



University of Antwerp  
Faculty of Medicine and  
Health Sciences

# Use of FVU urine in measuring HPV vaccination impact

HPV Prevention and Control board meeting.

Antwerp 2026

# Disclaimer

- The HPV Prevention and Control board and the Viral Hepatitis Prevention and Control boards are 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 and Novosanis NV.
- I have received, on my university funds, unrestricted research grants from MSD, and Seegene.
- I 'm cofounder and minority share holder of Sampl.id a UAntwerpen Spin-off that produces the Ini-Stream, a First Void Urine collection device.

# Content

- What can we learn from cervico-vaginal samples (CVS)
- Why collect first void urine for Ab testing
- Sampling vaccinated and none vaccinated women
- Use of FVU to monitor immune response after vaccination
- How good can we discriminate between vaccinated and non-vaccinated women
- Conclusion

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

Pattyn J., Van Keer S., Tjalma W., Matheussen V., Van Damme P., and Vorsters A. (2019)

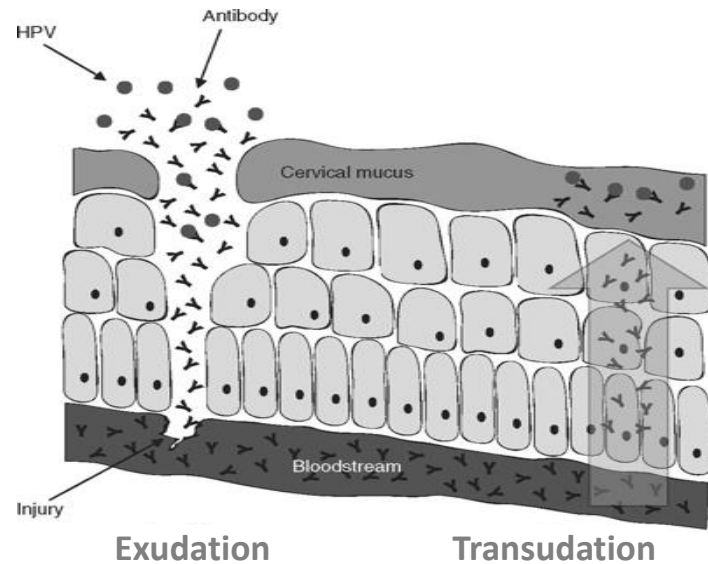
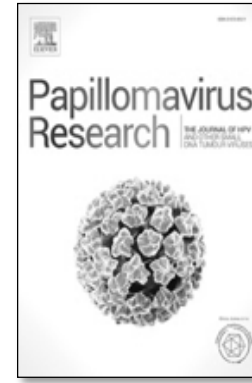
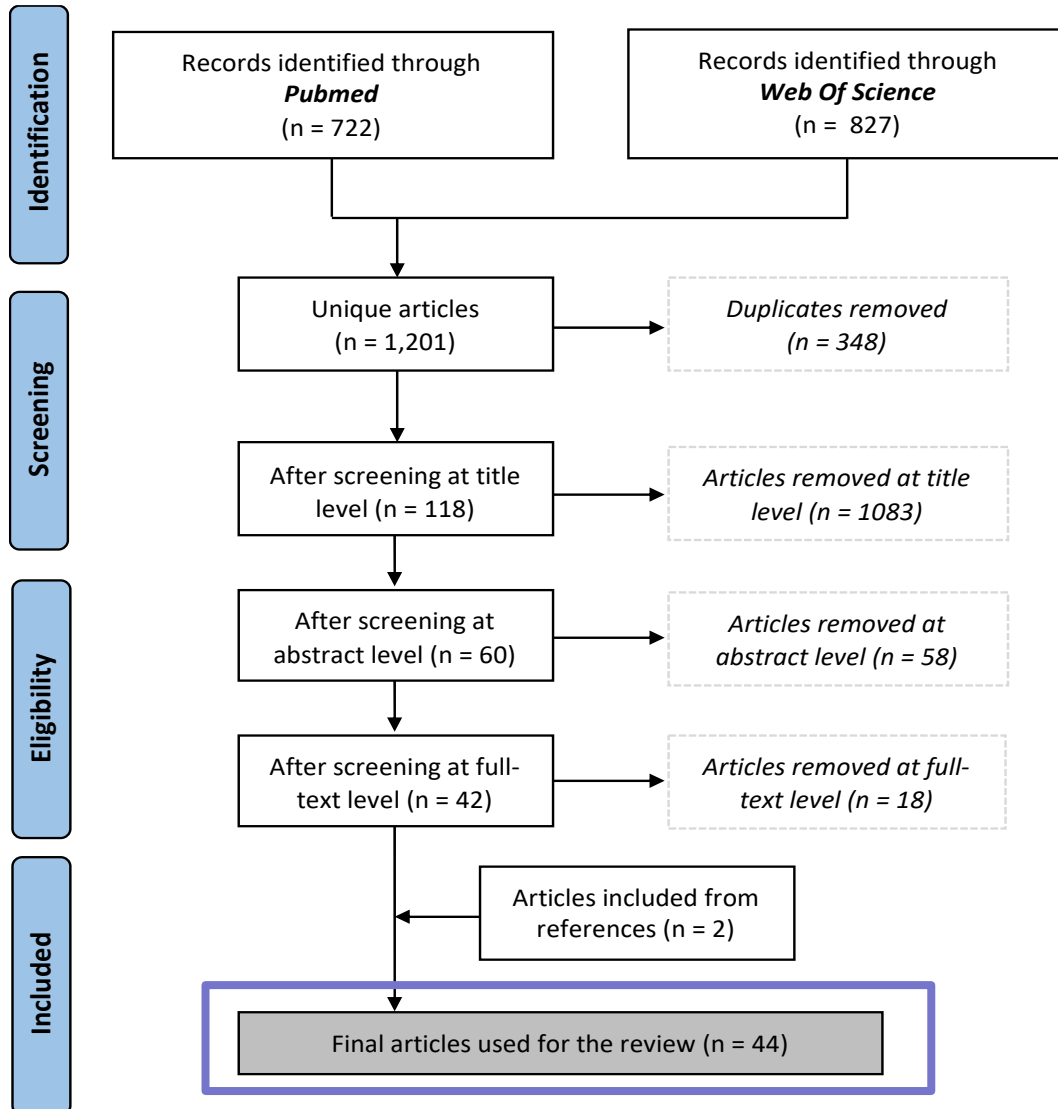


