

Jesper Bonde DENMARK

# **HPV Self-sampling**

Current situation and evolution in the future



# Jesper Bonde,

PhD, Dipl.Med.Sci Senior Researcher Laboratory Manager

Molecular Pathology
Dept. Pathology & Clinical Research Centre
Copenhagen University Hospital,
Hvidovre, Denmark

Member, National Health Authority, Cervical cancer screening guideline working group

Member, National Cervical Screening Steering Group

BD Diagnostics Genomica Hologic Self-Screen

### **SELF-SAMPLING**

A cervical screening sample taken by the woman either without medical staff assistance or with supervision; in the privacy of own home, or at clinic.

Self samples for cervical cancer screening are suitable for HPV tests

Self-sample material types include:

Self-sampling utensils (brush)
Urine collection devices



## SELF-SAMPLING IS AN EQUALLY GOOD SAMPLE AS A CLINICIAN COLLECTED SAMPLE

#### META ANALYSIS

#### COMPARATIVE PERFORMANCE CLINICAL IMPLEMENTATION VALIDATION METHODOLOGY **ANALYSIS STUDIES**

#### OPEN ACCESS Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated Marc Arbyn, 1 Sara B Smith, 2 Sarah Temin, 3 Farhana Sultana, 4,5 Philip Castle, 2,6 on behalf of the Collaboration on Self-Sampling and HPV Testing

OBJECTIVE
To evaluate the diagnostic accuracy of high-risk human papillomavirus (hritPV) assays on self samples and the efficacy of self sampling strategies to reach Medline (PubMed), Embase, and CENTRAL from 1 January 2013 to 15 April 2018 (accuracy review), and 1 January 2014 to 15 April 2018 (participation

REVIEW METHODS

WHAT IS ALREADY KNOWN ON THIS TOPIC

WHAT THIS STUDY ADDS

than on clinician samples, for hrHPV assays based on polymerase chain reaction or signal amplification, respectively. Mailing self sample kits to the woman's home address generated higher response rates to have a sample taken by a clinician than invitation intention to treat analysis of 2,3, 9% confidence intend 1.8 for 2,91, Opt-in strategies where women had to request a self sampling til were generally not more effective than invitation fleters (leaflatve participation of 1,22, 9% confidence interval (0.9) to 1,41). Direct offer of self sampling devices to women in communities that were underscreened generated high participation rates (27%), Substantial intensity heterogeneity was noted (b²-95%). intention-to-treat-analysis of 2-33-95% confidence

REVIEW MCTHOOS

Accuracy review: httpPV assay on a vaginal self sample and a clinician sample; and verification of the presence of cervical intraphibital neoplasta grade 2 or worse (CIN2-) by colposcopy and biopy in all enrolled women or its women with positive tests. Participation review: study population included CONCLUSIONS
When used with hrHPV assays based on polymerase chain reaction, testing on self samples was similarly accurate as on clinician samples. Offering self sampling kits generally is more effective in reaching underscrosed departs that exacting institutions. women who were irregularly or never screened; women in the self sampling arm (intervention arm) were invited to collect a self sample for hrHPV testing; ned women than sending invitations However, since response rates are highly variable among settings, pilots should be set up before women in the control arm were invited or reminded regional or national roll out of self sampling to undergo a screening test on a clinician sample; participation in both arms was documented; and a

56 accuracy studies and 25 participation trials were reaction were as sensitive on self samples as on low compared with rates in less developed cou clinician samples to detect CIN2+ or CIN3+ (pooled However, demographic and social disparities in the burden of disease exist. In the United States, incidence buttern of disease exist. in the United States, incidence is higher among Hispanie (8.) por 100000 women years in 2011-15, age adjusted using the 2000 US population as reference) and black (8.4) populations, versus the white population (7.a).<sup>2</sup> The contrasts can be explained by differences in access to screening. In western and northern Europe, both cervical cancer incidence and mortality have decreased after widespread screening.<sup>3</sup> In eastern Europe, where the med on clinician samples when using a high-risk human papillomavirus rage or quality, or both, of screening often is low onse rates for hrHPV testing are higher for self sampling kits than for coverage or quanty, or both, or screening onen is low to moderate, incidence has not dropped to the same extent and in some countries trends are even rising. \*4 To be noted, 85% of cases of cervical cancers occur in less developed countries, with incidence rates reaching 35 per 100 000 women years in eastern Africa. Most cervical cancer cases occur in women who have never been screened for cervical cancer, or

