komt enkel in aanmerking voor accreditatie indien u deze presentatie live (via Teams of ter plaatse) volgde.
 - U gaf reeds bij inschrijving uw Riziv-nummer mee. Op basis van de aanwezigheidslijst (inclusief Microsoft Teams) verzamelen wij deze gegevens en geven deze door voor accreditatie.

Programma

- 20.00 uur: Verwelkoming & introductie
Dr. Marc Coenen | Gynaecologie - Verloskunde Vitaz
Dr. Veroniek Saegeman | Klinische biologie Vitaz
- 20.10 uur: De roadmap naar primaire HPV-screening in België
Prof. dr. Elizaveta Padalko | Klinische biologie UZ Gent
- 20.40 uur: Surveillance van de effecten van HPV-vaccinatie in Europa
Prof. Alex Vorsters | Vaccinologie Universiteit Antwerpen
- 21.10 uur: Migratie van cytologie naar HPV-gebaseerde baarmoederhalskankerscreening: casus
Dr. Eva Verberckmoes | Huisarts
- 21.20 uur: Laboratoriumaspecten rond HPV PCR
Apr. biol. Elise Willems | Klinische biologie Vitaz
- 21.30 uur: Conclusie en zoete afsluiter

VERWELKOMING & INTRODUCTIE

DR. MARC COENEN | GYNAECOLOGIE – VERLOSKUNDE | VITAZ

DR. VERONIEK SAEGEMAN | KLINISCHE BIOLOGIE | VITAZ

VRAGEN?

VOOR ONLINE DEELNEMERS:

U KUNT STEEDS VRAGEN STELLEN VIA DE CHATFUNCTIE.

DEZE VRAGEN WORDEN VERZAMELD DOOR DE MODERATOR EN
SAMEN MET DE VRAGEN UIT DE ZAAL **OP HET EINDE VAN DE
AVOND** VOORGELEGD AAN DE SPREKERS.

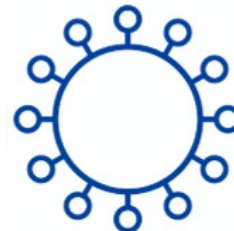
DE ROADMAP NAAR PRIMAIRE HPV-SCREENING IN BELGIË

PROF. DR. ELIZAVETA PADALKO
KLINISCHE BIOLOGIE | UZ GENT

De roadmap naar primaire HPV screening in België

Prof. Dr. Elizaveta Padalko

Laboratorium Klinische Biologie
UZ/UGent



Van **cytologie** naar **HPV**-gebaseerde screening naar baarmoederhalskanker



Van **cytologie** naar **HPV**-gebaseerde screening naar baarmoederhalskanker in **België**

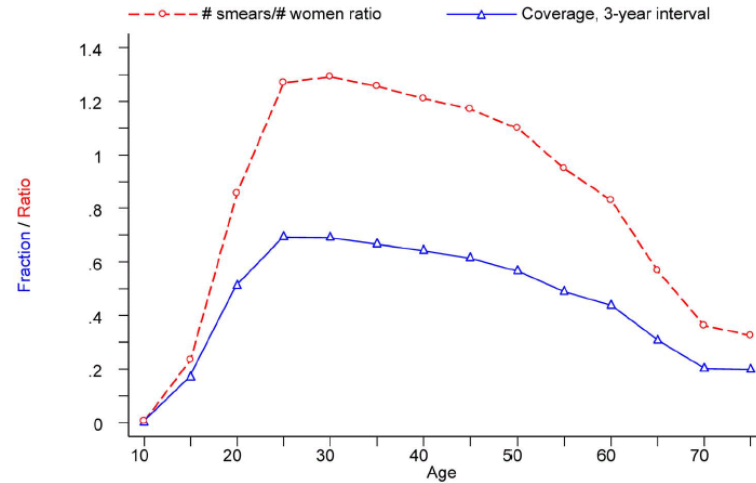


Van **cytologie** naar **HPV**-gebaseerde screening naar baarmoederhalskanker in **België**



Cytology-based screening: Belgian situation (2002-2006)

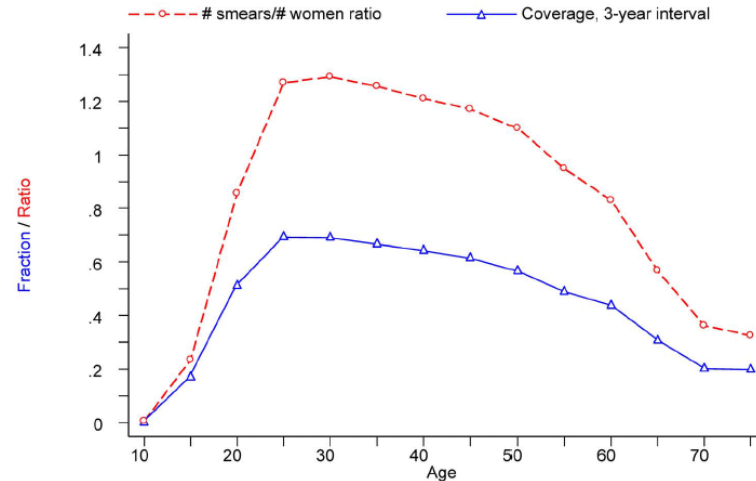
Area	Mean female population (25-64 years)	Number of smears taken	Number of women screened <3years ago	3-yr coverage	# smears / #women ratio
Belgium	2,785,516	3,199,984	1,706,043	61.2%	1.15
Flemish Region	1,614,285	1,778,783	968,385	60.0%	1.10
Walloon Region	897,182	1,091,051	568,004	63.3%	1.22
Brussels	274,052	330,150	169,654	61.9%	1.20



Cytology-based screening: Belgian situation (2002-2006)

Area	Mean female population (25-64 years)	Number of smears taken	Number of women screened <3years ago	3-yr coverage	# smears / #women ratio
Belgium	2,785,516	3,199,984	1,706,043	61.2%	1.15
Flemish Region	1,614,285	1,778,783	968,385	60.0%	1.10
Walloon Region	897,182	1,091,051	568,004	63.3%	1.22
Brussels	274,052	330,150	169,654	61.9%	1.20

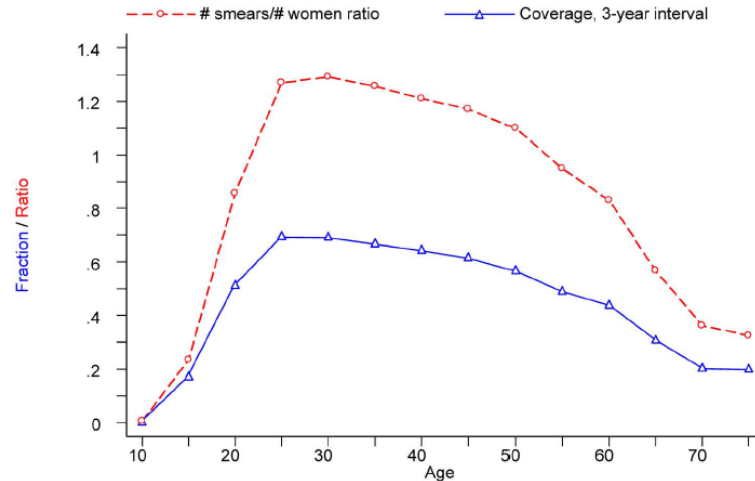
✓ Sufficient smears taken to cover 100% of target population (= **substantial overscreening**)



Cytology-based screening: Belgian situation (2002-2006)

Area	Mean female population (25-64 years)	Number of smears taken	Number of women screened <3years ago	3-yr coverage	# smears / #women ratio
Belgium	2,785,516	3,199,984	1,706,043	61.2%	1.15
Flemish Region	1,614,285	1,778,783	968,385	60.0%	1.10
Walloon Region	897,182	1,091,051	568,004	63.3%	1.22
Brussels	274,052	330,150	169,654	61.9%	1.20

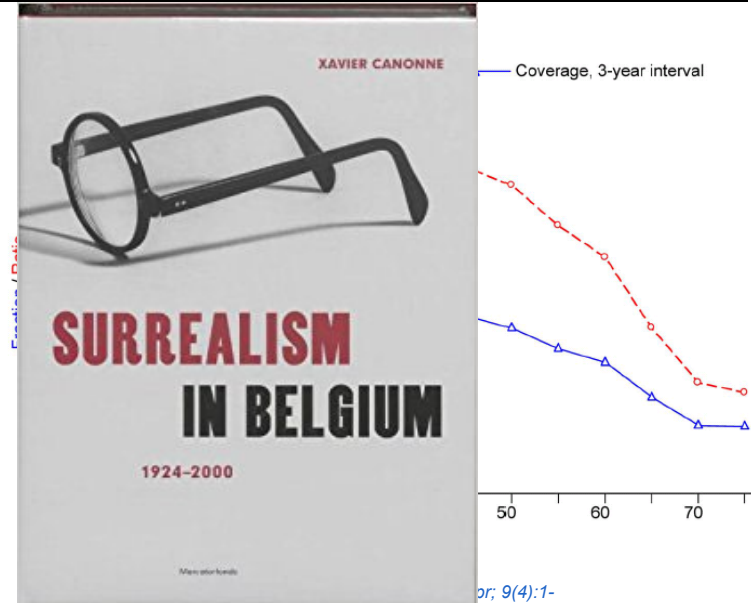
- ✓ Sufficient smears taken to cover 100% of target population (= **substantial overscreening**) but coverage only 61% (= **substantial underscreening**)
- ✓ The median screening interval was 13 months
- ✓ Differences between the 3 regions are small



Cytology-based screening: Belgian situation (2002-2006)

Area	Mean female population (25-64 years)	Number of smears taken	Number of women screened <3years ago	3-yr coverage	# smears / #women ratio
Belgium	2,785,516	3,199,984	1,706,043	61.2%	1.15
Flemish Region	1,614,285	1,778,783	968,385	60.0%	1.10
Walloon Region	897,182	1,091,051	568,004	63.3%	1.22
Brussels	274,052	330,150	169,654	61.9%	1.20

- ✓ Sufficient smears taken to cover 100% of target population (= **substantial overscreening**) but coverage only 61% (= **substantial underscreening**)
- ✓ The median screening interval was 13 months
- ✓ Differences between the 3 regions are small

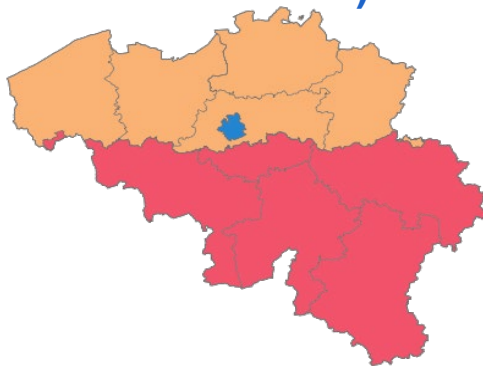


Cytology-based screening: Belgian situation (2013 - 2024)



- ✓ The **Flemish** region is **the only region where a formal cervical cancer screening program has been set up:**
 - ✓ since 06/2013 in women between 25 and 64 years of age once every 3 years (also reimbursement)
 - ✓ invitation by mail with encouragement to make an appointment with their GP or gynecologist for cervical smear
 - ✓ the test results are gathered in a centralized cyto-histo-pathology register by the Belgian Cancer Registry/Stichting Kankerregister/Fondations Registre du Cancer
 - ✓ clinicians are informed on the test results and are responsible to inform the screened woman and to organise the aftercare
- ✓ No formal screening program has been set up yet in **Walloon** region and **Brussels Capital** region.

Cytology-based screening: Belgian situation (2013 - 2024)



Intermutualistisch Agentschap - Agence Intermutualiste

Baarmoederhalskankerscreening 2008-2017

Vierde rapport van het Intermutualistisch Agentschap (IMA)

In samenwerking met het Kankercentrum, Sciensano en de Stichting Kankerregister

December 2019

www.atlas.ima-aim.be

4.1 EVOLUTIE VAN DE DEKKINGSGRAAD GEBASEERD OP HET CYTOLOGISCH ONDERZOEK VAN 2008 TOT 2017¹⁶

Tabel 1 : Dekkingsgraad gebaseerd op de verstrekking van het cytologisch onderzoek

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Brussels Hoofdstedelijk Gewest	65,3%	65,2%	63,8%	59,3%	56,7%	55,9%	48,2%	44,1%	47,0%	46,3%
Waals Gewest	64,0%	63,6%	62,4%	59,1%	57,5%	56,9%	48,5%	45,5%	48,9%	48,2%

Tabel 2: Evolutie van de dekkingsgraad gebaseerd op de verstrekking van het cytologisch onderzoek vergeleken met de situatie in 2008: proportionele evolutie als (dekkingsgraad jaar T - dekkingsgraad 2008) / dekkingsgraad 2008.

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Brussels Hoofdstedelijk Gewest		0,00	-0,02	-0,09	-0,13	-0,14	-0,26	-0,33	-0,28	-0,29
Waals Gewest		-0,01	-0,03	-0,08	-0,10	-0,11	-0,24	-0,29	-0,24	-0,25

✓ No formal screening program has been set up yet in **Walloon** region and **Brussels** Capital region.

Cervical cancer screening programs worldwide

Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis



Laia Bruni*, Beatriz Serrano*, Esther Roura, Laia Alemany, Melanie Cowan, Rolando Herrero, Mario Poljak, Raul Munillo, Nathalie Broutet, Leanne M Riley, Silvia de Sanjose



[Lancet Glob Health](#). 2022 Aug;10(8):e1115-e1127.

Methods In this review and synthetic analysis, we searched scientific literature, government websites, and official documentation to identify official national recommendations and coverage data for cervical cancer screening for the 194 WHO member states and eight associated countries and territories published from database inception until Oct 30, 2020, supplemented with a formal WHO country consultation from Nov 27, 2020, to Feb 12, 2021. We extracted

Findings We identified recommendations for cervical screening in 139 (69%) of 202 countries and territories. Cytology was the primary screening test in 109 (78%) of 139 countries. 48 (35%) of 139 countries recommended primary HPV-based screening. Visual inspection with acetic acid was the most recommended test in resource-limited settings. Estimated

Cervical cancer screening programs worldwide

Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis



Laia Bruni*, Beatriz Serrano*, Esther Roura, Laia Alemany, Melanie Cowan, Rolando Herrero, Mario Poljak, Raul Murillo, Nathalie Broutet, Leanne M Riley, Silvia de Sanjose



Lancet Glob Health. 2022 Aug;10(8):e1115-e1127.

Methods In this review and synthetic analysis, we searched scientific literature, government websites, and official documentation to identify official national recommendations and coverage data for cervical cancer screening for the 194 WHO member states and eight associated countries and territories published from database inception until Oct 30, 2020 supplemented with a formal WHO country consultation from Nov 27, 2020, to Feb 12, 2021. We extracted

Findings We identified recommendations for cervical screening in 139 (69%) of 202 countries and territories. Cytology was the primary screening test in 109 (78%) of 139 countries. 48 (35%) of 139 countries recommended primary HPV-based screening. Visual inspection with acetic acid was the most recommended test in resource-limited settings. Estimated

underserved populations). HPV testing was introduced as a triage test (and not recommended for primary use) for atypical squamous cells of undetermined significance or other indications in 18 countries. Six countries (Belarus, Belgium, Canada, Japan, New Zealand, and Trinidad and Tobago) announced plans in 2019 for introducing HPV-based screening by 2024. Combined or

Cervical cancer screening programs worldwide

Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis



Laia Bruni*, Beatriz Serrano*, Esther Roura, Laia Alemany, Melanie Cowan, Rolando Herrero, Mario Poljak, Raul Murillo, Nathalie Broutet, Leanne M Riley, Silvia de Sanjose



Lancet Glob Health. 2022 Aug;10(8):e1115-e1127.

Methods In this review and synthetic analysis, we searched scientific literature, government websites, and official documentation to identify official national recommendations and coverage data for cervical cancer screening for the 194 WHO member states and eight associated countries and territories published from database inception until Oct 30, 2020 supplemented with a formal WHO country consultation from Nov 27, 2020, to Feb 12, 2021. We extracted

Findings We identified recommendations for cervical screening in 139 (69%) of 202 countries and territories. Cytology was the primary screening test in 109 (78%) of 139 countries. 48 (35%) of 139 countries recommended primary HPV-based screening. Visual inspection with acetic acid was the most recommended test in resource-limited settings. Estimated

underserved populations). HPV testing was introduced as a triage test (and not recommended for primary use) for atypical squamous cells of undetermined significance or other indications in 18 countries. Six countries (Belarus, Belgium, Canada, Japan, New Zealand, and Trinidad and Tobago) announced plans in 2019 for introducing HPV-based screening by 2024. Combined or



Cervical cancer screening program in Belgium



Persbericht 8 december 2022

IMC beslist over nieuwe screening baarmoederhalskanker

De interministeriële conferentie Volksgezondheid bereikt een akkoord over de nieuwe baarmoederhalsscreening. Weldra kunnen vrouwen tussen 30 en 64 jaar om de vijf jaar een HPV-test laten afnemen. Experts pleiten al langer om boven de 30 jaar het cytologisch onderzoek te vervangen door een HPV-test. Voor vrouwen van 25 tot 29 jaar blijft het cytologisch onderzoek om de 3 jaar de beste manier om te screenen.

Om een groot effect op de volksgezondheid te hebben, moeten de deelstaten zorgen voor hogere deelname aan de screening. Bijna 40 procent van de vrouwen in Vlaanderen laat nooit een uitstrijkje doen, zelfs na een uitnodiging. In Wallonië en Brussel liggen de cijfers zelfs een pak hoger, respectievelijk 53 en 51 procent. Daar ligt dus een belangrijke opdracht voor de deelstaten. Zij kunnen ook vanaf 2025 zelfafnametesten organiseren, gericht op meer kwetsbare doelgroepen.

Cervical cancer screening program in Belgium

HPV
testing

↑ sensitivity



Persbericht 8 december 2022

IMC beslist over nieuwe screening baarmoederhalskanker

De interministeriële conferentie Volksgezondheid bereikt een akkoord over de nieuwe baarmoederhalsscreening. Weldra kunnen vrouwen tussen 30 en 64 jaar om de vijf jaar een HPV-test laten afnemen. Experts pleiten al langer om boven de 30 jaar het cytologisch onderzoek te vervangen door een HPV-test. Voor vrouwen van 25 tot 29 jaar blijft het cytologisch onderzoek om de 3 jaar de beste manier om te screenen.

Om een groot effect op de volksgezondheid te hebben, moeten de deelstaten zorgen voor hogere deelname aan de screening. Bijna 40 procent van de vrouwen in Vlaanderen laat nooit een uitstrijkje doen, zelfs na een uitnodiging. In Wallonië en Brussel liggen de cijfers zelfs een pak hoger, respectievelijk 53 en 51 procent. Daar ligt dus een belangrijke opdracht voor de deelstaten. Zij kunnen ook vanaf 2025 zelfafnametesten organiseren, gericht op meer kwetsbare doelgroepen.

Cervical cancer screening program in Belgium

HPV
testing

↑ sensitivity

↑ participation

HPV
testing



Persbericht 8 december 2022

IMC beslist over nieuwe screening baarmoederhalskanker

De interministeriële conferentie Volksgezondheid bereikt een akkoord over de nieuwe baarmoederhalsscreening. Weldra kunnen vrouwen tussen 30 en 64 jaar om de vijf jaar een HPV-test laten afnemen. Experts pleiten al langer om boven de 30 jaar het cytologisch onderzoek te vervangen door een HPV-test. Voor vrouwen van 25 tot 29 jaar blijft het cytologisch onderzoek om de 3 jaar de beste manier om te screenen.

Om een groot effect op de volksgezondheid te hebben, moeten de deelstaten zorgen voor hogere deelname aan de screening. Bijna 40 procent van de vrouwen in Vlaanderen laat nooit een uitstrijkje doen, zelfs na een uitnodiging. In Wallonië en Brussel liggen de cijfers zelfs een pak hoger, respectievelijk 53 en 51 procent. Daar ligt dus een belangrijke opdracht voor de deelstaten. Zij kunnen ook vanaf 2025 zelfafnametesten organiseren, gericht op meer kwetsbare doelgroepen.

Cervical cancer screening programs worldwide

Cervical cancer screening programmes and age-specific coverage estimates for 202 countries and territories worldwide: a review and synthetic analysis



Laia Bruni*, Beatriz Serrano*, Esther Roura, Laia Alemany, Melanie Cowan, Rolando Herrero, Mario Poljak, Raul Murillo, Nathalie Broutet, Leanne M Riley, Silvia de Sanjose



Lancet Glob Health. 2022 Aug;10(8):e1115-e1127.

Methods In this review and synthetic analysis, we searched scientific literature, government websites, and official documentation to identify official national recommendations and coverage data for cervical cancer screening for the 194 WHO member states and eight associated countries and territories published from database inception until Oct 30, 2020 supplemented with a formal WHO country consultation from Nov 27, 2020, to Feb 12, 2021. We extracted

Findings We identified recommendations for cervical screening in 139 (69%) of 202 countries and territories. Cytology was the primary screening test in 109 (78%) of 139 countries. 48 (35%) of 139 countries recommended primary HPV-based screening. Visual inspection with acetic acid was the most recommended test in resource-limited settings. Estimated

underserved populations). HPV testing was introduced as a triage test (and not recommended for primary use) for atypical squamous cells of undetermined significance or other indications in 18 countries. Six countries (Belarus, Belgium, Canada, Japan, New Zealand, and Trinidad and Tobago) announced plans in 2019 for introducing HPV-based screening by 2024. Combined or



Cervical cancer screening program in Belgium

HPV
testing

↑ sensitivity

↑ participation

HPV
testing



Persbericht 8 december 2022

IMC beslist over nieuwe screening voor baarmoederhalskanker

De interministeriële conferentie Volksgezondheid bereikt een akkoord over de nieuwe screening voor baarmoederhalskanker. Weldra kunnen vrouwen een HPV-test laten afnemen. Experts pleiten al langer om boven de 30 jaar het cytologisch onderzoek te vervangen door een HPV-test voor vrouwen van 25 tot 29 jaar blijft het cytologisch onderzoek om de 3 jaar de beste manier om te screenen.

Om een groot effect op de volksgezondheid te hebben, moeten de deelstaten zorgen voor hogere deelname aan de screening. Bijna 40 procent van de vrouwen in Vlaanderen laat nooit een uitstrijkje doen, zelfs na een uitnodiging. In Wallonië en Brussel liggen de cijfers zelfs een pak hoger, respectievelijk 53 en 51 procent. Daar ligt dus een belangrijke opdracht voor de deelstaten. Zij kunnen ook vanaf 2025 zelfafnametesten organiseren, gericht op meer kwetsbare doelgroepen.

Do we have
enough HPV
tests?

Currently available HPV tests: variety



2023 global inventory of commercial molecular tests for human papillomaviruses (HPV)

Mario Poljak^{a,*}, Anja Oštrbenk Valenčak^a, Kate Cuschieri^b, Klara B. Bohinc^a, Marc Arbyn^c

^a Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

^b Scottish HPV Reference Laboratory, Royal Infirmary of Edinburgh, Edinburgh, Scotland, United Kingdom

^c Belgian Cancer Centre / Unit of Cancer Epidemiology, Sciensano, Brussels, Belgium

J Clin Virol. 2024 Jun;172:105671. doi: 10.1016/j.jcv.2024.105671. Epub 2024 Mar 14.



SCITEIT

Currently available HPV tests: variety



Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv



2023 global inventory of commercial molecular tests for human papillomaviruses (HPV)

Mario Poljak^{a,*}, Anja Oštrbenk Valenčak^a, Kate Cuschieri^b, Klara B. Bohinc^a, Marc Arbyn^c

^a Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

^b Scottish HPV Reference Laboratory, Royal Infirmary of Edinburgh, Edinburgh, Scotland, United Kingdom

^c Belgian Cancer Centre / Unit of Cancer Epidemiology, Sciensano, Brussels, Belgium

J Clin Virol. 2024 Jun;172:105671. doi: 10.1016/j.jcv.2024.105671. Epub 2024 Mar 14.

SCITEIT



Currently available HPV tests: variety

Table S1: hr-HPV DNA screening tests without genotyping present on the global market in December 2023. All variants of a particular distinct HPV test are marked with the same superscript letter.