Figure derived from Garçon et al. (2011)

- Assess the **current knowledge of HPV antibody levels at the cervix**



- Is it feasible to detect infection-induced and/or vaccine-induced HPV-specific antibodies in cervicovaginal secretions?
- Do local and systemic HPV-specific antibodies levels correlate?



- Published between 1989 and 2018



Natural HPV infection (26/44)



HPV vaccination (18/44)



- Most papers reported paired CVS and serum data (36/44)

- Is it feasible to detect infection-induced HPV antibodies in CVS? **YES**
  - *Antibody levels were low and near the detection limit of the current assays*

- Do local and systemic HPV-specific antibodies levels correlate? **NO**
  - *Low concordance between CVS and serum*

- Is it feasible to detect vaccine-induced HPV antibodies in CVS? **YES**
  - *Detectable vaccine-induced Ab levels in CVS are lower than serum levels*

- Do local and systemic HPV-specific antibodies levels correlate? **YES**
  - *Moderate to good correlation with serum levels were reported in several studies*

Need for **specific methods to improve sensitivity and standardize the detection of (HPV) antibodies in CVS**

Characteristics	Cervical wick	Cervicovaginal lavages	Cytobrush/swab
Minimal trauma	+/-	+	☹️
Known dilution of secretions	+/-	☹️	+/-
Minimal dilution of secretions	+	☹️	+
Sufficient material collected	☹️	+	☹️
Ease of collection	+	+/-	+
Self-insertion/self-collection possible	+	☹️	+

