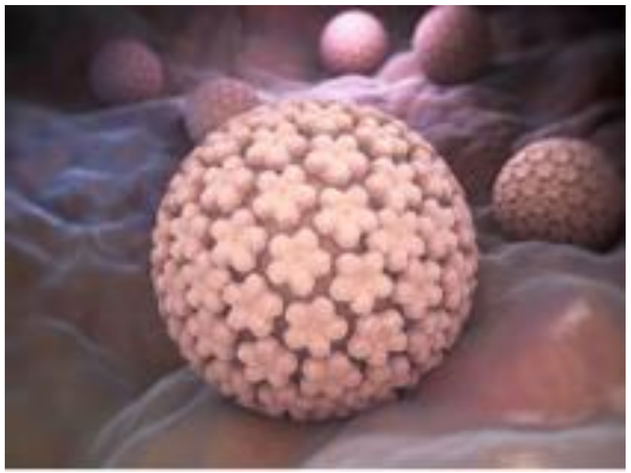
BD Solution for Cervical Cancer Screening

- and how it can help addressing current challenges

BD

Why cervical cancer screening?

- Cervical cancer is the 4th most common cancer among women globally, with an estimated 604 000 new cases and 342 000 deaths in 2020.[1]
- Human papillomavirus (HPV) infection is recognized as a major causative factor in the development of cervical cancer.[2]
- In sexually active people, the viral infection rate might be as high as 80%.[3]
- Vaccination against HPV and screening and treatment of pre-cancer lesions is a cost-effective way to prevent cervical cancer. [4]
- Cervical cancer can be cured if diagnosed at an early stage and treated promptly.[5]



1.Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021:71:209–49. doi:10.3322/caac.21660.
2. Zur Hausen, H. 2002. Papillomaviruses and cancer: from basic studies to clinical application. Nat. Rev. Cancer 2:342–350.
3. Szymonowicz KA, Chen J. Biological and clinical aspects of HPV-related cancers. Cancer Biol Med. 2020 Nov 15;17(4):864-878. doi: 10.20892/j.issn.2095-3941.2020.0370. Epub 2020 Dec 15. PMID: 33299640; PMCID: PMC7721094.
4. Lei et al. (2020) HPV Vaccination and the Risk of Invasive Cervical Cancer. N Engl J Med 2020;383:1340-8. DOI: 10.1056/NEJMoa1917338
5. WHO Global strategy towards the elimination of cervical cancer as a public health problem. 2019.

WHO Call for Action

Elimination by end of 21st century = Cervical cancer incidence < 4 cases/per 100 000 women/year

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

"2030" Targets 90-70-90

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

90% of women identified with cervical disease receive treatment and care

https://www.who.int/initiatives/cervical-cancer-elimination-initiative

WHO Call for Action

vrt nws

9-12-2022

Straks om de vijf jaar HPV-test voor vrouwen

De ministers van Volksgezondheid zijn het in de interministeriele conferentie eens geraakt over een nieuwe baarmoederhalsscreening.

Vrouwen tussen 30 en 64 jaar zullen binnenkort om de vijf jaar een HPV-test kunnen laten afnemen, in plaats van een klassiek uitstrijkje om de drie jaar. Dat meldt minister van Volksgezondheid Frank Vandenbroucke (Vooruit).

Tot nog toe werden vrouwen tussen 25 en 64 om de drie jaar uitgenodigd voor een gratis cytologisch onderzoek, het zogenaamde 'uitstrijkje', om te screenen op baarmoederhalskanker. Experts pleiten er echter al langer voor om dat onderzoek voor vrouwen boven de 30 jaar te vervangen door een HPV-test, die het humaan papillomavirus dat baarmoederhalskanker veroorzaakt opspoort.

De ministers van Volksgezondheid hebben daar nu een akkoord over bereikt, meldt Vandenbroucke. Is de HPV-test positief, dan volgt nog een klassiek uitstrijkje. De federale overheid trekt daar 40 miljoen euro voor uit. (BELGA)