Tests targeting 12 IARC-2009 hr-HPV genotypes plus HPV66 and/or HPV68

Hybrid Capture 2 (HC2) HPV DNA Test (Qiagen, Germantown, MD, USA)
 Cervista HPV HR Test (Hologic, Madison, WI, USA)
 CareHPV Test (Qiagen, Germantown, MD, USA)
 13 High-risk HPV Real-time PCR Kit (HybriBio, Beijing, China)
 RealLine HPV HCR Screen (Str-format) (Bioron Diagnostics GmbH, Ludwigshafen, Germany)
 CareGene HPV Screening Kit - PNT (WELLS BIO, Seoul, South Korea)
 Diagnostic Kit for Detection of Human Papillomavirus DNA (PCR-Fluorescent) (Genetel Pharmaceuticals, Shenzhen, China)
 HPV 13 High-risk Subtypes DNA Diagnostic Kit (CE marked) (Triplex International Biosciences (TIB), Xiamen, China)^a
 HR-HPV(14 types) Fluorescence PCR Detection Kit (Promega Biological Products, Shanghai, China)
 CERVASURE HPV Detection Kit (DSS Imagetech, New Delhi, India)
 High Risk HPV Genotyping Kit (Sanity 2.0) (Zeesan Biotech, Xiamen, China)
 High risk human papillomavirus nucleic acid Detection Kit (Tellgen Corporation, Shanghai, China)
 Human papillomavirus (HPV) nucleic acid Test Kit (Shenrui Bio, Wuxi, China)
 BioXsen Human Papillomavirus High-Risk qPCR T Panel (Takara Bio Inc, Shiga, Japan)
 RealBest DNA HPV HR screen (JSC "Vector-Best", Novosibirsk Region, Russia)
 Human Papillomavirus (HPV) Nucleic Acid Detection Kit (Hybrid Capture-CLIA) (DH2) (Hangzhou DALTON BioSciences, Ltd., Hangzhou, China)^b
 ABT HPV qPCR Kit (ABT Biological Solutions, Ho Chi Minh, Vietnam)ⁱ

Tests targeting 12 IARC-2009 hr-HPV genotypes only

HPV High Risk Screen Real-TM Quant (Sacace, Como, Italy)
 HPV High Risk Screen Real-TM Quant 2 x (Sacace, Como, Italy)
 Human Papilloma Virus (HPV) High Risk Screen PCR Kit (Biocore Diagnostics, Bad Homburg, Germany)
 AmpliSens HPV HCR screen-titre-FRT PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)^c
 AmpliSens HPV HCR screen-titre-FRT PCR kit (2x) (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)^c
 AmpliSens HPV HCR screen-titre-FRT PCR kit (4x) (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)^c

Tests targeting 12 IARC-2009 hr-HPV genotypes and additional alpha-HPV genotypes

STD Kit (Autoimmun Diagnostika GmbH, Strassberg, Germany)
 HPV-DNA Assay Kit (Tofema, Seoul, South Korea)
 Human Papilloma Virus (HPV Common/double check) (Genekam Biotechnology, Duisburg, Germany)
 BIOPAP Kit (Biotools, Nave, Spain)

Currently available HPV tests: variety

HPV 15HR – 15 High-risk Human Papillomavirus Nucleic Acid Diagnostic Kit (Sansure Biotech Inc., Changsha, Hunan, China)^d

HPV Genotyping test Kit (Isothermal Amplification + PCR detection) (National Bio-Founder, Taizhou, China)

HPV18 high risk HPV detection kit (PCR- Fluorescence Probing) (Heasbio, Guangzhou, China)

Human Papillomavirus DNA Test Kit (PCR- Fluorescence)-HPV18 (GZLBP, Guangzhou, China)

18 High-risk Human Papillomavirus Virus (HPV) Genotyping Kit (Real-Time PCR) (BACME Biotech, Suzhou, China)

Bosphore HPV Detection Kit v4 (Anatolia Geneworks, Istanbul, Türkiye)^k

HPV Selfy Extended - 30 HPV types (Ulisse BioMed, Udine, Italy)^{bb}

TopSENSI HPV genotype RDB Kit (ABT Biological Solutions, Ho Chi Minh, Vietnam)^j

TopSENSI HPV qPCR Kit (ABT Biological Solutions, Ho Chi Minh, Vietnam)ⁱ

Tests targeting a subset of 12 IARC-2009 hr-HPV genotypes

Bosphore HPV Detection Kit v1 (Anatolia Geneworks, Istanbul, Türkiye)^k

HPV 5 High-risk Subtypes DNA Diagnostic Kit (Triplex International Biosciences (TIB), Xiamen, China)^a

Table S2: hr-HPV DNA screening tests with concurrent partial (HPV16/18/45), concurrent extended or reflex partial genotyping for the main hr-HPV genotypes present on the global market in December 2023. All variants of a particular distinct HPV test are marked with the same superscript letter.

hr-HPV DNA screening tests with concurrent partial (HPV16/18/45) genotyping for the main hr-HPV genotypes

Cobas 4800 HPV Test (Roche Molecular Systems Inc., Alameda, CA, USA)

Cobas 6800/8800 HPV Test (Roche Molecular Systems Inc., Alameda, CA, USA)

RealTime High Risk HPV test (Abbott Molecular, Des Plaines, IL, USA)

Xpert HPV (Cepheid, Sunnyvale, CA, USA)

HPV-Risk assay (Fujirebio, Gent, Belgium)

QIAscreen HPV PCR Test (Qiagen Gaithersburg, Inc., Germantown, MD, USA)

NeuMoDx HPV assay (Qiagen Gaithersburg, Inc., Germantown, MD, USA)

14 High-risk HPV with 16/18 Genotyping Real-time PCR Kit (HybriBio, Beijing, China)

Realquality RQ-HPV Screen (AB Analitica, Padova, Italy)^f

Realquality RQ-HPV HR Multiplex (AB Analitica, Padova, Italy)^f

Realquality RQ-HPV HR/LR Multiplex (AB Analitica, Padova, Italy)^f

Realquality RQ-Multi HPV Detection (AB Analitica, Padova, Italy)^f

GenoFlow HPV-HR screening kit (FT-PRO) (DiagCor Bioscience, Hong Kong, China)

HPV Easy-Screening Kit (Autoimmun Diagnostika GmbH, Strassberg, Germany)

AmpliSens HPV HCR screen-FEP PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)

HarmoniaHPV High-risk Human Papillomavirus (HPV) and Genotyping 16&18 Real Time PCR Kit (Liferiver, Shanghai, China)

HPV 14 Screening & 16,18,45 Typing Real-TM Quant (Sacace, Como, Italy)

Currently available HPV tests: variety

Path-High Risk HPV (PrimerDesign, Southampton, United Kingdom)
Confidence HPV (Neumann Diagnostics, Budapest, Hungary)
14 hrHPV types and genotyping 16&18 Real Time PCR detection kit (Kangmei Tianhong, Beijing, China)
Nucleic Acid Detection and HPV 16/18 Genotyping Kit for 14 Types of High-Risk Human Papillomavirus (Kindmay Medical, Shenzhen, China)
PANA RealTyper Screening Kit (PANAGENE, Daejeon, South Korea)
Multiplex High Risk HPV Real Time Fluorescent Detection with HPV16/18 Genotyping (Atila BioSystems, Mountain View, CA, USA)⁸
2+16 HPV test kit (Mole Bioscience, Taizhou, China)
Diagnostic Kit for High-risk Human Papillomavirus DNA (Real-Time PCR) (Kehua Bio-Engineering, Shanghai, China)^h
HPV16+2 high risk HPV detection kit (PCR- Fluorescence Probing) (Heasbio, Guangzhou, China)
Gene-Dot Human Papillomavirus Test (Real Time PCR) (Shenrui Bio, Wuxi, China)
HPV Real Time PCR Kit (Bio Perfectus Technologies, Taizhou, China)
HPV nucleic acid detection kit (Real Time PCR) (TianLong Tec, Suzhou, China)
SILGOLBIO HPV 14+2 assay (Real Time PCR) (Mojin Bio-tech, Nanjing, China)
Human papillomavirus nucleic acid detection kit - HPV18 type (GZLBP, Guangzhou, China)
ABT DNA GENOTYPE qPCR Kit (ABT Biological Solutions, Ho Chi Minh, Vietnam)ⁱ
TopSENSI HPV 6, 11, 16, 18 & High Risk qPCR Kit (ABT Biological Solutions, Ho Chi Minh, Vietnam)ⁱ
AmpFire HPV Screening 16/18/HR (Atila BioSystems, Mountain View, CA, USA)^j
Aridia HPV 16/18 Real-Time PCR Test (CTK Biotech, San Diego, CA, USA)
Bosphore HPV Screening Kit v1 (Anatolia Geneworks, Istanbul, Türkiye)^k
Bosphore HPV Screening Kit v2 (Anatolia Geneworks, Istanbul, Türkiye)^k
CareStart HPV Screening Kit - H (Access Bio, Ewing Township, NJ, USA)
GeneNav HPV One qPCR Kit (GenomeMe Lab Inc., Richmond, Canada)^l
GeneNav HPV Complete qPCR Kit (GenomeMe Lab Inc., Richmond, Canada)^l
HPV 18 High-risk Types with 16/18 Genotyping Test Kit (Acon, Hangzhou, China)
High-Risk HPV's (Vitassay Healthcare, S.L.U., Huesca, Spain)
HPV 13+2 – Human Papillomavirus DNA Diagnostic Kit (Sansure Biotech Inc., Changsha, Hunan, China)
HPV 18 High-Risk with 16/18 Genotyping PCR Test Kit (Clongene Biotech Co., Hangzhou, China)
HPV Genotype 2+12 High Risk 16+18 Medium Risk PCR Detection Kit Lyophilized (Guangzhou BioKey Healthy Technology, Guangzhou, China)^m
High Risk HPV Real Time PCR kit (BioPerfectus, Jiangsu, China)
Human papillomavirus (18 high-risk types) nucleic acid amplification test kit (OUTDO Biotech, Shanghai, China)
Human papillomavirus (HPV) nucleic acid Test Kit (ZCON, Inner Mongolia, China)
Human Papillomavirus Nucleic Acid Detection and HPV16/18 Genotyping Kit -- HPV 18/2 (Yaneng BioScience, Shenzhen, China)
Human papillomavirus nucleic acid Detection Kit (HPV16+2) (Zybio Inc, Chongqing, China)
Human Papillomavirus Real Time PCR Kit (ViraxClear, London, United Kingdom)

SITEIT

Currently available HPV tests: variety

iSolutions HPV Fullplex qPCR kit (id solutions, Grabels, France)

Nucleic Acid Detection Kit for High-risk Human Papillomavirus (PCR-Fluorescence Probing) (Singuway Biotech Inc., Shenzhen City, China)

OncoPredict HPV SCR assay (Hiantis, Milano, Italy)

Primary screening HPV test kit (Mole Bioscience, Jiangsu, China)

RealBest HPV OncoScreen (JSC "Vector-Best", Novosibirsk Region, Russia)

ScreenFire HPV Risk Stratification Assay (Atila BioSystems, Mountain View, CA, USA)

SMARTCHEK HPV Detection Kit (Genesystem, Daejeon, South Korea)

STANDARD M10 HPV (SD BIOSENSOR, Gyeonggi-do, South Korea)

VIASURE High-Risk Human Papilloma Virus Real Time PCR Detection Kit (Certest Biotec S.L., Zaragoza, Spain)ⁿ

Vitro HPV Screening Kit (Master Diagnostika, Granada, Spain)^o

■ 14 High-Risk HPV with 16/18 Genotyping Test Kit (Fluorescence PCR) (Jiangsu Macro & Micro-Test Med-Tech Co., Ltd., Rudong County, China)^q

17 Types of Human Papillomavirus (16/18/6/11/44 Typing) Nucleic Acid Detection Kit (Fluorescence PCR) (Jiangsu Macro & Micro-Test Med-Tech Co., Ltd., Rudong County, China)^q

18 Types of High-risk Human Papilloma Virus Nucleic Acid Detection Kit (Fluorescence PCR) (Jiangsu Macro & Micro-Test Med-Tech Co., Ltd., Rudong County, China)^q

HPV 2+12 Test Kit (Tellgen Corporation, Shanghai, China)^p

hr-HPV DNA screening tests with concurrent extended genotyping for the main hr-HPV genotypes

BD Onclarity HPV Assay (BD Diagnostics, Sparks, MD, USA)

Alinity m HR HPV Assay (Abbott Molecular, Des Plaines, IL, USA)

RealLine HPV HCR Genotype (Str-format) (Bioron Diagnostics GmbH, Ludwigshafen, Germany)

HPV 5+9 Test Kit (Tellgen Corporation, Shanghai, China)^p

14 Types of High-risk Human Papillomavirus (16/18/52 Typing) Nucleic Acid Detection Kit (Fluorescence PCR) (Jiangsu Macro & Micro-Test Med-Tech Co., Ltd., Rudong County, China)^q

hr-HPV DNA screening tests with reflex partial genotyping for the main hr-HPV genotypes

Cervista HPV HR Test (Hologic, Madison, WI, USA) followed by Cervista HPV 16/18 Test (Hologic, Madison, WI, USA)

Hybrid Capture 2 (HC2) HPV DNA Test (Qiagen, Germantown, MD, USA) followed by digene HPV Genotyping PS Test (Qiagen, Germantown, MD, USA)

HPV High Risk Screen Real-TM Quant (Sacace, Como, Italy) followed by HPV 16/18 Real-TM Quant (Sacace, Como, Italy)

AmpliSens HPV HCR screen-titre-FRT PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)^c followed by AmpliSens HPV 16/18-FRT PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)^f

Currently available HPV tests: variety

Table S3: HPV DNA full genotyping tests present on the global market in December 2023. All variants of a particular distinct HPV test are marked with the same superscript letter(s).

Strip, filter or microtiter-well hybridisation-based full genotyping tests

- INNO-LiPA HPV Genotyping Extra II (Fujirebio, Gent, Belgium)
- RHA Kit SPF10-LiPA25^{version 1} (Cerba Research, Ghent, Belgium)
- DNA ELISA Kit HPV SPF10^{version 1} (Cerba Research, Ghent, Belgium)
- AmpliQuality HPV-type express v3.0 (AB Analitica, Padova, Italy)
- GenoFlow HPV Array Test (DiagCor Bioscience, Hong Kong, China)
- HPV Direct-Flow Chip Kit (Master Diagnostika, Granada, Spain)^s
- HPV Direct Flow Chip Kit (e-BRID) (Master Diagnostika, Granada, Spain)^s
- HPV Easy-Typing Kit (Autoimmun Diagnostika GmbH, Strassberg, Germany)
- High PapillomaStrip (Operon, Zaragoza, Spain)^t
- High+Low PapillomaStrip (Operon, Zaragoza, Spain)^t
- Human papillomavirus genotyping Assay Kit (PCR-RDB)-28 genotype (Daan Gene Co., Ltd. Of Sun Yat-Sen University, Guangdong, China)
- DR.HPV Genotyping IVD kit (DR. Chip Biotechnology Incorporation, Taichung City, Republic of China)
- PaxView HPV16/18/Others MPCR-ULFA Kit (PaxGenBio, Gyeonggi-do, South Korea)^u
- PaxView HPV 20 Genotyping MPCR-ULFA Kit (PaxGenBio, Gyeonggi-do, South Korea)^u
- VisionArray HPV Chip 1.0- Detection of 41 HPV types (ZytoVision, Bremerhaven, Germany)
- Human papillomavirus Genotyping Test Kit (GZLBP, Guangzhou, China)
- Human Papillomavirus Genotyping Kit for 15 Types - HPV15 (Yaneng BioScience, Shenzhen, China)^v
- Human Papillomavirus Genotyping kit for 23 Types -- HPV23 full-Genotyping (Yaneng BioScience, Shenzhen, China)^v
- HPV 23 Subtypes DNA Diagnostic Kit (Triplex International Biosciences (TIB), Xiamen, China)
- HPV28 full genotyping detection kit (PCR-RDB) (Heasbio, Guangzhou, China)
- MULTI HPV FLOW CHIP (Mobius Life Science, Curitiba, Brasil)
- HPV XpressMatrix Kit (PT KalGen DNA, Jakarta, Indonesia)
- Human papillomavirus (HPV) Genotyping Test Kit (Fosun Long March Medical Science, Shanghai, China)
- Human papillomavirus Genotyping (Type 25) Test Kit (Acon, Hangzhou, China)
- REBA HPV-ID IVD Diagnostica (Gyeonggi-do, South Korea)

Gel electrophoresis-based full genotyping tests

- PCR Human Papillomavirus Typing Set (Takara Bio Inc, Shiga, Japan)

Real time PCR-based full genotyping tests

- Anyplex II HPV HR Detection (Seegene, Seoul, South Korea)

Currently available HPV tests: variety

Allplex HPV HR Detection (Seegene, Seoul, South Korea)^w
Allplex HPV28 Detection (Seegene, Seoul, South Korea)^w
23 HPV Genotyping Real-time PCR Kit (HybriBio, Beijing, China)
VenusHPV High-Risk Human Papillomavirus (HPV) Genotyping Real Time PCR Kit (Liferiver, Shanghai, China)
AmpliSens HPV HCR genotype-FRT PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)
HPV genotypes 14 Real-TM Quant (Sacace, Como, Italy)^x
HPV genotypes 21 Real-TM Quant (Sacace, Como, Italy)^x
HPV QUANT-15 (HPV 6,11,16,18,31,33,35,39,45,51,52,56,58,59,68) (DNA-Technology LLC, Moscow, Russia)^y
HPV QUANT-21 (HPV 6,11,44,16,18,26,31,33,35,39,45,51,52,53,56,58,59,66,68,73,82) (DNA-Technology LLC, Moscow, Russia)^y
RealBest DNA HPV HR genotype (JSC "Vector-Best", Novosibirsk Region, Russia)^z
RealBest DNA HPV HR genotype quantitative (JSC "Vector-Best", Novosibirsk Region, Russia)^z
GeneProof Human Papillomavirus (HPV) PCR Kit (GeneProof, Brno, Czechia)
AmpliSens HPV HCR genotype-titre-FRT PCR kit (Federal State Institution of Science, Moscow, Russia; Ecoli s.r.o., Bratislava, Slovak Republic)
HPV (High Risk) TaqMan PCR Kit (Norgen, Thorold, Canada)^{aa}
HPV Selfy (Ulisse BioMed, Udine, Italy)^{bb}
HPV Selfy 16 HR/LR (Ulisse BioMed, Udine, Italy)^{bb}
HPV Selfy 19 HR (Ulisse BioMed, Udine, Italy)^{bb}
HPV Selfy HR (Ulisse BioMed, Udine, Italy)^{bb}
PANA RealTyper HPV Kit (PANAGENE, Daejeon, South Korea)
MeltPro High Risk HPV Genotyping Assay (QuanDx, San Jose, CA, USA)
Papilloplex HR-HPV DNA Kit (GeneFirst, Oxfordshire, United Kingdom)
AccuPower HPV Genotyping & Screening Kit (Bioneer, Daejeon, South Korea)
BGI SENTIS HPV test (BGI, Wuhan, China)
Human Papillomavirus (HPV) Genotyping Detection Kit (Amoy Diagnostics (AmoyDX), Xiamen, China)
HPV genotyping Real Time PCR Kit (Bio Perfectus Technologies, Taizhou, China)
High-Risk HPV Genotyping 12-well (AusDiagnostics, Sydney, Australia)^{dd}
HPV (High-Low Risk) 16-well (AusDiagnostics, Sydney, Australia)^{dd}
MeltPro High Risk HPV Genotyping Assay (MMCA) (Zeesan Biotech, Xiamen, China)^{cc}
Human papillomavirus genotyping detection kit (Fluorescence PCR method) (Amolli Biotechnology Co., Xiamen, China)
HPV G15 – High-risk Human Papillomavirus DNA (Genotype) Diagnostic Kit (Sansure Biotech Inc., Changsha, Hunan, China)^{ee}
HPV G23 – Human Papillomavirus DNA (23 genotypes) Diagnostic Kit (Sansure Biotech Inc., Changsha, Hunan, China)^{ee}
Human Papillomavirus (15 types) nucleic acid genotyping detection kit (Toneker Biotech, Shanghai, China)
24 Human Papillomavirus typing kit (Mole Bioscience, Taizhou, China)

ITEIT

Currently available HPV tests: variety

High Risk HPV Genotyping PCR Kit (Biocore Diagnostics, Bad Homburg, Germany)^{ff}

Human Papilloma Virus Genotyping PCR Kit (Biocore Diagnostics, Bad Homburg, Germany)^{ff}

High-risk human papillomavirus (14 types) Nucleic acid Typing Detection Kit (Promega Biological Products, Shanghai, China)

Human papillomavirus (18 high-risk and 6 low-risk) Genotyping Kit (OUTDO Biotech, Shanghai, China)

Human papillomavirus (HPV) nucleic acid Typing Test Kit (Bioer Technology, Hangzhou, China)

Human Papillomavirus 14 Types Detection Kit (Fluorescence PCR) (Zhejiang Orient Gene Biotech Co., Zhejiang, China)^{gg}

Nucleic Acid Genotyping Kit for Human Papillomavirus 18 Types (Zhejiang Orient Gene Biotech Co., Zhejiang, China)^{gg}

Nucleic Acid Genotyping Kit for Human Papillomavirus 29 Types (Zhejiang Orient Gene Biotech Co., Zhejiang, China)^{gg}

Human papillomavirus nucleic acid Typing Test Kit (BioPerfectus, Jiangsu, China)

NeoPlex™ HPV HR (GeneMatrix Co., Seoul, South Korea)^{hh}

NeoPlex™ HPV29 Detection Kit (GeneMatrix Co., Seoul, South Korea)^{hh}

Nucleic Acid Detection Kit for High-risk Human Papillomavirus (Typing) (PCR-Fluorescence Probing) (Singway Biotech Inc., Shenzhen City, China)

RevoDx HPV 14 Genotyping Kit (Idil Biotech, Gebze, Türkiye)ⁱⁱ

TRUPCR HPV high risk genotyping kit (38 BlackBio Dx Limited, Bhopal, India)

Bosphore HPV Genotyping High Risk Kit v1 (Anatolia Geneworks, Istanbul, Türkiye)^k

Bosphore HPV Genotyping High Risk Kit v4 (Fast Extraction) (Anatolia Geneworks, Istanbul, Türkiye)^k

Bosphore HPV HR-LR Genotyping Kit v1 (Anatolia Geneworks, Istanbul, Türkiye)^k

GeneNav HPV Genotyping qPCR Kit (GenomeMe Lab Inc., Richmond, Canada)^l

Genotyping High Risk HPV Real Time Fluorescent Detection (Atila BioSystems, Mountain View, CA, USA)^g

Human Papillomavirus (28 Types) Genotyping Detection Kit (Fluorescence PCR) (Jiangsu Macro & Micro-Test Med-Tech Co., Ltd., Rudong County, China)^a

MOLgen DNA HPV HCR genotype S1 (quantitative) Kit (Adaltis S.r.l., Guidonia Montecelio, Italy)^{yy}

MOLgen DNA HPV HCR genotype S1 Kit (Adaltis S.r.l., Guidonia Montecelio, Italy)^{yy}

Medium- or low-density microarray-based full genotyping tests

Clart HPV 4sHR (Genomica, Coslada, Spain)^{jj}

Clart HPV 4 (Genomica, Coslada, Spain)^{jj}

Clart HPV 4s (Genomica, Coslada, Spain)^{jj}

Clart HPV 3 (Genomica, Coslada, Spain)

21 HPV GenoArray Diagnostic Kit (HybriBio, Hong Kong, China)^{kk}

37 HPV GenoArray Diagnostic Kit (HybriBio, Hong Kong, China)^{kk}

T

Currently available HPV tests: **variety**

Table 2

Commercially available HPV molecular tests present on the global market in December 2023. For the purpose of this inventory distinct HPV tests and their variants are divided into seven main groups and several subgroups based on tests' technology used and targeted HPV genotypes. A full list of all individual HPV tests and their manufacturers is provided in Supplementary Tables S1–S6.

HPV test group	HPV distinct tests	HPV tests variants
hr-HPV DNA screening tests without genotyping	29	9
Tests targeting 12 IARC-2009 hr-HPV genotypes plus HPV66 and/or HPV68	16	1
Tests targeting 12 IARC-2009 hr-HPV genotypes only	4	2
Tests targeting 12 IARC-2009 hr-HPV genotypes and additional alpha-HPV genotypes	9	4
Tests targeting a subset of 12 IARC-2009 hr-HPV genotypes	0	2
hr-HPV DNA screening tests with concurrent partial (HPV16/18/45), concurrent extended or reflex partial genotyping for the main hr-HPV genotypes	64	10
hr-HPV DNA screening tests with concurrent partial (HPV16/18/45) genotyping for the main hr-HPV genotypes	55	10
hr-HPV DNA screening tests with concurrent extended genotyping for the main hr-HPV genotypes	5	0
hr-HPV DNA screening tests with reflex partial genotyping for the main hr-HPV genotypes	4	0
HPV DNA full genotyping tests	84	29
Strip, filter or microtiter-well hybridisation-based full genotyping tests	21	4
Gel electrophoresis-based full genotyping tests	1	0
Real time PCR-based full genotyping tests	38	21
Medium- or low-density microarray-based full genotyping tests	14	4
Microsphere bead-based full genotyping tests	5	0
Capillary electrophoresis-based full genotyping tests	2	0
Full genotyping tests based on PCR combined with matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry	1	0
Full genotyping tests based on PCR combined with sequencing	2	0
HPV DNA genotype- or group-specific genotyping tests	42	100
Strip, filter or microtiter-well hybridisation-based genotype- or group-specific genotyping tests	2	1
Gel electrophoresis-based genotype- or group-specific genotyping tests	2	22
Real time PCR-based genotype- or group-specific genotyping tests	36	75
Loop-mediated isothermal amplification and electrochemical DNA chip	2	2
hr-HPV E6/E7 mRNA tests	9	3
<i>in situ</i> hybridisation DNA- and mRNA-based HPV tests	35	360
HPV DNA tests targeting multiple non-Alpha HPV genotypes	1	0
Total number of HPV tests	264	511

Currently available HPV tests: variety

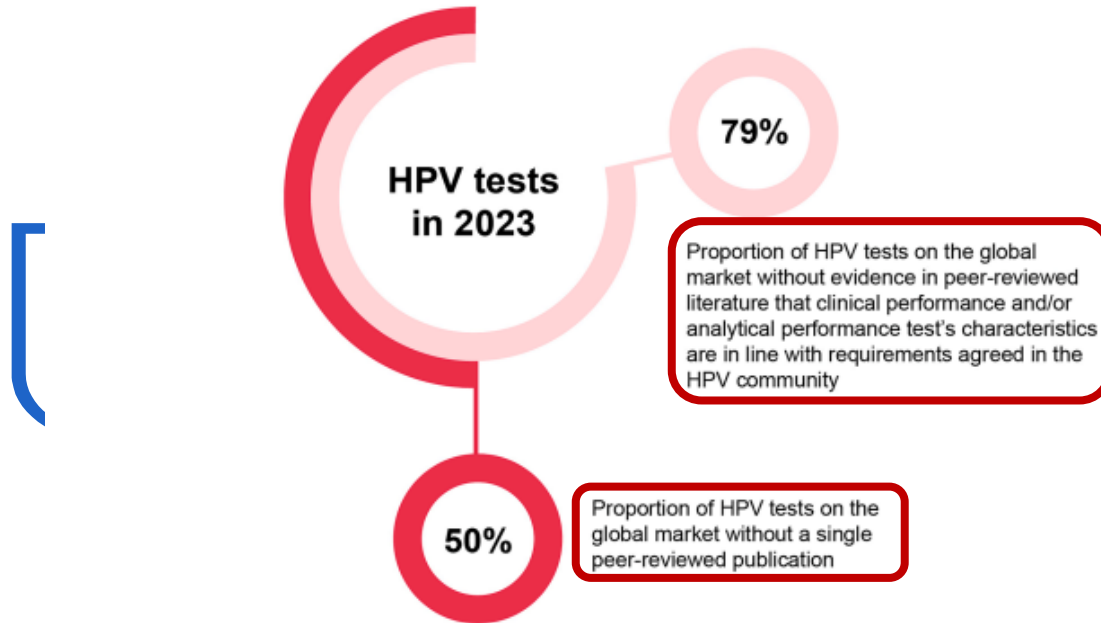


Fig. 4. Distinct commercial HPV tests available on the global market in December 2023 according to publication status. Proportion of distinct HPV tests without a single peer-reviewed publication and proportion of HPV tests without evidence in peer-reviewed literature that clinical performance and/or analytical performance test's characteristics are in line with requirements agreed in the HPV community.