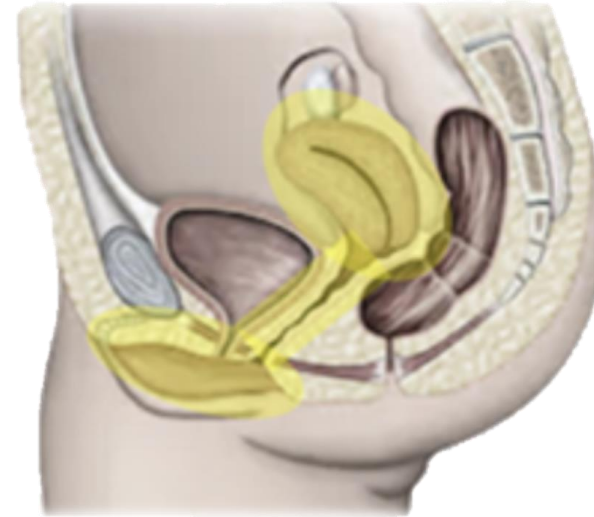
+ good; +/- moderate, ☹️ not good

# Why first-void urine?

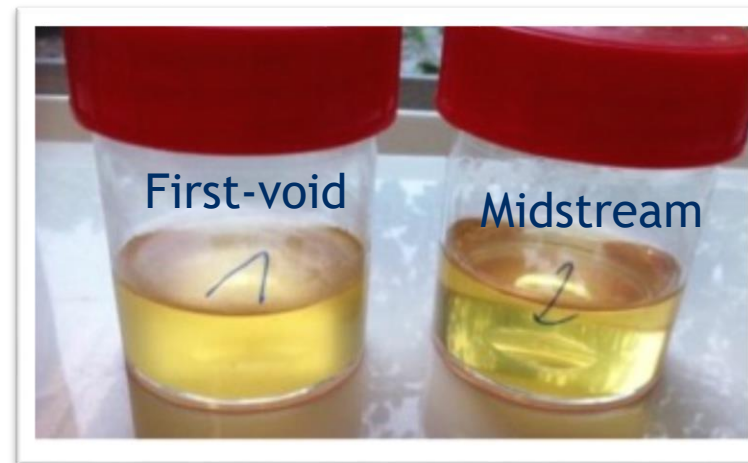
## Initial stream of urine

Captures impurities lining the urethra opening including transudated **antibodies** and **biomarker**-containing mucus and debris from exfoliated cells originating from **female** genital organs

- ✓ Non-invasive
- ✓ Preferred
- ✓ Home-based



- Neonatal Fc receptor (FcRn) involved in IgG transudation found across the whole FGT epithelia.
- Hysterectomy causes total IgG concentrations to decrease with ca. 95% in CVS



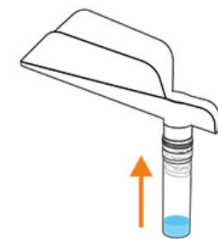


OTHER OPTION

First-void urine



- ✓ Young participants
- ✓ Increase participation
- ✓ Avoid sampling-induced microtrauma



Ini.Stream



Colli-Pee

Van Keer et al. (2019)