Journal of Citrical Virology 99-100 (2018) 22-30 Contents lists available at ScienceDirect Journal of Clinical Virology

Safety and acceptability of human papillomavirus testing of self-collected specimens: A methodologic study of the impact of collection devices and HPV assays on sensitivity for cervical cancer and high-grade lesions



Maarit K. Leinonena-, Kristina Scheea, Christine M. Jonassenb, C. A. Kathrine Lieb, Camilla F. Nystrand<sup>b</sup>, Anbjørg Rangberg<sup>b</sup>, Ingegerd E. Furre<sup>d</sup>, Marzena J. Johansson<sup>b</sup> Ameli Tropé<sup>6s</sup>, Katrine D. Sjøborg<sup>8</sup>, Philip E. Castle<sup>b</sup>, Mari Nygård<sup>a</sup>

Department of Benerols, Center Rajeary of Norwey, 625°9 Cale, Norwey
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#### ARTICLE INFO

Background: Comparative data on different self-collection methods is limited.

Objective: To assess the impact of hrMPV meting of two self-collection devices for detection of cervical cardinoma and high-yards lesions.

Study design: These hundred ten patients collected two cervicovaginal specimens using a brush (Evalyn Brush) and a swab (FLOQSwabs\*\*), and filled a questionnaire at home. Then, a physician at the clinic took a cervical secimen into PreservCyt, buffer for hrHPV testing and cytology. All specimens were tested using Anyplex." II PV28, Cobas. 4800 HPV Test and Xpert HPV.

Results: Performance comparison included 45 cervical carcinomas and 187 patients with premalignant lesions Compared to the physician specimen, hrHPV testing of Evalyn Brush showed non-inferior sensitivity for CIN3 -frelative sensitivity of Anyplex" 0.99; Cobas" 0.96; Xpen HPV 0.97) while hHPV testing of FLOQSwabs' privative sensitivity of largifact\* 0.90, Cabal 50%, Spec 1999 (197) adds 1897 vesting of FLOQNavid-tioned address controlled project\* 0.90, Cabal 50%, Spec 1999 (197) and 1970 (197) in State sensi-ted and the sensitivity of the sensitivit

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#### High-grade cervical intraepithelial neoplasia in human papillomavirus self-sampling of screening non-attenders

J U H Lam<sup>1</sup>, K M Elfström<sup>2</sup>, D M Ejegod<sup>1</sup>, H Pedersen<sup>1</sup>, C Rygaard<sup>1</sup>, M Rebolj<sup>3</sup>, E Lynge<sup>4</sup>, K E Juul<sup>5</sup>, S K Kjær<sup>5,6</sup>, J Dillner<sup>2,7</sup> and J Bonde\*,1,3

Department of Pathology, Copenhagen University Hospital Hydovre, Kettegård Allé 30, 2650 Hydovre, Copenhagen, Denmark \*Department of Laboratory Medicine, Karolinska Institutet, Stodsholm 14186, Sweden; \*Tolinical Research Centre, Copenhagen University Hospital Hvidovre, Kettegård Allé 30, 2650 Hvidovre, Copenhagen, Denmak; \*Department of Public Health, University of Copenhagen, Copenhagen 1014, Denmark; <sup>5</sup>Unit of Virus, Lifestyle and Genes, Danish Cancer Society Research Center, Openhagen 2100, Denmark; <sup>6</sup>Department of Obstetrics and Gynecology, Copenhagen University Hospital Rigshospitale Copenhagen 2100, Denmark and <sup>3</sup>Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm 14186,

Background: Self-sampling for human papillomavirus (HPV) offered to women who do not participate in cervical cancer screening is an increasingly popular method to increase screening coverage. The rationale behind self-sampling is that uncreened women harbour a high proportion of undetected precareer lesions. Here, we compare the cervical intrappithelial necolasis guide 2 or worse (s-CND2) detection rate between non-attenders who participated in self-sampling and women attending routine screen.