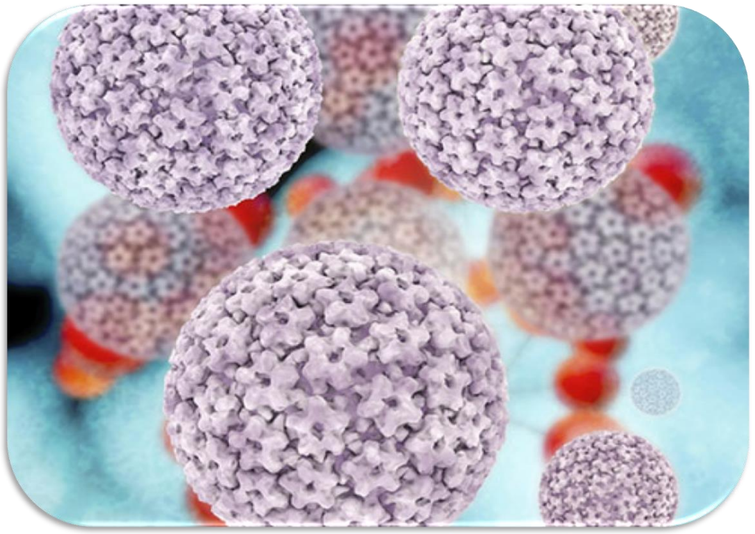
"Binnenkort om de vijf jaar HPV-test voor vrouwen tussen 30 en 64 jaar"

"...Vrouwen tussen 30 en de 64 jaar zullen voortaan om de vijf jaar uitgenodigd worden voor een HPV-test. Is die positief, dan volgt nog een klassiek uitstrijkje..."

https://www.vrt.be/vrtnws/nl/2022/12/09/binnenkort-om-de-vijf-jaar-hpv-test-voor-vrouwen-tussen-30-en-64/

The challenges

For HPV screening to deliver its promise, it needs...

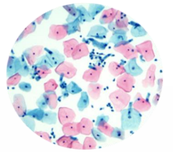


- Reliable, evidence-backed HPV-tests with well defined clinical cut-offs[1,2]
- The appropriate data resolution for optimal clinical management – extended GT information, accurate information on multiple infections
- Versatile high-throughput instrumentation
- A solution that can address the challenges of the future
- A partner company with experience in automation and high-throughput HPV screening (project management, technical and application support, production and supply chain)

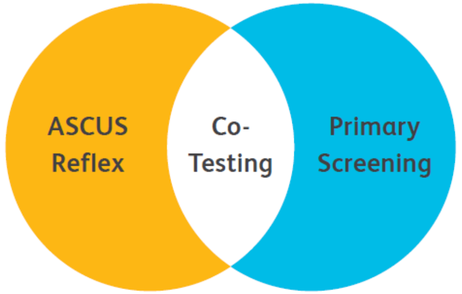
1. Meijer CLJM *et al.* **Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women of 30 years and older.** Int J Cancer. 2009 February 1; 124(3): 516–520. doi:10.1002/ijc.24010.
2. Arbyn M *et al.* 2020 list of human papillomavirus assays suitable for primary cervical cancer screening. 2021. Clinical Microbiology and Infection 27 (2021) 1083 - 1095