Currently available HPV tests: variety

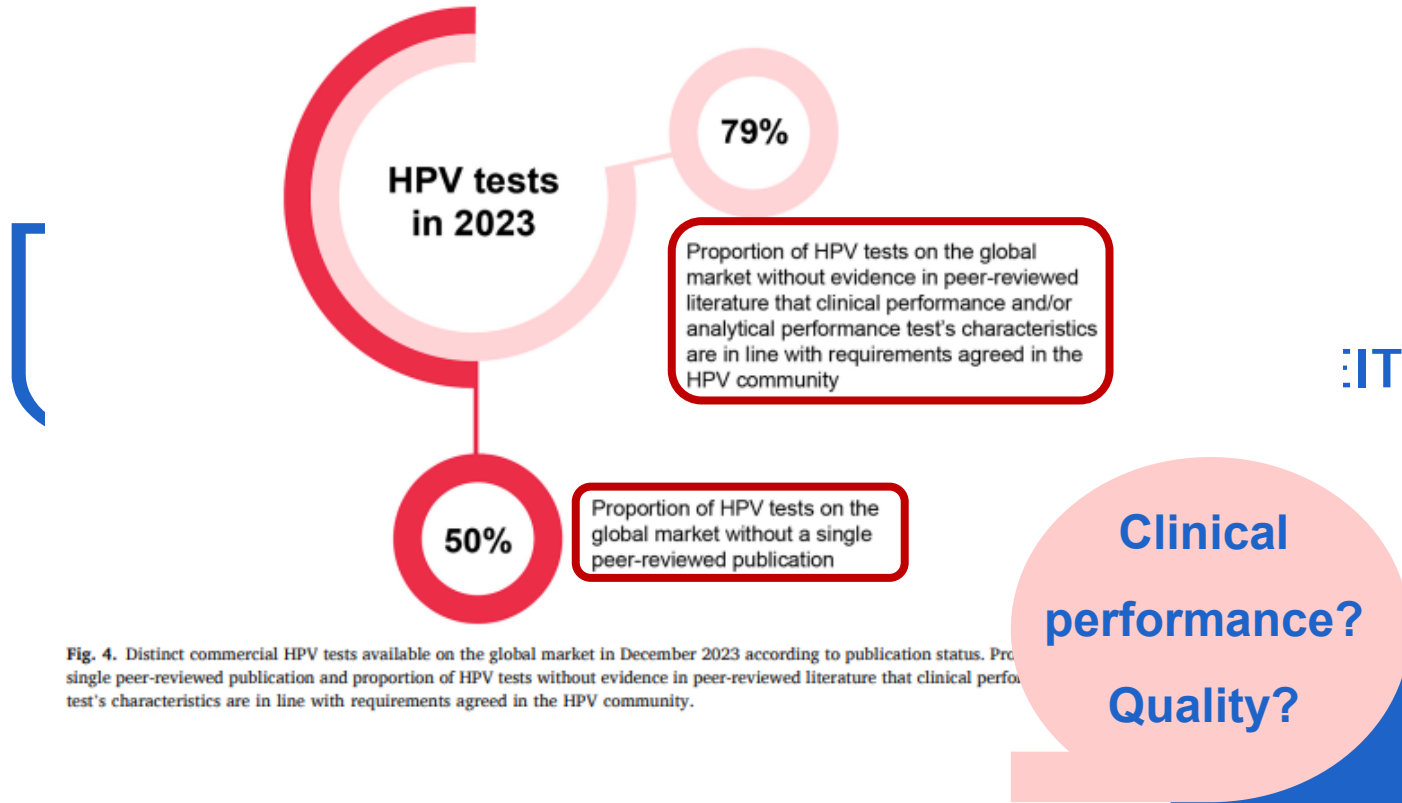


Fig. 4. Distinct commercial HPV tests available on the global market in December 2023 according to publication status. Proportion of HPV tests without a single peer-reviewed publication and proportion of HPV tests without evidence in peer-reviewed literature that clinical performance and/or analytical performance test's characteristics are in line with requirements agreed in the HPV community.

Cervical cancer screening program in Belgium

HPV
testing

↑ sensitivity

↑ participation

HPV
testing

Do we have enough HPV tests
for our particular purpose (= primary HPV screening) and with sufficient clinical validation and quality requirements?

De interministeriële werkgroep Cervix Screening bereikt een akkoord over de nieuwe baarmoederhalsscreening. Weldra kunnen vrouwen tussen 30 en 64 jaar om de vijf jaar een HPV-test laten afnemen. Experts pleiten al langer om boven de 30 jaar het cytologisch onderzoek te vervangen door een HPV-test. Voor vrouwen van 25 tot 29 jaar blijft het cytologisch onderzoek om de 3 jaar de beste manier om te screenen.

Om een groot effect op de volksgezondheid te hebben, moeten de deelstaten zorgen voor hogere deelname aan de screening. Bijna 40 procent van de vrouwen in Vlaanderen laat nooit een uitstrijkje doen, zelfs na een uitnodiging. In Wallonië en Brussel liggen de cijfers zelfs een pak hoger, respectievelijk 53 en 51 procent. Daar ligt dus een belangrijke opdracht voor de deelstaten. Zij kunnen ook vanaf 2025 zelfafnametesten organiseren, gericht op meer kwetsbare doelgroepen.

Tests to be used for primary HPV cervical cancer screening in Belgium

Home • National Reference Center (NRC) for Human papillomavirus

National Reference Center (NRC) for Human papillomavirus

Important information

Assays for the detection of high-risk human papillomaviruses in the context of Belgian cervical cancer primary screening.

The table below presents a list of molecular assays for the detection high-risk Human Papillomaviruses (hrHPV). These assays are clinically validated according to international criteria (Arbyn M. *et al.*, Clin Microbiol Infect 2021¹; Arbyn M *et al.*, ESGO Textbook of Gynaecological Oncology 2023²; Dhillon *et al.*, J Med 2023³; Arbyn *et al.*, Clin Microbiol Infect 2023⁴). The table below is updated at least twice a year, as new scientific evidence becomes available.

Clinical Microbiology and Infection 27 (2021) 1083–1095



Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com



Systematic review

2020 list of human papillomavirus assays suitable for primary cervical cancer screening

Marc Arbyn^{1,2,*}, Marie Simon³, Eliana Peeters¹, Lan Xu^{1,4}, Chris J.L.M. Meijer⁵, Johannes Berkhof⁶, Kate Cuschieri⁷, Jesper Bonde⁸, Anja Ostrbenk Vanlencak⁹, Fang-Hui Zhao¹⁰, Remila Rezhake^{1,10,11}, Murat Gultekin¹², Joakim Dillner¹³, Silvia de Sanjosé¹⁴, Karen Canfell^{15,16}, Peter Hillemanns¹⁷, Maribel Almonte¹⁸, Nicolas Wentzensen^{19,†}, Mario Poljak^{9,†}

Responsible laboratories

Coordinator

- [Sciensano](#)

Associated

- [Algemeen medisch laboratorium \(AML\)](#)
- [Sonic Healthcare](#)
- [UZGent](#)

ures. The hrHPV DNA assays fully matching the current criteria and which can be recommended today in HPV-based cervical cancer screening using clinician-collected cervical samples are: HC2, GP5+/6+ PCR-EIA, Abbott RealTime, Alinity, Anyplex HR, Cobas 4800, PapilloCheck, Onclarity, HPV-Risk and Xpert HPV. By accepting Cobas 4800, as alternative comparator, we can add Cobas 6800 also to the list of validated assays. This list of tests requires regular updating as evidence accrues.

Tests to be used for primary HPV cervical cancer screening in Belgium

Background: Only clinically validated HPV assays can be accepted in cervical cancer screening.

Objectives: To update the list of high-risk HPV assays that fulfil the 2009 international validation criteria (Meijer-2009).

Data Sources: PubMed/Medline, Embase, Scopus, references from selected studies; published in January 2014 to August 2020.

Study eligibility criteria: HPV test validation studies and primary screening studies, involving testing with an index HPV test and a comparator HPV test with reporting of disease outcome (occurrence of histologically confirmed cervical precancer; CIN2+).

Participants: Women participating in cervical cancer screening.

Interventions: Testing with an index and a comparator HPV test of clinician-collected cervical specimens and assessment of disease outcome (<CIN2, CIN2+). Comparator HPV assays were HC2, GP5+/6+ PCR-EIA, recommended in validation guidelines, or tests with consistent previous validations.

Methods: Assessment of relative clinical accuracy (including non-inferiority statistics index vs comparator assay) and test reproducibility in individual studies; random effects meta-analyses of the relative clinical sensitivity and specificity of index vs comparator tests.

Clinical Microbiology and Infection 27 (2021) 1083–1095



Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com



Systematic review

2020 list of human papillomavirus assays suitable for primary cervical cancer screening

Marc Arbyn^{1,2,*}, Marie Simon³, Eliana Peeters¹, Lan Xu^{1,4}, Chris J.L.M. Meijer⁵, Johannes Berkhof⁶, Kate Cuschieri⁷, Jesper Bonde⁸, Anja Ostrbenk Vanlencak⁹, Fang-Hui Zhao¹⁰, Remila Rezhake^{1,10,11}, Murat Gultekin¹², Joakim Dillner¹³, Silvia de Sanjosé¹⁴, Karen Canfell^{15,16}, Peter Hillemanns¹⁷, Maribel Almonte¹⁸, Nicolas Wentzensen^{19,†}, Mario Poljak^{9,†}

ures. The hrHPV DNA assays fully matching the current criteria and which can be recommended today in HPV-based cervical cancer screening using clinician-collected cervical samples are: HC2, GP5+/6+ PCR-EIA, Abbott RealTime, Alinity, Anyplex HR, Cobas 4800, PapilloCheck, Onclarity, HPV-Risk and Xpert HPV. By accepting Cobas 4800, as alternative comparator, we can add Cobas 6800 also to the list of validated assays. This list of tests requires regular updating as evidence accrues.

Tests to be used for primary HPV cervical cancer screening in Belgium

Home • National Reference Center (NRC) for Human papillomavirus

National Reference Center (NRC) for Human papillomavirus

Important information

Assays for the detection of high-risk human papillomaviruses in the context of Belgian cervical cancer primary screening.

The table below presents a list of molecular assays for the detection high-risk Human Papillomaviruses (hrHPV). These assays are clinically validated according to international criteria (Arbyn M. *et al.*, Clin Microbiol Infect 2021¹; Arbyn M *et al.*, ESGO Textbook of Gynaecological Oncology 2023²; Dhillon *et al.*, J Med 2023³; Arbyn *et al.*, Clin Microbiol Infect 2023⁴). The table below is updated at least twice a year, as new scientific evidence becomes available.

Clinical Microbiology and Infection 27 (2021) 1083–1095



Systematic review

2020 list of human papillomavirus assays suitable for primary cervical cancer screening

Marc Arbyn^{1,2,*}, Marie Simon³, Eliana Peeters¹, Lan Xu^{1,4}, Chris J.L.M. Meijer⁵, Johannes Berkhof⁶, Kate Cuschieri⁷, Jesper Bonde⁸, Anja Ostrbenk Vanlencak⁹, Fang-Hui Zhao¹⁰, Remila Rezhake^{1,10,11}, Murat Gultekin¹², Joakim Dillner¹³, Silvia de Sanjosé¹⁴, Karen Canfell^{15,16}, Peter Hillemanns¹⁷, Maribel Almonte¹⁸, Nicolas Wentzensen^{19,†}, Mario Poljak^{9,†}

Responsible laboratories

Coordinator

- Sciensano

Associated

- Algemeen medisch laboratorium (AML)
- Sonic Healthcare
- UZGent

ures. The hrHPV DNA assays fully matching the current criteria and which can be recommended today in HPV-based cervical cancer screening using clinician-collected cervical samples are: HC2, GP5+/6+ PCR-EIA, Abbott RealTime, Alinity, Anyplex HR, Cobas 4800, PapilloCheck, Onclarity, HPV-Risk and Xpert HPV. By accepting Cobas 4800, as alternative comparator, we can add Cobas 6800 also to the list of validated assays. This list of tests requires regular updating as evidence accrues.

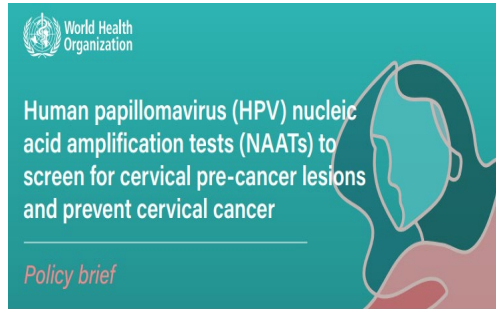
Tests to be used for primary HPV cervical cancer screening in Belgium

<u>Assay</u>	<u>Manufacturer</u>
Alinity m HR HPV Assay	Abbott, Wiesbaden, Germany
Allplex II HR	Seegene, Seoul, South Korea
Anyplex II HPV HR Detection	Seegene, Seoul, South Korea
APTIMA HPV Assay*	Hologic, Bedford, MA, USA
*in combination with another mRNA assay (APTIMA HPV16, 18, 45; Hologic) which can identify HPV16 and HPV18,45	
CLART HPV45	GENOMICA SAU, Madrid, Spain
Cobas 4800 HPV Test	Roche Molecular System, Pleasanton, CA, USA
Cobas® HPV test (for use on the Cobas® 5800/6800/8800 Systems)	Roche Molecular System, Pleasanton, CA, USA
HPV-Risk Assay	Self-Screen BV, Amsterdam, The Netherlands
HPV Test Onclarity HPV Assay	BD Diagnostics, Sparks, MD, USA
NeuMoDX	Qiagen, Ann Arbor, MI, USA
RealTime High Risk HPV Test	Abbott, Wiesbaden, Germany
RIATOL HPV genotyping qPCR assay	in house, AML, Antwerp, Belgium
Xpert HPV	Cepheid, Sunnyvale, CA, USA

List of internationally validated hrHPV assays which can be applied in the Belgian cervical cancer screening (ordered alphabetically).

Updated on 05/08/2024.

WHO Guidance on HPV based screening



WHO recommendations, by population, on HPV NAATs for cervical screening to prevent cervical cancer

 For the general population of women, HPV DNA NAATs are the **recommended*** primary screening test, but HPV mRNA detection may also be used. Both can be used in a "screen-and-treat" or "screen, triage and treat" approach, starting at age 30 and with a screening interval of 5–10 years when using HPV DNA tests and 5 years when using HPV mRNA tests.

Remark: Choosing HPV mRNA testing implies having the capacity to provide follow-up screening at 5-year intervals, and having health-care providers take the samples.

 For the population of women living with HIV, HPV DNA NAATs are the **recommended*** primary screening test. It is **suggested*** that these tests be used in a "screen, triage and treat" approach rather than in a "screen-and-treat" approach, starting at age 25 and with a screening interval of 3–5 years.

Note: No recommendation was made for the use of HPV mRNA NAATs for women living with HIV because no applicable evidence was identified.

* "Recommended" = strong recommendation; "suggested" = conditional recommendation.

2030 targets to accelerate the elimination of cervical cancer as a public health problem

VACCINATION

90% of girls fully vaccinated with HPV vaccine by age 15

SCREENING

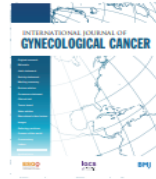
70% of women screened with a high-performance test by age 35 and again by age 45

TREATMENT

90% of women identified with cervical disease (pre-cancer or invasive cancer) receive treatment and care

Quality assurance in HPV based screening: guidance

Review



Quality assurance in human papillomavirus testing for primary cervical screening

Kate Cuschieri,¹ Maria Dolores Fellner,² Laila Sara Arroyo Mühr ,^{3,4} Elizaveta Padalko,⁵ Rita Mariel Correa,² Joakim Dillner,^{3,4} Murat Gultekin ,⁶ Maria Alejandra Picconi²

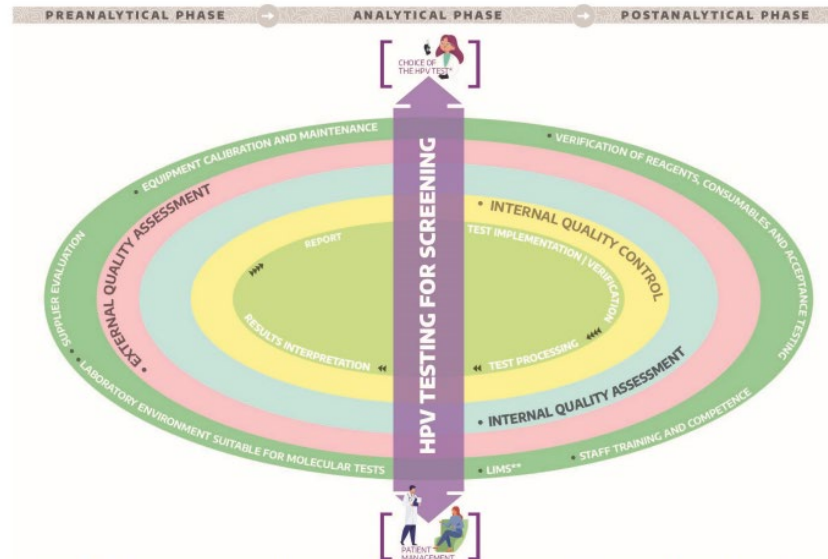


Figure 1 Quality assurance universe for human papillomavirus (HPV) testing in cervical screening. *Test analytically and clinically validated. **LIMS: Interfacing between HPV assay platform and the laboratory information management system.

Quality assurance in HPV based screening: international NRC HPV network

Journal of Clinical Virology 171 (2024) 105657



Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv



Full Length Article

Human papillomavirus negative high grade cervical lesions and cancers: Suggested guidance for HPV testing quality assurance



Jean Luc Pr  tet^{a,1}, Laila Sara Arroyo M  hr^{b,1}, Kate Cuschieri^c, Mar  a Dolores Fellner^d, Rita Mariel Correa^d, Mar  a Alejandra Picconi^d, Suzanne M. Garland^{e,f}, Gerald L. Murray^{e,f}, Monica Molano^e, Michael Peeters^g, Steven Van Gucht^g, Charlotte Lambrecht^h, Davy Vanden Broeck^h, Elizaveta Padalkoⁱ, Marc Arbyn^j, Quentin Lepiller^a, Alice Brunier^a, Steffi Silling^k, Kristiane S  reng^l, Irene Kraus Christiansen^l, Mario Poljak^m, Camilla Lagheden^b, Emel Yilmaz^b, Carina Eklund^b, Hem R. Thapaⁿ, Troy D. Querecⁿ, Elizabeth R. Ungerⁿ, Joakim Dillner^{b,*}



^a French National Papillomavirus Reference Center, CHU de Besan  on, EA3181, Universit   de Franche-Comt  , F-25000 Besan  on, France

^b Swedish National HPV Reference Laboratory, Center for Cervical Cancer Elimination, Karolinska Institutet and Karolinska University Hospital F56, 141 86 Stockholm, Sweden

^c Scottish HPV Reference Laboratory, Department of Lab Medicine, Royal Infirmary of Edinburgh, Edinburgh, EH16 4SA, UK

^d Laboratorio Nacional y Regional de Referencia de Papilomavirus Humanos, Instituto Nacional de Enfermedades Infecciosas-ANLIS "Dr Malbr  n", C1282AFF Buenos Aires, Argentina

^e Royal Women's Hospital, Parkville 3052 VIC, Australia

^f Department of Obstetrics and Gynaecology, University of Melbourne, Parkville 3052 VIC, Australia

^g National Reference Centre for Human Papillomaviruses, Viral Diseases, Infectious Diseases in Humans, Sciensano. Rue Juliette Wytsman 14, 1050 Brussels, Belgium

^h National Reference Centre for Human Papillomaviruses, Algemeen Medisch Laboratorium, Emiel Vloorsstraat 9, 2020 Antwerp, Belgium

ⁱ National Reference Centre for Human Papillomaviruses, Laboratory of Medical Microbiology, University Hospital Ghent. C. Heymanslaan 10, 9000 Ghent, Belgium

^j Unit Cancer Epidemiology, Cancer centre, Sciensano. Rue Juliette Wytsman 14, 1050 Brussels, Belgium

^k Institute of Virology, National Reference Center for Papilloma- and Polyomaviruses, University of Cologne, Faculty of Medicine and University Hospital of Cologne, 50935 Cologne, Germany

^l Norwegian HPV Reference Laboratory, Department of Microbiology and Infection Control, Akerhus University Hospital, L  renskog, Norway

^m Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Zalo  ka 4, 1000 Ljubljana, Slovenia

ⁿ Division of High-Consequence Pathogens and Pathology, Centers for Disease Control and Prevention, Atlanta, GA 30329, USA

Van **cytologie** naar **HPV**-gebaseerde screening naar baarmoederhalskanker in **België**



01/01/2025

Van **cytologie** naar **HPV**-gebaseerde screening naar baarmoederhalskanker in **België**



Van **cytologie** naar **HPV**-gebaseerde screening naar baarmoederhalskanker in **België**



Van **cytologie** naar **HPV**-gebaseerde screening naar baarmoederhalskanker in **België**



VRAGEN?

VOOR ONLINE DEELNEMERS:

U KUNT STEEDS VRAGEN STELLEN VIA DE CHATFUNCTIE.

DEZE VRAGEN WORDEN VERZAMELD DOOR DE MODERATOR EN
SAMEN MET DE VRAGEN UIT DE ZAAL **OP HET EINDE VAN DE
AVOND** VOORGELEGD AAN DE SPREKERS.

SURVEILLANCE VAN DE EFFECTEN VAN HPV-VACCINATIE IN EUROPA

PROF. ALEX VORSTERS

VACCINOLOGIE | UNIVERSITEIT ANTWERPEN

Surveillance van de effecten van HPV vaccinatie in Europa

Alex Vorsters

University of Antwerp



University
of Antwerp



HPV Prevention
and Control Board



COALITION to STRENGTHEN
the HPV IMMUNIZATION
COMMUNITY

Disclosure relevant to this presentation.

- The HPV Prevention and Control board is supported by in kind contributions and support from the involved international experts and their institutions. To set up the activities the secretariat does receive unrestricted grants from industry. All funds are handled according to the rules of the University of Antwerp. No remuneration for experts or speakers is provided.
- I received on my university funds speakers' fees and scientific advisory board fees from MSD, Janssen, Hologic and Novosanis NV.
- I received unrestricted research grants from MSD and Abbott.
- Co-founder and former board member of Uantwerp spinoff company Novosanis. Since 2019 fully owned by Orasure in which I have no financial interest.

Inhoud

- Inleiding HPV
- HPV vaccin en HPV vaccinatie
- Impact van Vaccinatie in Europa
- Potentieel van eerste fractie urine in de opvolging van HPV vaccinatie programma's.

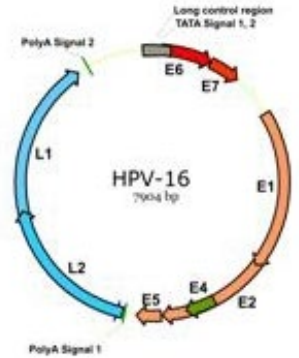
2008 Nobel Prize in Medicine awards discovery that Human Papilloma Virus can cause cervical cancer



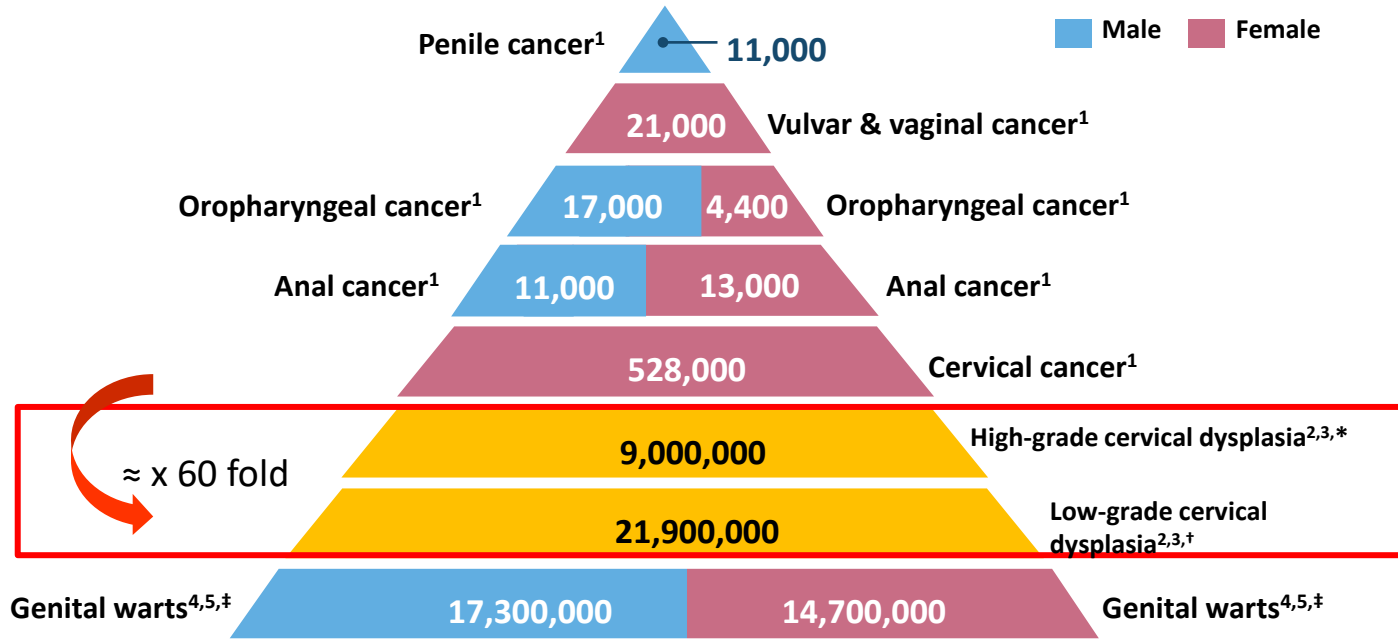
Harald zur Hausen

"His discovery has led to characterisation of the natural history of HPV infection, an understanding of mechanisms of HPV-induced carcinogenesis and the development of prophylactic vaccines against HPV acquisition."