Methods: A total of 23632 women who were qualified as non-attenders in the Copenhagen Region were invited for HPV-based self-sampling. Of these, 4824 women returned a self-sample, and HPV-positive women were referred for oxtology and HPV co-Sensanjunja. O unione were relative as sensanjung, and in "Publisher where relative to springly and in "Or testing as follow-up. The entire cohort and a efference cohort (3447 noutrinely screened women) were followed for histopathology confirmed  $\geqslant$  CIN2. Odds ratio (OR) and the relative positive predictive value of  $\geqslant$  CIN2 detection between the two populations

Results: Women participating in self-sampling had a higher ≥ CIN2 detection than women undergoing routine cytology-based screening (OR = 1.83, 95% Ct: 1.21–2.77) and a similar detection as routinely screened women tested with cytology and HPV testing (OR = 1.03, 95% Ct: 0.75–1.40). The positive predictive value for \$CINZ was higher in screening non-attenders than in routinely HPV- and cytology-screened screened women (36.5% vs 25.6%, respectively).

Condusions: Self-sampling offered to non-attenders showed higher detection rates for >CIN2 than routine cytology-based creening, and similar detection rates as HPV and cytology co-testing. This reinforces the importance of self-sampling for screening non-attenders in organised cervical cancer screening.

Published by Springer Nature on behalf of Cancer Research UK.

A major challenge in presenting cervical cancer is the large women 90-05 years of age are invoked every 5-years. Approximately proportion of vowen who are exercining programme, women recommendations, with mixor regional and annual flactuations and 32-09 year are invoked every 5 years for exercining, and (Danish) Quality, Assumence Danishes for the Gervical General Consistence of the Carvical Construction of the Construction of the Carvical Constru

\*Correspondence: Dr J Bonde; E-mail: jesper.hansen.bonde@regjonh.dk Received 10 April 2017; revised 15 September 2017; accepted 26 September 2017



Advance Online Publication: 14 November 2017



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



 $M. \ Arbyn^{a_{a^{n}}}, E. \ Peeters^{n}, I. \ Benoy^{b_{a^{n}},c_{a^{n}}}, D. \ Vanden \ Broeck^{b_{a^{n}},c_{a^{n}},c_{a^{n}}}, \ J. \ Bogers^{b_{a^{n}},c_{a^{n}},c_{a^{n}}}, P. \ De \ Sutter^{f},$ G. Donders gh., W. Tjalma, S. Weyers, K. Cuschieri, M. Poljak, J. Bonde, C. Cocuzza, F.H. Zhaoq, S. Van Keer, A. Vorsters

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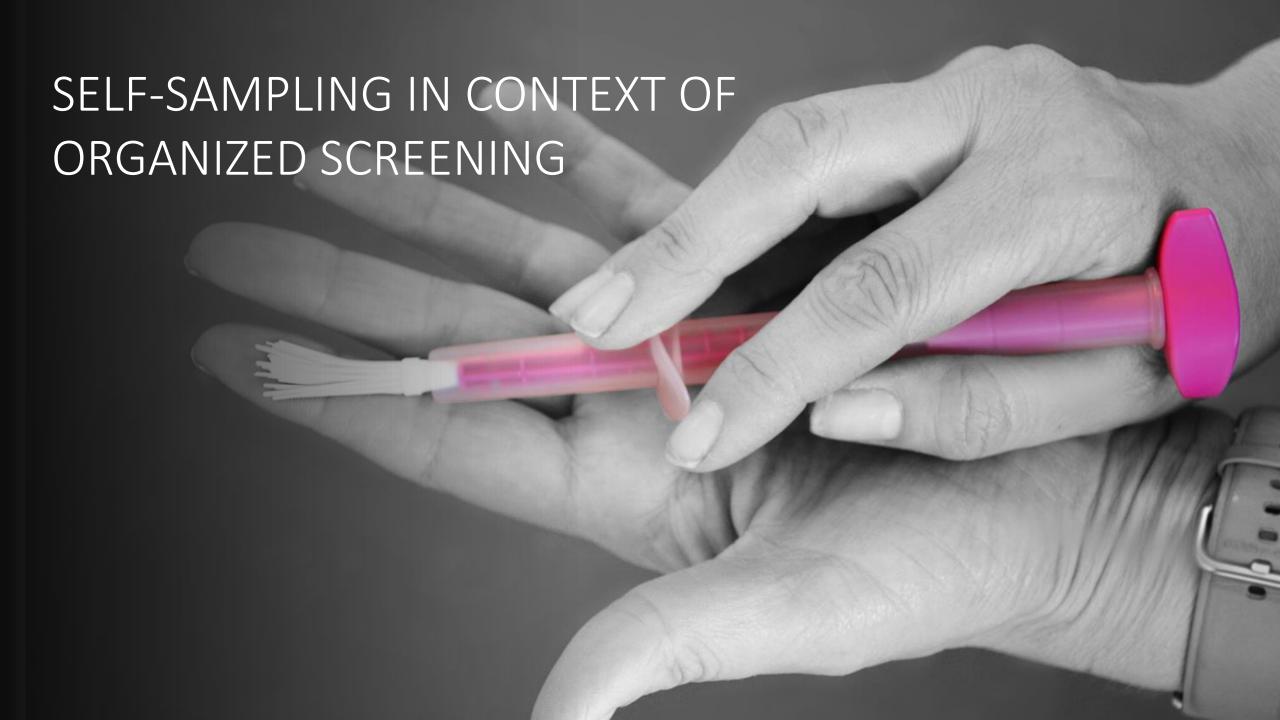
#### ARTICLE INFO