BD's Cervical Cancer Screening Solution

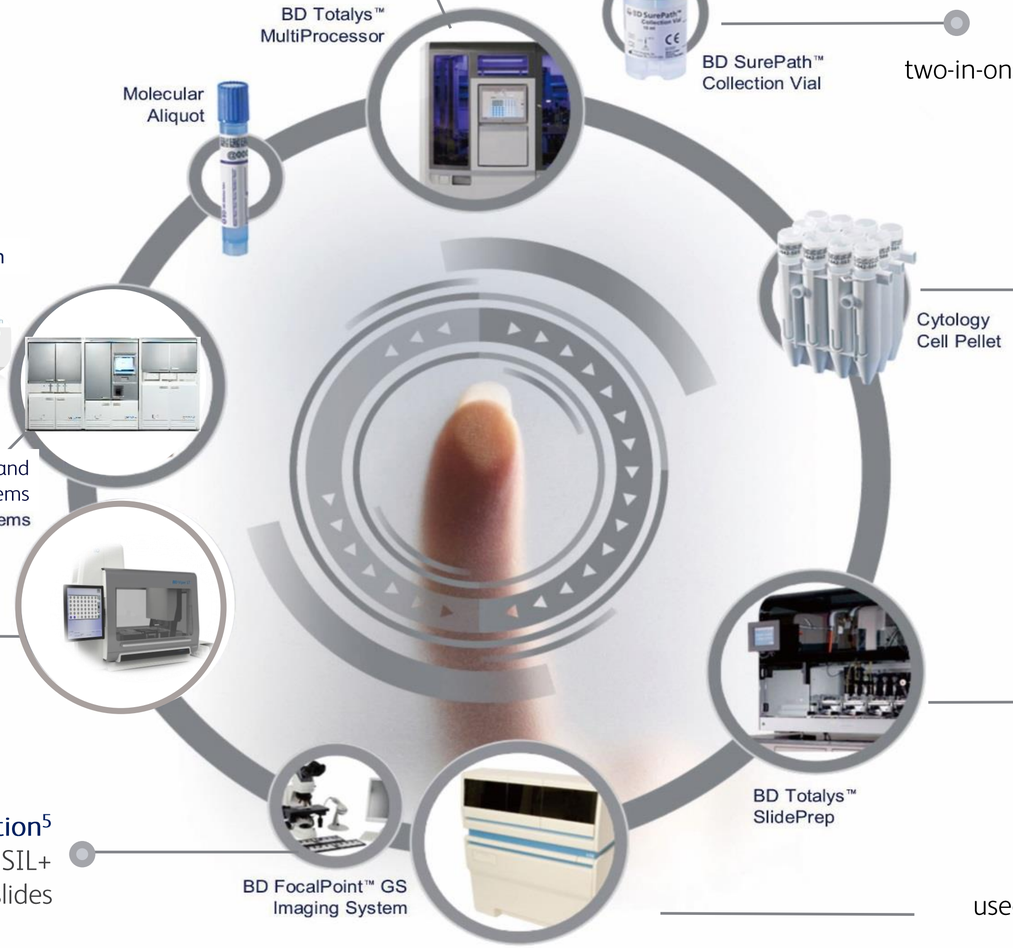
Flexible sample runs
Processes up to 96 samples simultaneously, optional molecular aliquots, ensures chain of custody



100% of cells to the lab[1,4]
two-in-one brushes with detachable heads, and ethanol-based vials that preserve sample



CE marked & FDA approved



Through **cell enrichment**[2,3,4]
the test exhibits lower unsats than any other method, decreasing patient callbacks and sample reprocessing

Fully automated HPV testing with the BD Onclarity™ HPV Assay

Up to **336 prepared and stained slides** in a single shift with one operator[6]

Increased abnormal cell detection[5]
process results in a clear presentation of cells to increase HSIL+ detection compared to that of conventional pap slides

Advanced algorithms[7]
used to determine potential abnormalities and rank slides

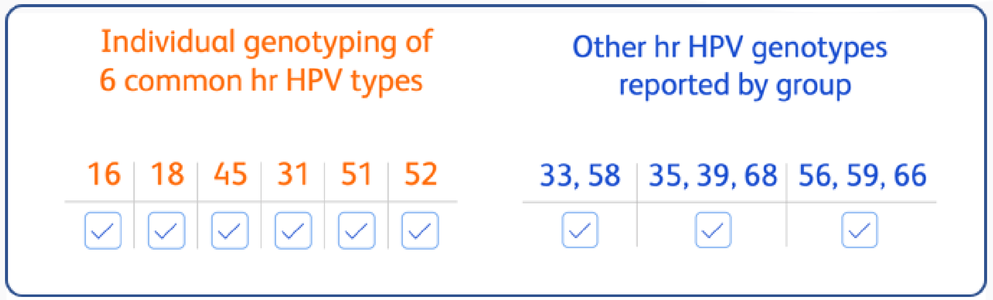
1. Bigras G, *et al.* Keeping Collecting Device in Liquid Medium Is Mandatory to Ensure Optimized Liquid-Based Cervical Cytologic Sampling. *J Low Genit Tract Dis.* 7(3), 2003:168-174
2. Moriarty A *et al.* Unsatisfactory Reporting Rates .Arch Pathol Lab Med. 2009;133(12):1912–1916.
3. Sweeney B *et al.* Comparison of the Effectiveness of Two Liquid-Based Papanicolaou Systems in the Handling of Adverse Limiting Factors, such as Excessive Blood. *Cancer.* 2006;108(1):27
4. Marino J *et al.* Direct to vial experience with Autocyte PREP in a small new England regional cytology practice. *J Reprod Med.* 2001;46(4):353–358
5. Nance KV. Evolution of Pap testing at a community hospital , 10 years experience. *Diagn Cytopathol.* 2007;35(3):148–153.
6. Internal BD document, PD-08129-67
7. BD FocalPoint™ GS Imaging System (exUS User's Manual 500027657)

The assay at a glance

The BD Onclarity™ HPV Assay

Detects 14 hr-HPV genotypes and reports up to 9 results[1]