Nobel Assembly of the Swedish Karolinska Institute



Worldwide HPV-Related Disease Burden: 607,000 Cancer Cases in Men and Women



*Estimated 90% of high-grade cervical lesions are HPV related³; †Estimated 73% of low-grade cervical lesions are HPV related³;

‡Estimated gender ratio of genital warts: 54% males; 46% females⁶

1. Forman D, et al. *Vaccine*. 2012;30:F12-F23; 2. World Health Organization; 3. Guan P, et al. *Int J Cancer*. 2012;131:2349-2359;

4. World Health Organization; 5. Greer CE, et al. *J Clin Microbiol*. 1995;33:2058-2063;

6. Public Health England.

HUMAN PAPILLOMAVIRUS IS A NECESSARY CAUSE OF INVASIVE CERVICAL CANCER WORLDWIDE

JAN M. M. WALBOOMERS^{1*}, MARCEL V. JACOBS¹, M. MICHELE MANOS², F. XAVIER BOSCH³, J. ALAIN KUMMER¹,
KEERTI V. SHAH², PETER J. F. SNIJDERS¹, JULIAN PETO⁴, CHRIS J. L. M. MEIJER¹ AND NUBIA MUÑOZ⁵

¹*Department of Pathology, University Hospital Vrije Universiteit, Amsterdam, The Netherlands*

²*Department of Molecular Microbiology and Immunology, Johns Hopkins University, Baltimore, MD, U.S.A.*

³*Institute Catala d'Oncologia, Barcelona, Spain*

⁴*Institute of Cancer Research, Belmont, Surrey, U.K.*

⁵*Unit of Field and Intervention Studies, IARC, Lyon, France*

SUMMARY

A recent report that 93 per cent of invasive cervical cancers worldwide contain human papillomavirus (HPV) may be an underestimate, due to sample inadequacy or integration events affecting the HPV L1 gene, which is the target of the polymerase chain reaction (PCR)-based test which was used. The formerly HPV-negative cases from this study have therefore been reanalysed for HPV serum

Prevalence of HPV DNA in 932 cervical cancer biopsies from 22 countries :
99.7%

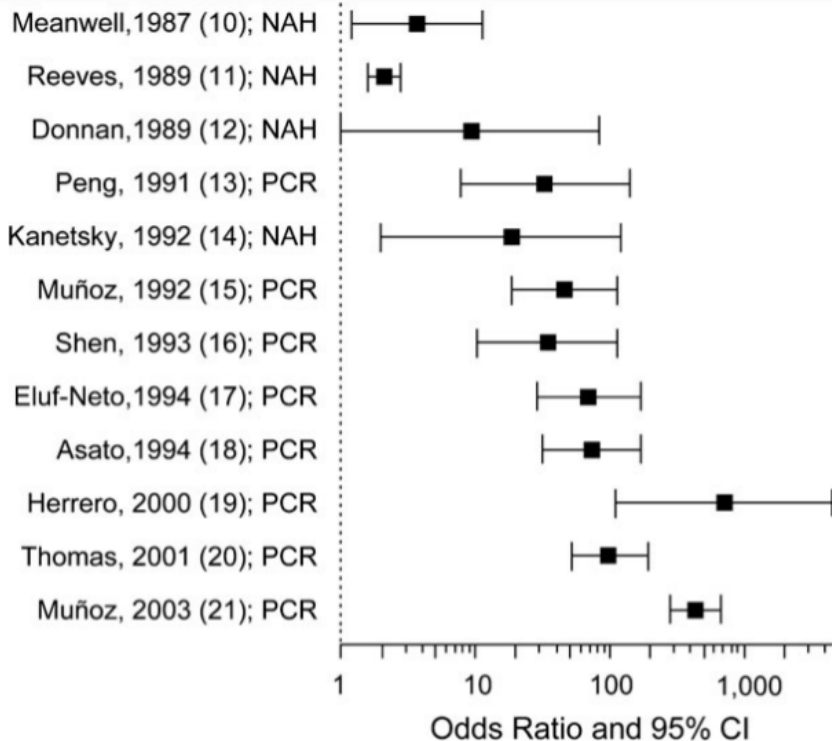


Figure 2. Odds ratios and 95% confidence intervals for the association between human papillomavirus (HPV) infection (via HPV DNA detection) and invasive cervical cancer risk in successive molecular epidemiologic studies (mostly case-control) (from top to bottom, references 10–21). CI, confidence interval; NAH, nonamplified hybridization; PCR, polymerase chain reaction.



Invited Commentary

Invited Commentary: Human Papillomavirus Infection and Risk of Cervical Precancer—Using the Right Methods to Answer the Right Questions

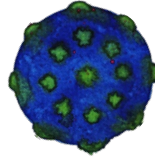
Eduardo L. Franco* and Joseph Tota

* Correspondence to Dr. Eduardo L. Franco, Division of Cancer Epidemiology, McGill University, 546 Pine Avenue West, Montreal, Quebec H2W 1S6, Canada (e-mail: eduardo.franco@mcgill.ca).

Initially submitted August 28, 2009; accepted for publication October 2, 2009.

Caused by an infection with HPV 'Human Papillomavirus'

- Small non-enveloped dsDNA virus
- > 200 genotypes



Low-risk types; e.g. HPV6, 11

Carcinogenic of HR types; HPV16, 18,
31, 33, 35, 39, 45, 51, 52, 56, 58, 59

- Transmitted primarily via skin-skin contact during sexual activities
- Cause of **other cancers** as well:
vagina (78%), vulva (25%), penis (50%),
anus (88%), oropharynx (31%), larynx (2%)

Cervical cancer

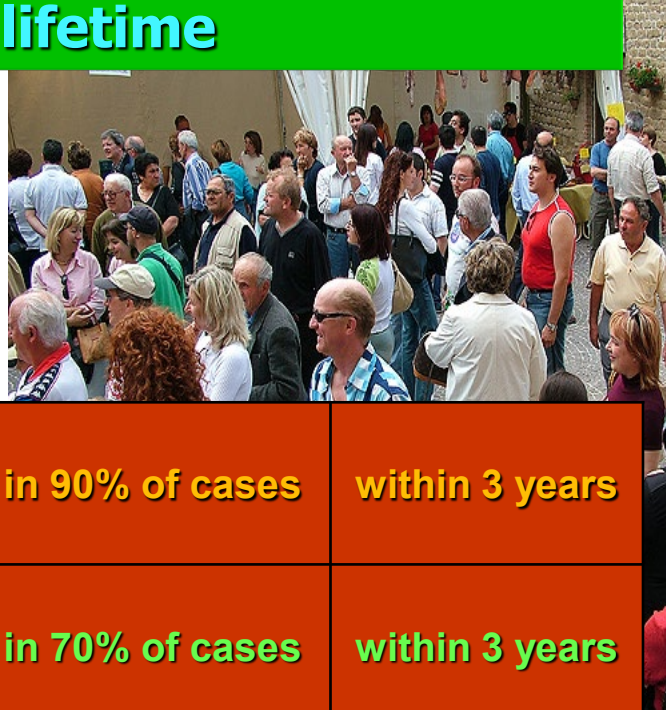
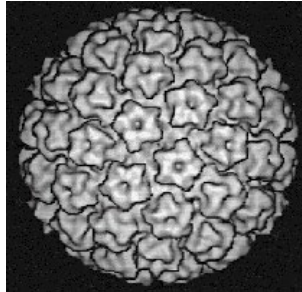
4th most common cause
of cancer (death) among
women worldwide

Belgium (2016)



- Incidence 640 –
7.8/100,000
- Mortality 235 –
2.0/100,000

**~ 70% population acquires HPV
during lifetime**

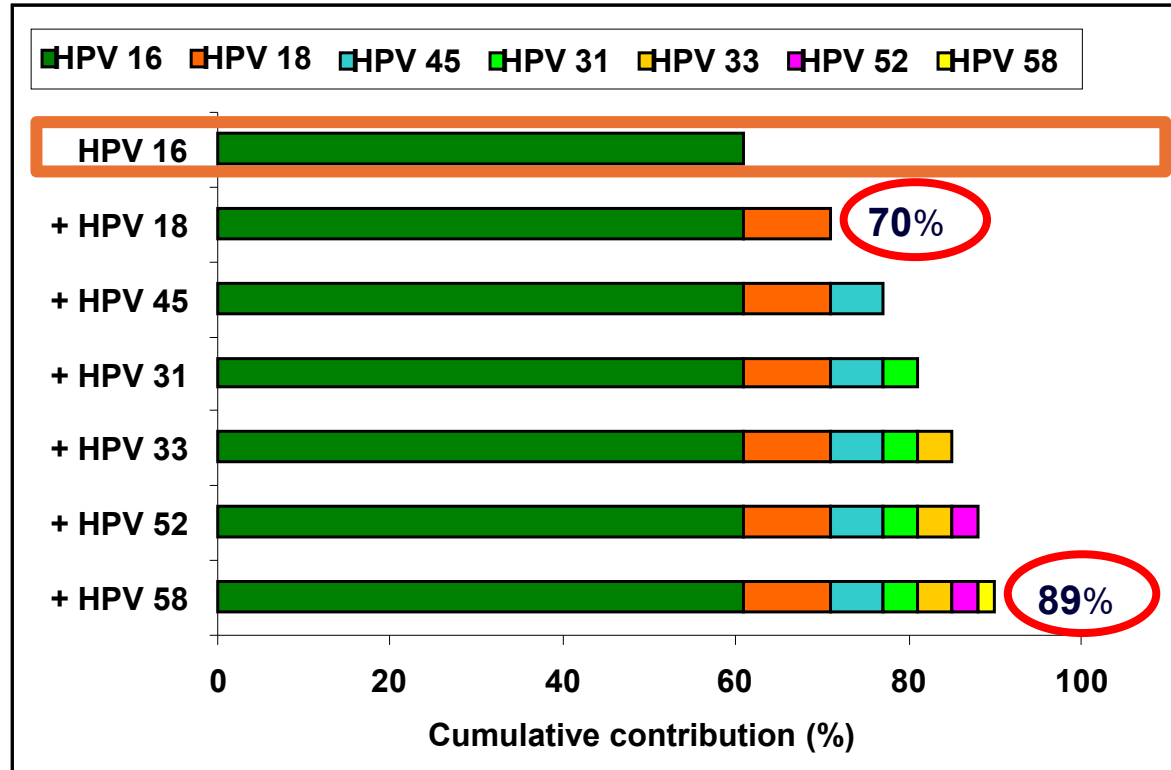


Low risk HPV	eliminated in 90% of cases	within 3 years
High risk HPV	eliminated in 70% of cases	within 3 years

Ho GY et al, NEJM 1998; 338:423-428

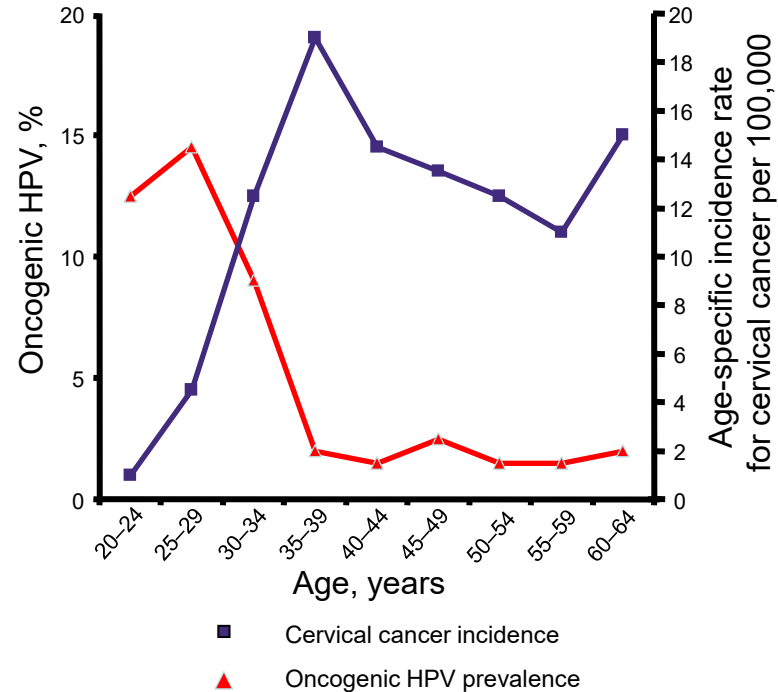
Moscicki AB et al, J Infect Dis 1994; 169:235-240

Relative Contribution of HPV types in cervical cancers worldwide (The ICO HPV survey)



Relationship between age of incidence of cervical cancer and age of HPV infection

- HPV infection precedes cervical cancer of some decades¹
- Most cervical cancers (~70%) are observed in women > 45 years²
- Regional differences in the prevalence of infections with oncogenic HPV types are observed³

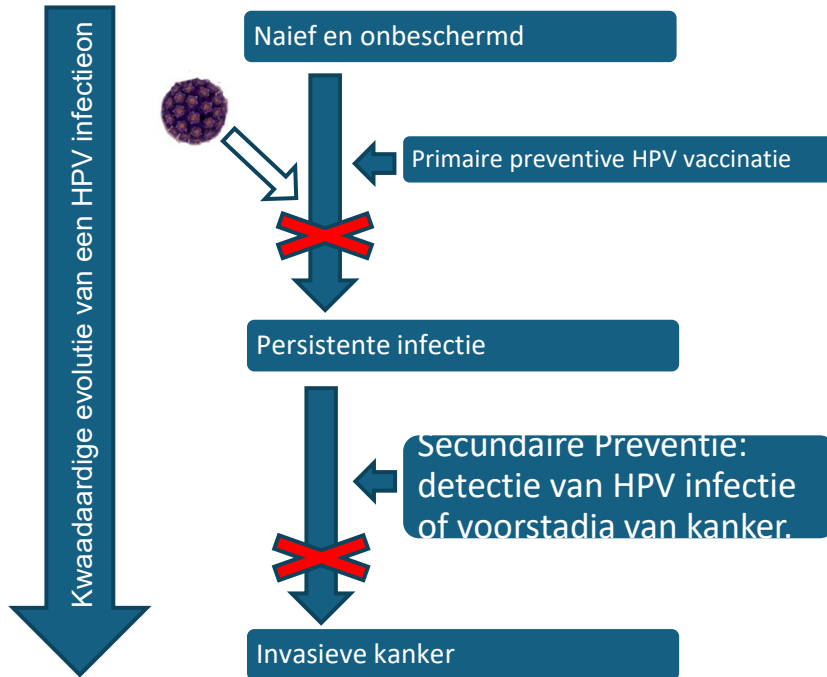


1. Bosch FX, et al. *J Clin Pathol* 2002; 55:244-265;

2. Ferlay J, et al. *GLOBOCAN 2002 Cancer Incidence, Mortality and Prevalence Worldwide*. IARC CancerBase; Lyon, 2004;

3. Bosch FX, et al. *Vaccine* 2008; S26:K1-K16.

Verband tussen screening, vaccinatie en detectie van HPV DNA of abnormale cellen.



Adapted from Franco et al Vaccine 2008

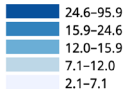
Global and regional burden of cervical cancer

Age-Standardized Rate (World) per 100 000, Incidence, Females, in 2022

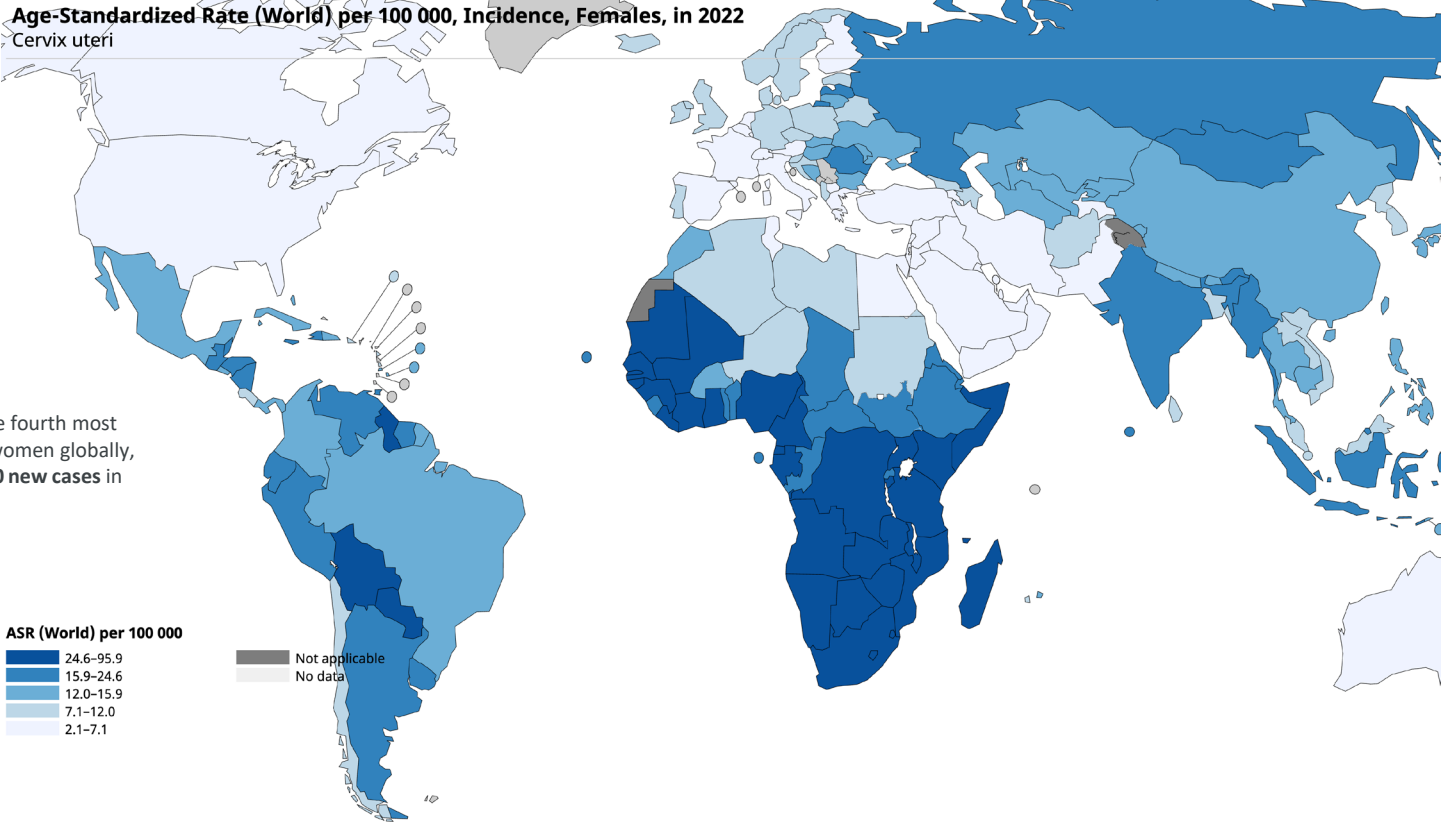
Cervix uteri

Cervical cancer is the fourth most common cancer in women globally, with around **660,000** new cases in 2022.

ASR (World) per 100 000



Not applicable
No data



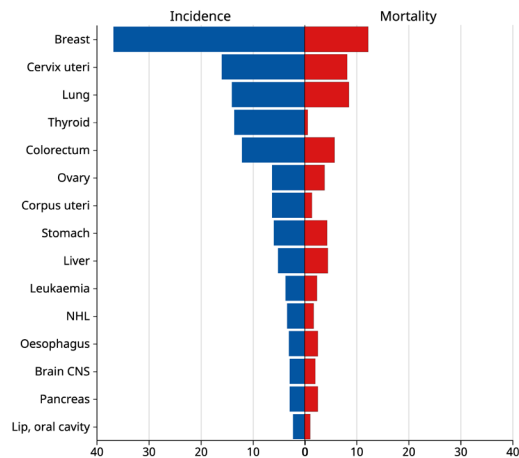
All rights reserved. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization / International Agency for Research on Cancer concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate borderlines for which there may not yet be full agreement.

Cancer TODAY | IARC
<https://gco.iarc.who.int/today>
Data version: Globocan 2022 (version 1.1) - 08.02.2024
© All Rights Reserved 2024

The second most common cancer among women

Age-Standardized Rate (World) per 100 000, Incidence and Mortality, Females, in 2022

Upper middle income + Lower middle income + Low income
(Top 15 cancer sites)



ASR (World) per 100 000

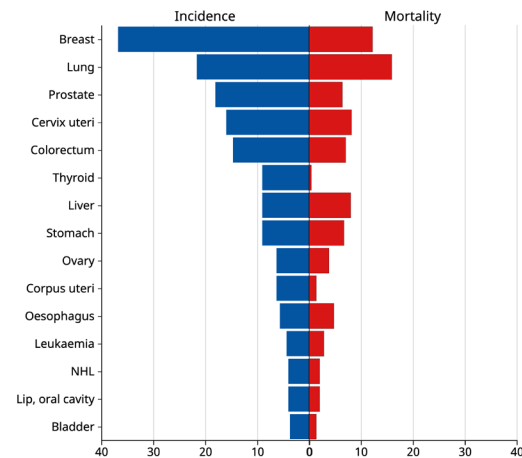
Cancer TODAY | IARC - <https://gco.iarc.who.int/today>

Data version : Globocan 2022 (version 1.1)

© All Rights Reserved 2024

Age-Standardized Rate (World) per 100 000, Incidence and Mortality, Both sexes, in 2022

Upper middle income + Lower middle income + Low income
(Top 15 cancer sites)



ASR (World) per 100 000

Cancer TODAY | IARC - <https://gco.iarc.who.int/today>

Data version : Globocan 2022 (version 1.1)

© All Rights Reserved 2024

Global strategy to accelerate elimination of cervical cancer

VISION: A world without cervical cancer

THRESHOLD: All countries to reach < 4 cases per 100,000 women years

2030 CONTROL TARGETS

90%

of girls fully
vaccinated with HPV
vaccine by 15 years of
age

70%

of women screened
with a high precision
test at 35 and 45 years
of age

90%

of women identified
with cervical disease
receive treatment
and care

Estimated 45
million lives can
be saved over
next 100 years in
LMICs

Canfell et al Lancet 2020

SDG 2030: Target 3.4 – 30% reduction in mortality from cervical cancer

Adopted strategies for EU target population

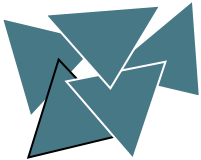
	World Health Organization		Europe's Beating Cancer Plan [*]	
Vaccination	90%	Of girls fully vaccinated with HPV vaccine by 15 years old.	90%	Of the EU target population of girls fully vaccinated with HPV vaccine and the vaccination of boys significantly increased by 2030.
Screening	70%	Of women are screened using a high-performance test ¹ by 35 years of age and by 45 years of age.	90%	Of the EU target population offered cervical cancer screening by 2025.
Treatment	90%	Of women identified with cervical disease receive treatment.	90%	Of eligible patients have access to tertiary specialized centers for treatment by 2030.

^{*}European Parliament resolution of 16 February 2022 on strengthening Europe in the fight against cancer.

Assembly of Virus-like Particles

Structural model of papilloma VLP

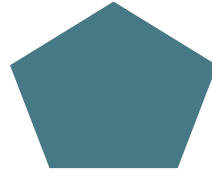
L1 proteins
(55 to 57 kD)



5 x L1



L1 capsomere
(~280 kD)

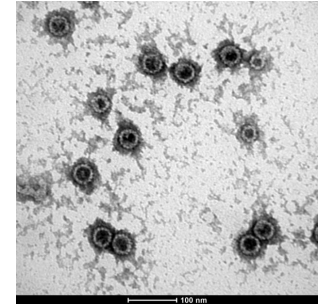
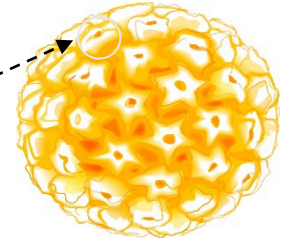


(Atomic force microscopy
image of a single VLP)

Virus-Like Particle
(~20,000 kD)

72

capsomeres



Atomic force microscopic picture: Merck Research Laboratories).

1. Kirnbauer et al. Proc Natl Acad Sci USA 1992;89:12180–4. 2. Kirnbauer et al. J Virol 1993;67:6929–36. 3. Galloway. In Current Research on Papillomaviruses. (Ed). C. Lacey. Leeds Medical Information, Leeds University Press, Leeds, 1996:113–9. 4. Brown et al. Virology 1996;222:43–50. 5. Carter et al. Clin Dermatol 1997;15:249–59.