However, insufficient evidence is available for specific HPV assay/self-sample device combinations. Objectives: The VALHUDES protocol is designed as a diagnostic test accuracy study that aims to compare the clinical sensitivity and specificity of particular hrHPV assay(s) on vaginal self-samples and first-void-urine, collected in agreement with standardized protocols, with hrHPV testing on matched clinician-taken samples. collected in agreement with instandarded portocols, with InPPS watering on matched clinicians labes amplies. Stayl design: We have invested entailed women referred to a colposcopy clinic are invitation to cellate at flat revolutions sample and one or more variety at self-amplies with particular devices from collection of a cervical sample by a children and one or more variety at self-amplies with particular devices force collection of a cervical sample by a children and consideration of a cervical sample by a substantial consideration of a cervical sample by a children and consideration of the collection of the collection of a cervical sample by a Realize. A first VALITATIONS startly hast strain in heightum in Denmier 2017 with memoliant from face or optocopy recent The Hold National assists of best and the second Hold Hold National Hold Nation

\* Corresponding author at Unit of Cancer Epidemiology, Belgian Cancer Centre, Sciencano, J. Wytsmansteet 14, 21050 Brussels, Belgium.

Emuli address: marc.arbyn@sciencano.br (M. Adve-\

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#### ORGANISED CERVICAL SCREENING IS CHALLENGED BY DECLINING PARTICIPATION RATES

In Denmark, women between 23-65 years are recommanded to attend cervial cancer screening at their own general practicioner (GP)

Screening coverage: 75% (~25% do not attend screening)

~45% of all newly diagnosed cancer cases are found women, who do not attend screening (non-attenders)1

Similar situation in all countries with organized screening



~ 75% are covered by screening (by invitation or opportunistic)

~ 45% cancers in non-attenders<sup>1,2</sup>

## SCREENING NON-ATTENDERS

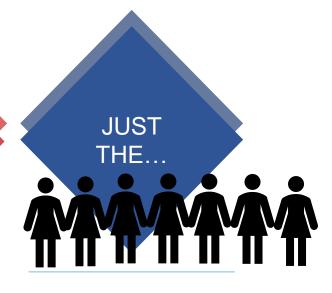


Socio-economic challenged women difficult to reach

low income, little or no education besides primary school



Non-responders are mainly EU/non-EU emigrants living and working in Dk



Just regular women...

### CREATING A USER FOCUSED VALUE-CHAIN

Availability of service is paramount to recruitment of non-attenders!

 $\setminus$  SIMPLE

Women don't go for screening because..

- Embarrassment
- Fear of examination
- Dont believe its relevant for them
- Thinks vaccination gives full cover
- Procrastinating...