# The initial stream of urine captures a concentrated wash of biomarkers from the female genital tract

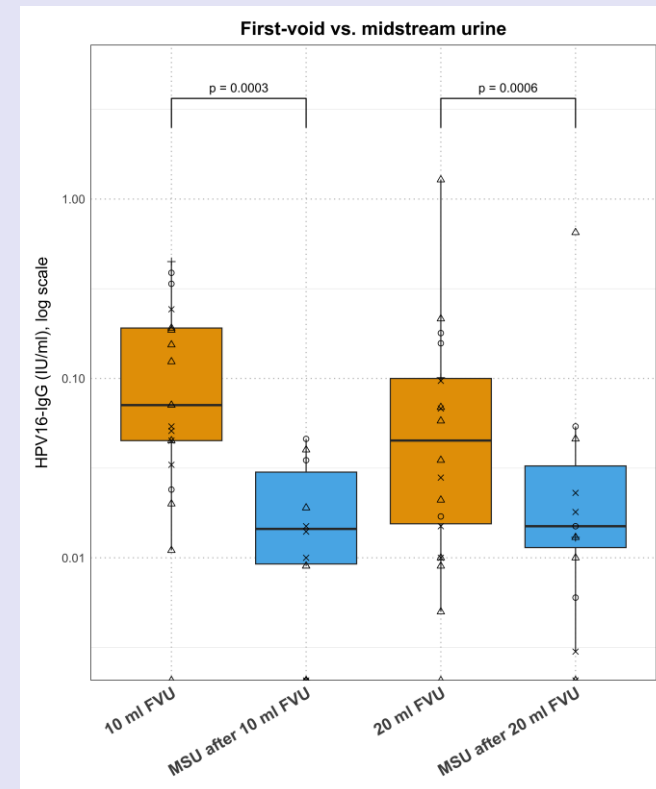


## DNA copies FVU > Mid-stream urine

Sample number	DNA copies		HPV FV/MID	hDNA	
	HPV FV	HPV MID		hDNA FV	hDNA MID
1	0.6	0	DIV/0	1880	233
2	1450	24.4	59.4	1710	200
3	14.4	2.99	4.8	4110	192
4	6400	626	10.2	552	387
5	767	7.6	100	2830	327
6	0	0	DIV/0	56.9	142
7	2.6	0	DIV/0	204	44.6
8	392000	15600	25.1	17300	2760
9	36.4	0.227	160.4	314	64.1
10	51	4.18	12.2	5900	1500

$P = 0.008$ 
 $P = 0.007$

## HPV16-IgG FVU > Mid-stream urine



# Secondary prevention – OUTPUT

## *Detection of HPV DNA and methylation markers*

European Journal of Clinical Microbiology & Infectious Diseases (2018) 37:859–869  
https://doi.org/10.1007/s10096-017-3179-1

ORIGINAL ARTICLE

**Human papillomavirus genotype and viral load agreement between paired first-void urine and clinician-collected cervical samples**

Severien Van Keer<sup>1</sup> · Wiebren A. A. Tjalma<sup>2,3</sup> · Jade Pattyn<sup>1</sup> · Samantha Biesmans<sup>1</sup> · Zoë Pieters<sup>4,5</sup> · Xaveer Van Ostade<sup>6</sup> · Margareta Ieven<sup>7</sup> · Pierre Van Damme<sup>1</sup> · Alex Vorsters<sup>1</sup>

Contents lists available at ScienceDirect

Journal of Clinical Virology

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

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

M. Arbyn<sup>1,2</sup>, E. Peeters<sup>1</sup>, I. Benoy<sup>3,4,5</sup>, D. Vanden Broeck<sup>6,7,8,9</sup>, J. Bogers<sup>10,11,12</sup>, P. De Sutter<sup>13</sup>, G. Donders<sup>14</sup>, W. Tjalma<sup>15</sup>, S. Weyers<sup>16</sup>, K. Cuschieri<sup>17</sup>, M. Poljak<sup>18</sup>, J. Bonde<sup>19</sup>, C. Cocuzza<sup>20</sup>, F.H. Zhao<sup>21</sup>, S. Van Keer<sup>22</sup>, A. Vorsters<sup>23</sup>

**HPV DNA detection in urine samples of women: 'an efficacious and accurate alternative to cervical samples?'**

Jade Pattyn, Severien Van Keer, Laura Téblick, Pierre Van Damme & Alex Vorsters

Contents lists available at ScienceDirect

Journal of Virological Methods

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

**Optimization of HPV DNA detection in urine by improving collection, storage, and extraction**

A. Vorsters · J. Van den Bergh · I. Micalessi · S. Biesmans · J. Bogers · A. Hens · I. De Coster · M. Ieven · P. Van Damme