Prophylactic HPV VLP Vaccine Profiles

	Cervarix Bivalent vaccine		Gardasil Quadrivalent vaccine		Gardasil9 Nonavalent vaccine	
Manufacturer	Glaxo Smith Kline		Merck		Merck	
Volume	Per dose	0.5ml	Per dose	0.5ml	Per dose	0.5ml
Adjuvant	ASO4: Al(OH) ₃ 500mg MPL® 50mg		Amorphous Aluminium 225mg Hydroxyphosphate sulphate®		Amorphous Aluminium 500mg Hydroxyphosphate sulphate®	
Antigens	L1 HPV16 20µg L1 HPV18 20µg		L1 HPV6 20µg L1 HPV11 40µg L1 HPV16 40µg L1 HPV18 20µg		L1 HPV6 30µg L1 HPV11 40µg L1 HPV16 60µg L1 HPV18 40µg L1 HPV31 20µg L1 HPV33 20µg L1 HPV45 20µg L1 HPV52 20µg L1 HPV58 20µg	
FDA Licenses	2007		2006		2014	
EMA Licensed	2007		2007		2015	

Two other vaccines have WHO pre-qualification:

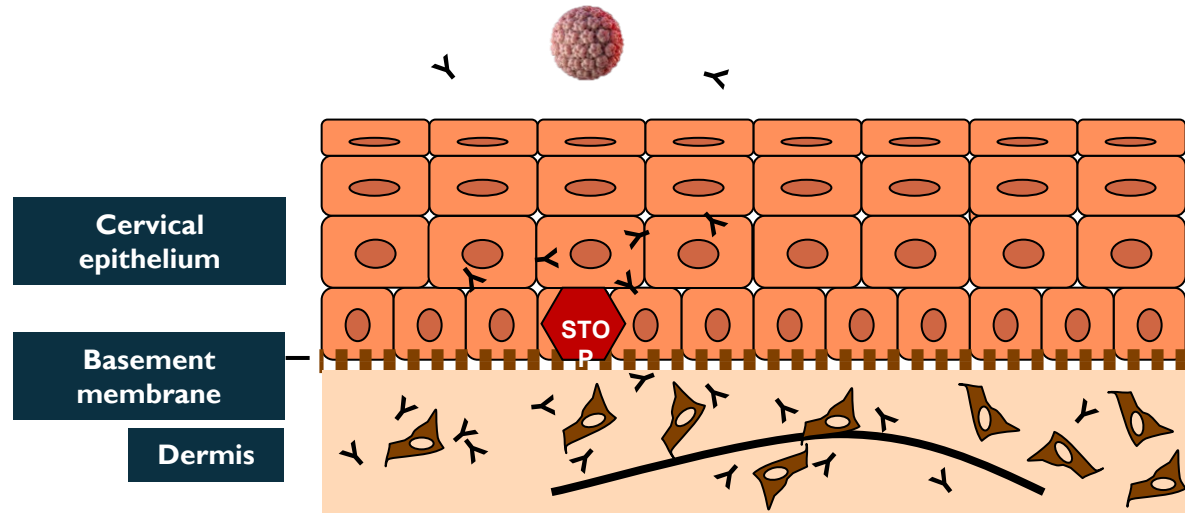
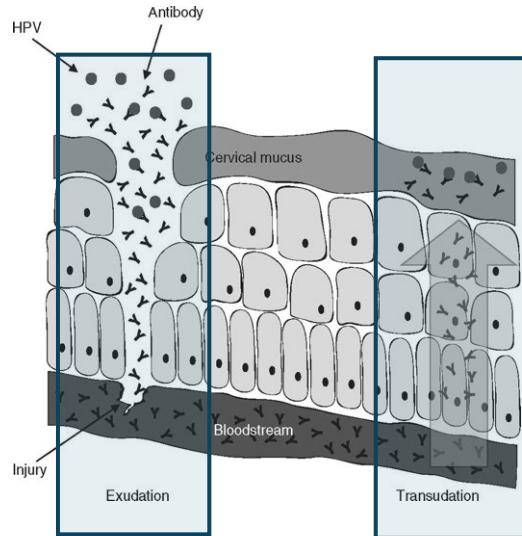
- Innovax's Cecolin® with aluminium-containing adjuvant, indicated for girls and women aged 9-45 years.
»

- Walvax Biotechnology's product with aluminium-containing adjuvant, indicated for girls and women aged 9-30 years (developed by its subsidiary Shanghai Zerun Biotech).

Background: the HPV infection/vaccine

- Three specific characteristics of the HPV infection and the HPV vaccine
 - HPV causes a “hidden” infection (remains in the epithelium with limited interaction with the immune system)[1,2]
 - The vaccine due to its viral-like structure (dense optimal spaced, repetitive protein arrays) induces a very strong and potent (high avidity) humoral immune response.[3]
 - Titres much higher than induced by natural infection (due to parenteral injection)
 - One dose options are being given as option by WHO
 - Anti-HPV antibodies have a unique and decisive role in the protection against HPV infection. Confirmed in animal models. [4]

Protection: based on vaccine-induced neutralizing HPV antibodies



Global Map area

Country profile area

Coverage Analysis
Global/Regional

Effectiveness studies

194

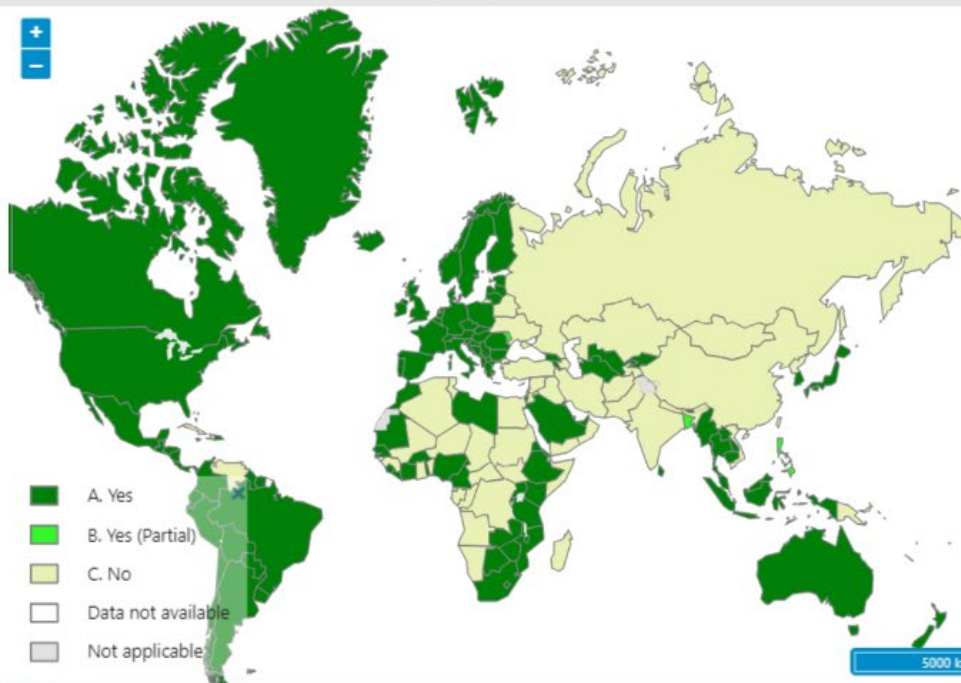
Total countries reported

HPV national schedule	No. of countries
A. Yes	141
B. Yes (Partial)	3
C. No	50

Last update:

10/10/2024 4:48...

HPV vaccine included in national immunization programme



2030 Target
194 countries

144 (74%) countries
introduced HPV
vaccination

50 (26%) countries
did not introduce

Disclaimer

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.



World Health Organization

WHO 2024. All rights reserved.

Meta data

RIGHT CLICK TO DOWNLOAD —

[Export csv data](#) [Export excel data](#)

Global Map area

Country profile area

Coverage Analysis
Global/Regional

Effectiveness studies

132

Total countries estimated

Mean of programme coverage in
the region/world

Region HPVc (%)

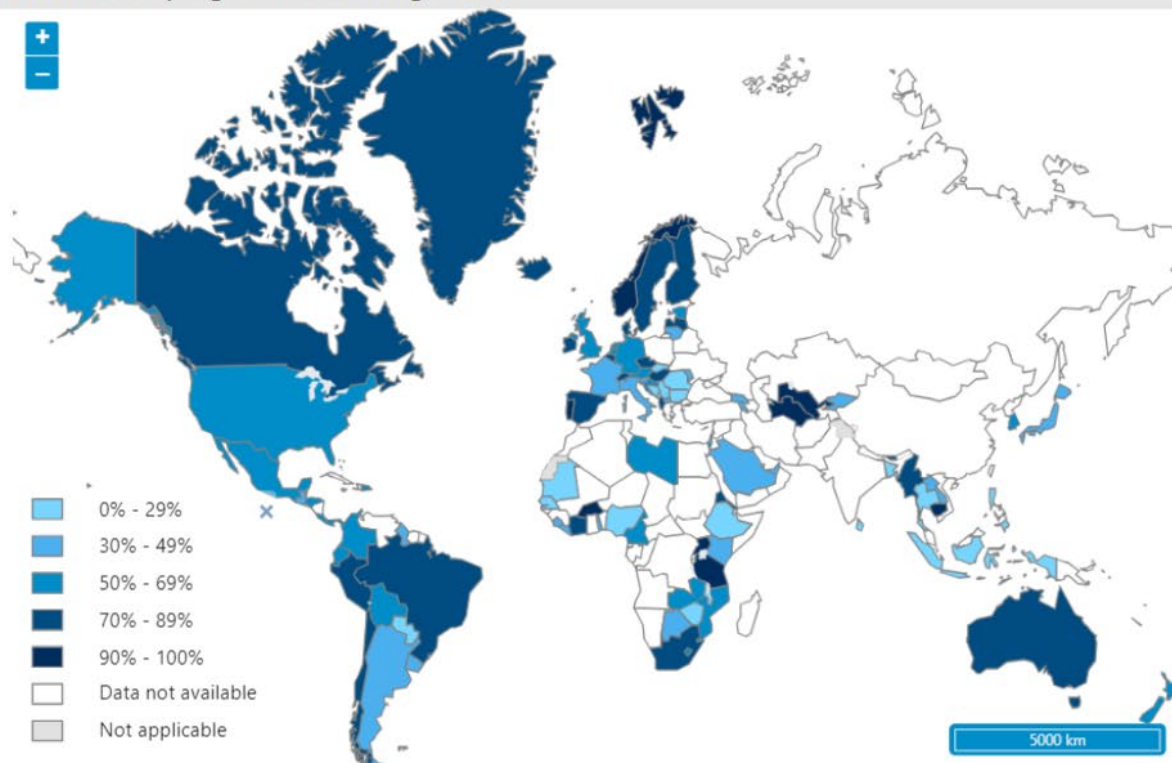
AFRO	52
AMRO	47
EMRO	44
EURO	57
SEARO	44
WPRO	55

Global HPVc (%)

Global	52
--------	----

Meta data

HPV vaccine full dose programme coverage 2023



Disclaimer

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

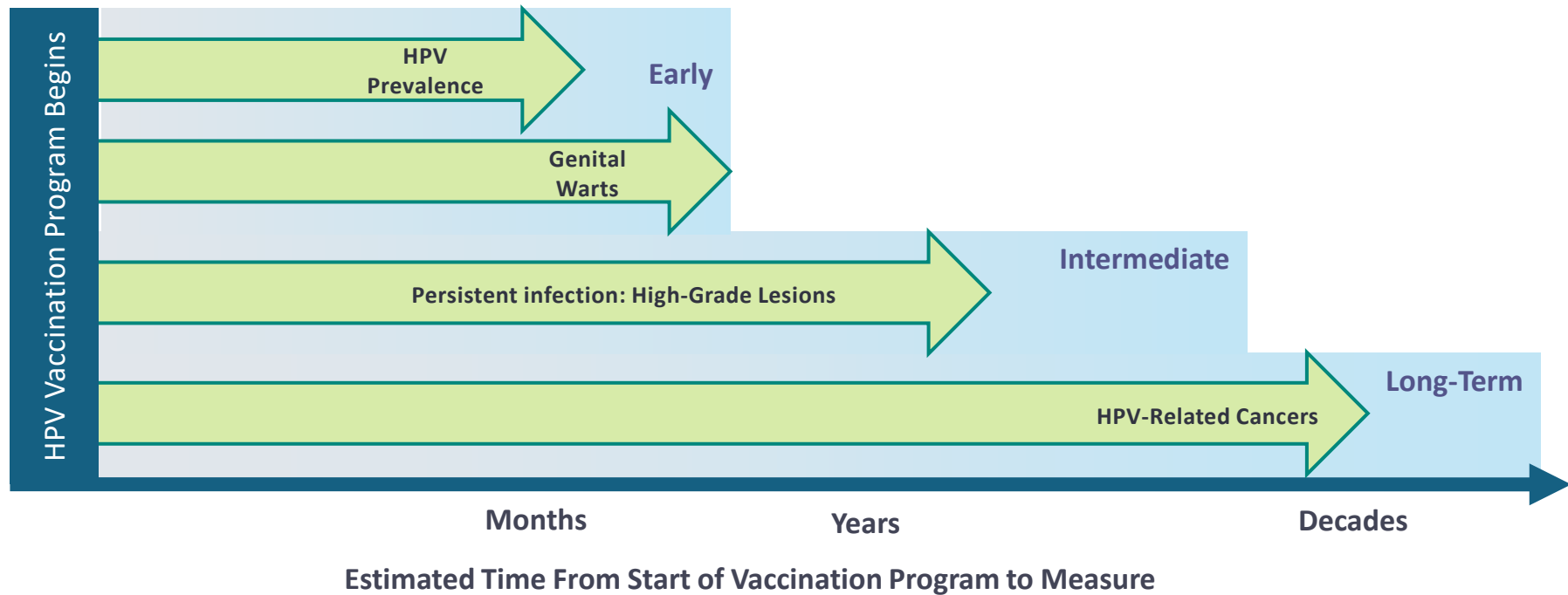

World Health Organization

© WHO 2024. All rights reserved.

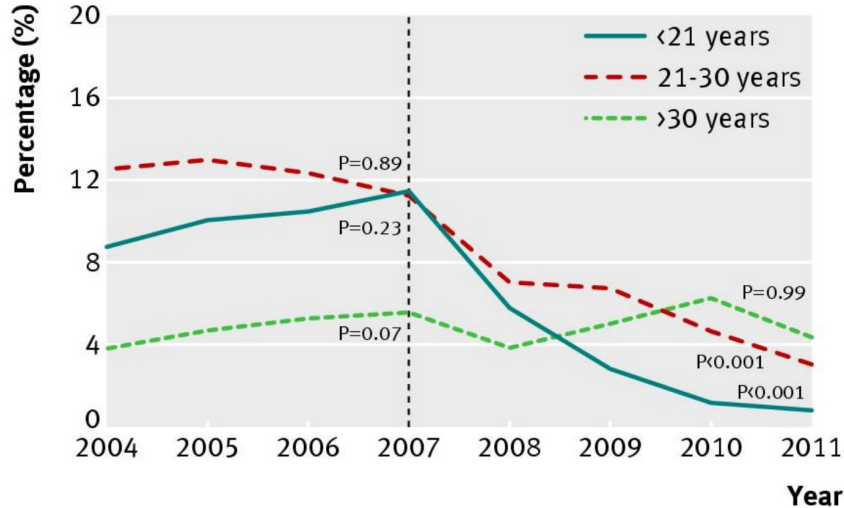
RIGHT CLICK TO DOWNLOAD →

[Export csv data](#) [Export excel data](#)

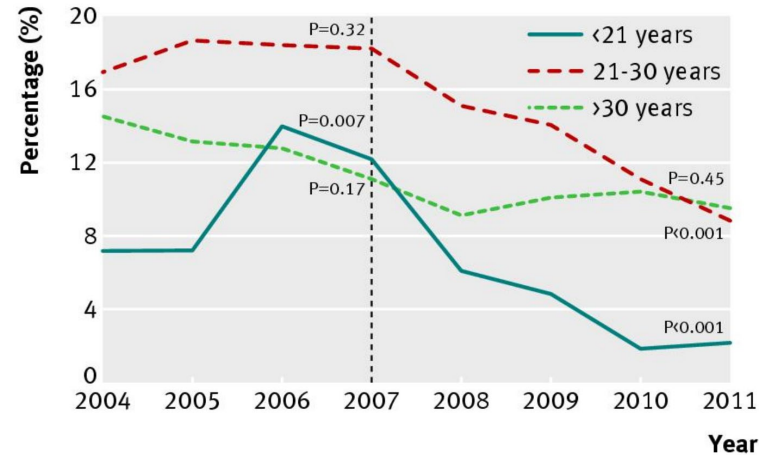
Multiple Endpoints Can Be Used To Monitor the Real World Effectiveness and Impact of HPV Vaccination¹



Australian born women having genital warts at first visit of sexual health service.

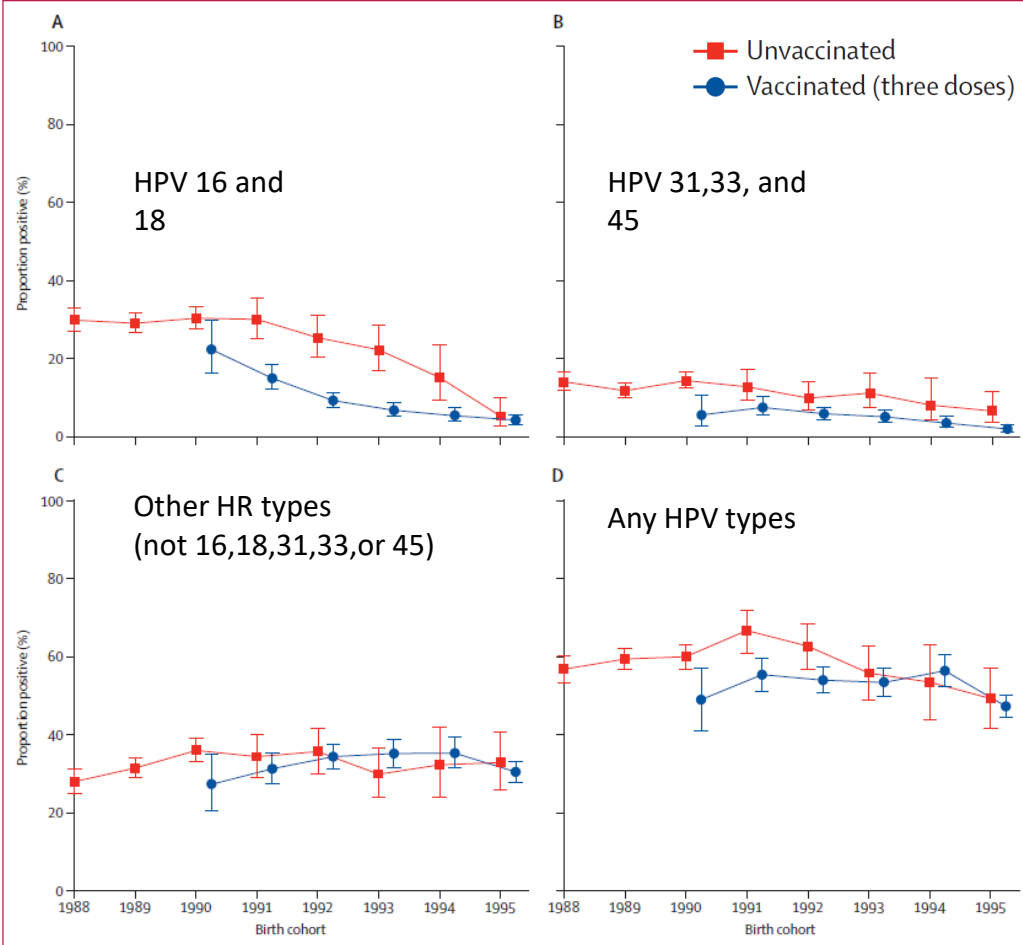


Australian born heterosexual men having genital warts at first visit of sexual health service.



- showed substantial decline of GW in vaccinated women
- showed herd protection by substantial decline of GW in heterosexual men, whereas this decline was not observed in bisexual or homosexual males.

Real life impact of HPV vaccination



Changes in the prevalence of human papillomavirus following a national bivalent human papillomavirus vaccination programme in Scotland: a 7-year cross-sectional study

Kimberley Kavanagh, Kevin G Pollock, Kate Cuschieri, Tim Palmer, Ross L Cameron, Cameron Watt, Ramya Bhatia, Catherine Moore, Heather Cubie, Margaret Cruickshank, Chris Robertson
www.thelancet.com/infection Vol 17 December 2017

- Vaccination started 2008
- 92.4% coverage of 12-13 year olds
- HPV was assessed in women attending their first cervical screen (i.e. age 20-21)
- Between 2009-2015 yearly 1000 samples were tested for HPV DNA

⇒ **Impressive reduction of vaccine and cross-protective types (HPV16 and 18 from 30% to 4.5%)**

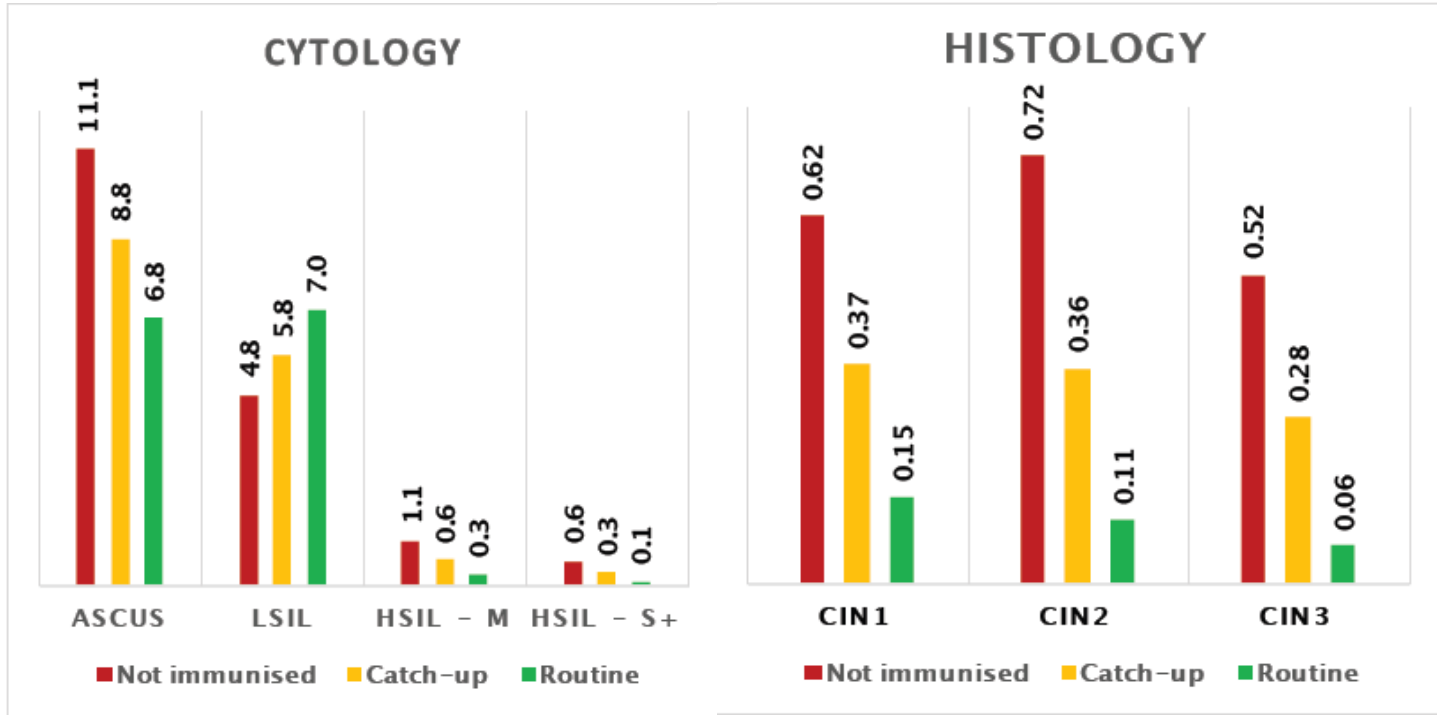
⇒ **Evidence of herd protection**

Figure: Impact of vaccination on the prevalence of human papillomavirus (HPV) by birth cohort 1988-1995 for (A) HPV types 16 and 18, (B) HPV types 31, 33, and 45, (C) other high-risk HPV types (not types 16, 18, 31, 33, or 45), and (D) any HPV types

Impact of vaccination on cervical abnormalities

- Assessment of screened cohort for women born 1988-1995
 - 1988,1989 – pre-vaccine
 - 1990-94 – vaccine eligible; catch-up cohort
 - 1995,96 – vaccine eligible; routine cohort
- Omission of small number of episodes (referred to colposcopy before screening)
- Inclusion of incident abnormal cytology cases in 1st year after 1st screen, by cohort year
- Poisson regression model adjustment for birth cohort and deprivation
- **139,000 records** censored to August 2017

Impact of vaccination on cervical abnormalities (% women screened)



Treatment for CIN at colposcopy for women aged 20/21, total number: 7013) by year of referral in Scotland

Referral year	2008–09	2009–10	2010–11	2011–12	2012–13	2013–14	Trend test
Total number of colposcopy patients	(n = 1344)	(n = 1434)	(n = 1237)	(n = 1254)	(n = 942)	(n = 802)	<i>P</i>
Treatment at colposcopy							
Ablation (cold coagulation/cryotherapy) , %	7.74 (104)	7.81 (112)	3.56 (44)	2.79 (35)	3.08 (29)	0.75 (6)	<0.0001
LLETZ/type-3 excision, %	15.92 (214)	11.65 (167)	11.72 (145)	12.44 (156)	8.92 (84)	6.98 (56)	<0.0001

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

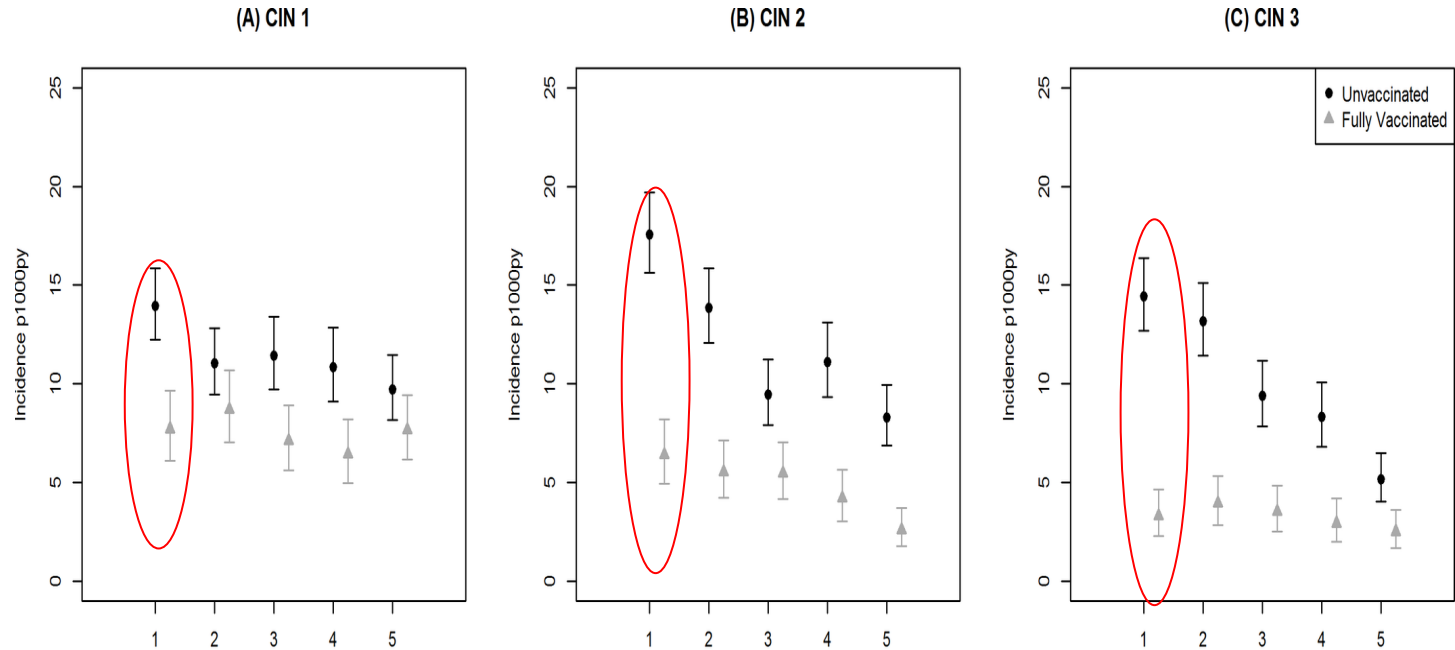
ME Cruickshank,^a J Pan,^b SC Cotton,^a K Kavanagh,^b C Robertson,^{b,c} K Cuschieri,^d H Cubie,^d T Palmer,^a KG Pollock^c