EASY

Adding to the value-chain

- In privacy of own home
- Multi-language information material
- On-line ordering
- No paperwork to fill out
- Ease of use
- Web/App portal
- E-Mail contact address
- Call-in Hot-line
- No cost

3 SAFE

Quality Assurance for the Lab

- Validated stability of device
- Validated performance of the HPV diagnostic test
- Safe patient identification

# SELF-SAMPLING INVITATION STRATEGIES & OUTCOMES

#### **OPT-IN:**

Women are invited and actively accepts

#### **OPT-OUT:**

Women are invited and must actively decline to not receive self-sample

#### DIRECT-MAIL/MAIL-TO-ALL:

Women are mailed self-sampling kit directly

Invitation strategy	Country & Study design	Study size	Target age (years)	Participation	Reference
				Rate	
	Denmark Cross sectional	N=4874	27-64	20% by self- sampling+ 10% by clinician taken samples after invitation	Lam JUH et al., 2017 (1)
Opt-in	Sweden Cross sectional	N=369	35-50	32.0%	Stenvall et al., 2007
	Sweden Cross sectional	N=3000	30-58	39.0%	Sanner K et al., 2009
	Sweden RCT	N=800	30-62	16.0%	Broberg et al., 2013
Opt-in & mail-to-all	Italy RCT	Opt in: N=622 Mail-to-all: N=622	35-65	Opt-In : 8.7% Mail-to-all: 19.6%	Giorgi Rossi et al., 2011
	Italy RCT	Opt in: 4513 Mail-to-all: 4516	30-64	Opt-In: 10.5% Opt-out: 19.6%	Giorgi Rossi et al., 2015
<b>Opt-out</b>	Netherlands RCT	N= 2546	30-50	28.9%	Bais et al., 2007
	Netherlands Cohort	N=27,792	30-60	26.6%	Gök et al., 2010
	Sweden Cross sectional	N=8000	30-65	39.0%	Gyllensten et al., 2011
	UK RCT	N=1500	NR	6.4%	Szarewski et al., 2011
	Finland RCT	N=2,397	30-60	27.7%	Virtanen et al., 2011
	Sweden RCT	N=2000	39-60	34.0%	Wikström et al., 2011
	Netherlands RCT	N=26,145	26-63	30.8%	Gök et al., 2012
	Sweden RCT	N=1000	32-65	14.7%	Darlin et al., 2013
	France RCT	N=8,829	35-69	18.4%	Sancho-Garnier et al., 2013
	UK RCT	N=3,000	25-65	13.0%	Cadman et al., 2014

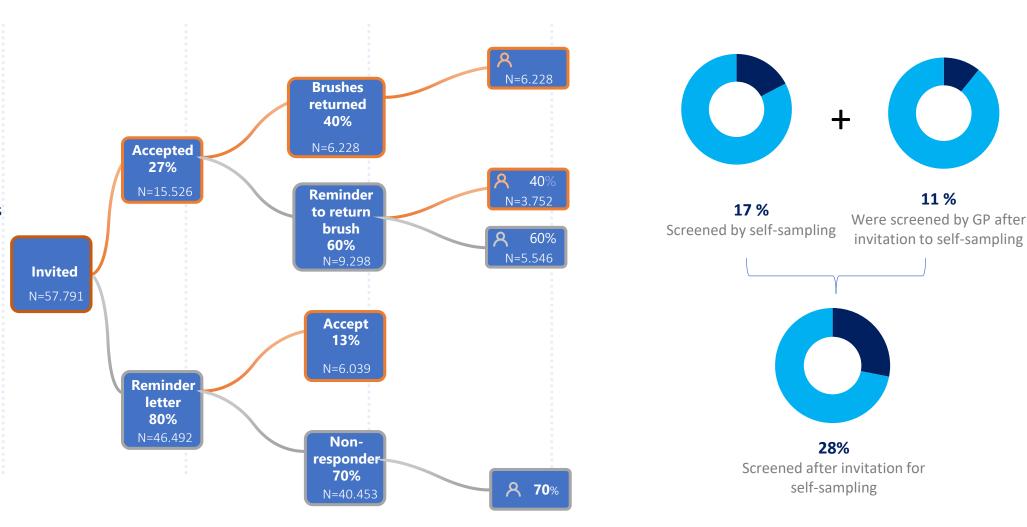
# SELF-SAMPLING UPTAKE AND RETURN RATES IN CAPITAL REGION OF DENMARK IMPLEMENTATION 2017-2019