- **Individual results** for HPV genotypes with highest-risk for disease: **16, 18, 45, 31, 51** and **52**
- **Strategic grouped** results for lower risk HPV genotypes: **35/39/68, 33/58** and **56/59/66**



BD Onclarity™ HPV Assay provides accuracy of results to elevate your laboratory's performance

- **Individual results for 6 HPV genotypes** with highest risk for disease, 3 strategic grouped results for the other 8 high-risk genotypes[1]
- **DNA-based PCR assay** which makes the assay suitable for self-collection[1, 3]
- **E6/E7- based PCR design** significantly reduces the risk of false-negative results due to gene deletion after HPV integration[2]
- **No cross-reactivity** with low-risk HPV types minimizes the risk of false-positives[1]
- Validated for vaccinated women
- β-Hemoglobin as **internal control** - sample adequacy- and process control[1]
- **Negative and positive controls** with each batch of 30 specimens[1]

1. BD Onclarity™ HPV EU Package Insert (8089899, 2022-05)
2. Arroyo Muehr LS *et al.* Sequencing detects human papillomavirus in some apparently HPV-negative invasive cervical cancers *J Gen Virol*. 2020; 101:265-70
3. Arbyn, M. *et al.* Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. 2018. *Bmj* 363, k4823

Extended Genotyping

While HPV vaccination changed the landscape, some women REMAIN AT RISK and unmonitored

There are three different types of HPV vaccines:

The bi-valent HPV vaccine

- Protects against hrHPV genotypes **16** and **18**.[1,2]
- Initially approved by the EMA in 2007 and the FDA in 2009.[1,2]
- Voluntary withdrawn from the US in 2016.

The 4-valent HPV vaccine

- Protects against two hrHPV genotypes (HPV **16** and **18**) and two low-risk genotypes involved in genital warts (HPV **6** and **11**).[3,4]
- Initially approved by the EMA and the FDA in 2006.[3,4]
- No longer distributed in the US.

The 9-valent HPV vaccine

- Targets the same genotypes as the 4-valent vaccine and 5 additional hrHPV genotypes **HPV 31, 33, 45, 52** and **58**.[5,6*]
- Approved by the FDA in 2014 and by the EMA in 2015.[5,6]

While the **9-valent** HPV vaccine is now exclusively used in many countries, women who received the **earlier** vaccines have now entered the screening population.

Additionally, as the vaccinated population increases, HPV **16** and **18** (high-risk genotypes covered by the **bi-valent**, **4-valent** and **9-valent** vaccines) are decreasing in prevalence.[7]

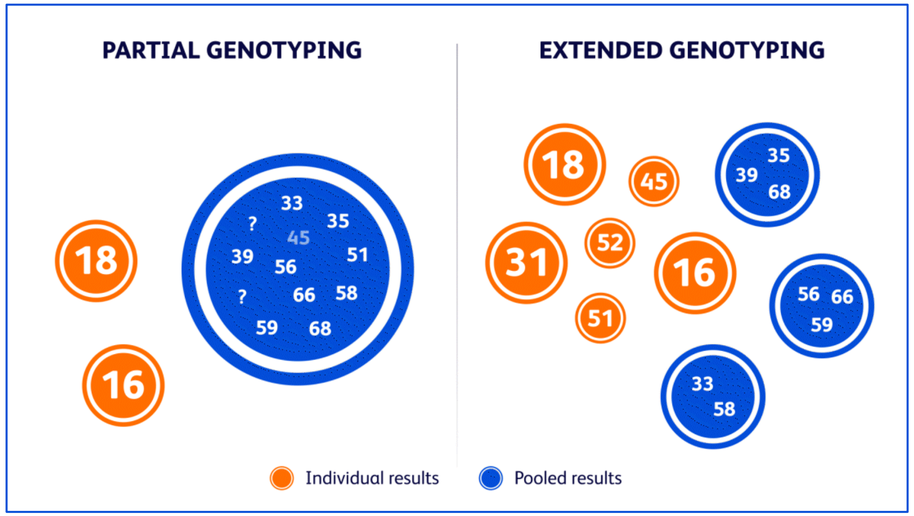
EMA, European Medicines Agency; FDA, Food and Drug Administration; HPV, human papillomavirus; hr, high-risk; OR, odds ratio; US, United States.