BJOG

An International Journal of
Obstetrics and Gynaecology

Incidence rate per 1000 person-years (p1000py) of CIN by deprivation



Scottish Index of Multiple Deprivation

Scottish Index of Multiple Deprivation

Scottish Index of Multiple Deprivation



Research Paper

Final analysis of a 14-year long-term follow-up study of the effectiveness and immunogenicity of the quadrivalent human papillomavirus vaccine in women from four nordic countries

Susanne K. Kjaer^{a,*}, Mari Nygård^b, Karin Sundström^c, Joakim Dillner^c, Laufey Tryggvadottir^d, Christian Munk^e, Sophie Berger^b, Espen Enerly^b, Maria Hortlund^c, Ágúst Ingi Ágústsson^f, Kaj Bjelkenkrantz^g, Katrin Fridrich^h, Ingibjorg Guðmundsdóttirⁱ, Sveinung Wergeland Sørbye^j, Oliver Bautista^k, Thomas Group^k, Alain Luxembourg^k, J. Brooke Marshall^k, David Radley^k, Yi Shen Yang^k, Cyrus Badshah^k, Alfred Saah^k

- Extension of the FUTURE II study making use of the national registries present in Denmark, Iceland, Norway, and Sweden.
- Of note 10% of participants that consented for registry-based analysis did not consent for serum sample

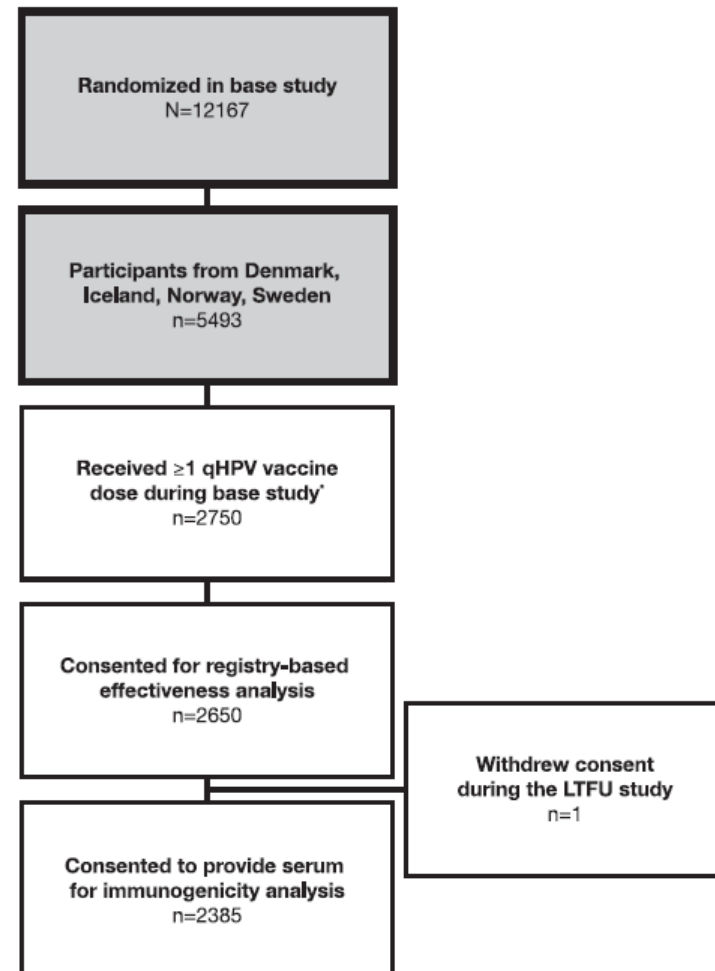


Table 1

Analysis of qHPV vaccine effectiveness against HPV16/18-related CIN2 or worse by time since qHPV vaccination, HPV type, and lesion type

	Young women 16–23 years of age (N=2650)			Vaccine effectiveness,* % (95% CI)
	Cases/n	Person-years' follow-up	Rate per 100 person-years (95% CI)	
PPE population[†]				
HPV16/18-related CIN2 or worse	0/2121	24099.0	0.0 (0.0–<0.1)	100 (94.7–100.0)
By time since qHPV vaccine Dose 1				
≤4 years	0/2121	7246.8	0.0 (0.0–0.1)	
>4 to 6 years	0/2121	4220.4	0.0 (0.0–0.1)	
>6 to 8 years	0/2089	4121.8	0.0 (0.0–0.1)	
>8 to 10 years	0/2022	3901.0	0.0 (0.0–0.1)	
>10 to 12 years	0/1855	3197.6	0.0 (0.0–0.1)	
>12 to 14 years	0/1211	1393.4	0.0 (0.0–0.3)	
>14 to 16 years	0/122	18.0	0.0 (0.0–20.5)	
By HPV type				
HPV16-related	0/1814	20583.9	0.0 (0.0–<0.1)	
HPV18-related	0/2018	22940.6	0.0 (0.0–<0.1)	
By lesion type				
CIN2	0/2121	24099.0	0.0 (0.0–<0.1)	
CIN3	0/2121	24099.0	0.0 (0.0–<0.1)	
AIS	0/2121	24099.0	0.0 (0.0–<0.1)	
Cervical cancer	0/2121	24099.0	0.0 (0.0–<0.1)	

No cases of HPV16/18-related high grade cervical dysplasia were observed in the PPE population (N=2121;24,099 person-years of follow-up)

Seropositivity rates at study conclusion were > 90% (HPV 6/11/16) and 52% (HPV18) using competitive Luminex immunoassay, and > 90% (all four HPV types) using the more sensitive IgG Luminex immunoassay.

2018: Finland shows effect on HPV cancer rates

Int J Cancer. 2018 May 15;142(10):2186-2187. doi: 10.1002/ijc.31231. Epub 2018 Jan 4.

Vaccination protects against invasive HPV-associated cancers.

Luostarinen T^{1,2}, Apter D³, Dillner J², Eriksson T⁴, Harjula K⁴, Natunen K⁴, Paavonen J⁵, Pukkala E^{1,4}, Lehtinen M^{2,4}.

Finland: June 2007 – Dec 2015 (8.5 years)

- 9,529 HPV vaccinated women
- 17,838 age-matched unvaccinated women
- Incidence of cervix, vulvar, vaginal, anal, oropharyngeal cancers

Vaccination protects against invasive HPV-associated cancers. Luostarinen T, Apter D, Dillner J, Eriksson T, Harjula K, Natunen K, Paavonen J, Pukkala E, Lehtinen M. Int J Cancer 2018 May 15;142(10):2186-2187. doi: 10.1002/ijc.31231. Epub 2018 Jan 4.



Vaccination Protects Against Invasive HPV-associated Cancers

Table 1. Numbers (*n*) and incidence rates (/100,000 woman-years) of human papillomavirus (HPV) associated invasive cancers in cluster-randomized cohorts of altogether 9,529 14- to 17-year-old female HPV16/18 or HPV6/11/16/18 vaccine recipients and 17,838 non-HPV vaccinated, originally 14- to 19-year-old women²⁻⁴

Malignancy	HPV vaccinated women			Non-HPV vaccinated women		
	Person years	<i>n</i>	Rate (95% CI)	Person years	<i>n</i>	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)
Breast cancer	65,656	2	3.0 (0.8, 12)	124,245	10	8.0 (4.3, 15)
Thyroid cancer	65,656	1	1.5 (0.2, 11)	124,245	9	7.2 (3.8, 14)
Melanoma	65,656	3	4.6 (1.5, 14)	124,245	13	10.5 (6.1, 18)
Non-melanoma skin cancer	65,656	2	3.0 (0.8, 12)	124,245	3	2.4 (0.8, 7.5)

¹Vaginal carcinoma, anal carcinoma.

For corresponding sub-cohorts age-aligned, 7-year periods of passive follow-up were by the population-based Finnish Cancer Registry.

Vaccination protects against invasive HPV-associated cancers. Luostarinen T, Apter D, Dillner J, Eriksson T, Harjula K, Natunen K, Paavonen J, Pukkala E, Lehtinen M. Int J Cancer 2018 May 15;142(10):2186-2187. doi: 10.1002/ijc.31231. Epub 2018 Jan 4.



Invasive cervical cancer incidence following bivalent human papillomavirus vaccination: a population-based observational study of age at immunization, dose, and deprivation

Tim J Palmer^{1,2}, Kimberley Kavanagh^{1,3}, Kate Cuschieri⁴, Ross Cameron¹, Catriona Graham⁵, Allan Wilson⁶, Kirsty Roy¹

Affiliations + expand

PMID: 38247547 DOI: [10.1093/jnci/djad263](https://doi.org/10.1093/jnci/djad263)

Results: No cases of invasive cancer were recorded in women immunized at 12 or 13 years of age irrespective of the number of doses. Women vaccinated at 14 to 22 years of age and given 3 doses of the bivalent vaccine showed a significant reduction in incidence compared with all unvaccinated women (3.2/100 000 [95% confidence interval (CI) = 2.1 to 4.6] vs 8.4 [95% CI = 7.2 to 9.6]).

Scotland

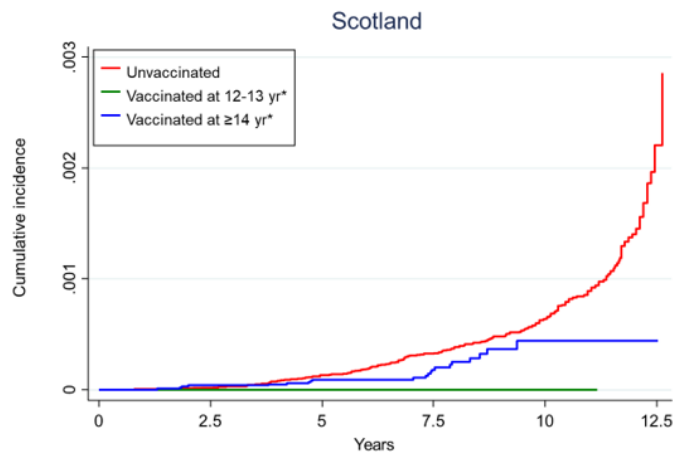


Figure1. Cumulative incidence of cervical cancer stratified by HPV vaccination status and age at vaccination (see legend), observed in linkage studies conducted in Scotland¹, joining individual patient data from vaccination and cancer registries. The X-axis expresses the years since start of screening invitation restricted to girls who were completely vaccinated.

Arbyn et al. *NCI: Journal of the National Cancer Institute*,
djae042, <https://doi.org/10.1093/jnci/djae042>

ORIGINAL ARTICLE

HPV Vaccination and the Risk of Invasive Cervical Cancer

Jiayao Lei, Ph.D., Alexander Ploner, Ph.D., K. Miriam Elfström, Ph.D.,
Jiangrong Wang, Ph.D., Adam Roth, M.D., Ph.D., Fang Fang, M.D., Ph.D.,
Karin Sundström, M.D., Ph.D., Joakim Dillner, M.D., Ph.D.,
and Pär Sparén, Ph.D.

- Registry based
- 10 year follow-up; 2006 to 2017.
- Girls between 10 and 30 years old.

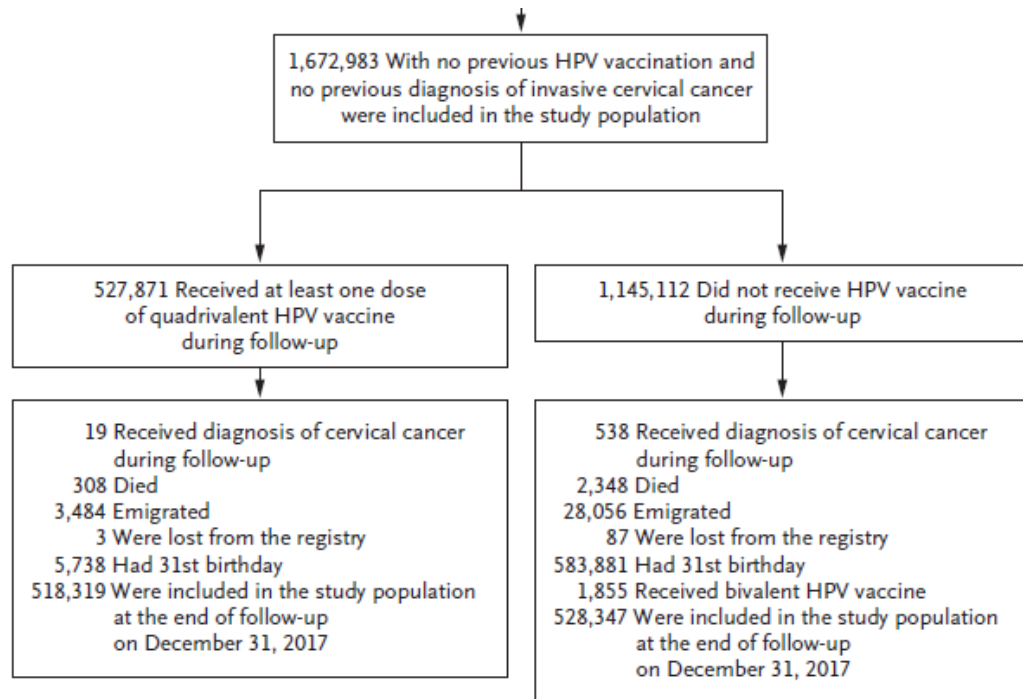
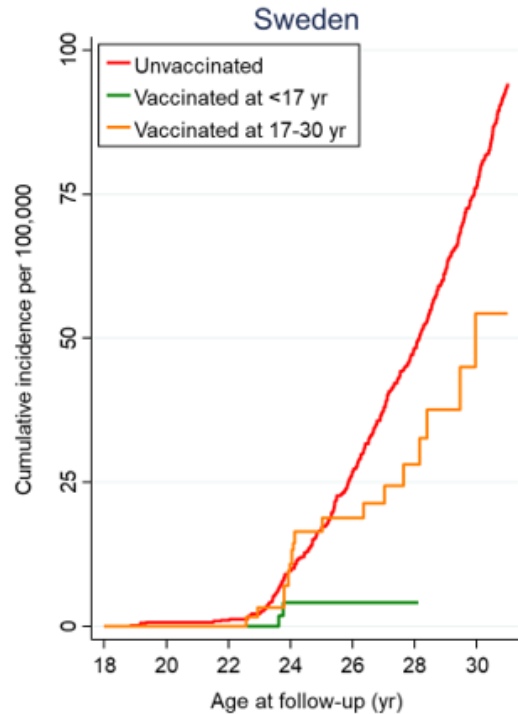


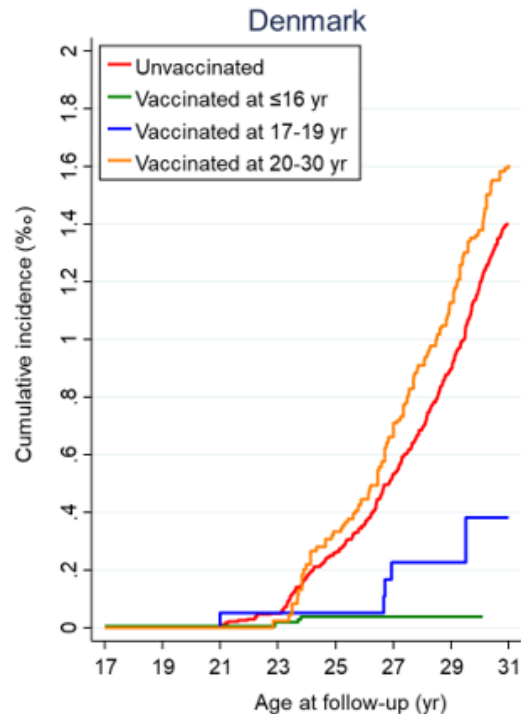
Table 2. HPV Vaccination and Invasive Cervical Cancer.

HPV Vaccination Status	No. of Cases of Cervical Cancer	Crude Incidence Rate per 100,000 Person-Yr (95% CI)	Age-Adjusted Incidence Rate Ratio (95% CI)	Adjusted Incidence Rate Ratio (95% CI)*
Unvaccinated	538	5.27 (4.84–5.73)	Reference	Reference
Vaccinated	19	0.73 (0.47–1.14)	0.51 (0.32–0.82)	0.37 (0.21–0.57)
Status according to age cutoff of 17 yr				
Vaccinated before age 17 yr	2	0.10 (0.02–0.39)	0.19 (0.05–0.75)	0.12 (0.00–0.34)
Vaccinated at age 17–30 yr	17	3.02 (1.88–4.86)	0.64 (0.39–1.04)	0.47 (0.27–0.75)
Status according to age cutoff of 20 yr				
Vaccinated before age 20 yr	12	0.49 (0.28–5.73)	0.52 (0.29–0.94)	0.36 (0.18–0.61)
Vaccinated at age 20–30 yr	7	5.16 (2.46–10.83)	0.50 (0.24–1.06)	0.38 (0.12–0.72)

* The adjusted incidence rate ratios were adjusted for age as a spline term with 3 degrees of freedom, county of residence, calendar year, mother's country of birth, highest parental education level, highest annual household income level, previous diagnosis in mother of CIN3+, and previous diagnosis in mother of cancers other than cervical cancer. The 95% confidence intervals were bias-corrected percentile confidence intervals that were estimated with the use of bootstrapping with a resampling frequency of 2000 times.



Lei, N Engl J Med 2020



Kjaer, JNCI 2021

Arbyn et al. *NCI: Journal of the National Cancer Institute*,
djae042, <https://doi.org/10.1093/jnci/djae042>

Figure1. Cumulative incidence of cervical cancer stratified by HPV vaccination status and age at vaccination (see legend), observed in linkage studies conducted in Sweden¹⁴, Denmark¹⁵ and Scotland¹, joining individual patient data from vaccination and cancer registries. The X-axis in the two plots on top expresses the years at follow-up, whereas in the plot at the bottom, expresses the years since start of screening invitation.

* For Scotland, restricted to girls who were completely vaccinated.

A few words on 'urine samples'

- Use urine samples to monitor impact of HPV vaccination
- Comparing first void urine sampling at home with clinician collected cervical sampling.
- Can first void urine replace a blood sample?

Importance of sample collection

- Providing a sample must be easy and convenient for the target group.
- Often performed with the support of a medically trained person
- Eg of hurdles:
 - Monitoring immune response after vaccination is performed using a blood sample.
 - Impact of vaccination based on cervical sampling is only determined in sexually active women
- The introduction of HPV DNA testing has opened the door for self-sampling.

Short Communication

Worldwide use of HPV self-sampling for cervical cancer screening

B. Serrano^{a,b,*}, R. Ibáñez^{a,b}, C. Robles^a, P. Peremiquel-Trillas^{a,b}, S. de Sanjosé^{c,d}, L. Bruni^{a,b}

- 17 countries use self-sampling (2020):
 - 9 in primary screening program
 - 8 only for under screened women
- 10 pilots were identified

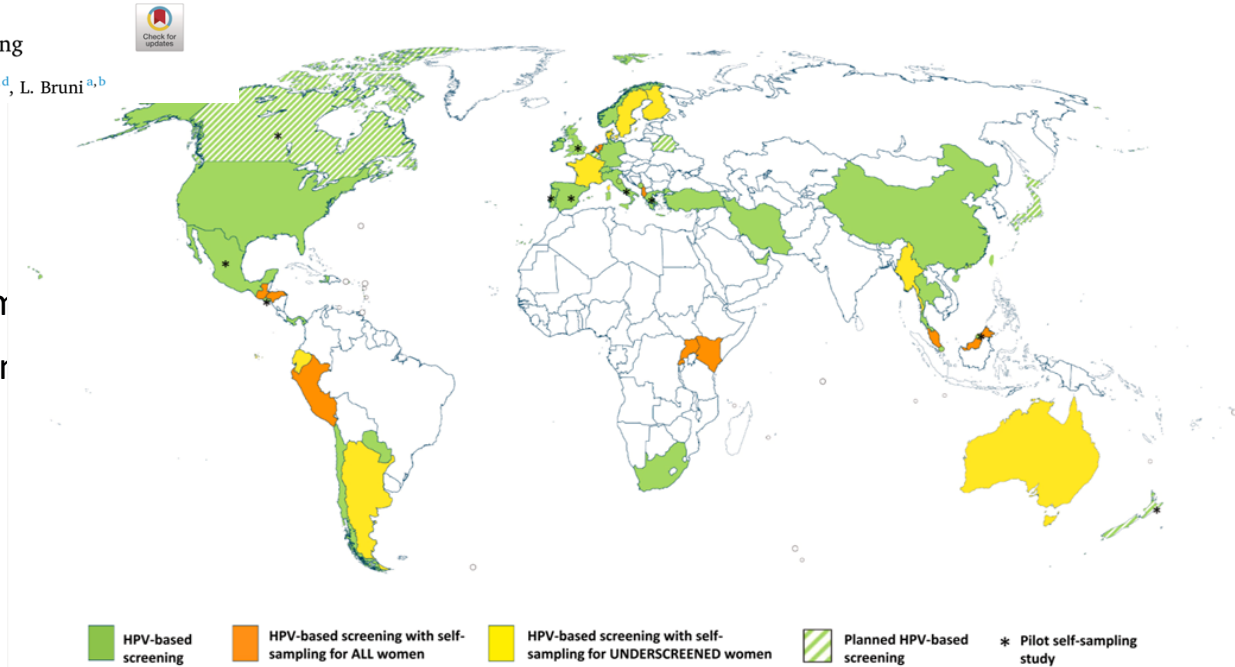


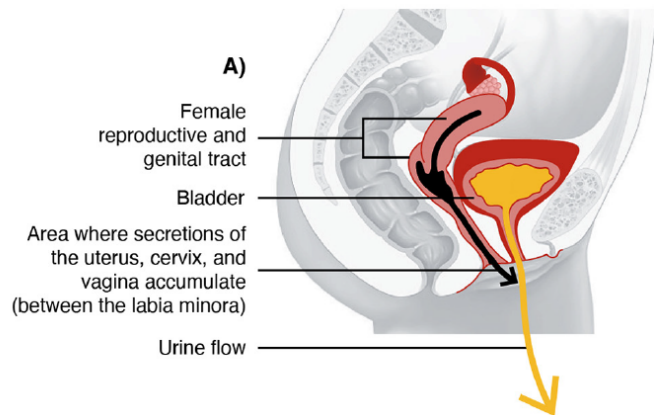
Fig. 1. Self-sampling approach in countries officially recommending HPV-based screening.

The solid pattern indicates that the country recommends HPV-based screening (either alone or combined with cytology and/or VIA), the stripped pattern indicates that the country plans the introduction of primary HPV screening in the coming years. The boundaries shown and the designations used on this map do not imply the expression of any opinion whatsoever concerning the legal status of any country, territory, city or area or its authorities, or concerning the delimitation of its frontiers or boundaries.



Testing for Human Papillomaviruses in Urine, Blood, and Oral Specimens: an Update for the Laboratory

© Mario Poljak,^a © Kate Cuschieri,^b © Laia Alemany,^{c,d} © Alex Vorsters^e



Urine testing to monitor the impact of HPV vaccination in Bhutan and Rwanda

S. Franceschi, et al. International Journal of Cancer. 2016

- High return rate of the samples:
 - in Bhutan of 1,148 consented girls 92.7% returned the urine sample;
 - in Rwanda of the 1,130 consented girls 88.3% returned the urine sample as well

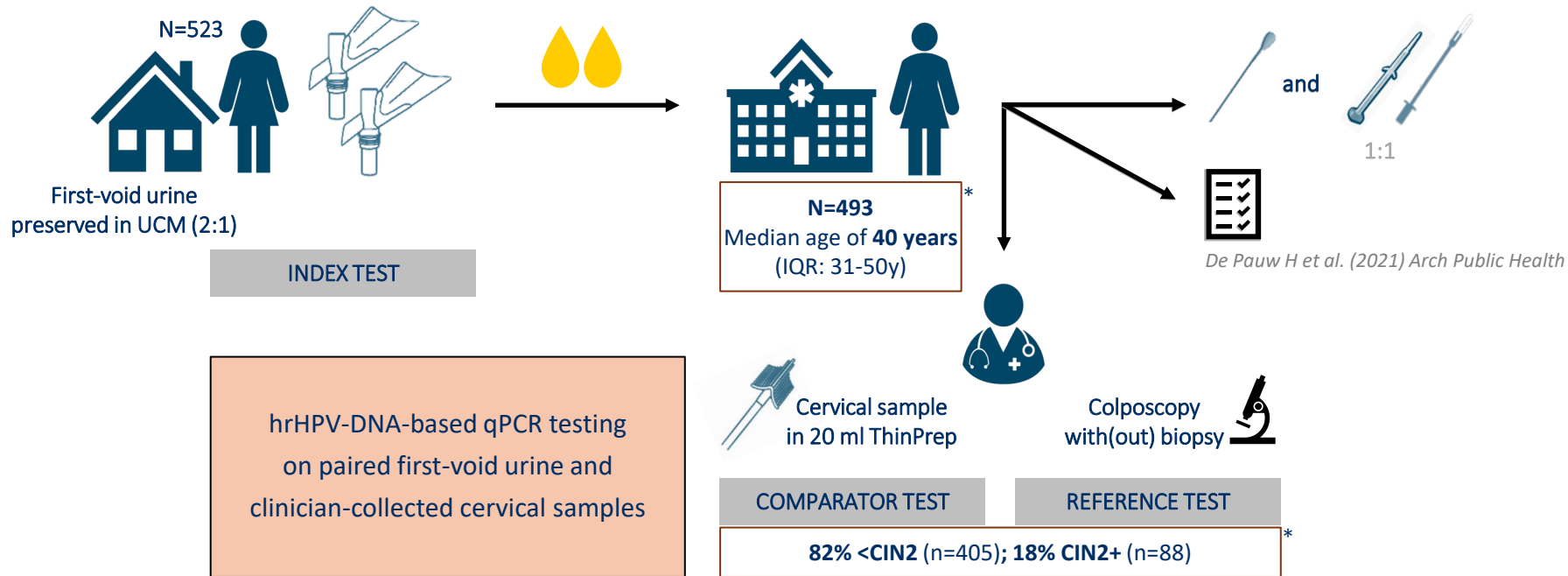
Prevalence ratios (PRs) and vaccine effectiveness (VE) with corresponding 95% confidence intervals (CIs) for positivity for human papillomavirus by GP5+/6+. Rwanda.