The flow of activities from invitation to end-of-algorithm

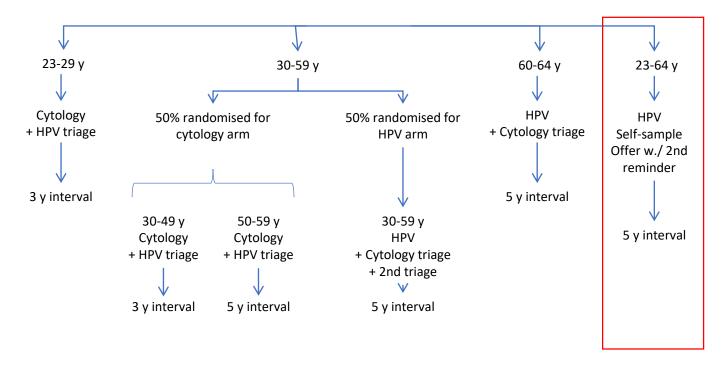
Screened by self-sampling 17.3% of all invited

82.7% Non-responders of all invited



### SELF-SAMPLING IN CONTEXT OF ORGANIZED SCREENING – DENMARK 2020

#### [ Implementation date 1st September 2020]



[Implementation date undecided but 1st January 2021 suggested]

# SELF-SAMPLING IN COUNTRIES WITHOUT ORGANIZED SCREENING

**AND** 

LOW- AND MIDDLE INCOME COUNTRIES

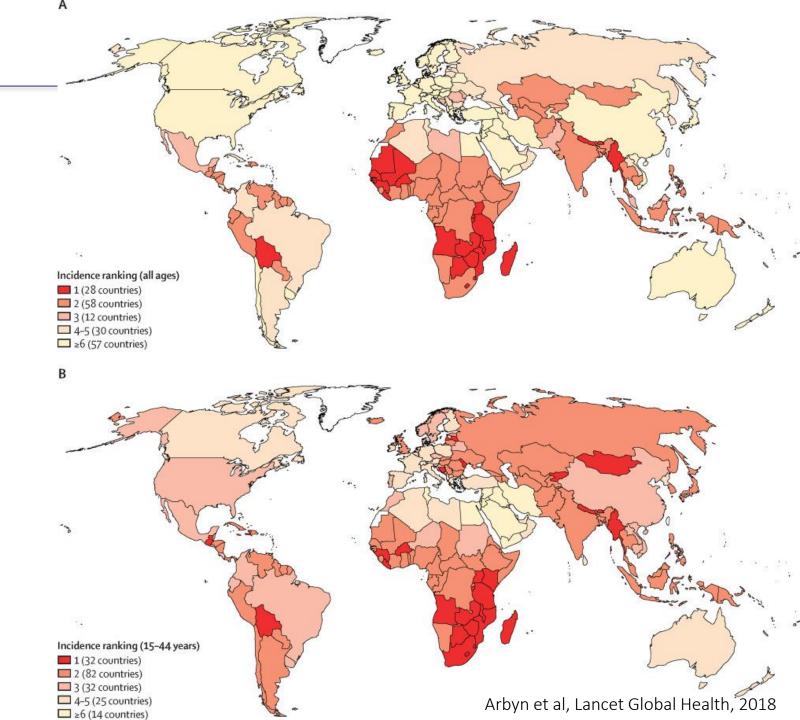
# ACCESS TO SELF-CARE INTERVENTIONS IMPROVE PEOPLE'S AUTONOMY

#### **SELF CARE CAN BE ACCESSED THROUGH:**



# SELF-SAMPLING IN CONTEXT OF COUNTRIES WITHOUT ORGANIZED SCREENING

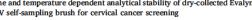
Ranking of cervical cancer incidence burden in 2018 relative to all other cancer sites in women of all ages (A) and aged 15–44 years (B)



# ANALYTICAL STABILITY OF COLLECTED HPV SFLF-SAMPLES ALLOWS FOR ADAPTION TO LOCAL HEALTH CARE INFRASTRUCTURE AND GEOGRAPHICAL CHALLENGES



Time and temperature dependent analytical stability of dry-collected Evalyn HPV self-sampling brush for cervical cancer screening



Ditte Møller Ejegod\*, Helle Pedersen, Garazi Peña Alzua, Camilla Pedersen, Jesper Bonde