1. European Medicines Agency. Cervarix Product information. 2021. 2. Food and Drug Administration. Cervarix Package insert.. 3. European Medicines Agency. Gardasil Product information. 2022. 4. Food and Drug Administration. Gardasil Package insert. 5. European Medicines Agency. Gardasil 9 Product information. 2022. 6. Food and Drug Administration. Gardasil 9 Package insert. 7. Wright TC *et al.* HPV infections and cytologic abnormalities in vaccinated women 21–34 years of age: Results from the baseline phase of the Onclarity trial. *Gynecol Oncol.* 2019;153(2):259–65.

What are the MAIN Differences between an HPV assay with partial genotyping versus EXTENDED GENOTYPING?

The difference is in the data.

HPV assays with extended genotyping detect at least 6 individual high-risk HPV genotypes.[1]



Individual identification of high-risk genotypes is essential to reveal the true risk of CIN3+ disease.[1]

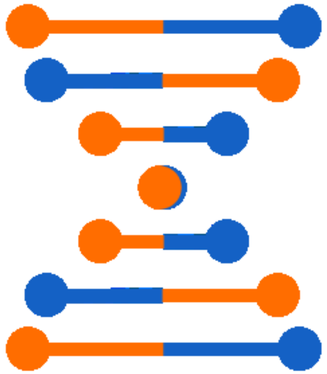
CIN, cervical intraepithelial neoplasia.

1. Bonde JH *et al.* Clinical Utility of Human Papillomavirus Genotyping in Cervical Cancer Screening: A Systematic Review. *J Low Genit Tract Dis.* 2020;24:1–13.

SO, WHAT IS the CLINICAL Value of an HPV assay with EXTENDED GENOTYPING?

Extended genotyping provides specific, actionable insights on an extended set of HPV genotypes.[1-6]

Extended genotyping can identify HPV 31.[1]



Extended genotyping enables tracking of genotype-specific hrHPV persistence.[3-6]

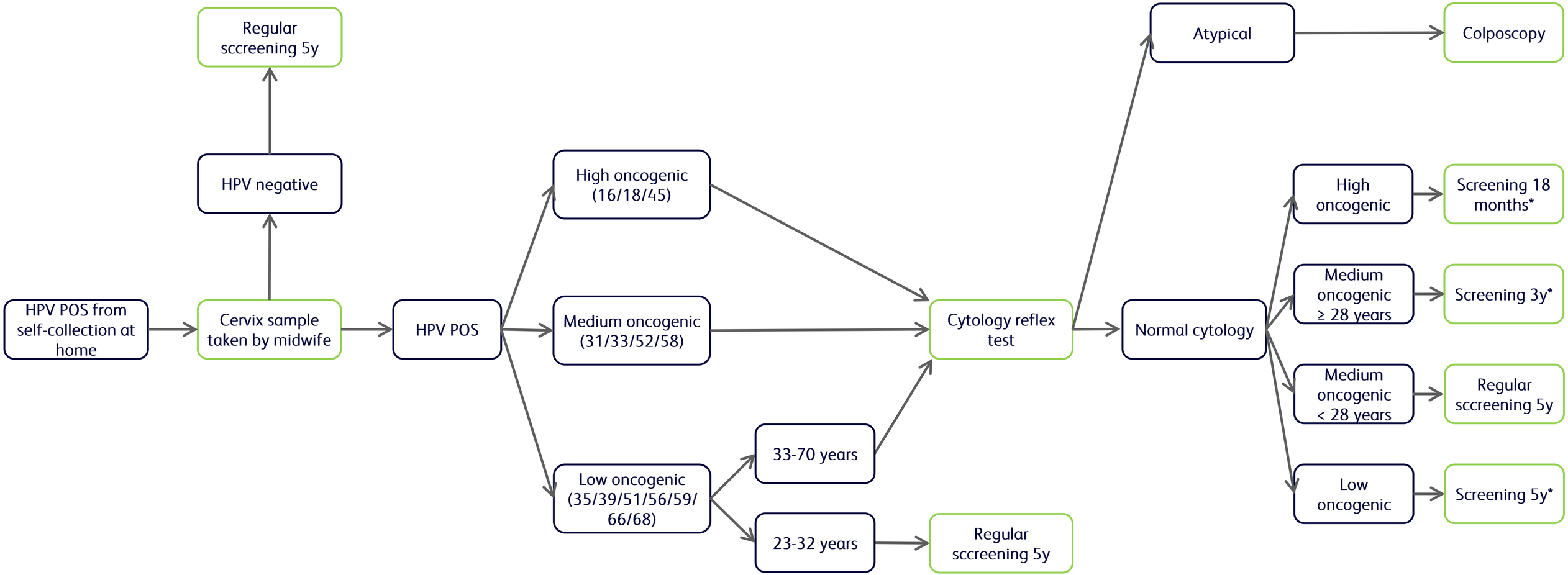
Extended genotyping enhances clinical management by providing insight to assist in reducing patient callbacks and unnecessary colposcopies,[1-6] thus potentially reducing costs and patient's anxiety