Country	Type of effectiveness	HPV type ^a	N. (%) by vaccination status		Adjusted PRs ^b	Adjusted VE (%) ^b	
			Baseline survey	Repeat survey			
Rwanda	Overall		All	All			
		N	912	1087			
		Vaccine-targeted	23 (2.5)	8 (0.7)	0.2 (0.1-0.5)	78 (51 to 90)	- Adjusted for age, ever had sexual intercourse, chlamydia and place where born
		Other alpha-9	26 (2.9)	16 (1.5)	0.4 (0.2-0.8)	59 (23 to 78)	- Vaccine-targeted types (HPV 6, 11, 16, 18)
		Other alpha-7	19 (2.1)	23 (2.1)	0.8 (0.4-1.4)	22 (-45 to 58)	- Alpha-9 types (HPV31, 33, 35, 52, 58)
		Non-alpha 7/9	29 (3.2)	42 (3.9)	0.9 (0.6-1.4)	11 (-41 to 44)	- Alpha-7 types (HPV39, 45, 59, 68)
	Restricted		Unvaccinated	All			- Other-HPV types (HPV26, 51, 53, 56, 66, 67, 69, 70, 73, 82)
		N	519	1087			
		Vaccine-targeted	21 (4.0)	8 (0.7)	0.1 (0.1-0.3)	86 (69 to 94)	
		Other alpha-9	17 (3.3)	16 (1.5)	0.4 (0.2-0.7)	63 (27 to 81)	
		Other alpha-7	12 (2.3)	23 (2.1)	0.7 (0.3-1.4)	31 (-39 to 66)	
		Non-alpha 7/9	15 (2.9)	42 (3.9)	1.0 (0.6-1.7)	2 (-73 to 45)	
	Total		Unvaccinated	Vaccinated			
		N	519	962			
		Vaccine-targeted	21 (4.0)	3 (0.3)	0.0 (0.0-0.2)	95 (84 to 99)	
		Other alpha-9	17 (3.3)	15 (1.6)	0.4 (0.2-0.8)	61 (22 to 81)	
		Other alpha-7	12 (2.3)	19 (2.0)	0.6 (0.3-1.3)	37 (-32 to 70)	
		Non-alpha 7/9	15 (2.9)	36 (3.7)	0.9 (0.5-1.7)	7 (-67 to 49)	

VALHUDES - A protocol for validation of HPV assays and collection devices for HPV testing on self-samples and urine samples

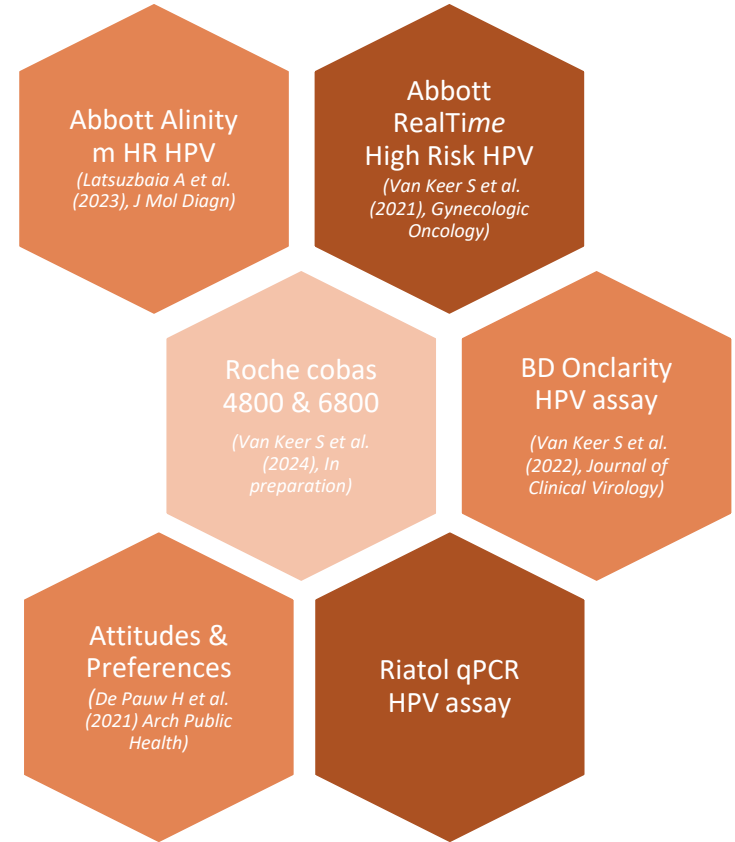
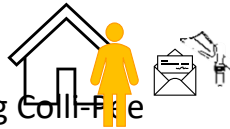


VALHUDES - A protocol for validation of HPV assays and collection devices for HPV testing on self-samples and urine samples



Strengths and conclusions VALHUDES Urine

- HrHPV DNA-based PCR assays used in routine cervical screening have similar clinical sensitivity (CIN2+) and specificity (<CIN2) in first-void urine compared to clinician-collected cervical samples
- No need for additional sample handling steps on first-void urine as for manufacturer-validated cervical samples
- First-void urine samples
 - Collected at home
 - Standardized and DNA-preserved samples using Coll-File
- Well-accepted by women for cervical screening purposes
- Women feel confident about sampling correctly



Main research questions

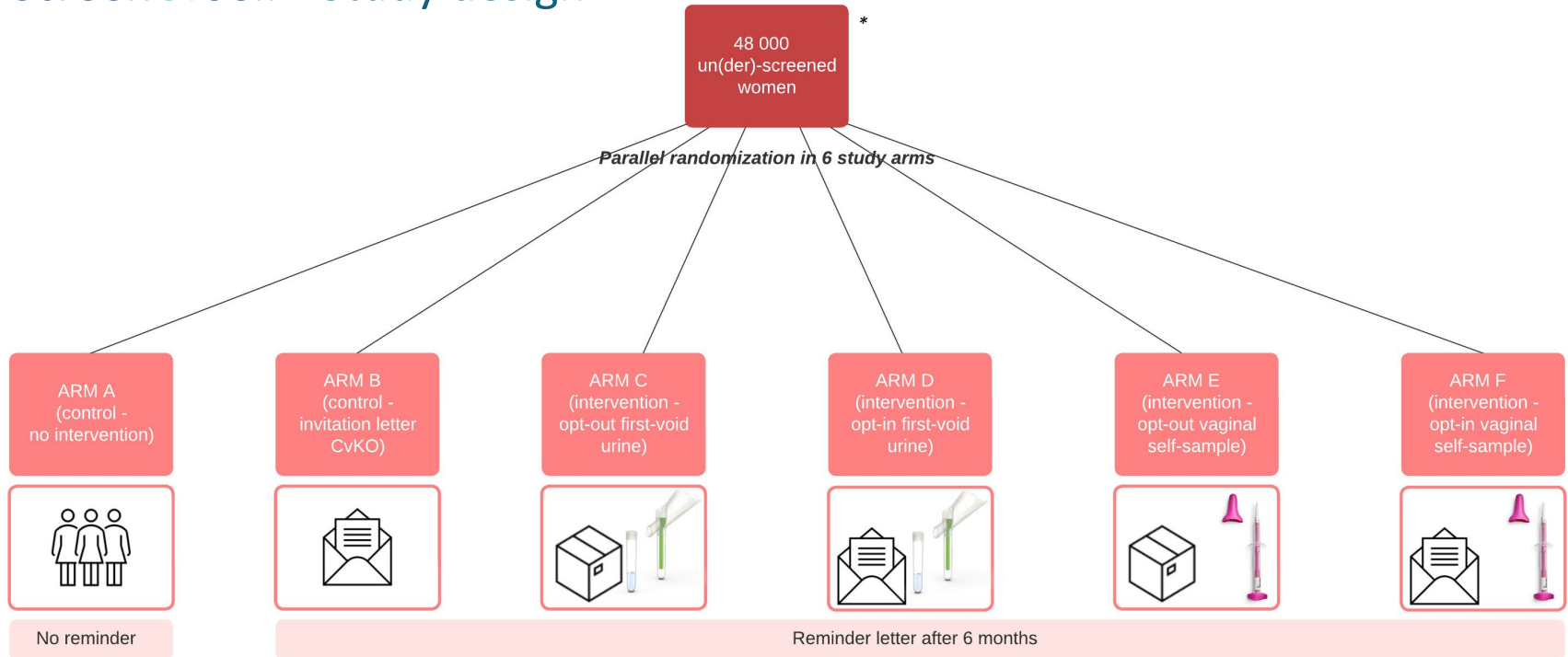
“Can we reach more un(der)-screened, Flemish women for cervical screening by offering home-based self-sampling opportunities?

Without negatively impacting compliance to follow-up?

If so, is urine self-sampling more preferred compared to vaginal self-sampling?”



ScreenUrSelf - Study design



**Un(der)-screened women: No cytological, histological, pathological reports in Belgian Cancer Register for ≥ 2 screening rounds (31-64y), residing in Flanders, not included in other CvKO research projects, no history of total hysterectomy nor uterine/cervical cancer, and not actively opted out of the organized screening program.*





CASUS trial

Methylation – Clinical performance of bi-marker panel ASCL1/LHX8 in first-void urine

- Device under study: Colli-Pee Small Volumes (with UCM, Novosanis)
- Assay: PreCursorM-Gold (Self-Screen)



molecules



Article

Impact of Collection Volume and DNA Extraction Method on the Detection of Biomarkers and HPV DNA in First-Void Urine

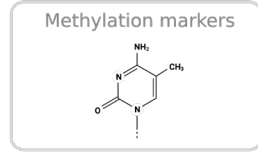
Laura Téblick ^{1,*}, Severien Van Keer ¹, Annemie De Smet ¹, Pierre Van Damme ¹, Michelle Laeremans ², Alejandra Rios Cortes ², Koen Beyers ², Vanessa Vankerckhoven ^{1,2}, Veerle Matheussen ^{3,4,5}, Renee Mandersloot ⁶, Arno Floore ⁶, Chris J. L. M. Meijer ^{6,7}, Renske D. M. Steenberg ⁷ and Alex Vorsters ¹



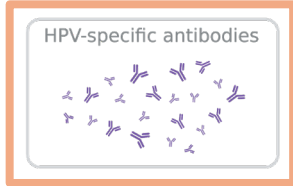
First-void urine



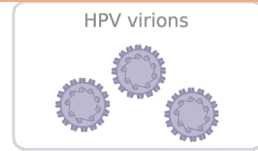
HPV DNA



Methylation markers



HPV-specific antibodies



HPV virions

First-void urine as a non-invasive liquid biopsy source to detect vaccine-induced human papillomavirus antibodies originating from cervicovaginal secretions

Severien Van Keer^{a,*}, Martina Willhauck-Fleckenstein^a, Jade Pattyn^a, Julia Butt^a, Wiebren A.A. Tjalma^{a,b}, Xaveer Van Ostade^a, Niel Hens^{a,b}, Pierre Van Damme^a, Tim Waterboer^a, Alex Vorsters^a

Comparison of a VLP-based and GST-L1-based multiplex immunoassay to detect vaccine-induced HPV-specific antibodies in first-void urine

Jade Pattyn^a, Gitika Panicker^a, Martina Willhauck-Fleckenstein^a, Severien Van Keer^a, Laura Téblick^a, Zoë Pieters^{a,b}, Wiebren A. A. Tjalma^{a,b}, Veerle Matheussen^{a,b,10}, Pierre Van Damme^a, Tim Waterboer^a, Elizabeth R. Unger^a, Alex Vorsters^a

Infection and vaccine-induced HPV-specific antibodies in cervicovaginal secretions. A review of the literature

Jade Pattyn^{a,*}, Severien Van Keer^a, Wiebren Tjalma^a, Veerle Matheussen^a, Pierre Van Damme^a, Alex Vorsters^a

Non-invasive Assessment of Vaccine-Induced HPV Antibodies via First-Void Urine

Jade Pattyn^a, Severien Van Keer^a, Laura Téblick^a, Pierre Van Damme^a and Alex Vorsters^a

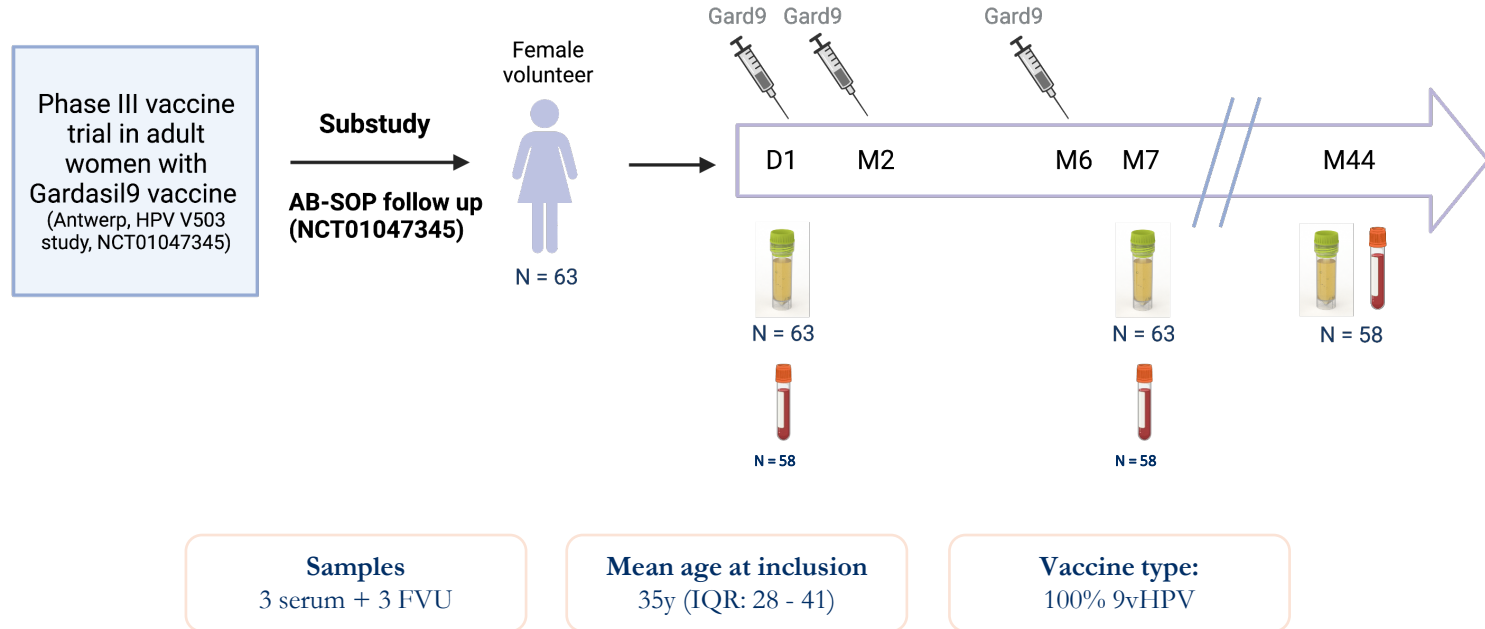
Faculty of Medicine and Health Sciences, Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute (VIMINFECTION), University of Antwerp, Antwerp, Belgium

HPV-specific antibodies are detectable in FVU samples

HPV-specific antibody concentrations detected in FVU correlate with concentrations in serum

AB-SOP follow-up study / 2018-2022

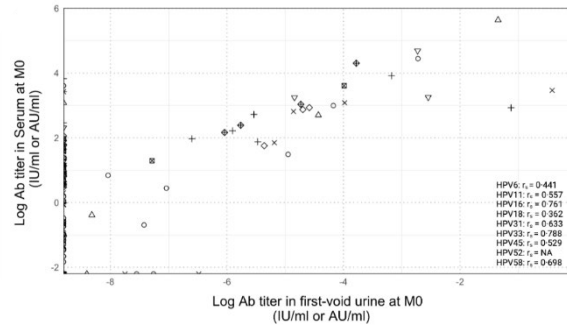
NCT03542227



Good correlations between HPV-specific antibody titers in paired FVU and serum

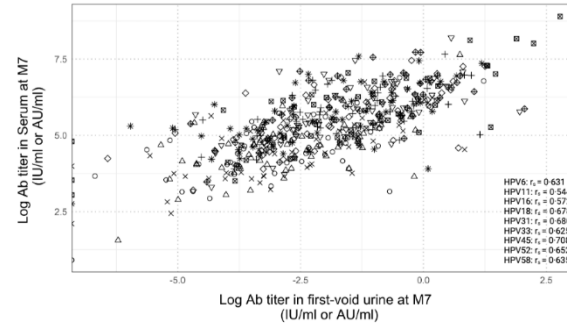
Before vaccination

$r_s: 0.36-0.78$



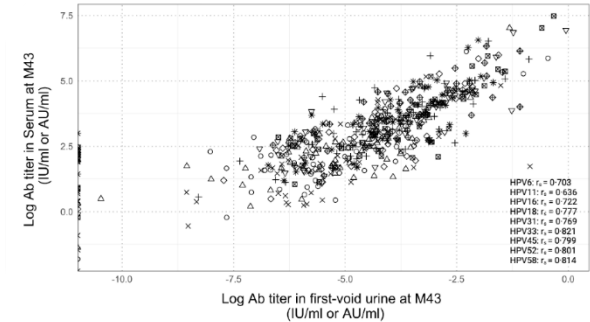
1 month after full vaccination

$r_s: 0.54-0.71$



3 years after full vaccination

$r_s: 0.64-0.82$



○ HPV6 + HPV16 ◇ HPV31 ■ HPV45 ◆ HPV58 △ HPV11 × HPV18 ▽ HPV33 * HPV52

First-void urine

Conclusies

- Impact van HPV vaccinatie op HPV infectie, hooggradige laesies en HPV gerelateerde kankers is indrukwekkend.
- Eerste fractie urine heeft potentieel om gebruikt te worden voor zelfafname en voor het opvolgen van impact van HPV vaccinatie programma's.

HPV plus TEAM

PI: Prof. Alex Vorsters, PhD

Current research team:

- Severien Van Keer, PhD
- Annemie De Smet, lab technician
- Laura Téblick, PhD researcher
- Eef van den Borst, PhD researcher
- Margo Bell, PhD researcher
- Marijana Lipovac, PhD researcher
- Anne Van Caesbroeck, PhD researcher



HPV Prevention and Control Board & Coalition to Strengthen the HPV Immunization

Community:

- Nayab Waheed, PhD researcher
- Ricardo Burdier, MD researcher
- Xenia Mikulla, secretariat

Collaborating Partners :



University of Antwerp
Center for the Evaluation of Vaccination
Vaccine and Infectious Disease Institute



Vaccinopolis
Powered by UAntwerp



European Research Council
Established by the European Commission



URISAMP



International Agency
Research on Cancer



World Health
Organization

VRAGEN?

VOOR ONLINE DEELNEMERS:

U KUNT STEEDS VRAGEN STELLEN VIA DE CHATFUNCTIE.

DEZE VRAGEN WORDEN VERZAMELD DOOR DE MODERATOR EN
SAMEN MET DE VRAGEN UIT DE ZAAL **OP HET EINDE VAN DE
AVOND** VOORGELEGD AAN DE SPREKERS.

LABORATORIUMASPECTEN ROND HPV PCR

APR. BIOL. ELISE WILLEMS & DR. VERONIEK SAEGEMAN
KLINISCHE BIOLOGIE | VITAZ

Introductie

- Heel veel commerciële HPV PCR assays
- 79% onvoldoende evidentie m.b.t. klinische en analytische performantie als 1^e HPV screening strategie
- Enkel assays klinisch gevalideerd volgens internationale richtlijnen, komen in aanmerking voor RIZIV terugbetaling.

Assays for the detection of high-risk human papillomaviruses in the context of Belgian cervical cancer primary screening.

The table below presents a list of molecular assays for the detection high-risk Human Papillomaviruses (hrHPV). These assays are clinically validated according to international criteria (Arbyn M. *et al.*, Clin Microbiol Infect 2021¹®; Arbyn M *et al.*, ESGO Textbook of Gynaecological Oncology 2023²®; Dhillon *et al.*, J Med 2023³®; Arbyn *et al.*, Clin Microbiol Infect 2023⁴®). The table below is updated at least twice a year, as new scientific evidence becomes available.

Assay	Manufacturer
Alinity m HR HPV Assay	Abbott, Wiesbaden, Germany
Alplex II HPV HR Detection	Seegene, Seoul, South Korea
Anplex II HPV HR Detection	Seegene, Seoul, South Korea
APTIMA HPV Assay*	Hologic, Bedford, MA, USA
*in combination with another mRNA assay (APTIMA HPV16, 18, 45, Hologic) which can identify HPV16 and HPV18.45	
CLART HPV4S	GENOMICA SAU, Madrid, Spain
Cobas 4800 HPV Test	Roche Molecular System, Pleasanton, CA, USA
Cobas® HPV test (for use on the Cobas® 5800/6800/8800 Systems)	Roche Molecular System, Pleasanton, CA, USA
HPV-Risk Assay	Self-Screen BV, Amsterdam, The Netherlands
HPV Test Onclearity HPV Assay	BD Diagnostics, Sparks, MD, USA
NeuMoDX	Qiagen, Ann Arbor, MI, USA
RealTime High Risk HPV Test	Abbott, Wiesbaden, Germany
RIATOL HPV genotyping qPCR assay	in house, AML, Antwerp, Belgium
Xpert HPV	Cepheid, Sunnyvale, CA, USA

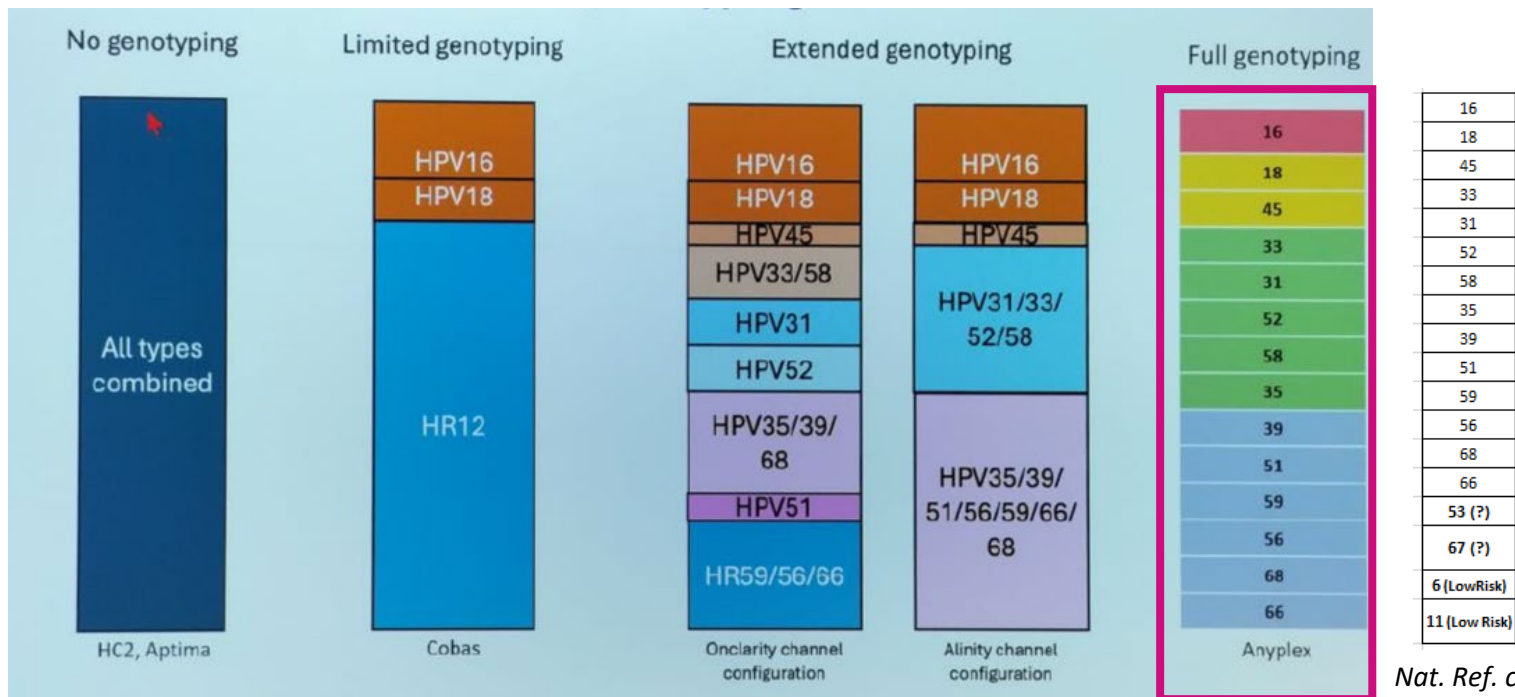
List of internationally validated hrHPV assays which can be applied in the Belgian cervical cancer screening (ordered alphabetically).
Updated on 05/08/2024.