Molecular Pathology Laboratory, Department of Pathology, Copenhaum University Husbial, Kateeded Alle 30, 2650, Heidove, Department

#### ARTICLE INFO

#### ABSTRACT

As a new initiative, EW self-ampling to non-attenders using the dry Evalyn self-ampling bash is offered in the Capital Region of Denmark. The use of a dry brush is largely uncharted territory in terms of analytical stability. In this study we aim to provide evidence on the analytical quality of dry HPV self-ampling brushes as a function

We assessed the analytical stability of day stored Evalvo brushes at three different temperatures, (4 °C. mon temperature, 30 °C) and five different storage time points; T = 0 (baseline), 2, 4, 8, 16, and 32 weeks prior a HPV analysis using the BD Onclarity HPV assay.

Mean Ct value of the Onclarity internal control was used as companior of cellularity across time and tem-peratures, with no or only bonderline statistical differences observed. BPV detection was stable through out the five time points. In addition, analytically amplifiable DNA copy numbers and DNA fragmentation was assessed. using the Agena IPLEX Exome QC assay, with no or only borderline statistical differences observed.

In conclusion, the Evalyn brush is analytically stable with respect to human genomic material and HP

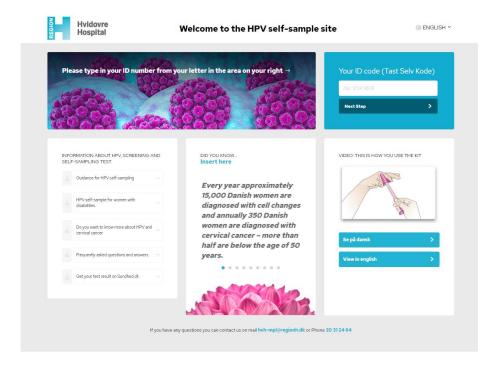
detection for up to 32 weeks at temperatures ranging from 4 °C to 30 °C.

Human papillomavirus (HPV) based cervical cancer screening [1-7] in combination with self-collected samples is increasingly being investigated as an alternative to dinician collected samples aiming at increasing the coverage of cervical screening worldwide [8-12]. In organized screening programs, HPV self-sampling is considered as a potential alternative to screening non-attending women [13-15]. In Denmark, women aged 23-65 years are invited for screening for cervical cancer free of charge as a public cancer prevention program. In Denmark approximately 50% of all cervical cancers are diagnosed amongst the 25% women who do not participate in screening after being invited [16,17], as also observed in similar North European countries with nationwide cervical cancer screening programs [18,19]. In qualitative studies evaluating women's preferences in screening, the main reasons for non-participation are reported as a combination beexamination and the general inconvenience of the doctor's visit [20-22]. To address the screening non-attendance, the Capital Region of Dermark launched a pilot implementation program in 2014, the

Copenhagen Self-sampling initiative (CSi), offering HPV self-sampling brushes to approx. 24,000 screening non-attenders [9,14,23]. In CSi, we distributed the Evalyn self-sampling brush to invited women who ac tively opted in after invitation using a purpose designed and developed self-sampling kit [9]. After sampling in the privacy of the woman's own home, the women returned the brush in a dry state to the laboratory for HPV analysis using a postage pre-paid envelope.

Multiple approaches to self-sampling have been described but two types of self-sampling devices have predominantly been used for larger self-sampling initiatives; a "wet" brush that requires the woman to re suspend the brush in a supplied media immediately after sampling or "dry" brush, shipped directly to the laboratory after sampling without further interaction by the woman. Comparing these two approaches, the use of a dry shipped self-sampling brush in our opinion holds : the self-sampling device. Firstly, a dry brush can be transported by mail lage and leakage during collection and transport. Secondly, any risk of





WEB & TELECOMMUNICATION INFRASTRUCTURE ALLOWS FOR "EASY" ADMINISTRATION OF SERVICE

### SELF-SAMPLING IN THE FUTURE

# Organized screening programs

Self-sampling will become a free-of-choice offer along with clinician collected samples, allowing for resource re-allocation in the primary health care sector, making cervical screening more accessible, cheaper, convenient

# Without organized screening programs

Self-sampling enables cervical cancer screening outside the classical restraints of health care infrastructure; cheap, effective, mobile, community engaging