EXTENDED GENOTPYING ENHANCES CLINICAL MANAGEMENT AND ENABLES LONG-TERM PATIENT MONITORING, WITH RESULTS YOU CAN TRUST[1-6]

HPV, human papillomavirus; hr, high risk.

1. Stoler MH *et al.* Stratified risk of high-grade cervical disease using onclarity HPV extended genotyping in women, ≥25 years of age, with NILM cytology. *Gynecologic Oncology.* 2019;153(1):26–33. 2. Bonde JH *et al.* Bayesian analysis of baseline risk of CIN2 and ≥CIN3 by HPV genotype in a European referral cohort *Int J Cancer*. 2019;145:1033–41. 3. Bonde JH *et al.* Clinical Utility of Human Papillomavirus Genotyping in Cervical Cancer Screening: A Systematic Review. J *Low Genit Tract Dis.* 2020;24:1–13. 4. Elfgren K *et al.* Management of women with human papillomavirus persistence: long-term follow-up of a randomized clinical trial. *Am J Obstet Gynecol.* 2017;216:264.e1–7. 5. Radley D *et al.* Persistent infection with human papillomavirus 16 or 18 is strongly linked with high-grade cervical disease. *Hum Vaccin Immunother* 2016;12(3):768–72. 6. . Bodily J, Laimins LA. Persistence of human papillomavirus infection: keys to malignant progression. *Trends Microbiol.* 2011;19(1):33–9.

Extended genotyping in practice: Sweden[1]



*special monitoring of selected parameters based on oncogenic type may lead to different call intervals/follow-ups

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Self-collection

BD's offer for HPV Screening from at-home or at clinics self-collected vaginal samples

May 2021

BD Onclarity™ HPV Assay CE marked for Self-Collection[1]

Available on BD Viper™ LT and BD COR™ Systems for molecular testing[1]

At-home self-collection in cervical cancer screening

Convenient, easy and safe for women[2]

Equals doctor-collected samples in diagnostic quality[3]

HPV self-sampling makes screening accessible to women who don't participate in screening or have limited access to screening[2]

Extended Genotyping

Combining HPV self-sampling with extended genotyping allows for focus on those women at highest risk while not overtreating[4]

Screening strategies employing HPV tests with simultaneous genotyping can improve cervical cancer screening for women and health care providers by allowing risk stratification[4]

1. http://www.pd-announces-industry-first-ce-marked-assay-for-hpvscreening-from-at-home-self-collected-vaginal-samples-301290462.html newswire.com/news-releases/b
2. Nishimura H, *et al.* HPV self-sampling for cervical cancer screening: a systematic review of values and preferences. *BMJ Global Health* 2021;6:e003743. doi:10.1136/bmjgh-2020-003743
3. Arbyn, M. *et al.* (2018) Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. *Bmj* 363, k4823
4. Rohner E. *et al.* **Extended HPV genotyping to compare HPV type-distribution in self and provider-collected samples for cervical cancer screening.** Cancer Epidemiol Biomarkers Prev. 2020 December ; 29(12): 2651–2661. doi:10.1158/1055-9965.EPI-20-0674.

BD Viper™ LT and BD COR™

Flexible HPV testing automation for any lab volume

BD Viper™ LT System[1]

HPV testing automation for low- to mid-volume laboratories

The BD Viper™ LT System is a compact, self-contained table-top system, that automates sample extraction and real-time PCR for extended genotyping with the BD Onclarity™ HPV Assay all in one instrument for added ease, convenience, and walkaway time.

BD COR™ System[1]

Integrated high-throughput automation

The BD COR™ System is a scalable solution that fully automates the processing of the BD Onclarity™ HPV Assay with extended genotyping. It is suited for high-volume laboratories requiring advanced integrated automation from sample to result, with minimal user interventions and outstanding long walkaway times.

1, BD-60230_BD Onclarity Sales Sheet_EMEA

THANK YOU!