Moleculaire techniek gebruikt in VITAZ

AnyplexII HPV HR Detection (Firma: Seegene- Leverancier: Accuramed)

- Implementatie 2019 in VITAZ - 1 van de eerste labo's in België
 - Literatuur:
 - Voldoende evidentie over klinische & analytische prestatie
 - Meer en meer evidentie over het belang van genotypering (vaccin optimalisatie- screening strategieën optimaliseren)
 - Interne validatie: prestatie bevestigd
- **Full genotyping (14 types)**
 - ✓ HPV 16 ✓ HPV 33 ✓ HPV 45 ✓ HPV 56 ✓ HPV 66
 - ✓ HPV 18 ✓ HPV 35 ✓ HPV 51 ✓ HPV 58 ✓ HPV 68
 - ✓ HPV 31 ✓ HPV 39 ✓ HPV 52 ✓ HPV 59
- More future proof voor adapting guidelines
 - Wijzigingen in triage richtlijnen o.b.v. bijkomende evidentie
 - Meer genotypes
 - Differentiëren tussen persistente-genotypes, transitie van genotypes, clearance genotypes
 - Monitoring van veranderingen in HPV GT gevaccineerd vs niet-gevaccineerd; monitoring vaccin efficacy – kruisbescherming
- Principe: oligonucleotide cleavage and extension (TOCE) technology





Eurogin 2024 - Real-life experiences of extended HPV genotyping in screening Bonde J. (Denmark)





Alle toestellen 2x → voldoende capaciteit & continuïteit gegarandeerd

Impact praktisch –

HPV-test als 1^e screeningtool voor baarmoederhalskanker bij 30-64 j vrouw

REGULIERE screening 30-64 jaar:

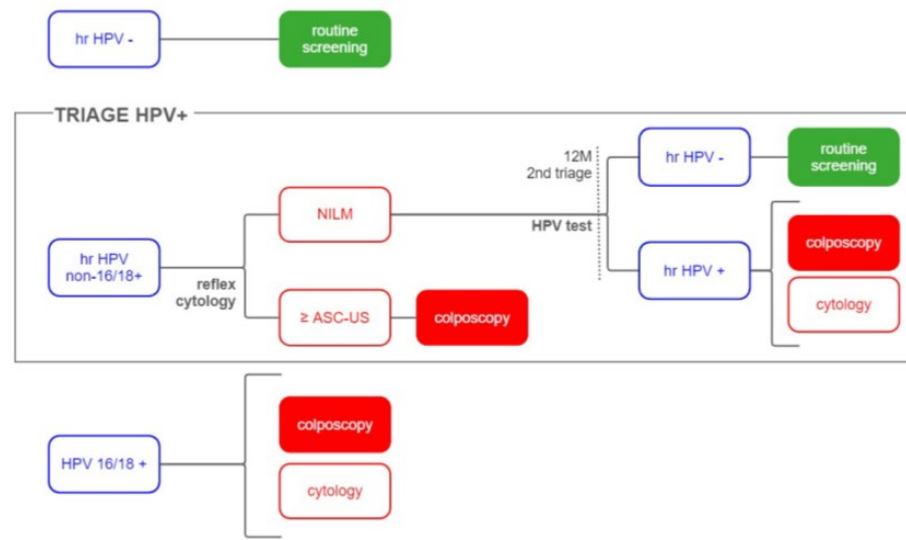
HEDEN (om de 3 kalenderjaren):

Cytologie → PCR HPV bij atypische cellen
LABO APD → *KLINISCH LABO*

VANAF 1/1/2025 (om de 5 kalenderjaren):

PCR HPV →
negatief: STOP indien hrHPV negatief
HPV 16/18+ : cytologie & colposcopie
ander hrHPV type → cytologie → colposcopie /na 12m retest

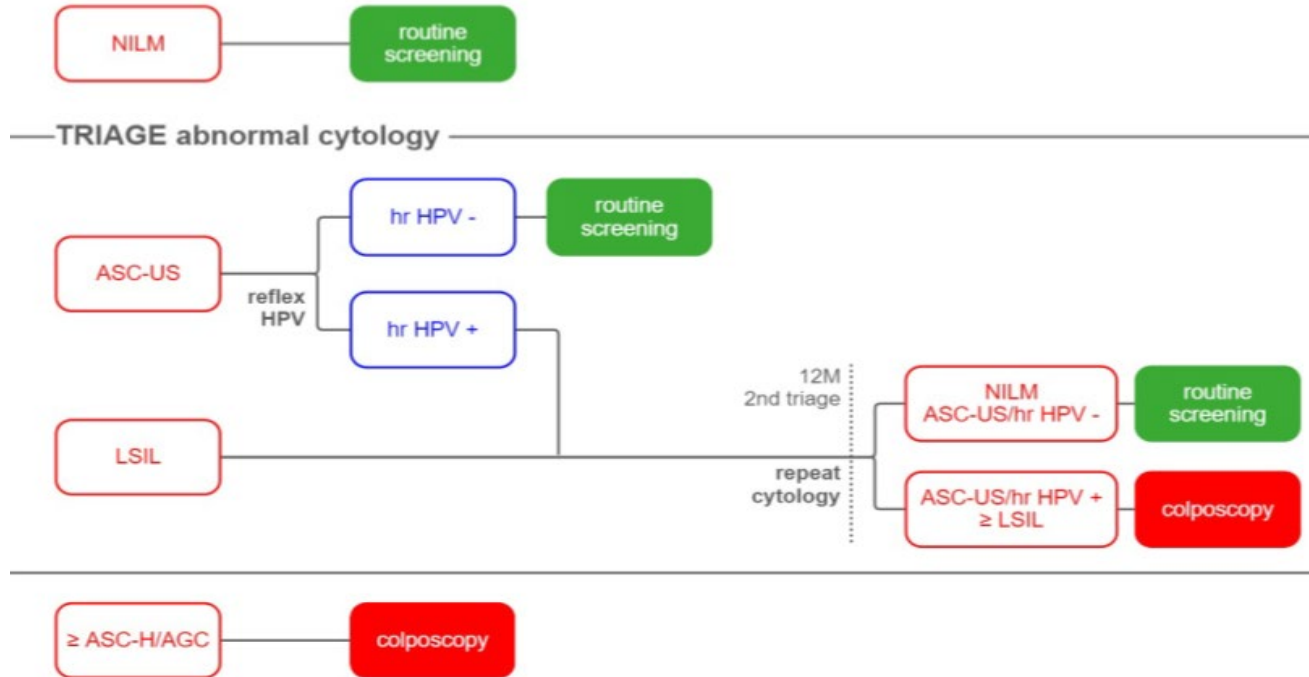
KLINISCH LABO → APD



Wat met <30 jarige?

Age category	Primary screening	Frequency	Triage - reflex test (after a positive primary test)	2nd triage - repeat testing (in 12 months)
≤24y	No	NA	NA	NA
25-29y (Figure 1)	Cytology	Every 3 calendar years	ASC-US result -> HPV test	hrHPV pos. -> repeat cytology Primary screening result LSIL -> repeat cytology

25 - 29 jarige



≥ASC-H/AGC = ASC-H/AGC or a more severe lesion (HSIL, SCC, AIS, AC)

≥ 65 jaar

Age category	Primary screening	Frequency	Triage - reflex test (after a positive primary test)	2nd triage - repeat testing (in 12 months)
65+ (exit or catch-up screening) ¹	Cotesting (cytology+HPV), on the same sample	Once	NA	hrHPV non-16/18 pos. + NILM -> HPV test hrHPV neg. + ASC-US -> HPV test

¹ If no screening was reimbursed in the previous 10 years.

Diagnostische/therapeutische FU

Richtlijnen Sciensano in consensus met beroeps- en wetenschappelijke verenigingen **volgen**

FOLLOW-UP			
	Test type	Frequency reimbursement	Notification advising physician
Diagnostic or therapeutic follow-up	Cytology and/or HPV-test (not to be interpreted as cotesting)	One reimbursement/calendar year, both for cytology and HPV-testing	Temporary high-risk with the possibility of testing twice per calendar year (e.g. in HSIL without treatment)

KLINIEK/HOOG Risicogroep

Meer info over hoe RIZIV te notifiëren volgt

CLINICAL/DIAGNOSTIC			
Clinical testing (with symptoms) ²	Cotesting (cytology + HPV)	No limitation	Notification with reimbursement of one diagnostic cotest
HIGH-RISK GROUPS			
DES ³ AIS ⁴	Cotesting (cytology + HPV)	No limitation Recommendation: yearly	Notification with reimbursement of all required tests
Others ⁵ (immunocompromised)	HPV-test or cytology, depending on age	No limitation Recommendation: 3-yearly HPV-test or yearly cytology, depending on age ^o	Notification with reimbursement of all required tests

Richtlijnen: Screening, triage and follow-up in high-risk populations (to be published at [Cervical cancer screening | sciensano.be](https://www.sciensano.be))

² Postmenopausaal bloedverlies, abnormaal therapie resistent uterinen bloedverlies, onverklaard postcoïtaal bloedverlies

³ DES= kinderen van vrouwen die DES (diethylstilbestrol) voorgeschreven kregen (1938-1971) i.k.v. miskraam preventie .

⁴ AIS=adenocarcinoma in situ

⁵ HIV positives (CD4 <350/μl or HIVRNA >200 cp/ml), na orgaan txp, na allo-SCT, SLE, congenitale 1^e ID, patiënten onder langdurige continue IS
! Zo lang IS wordt toegediend.

Overgangsregeling voor 30-64 jarige

Transitional arrangement

According to the RIZIV/INAMI nomenclature, all insured people aged between 30 and 64 will enter the new system three years after the last reimbursed test for cervical cancer screening. They will at that point be entitled to a reimbursed HPV test that will be repeated every five years from that moment on.

Although nomenclature allows an HPV test for each woman 30-64 years old after 3 years, regardless of the previous test (cytology or HPV), the experts want to take previous HPV test results into account. This means that women with a previous negative reflex HPV test result or a not-reimbursed negative HPV test result (and normal cytology) should only be advised for the next screening round in 5 years' time.

Staal-transportmedium = idem

Staal: Cervicovaginale brush

TPM: Liquid- based cytology media

Waarom dit TPM?

- Geschikt voor HPV PCR & cytologie
- Langere bewaartermijn
- Transport op kamertemperatuur



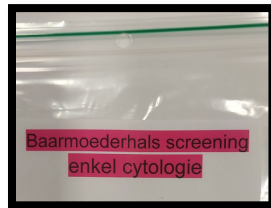
➡ VITAZ : Thinprep® met cervico-vaginale brush

Staaltransport - triage

- Extern: IDEM - bode (vaste momenten/afroep) richting klinisch labo
- Intern: **ALTIJD klinisch labo → OPTIMALE TRIAGE i.f.v. testindicatie**
 - SN/SM: buizenpost - afgifte klinisch labo
 - Perifere campi:
 - LO + BE: prikplaats klinisch labo
 - SG/TEMSE/HAMME: onthaal → meerdere bodes/dag → klin. labo

! Indien 1^e **ENKEL cytologie: zakje met roze sticker**

- Snellere triage!



Quality assurance labo resultaten VITAZ

Accreditatie:

- Klinisch labo: BELAC ISO 15189 sinds 2019
 - Interne QC
 - **Kwaliteit staal:** hBèta-globine (endogene QC) – **wordt gerapporteerd**
 - Kwaliteit analyse: negatieve en (zwak) positieve QC-staal
 - Externe QC
 - KPI:
 - % invalid results < 5% (WHO criterium)
 - TAT opvolging
- APD: Sciensano praktijkrichtlijn
 - Externe QC
 - AI-ondersteund cytologisch onderzoek (FDA- approved)

Quality assurance labo resultaten VITAZ

- Goede samenwerking tussen APD en klin. labo
 - Dagelijkse /op afroep ophalen van stalen bij aanvragende arts
 - Vlot stalentransport tussen beide labo's, gelegen op campus St-Niklaas
 - Vlotte communicatie van resultaten tussen beide laboratoria
- 1 gemeenschappelijk & duidelijk aanvraagformulier
- Rapportering:
 - hrHPV PCR resultaten: 1-3 werkdagen
 - PCR + cytologie: <= 28 d

Entiteit	01-10-2024 16:27
Aanvraag	5459281
☐ ALGEMENE INFO	
Extra info	afnamedatum: 13/09/2024
☐ Molec.ond.micro	
HPV type 16 DNA	Niet detecteerbaar
HPV type 18 DNA	Niet detecteerbaar
HPV type 31 DNA	Niet detecteerbaar
HPV type 33 DNA	Niet detecteerbaar
HPV type 35 DNA	Niet detecteerbaar
HPV type 39 DNA	Niet detecteerbaar
HPV type 45 DNA	Niet detecteerbaar
HPV type 51 DNA	Niet detecteerbaar
HPV type 52 DNA	Niet detecteerbaar
HPV type 56 DNA	Niet detecteerbaar
HPV type 58 DNA	Niet detecteerbaar
HPV type 59 DNA	Niet detecteerbaar
HPV type 66 DNA	Niet detecteerbaar
HPV type 68 DNA	Niet detecteerbaar
HPV controle staalkwaliteit	kwaliteitsvol staal

Besluit: Laboratoriumaspecten rond HPV PCR

- ✓ Kwaliteitsvolle- evidence based analyses (full genotyping)
- ✓ 1 duidelijk aanvraagformulier
- ✓ Georganiseerde externe staalophaling
- ✓ Alle stalen naar klinisch labo
- ✓ Efficiënte staal & data-flow tussen beide labo's

Samenwerken met VITAZ

Neem contact op met één van de klinisch biologen of anatoom pathologen

KLIN. BIOLOGEN



Veroniek Saegeman



Elise Willems



Pascal Van Ranst



Karin Van Poucke



Greet Van der Jonckheyd



Leen Sergooris



Geert Mistiaen

Anatoom pathologen



Elisabeth Beerens



Saskia Deprez



Heidi Woestenborghs



Jonathan Eben



Sofie Van Renterghem

VRAGEN?

VOOR ONLINE DEELNEMERS:

U KUNT STEEDS VRAGEN STELLEN VIA DE CHATFUNCTIE.

DEZE VRAGEN WORDEN VERZAMELD DOOR DE MODERATOR EN
SAMEN MET DE VRAGEN UIT DE ZAAL **OP HET EINDE VAN DE
AVOND** VOORGELEGD AAN DE SPREKERS.

MIGRATIE VAN CYTOLOGIE NAAR HPV-GEBASEERDE BAARMOEDERHALSKANKERSCREENING: CASUS

DR. EVA VERBERCKMOES
HUISARTS

CASUS 1

Dame, 39j

G2P2A0, niet gevaccineerd voor HPV, eerder uitstrijkjes
NILM

02/2024: screeningsuitstrijkje toont L-SIL, geen HPV-
bepaling

Advies: Herhalen na 6 maanden

08/2024: controle-uitstrijkje: opnieuw L-SIL

Adviezen opvolging afwijkende uitstrijkjes ^{66,67}

Algemene beoordeling van het cervixepitheel	Beleidsvoorstel
Kwaliteit is onvoldoende.	Herhaal het uitstrijkje na 3-6 maanden.
Negatief voor intra-epitheliale leasie of maligniteit (NILM): deze categorie bevat alle normale uitstrijkjes en alle uitstrijkjes met uitsluitend reactieve veranderingen.	Normaal screeningsinterval: 3 jaar, behalve na eerste uitstrijkje: interval van 1 jaar ⁶⁶ . Begin screening: 25 jaar Eindeleeftijd screening: 64 jaar
'Atypical Squamous Cells of Undetermined Significance' (ASC-US)	hrHPV-test: • hrHPV-positief: onmiddellijke verwijzing voor colposcopie en biopsie. • hrHPV-negatief: uitstrijkje na 12 maanden ⁶⁶ .
ASC-US+infectie	Infectie + hrHPV-negatief: herhaling na behandeling van de infectie maar ten vroegste 3 maanden na het vorige uitstrijkje. Infectie + hrHPV-positief: eerst infectie behandelen, dan colposcopie.
ASC-H (atypische squameuze cellen, H-SIL kan niet met zekerheid uitgesloten worden)	Verwijzen naar gynaecoloog voor colposcopie en biopsie.
L-SIL (HPV-effect, CIN I)	Uitstrijkje na 6 maanden: • HPV-positief: colposcopie en biopsie. • HPV-negatief: herhaal na 12 maanden.
H-SIL (CIN II, CIN III, CIS)	Verwijzen naar gynaecoloog voor colposcopie en biopsie.
Aanwezigheid van normale endometriumcellen: <40 jaar: wordt niet vermeld >40 jaar: aanwezigheid wordt vermeld, doch wordt niet beschouwd als epitheliale afwijking	Aanwezigheid van endometriumcellen interpreteren in de klinische context: men- ses? Eerste helft menstruele cyclus? Hormonale substitutie? Intra-uterien voorbehoedsmiddel? Endometriumcellen na de menopauze moet steeds verder onderzocht worden: verwijzing naar de gynaecoloog voor gecombineerde colposcopie en hysterosco- pie, met eventueel biopsienamen indien mogelijk.
'Atypical Glandular Cells' (AGC): atypische glandulaire cellen, endocervicaal, endometriaal of NOS (Not Otherwise Specified: niet nader gespecificeerd)	Verwijzen naar gynaecoloog voor colposcopie, biopsie, endocervicale en endo- metriale weefselafname.
AGC-voorkeur neoplasie	Verwijzen naar gynaecoloog.
AIS-ecc: endocervicaal adenocarcinoma in situ	Verwijzen naar gynaecoloog.
Invasief carcinoom, plaveiselcel- of adenocarcinoom	Verwijzen naar gynaecoloog.
Normaal uitstrijkje na behandeling voor H-SIL of AIS-ecc	Na excisionele of ablatieve behandeling voor CIN II, CIN III of AIS: uitstrijkje 6, 12 en 24 maanden na behandeling. Ook colposcopie en hrHPV-test 6 maanden na behandeling. Jaarlijks uitstrijkje tot 5 jaar na behandeling. Daarna normaal screeningsinterval. Na excisionele of ablatieve behandeling voor CIN I: uitstrijkje 6, 12 en 24 maanden na behandeling. Daarna normaal screeningsinterval.

Waarom HPV bepaling?

Impact wachttijd na afwijkend uitstrijkje en verdere onderzoeken



Snelle actie na positieve HPV test

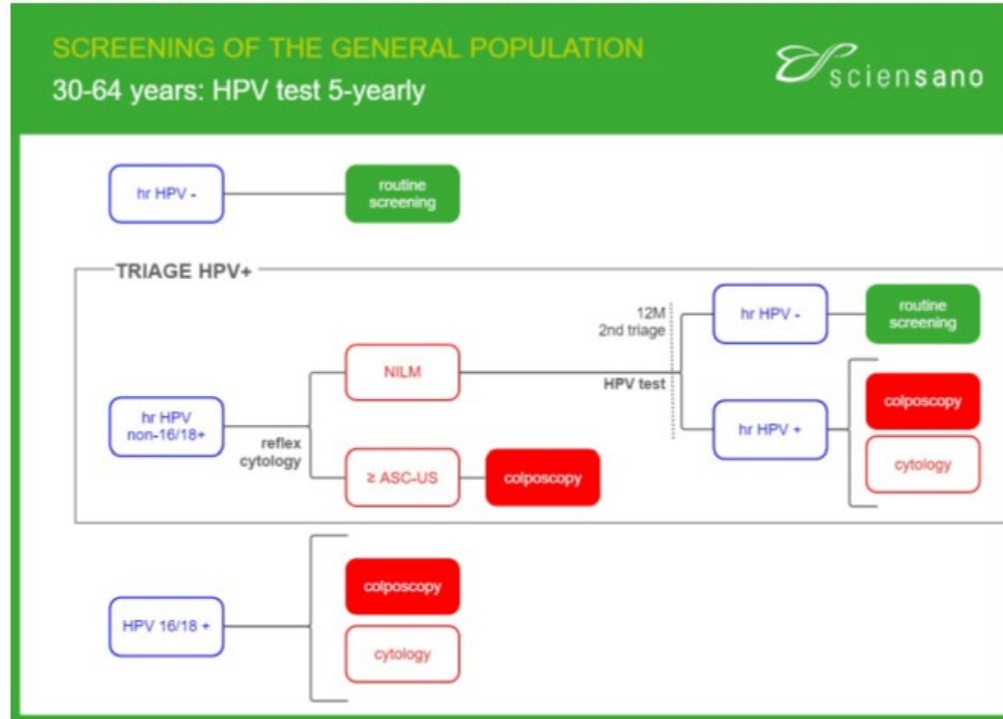
Dame, 39j

Bijkomende HPV bepaling :
NEGATIEF voor een hoog-risico HPV

Contact met gynaecoloog: controle na 6-12 maanden.

Nieuwe richtlijnen:

FIGURE 2: SCREENING ALGORITHM FOR 30-64 YEAR OLDS, IN THE GENERAL POPULATION (version 1 - dd 20241015)



Remark: A hrHPV positive result is always followed by a reflex cytology (both in the initial screening and 2nd triage 12 months later)

Casus 2

Dame, 25 jaar, gevaccineerd voor HPV

09/2020: L-SIL

controle na 6 maanden

10/2021: ASC-US, HPV type 53 (intermediair risico)

Controle na 6-12 maanden

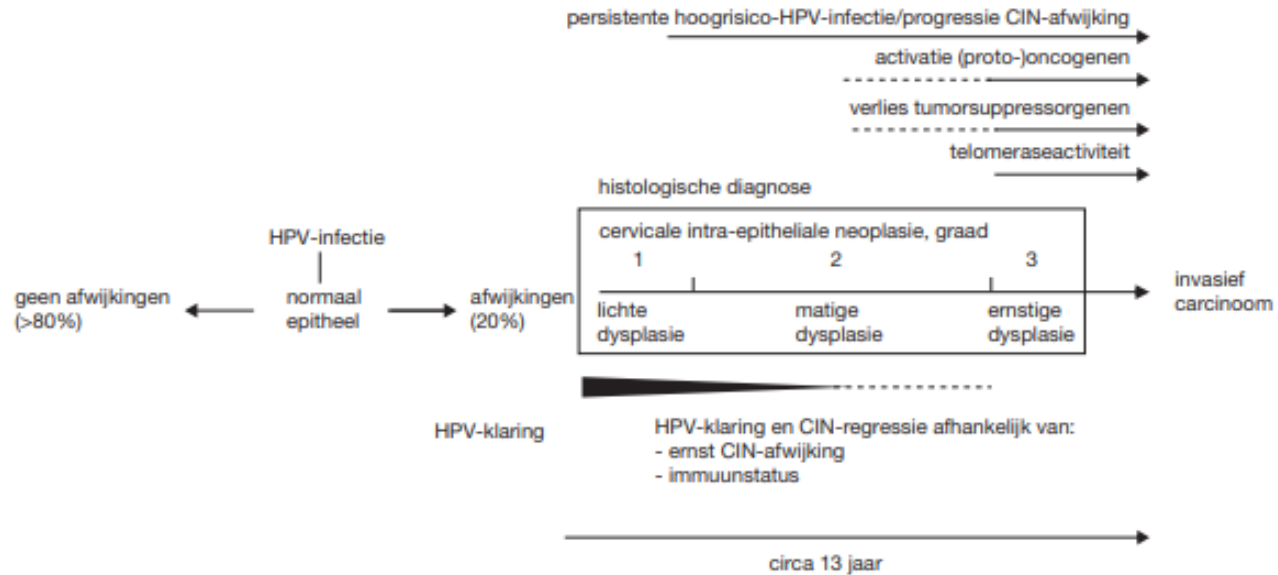
09/2022: ASC-US, negatief voor hoogrisico HPV

Controle na 1 jaar

07/2023: NILM, negatief voor hoogrisico HPV

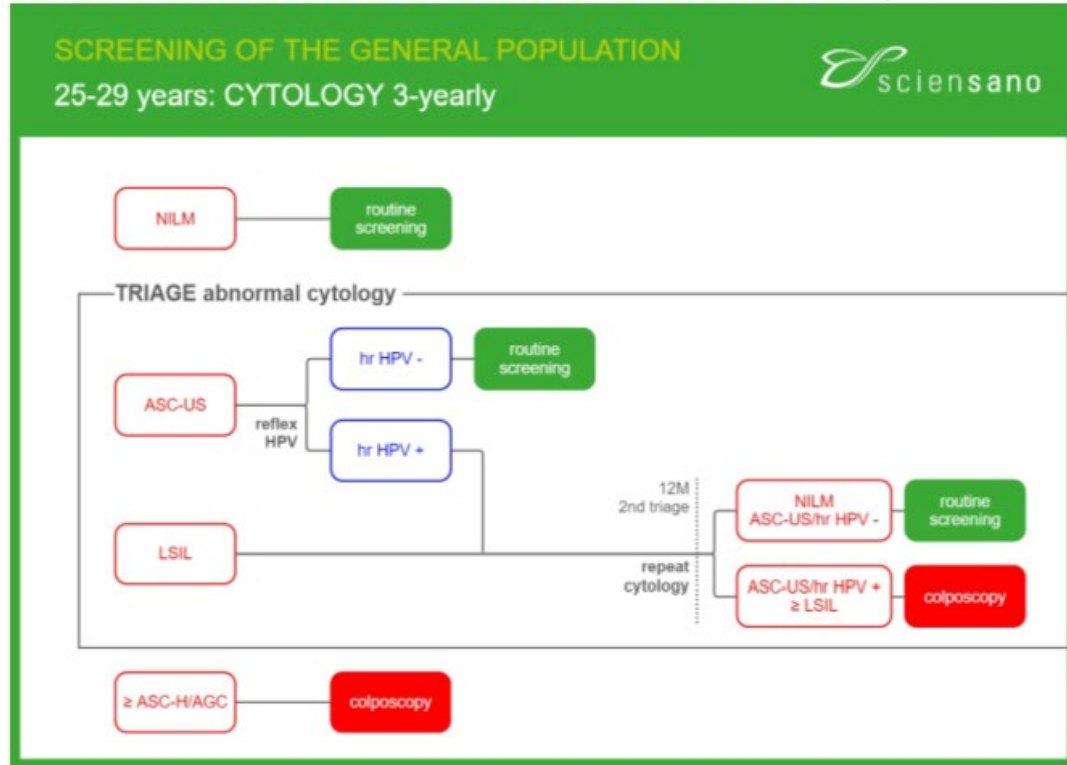
VITAZ

Figuur: Model van HPV-infectie en pathogenese van baarmoederhalskanker.



Nieuwe richtlijnen

FIGURE 1: SCREENING ALGORITHM FOR 25-29 YEAR OLDS, IN THE GENERAL POPULATION (version 1 - dd 20241015)



≥ASC-H/AGC = ASC-H/AGC or a more severe lesion (HSIL, SCC, AIS, AC)

Remark: An ASC-US result is always followed by a reflex HPV test (both in the initial screening and in the 2nd triage 12 months later)

VRAGEN?

VOOR ONLINE DEELNEMERS:

U KUNT STEEDS VRAGEN STELLEN VIA DE CHATFUNCTIE.

DEZE VRAGEN WORDEN VERZAMELD DOOR DE MODERATOR EN
SAMEN MET DE VRAGEN UIT DE ZAAL **OP HET EINDE VAN DE
AVOND** VOORGELEGD AAN DE SPREKERS.

VRAGEN & CONCLUSIE

DR. MARC COENEN | GYNAECOLOGIE – VERLOSKUNDE | VITAZ

DR. VERONIEK SAEGEMAN | KLINISCHE BIOLOGIE | VITAZ

U ONTVANGT KORTELIJNS EEN MAIL MET DE LINK NAAR DE PRESENTATIES EN
DE VIDEO-OPNAME.