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

Silvia Franceschi<sup>1</sup>, M. Chantal Umulisa<sup>2</sup>, Ugyen Tshomo<sup>3</sup>, Tarik Gheit<sup>4</sup>, Iacopo Baussano<sup>5</sup>, Vanessa Tenet<sup>6</sup>, Tshokey Tshokey<sup>7</sup>, Maurice Gatera<sup>8</sup>, Fidele Ngabo<sup>9</sup>, Pierre Van Damme<sup>10</sup>, Peter J.F. Snijders<sup>11</sup>, Massimo Tommasino<sup>12</sup>, Alex Vorsters<sup>13</sup> and Gary M. Clifford<sup>14</sup>

**Impact of Human Papillomavirus Vaccination, Rwanda and Bhutan**

Iacopo Baussano, Felix Sayinzoga, Ugyen Tshomo, Vanessa Tenet, Alex Vorsters, Daniëlle A.M. Heideman, Tarik Gheit, Massimo Tommasino, Marie Chantal Umulisa, Silvia Franceschi, Gary M. Clifford

Contents lists available at ScienceDirect

Gynecologic Oncology

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

**Clinical and analytical evaluation of the RealTime High Risk HPV assay in Colli-Pee collected first-void urine using the VALHUDES protocol**

Severien Van Keer<sup>1,2</sup>, Eliana Peeters<sup>3</sup>, Davy Vanden Broeck<sup>4,5,6</sup>, Philippe De Sutter<sup>7</sup>, Gilbert Donders<sup>8,9</sup>, Jean Doyen<sup>10</sup>, Wiebren A.A. Tjalma<sup>11</sup>, Steven Weyers<sup>12</sup>, Alex Vorsters<sup>13</sup>, Marc Arbyn<sup>14</sup>

Contents lists available at ScienceDirect

Journal of Virological Methods

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

**Human papillomavirus detection in urine: Effect of a first-void urine collection device and timing of collection**

Jade Pattyn<sup>1</sup>, Severien Van Keer<sup>1</sup>, Samantha Biesmans<sup>2</sup>, Margareta Ieven<sup>3,4</sup>, Charlotte Vanderborgh<sup>5</sup>, Koen Beyers<sup>6</sup>, Vanessa Vankerckhoven<sup>7,8</sup>, Robin Bruyndonckx<sup>9,10</sup>, Pierre Van Damme<sup>11</sup>, Alex Vorsters<sup>12</sup>

**Urine testing for HPV: rationale for using first void**

Alex Vorsters<sup>1</sup>, researcher<sup>1</sup>, Pierre Van Damme<sup>2</sup>, professor<sup>2</sup>, Gary Clifford<sup>3</sup>, cancer epidemiologist<sup>3</sup>

<sup>1</sup>Faculty of Medicine and Health Sciences, Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, University of Antwerp, 2010 Antwerpen (Wijk), Belgium; <sup>2</sup>Infections and Cancer Epidemiology Group, International Agency for Research on Cancer, Lyon, Cedex 08, France

Article

**Long-Term Follow-up of HPV Infection Using Urine and Cervical Quantitative HPV DNA Testing**

Alex Vorsters<sup>1,2,3</sup>, Severien Van Keer<sup>1</sup>, Samantha Biesmans<sup>1</sup>, Annick Hens<sup>1</sup>, Ilse De Coster<sup>1</sup>, Herman Goossens<sup>2,3</sup>, Margareta Ieven<sup>2,3</sup> and Pierre Van Damme<sup>1</sup>

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

Laura Téblick<sup>1,2</sup>, Severien Van Keer<sup>1</sup>, Annemie De Smet<sup>1</sup>, Pierre Van Damme<sup>1</sup>, Michelle Laeremans<sup>2</sup>, Alejandra Rios Cortes<sup>3</sup>, Koen Beyers<sup>4</sup>, Vanessa Vankerckhoven<sup>5,6</sup>, Veerle Matheussen<sup>3,4,5</sup>, Renee Manderstoot<sup>7</sup>, Arno Floore<sup>8</sup>, Chris J. L. M. Meijer<sup>9,10</sup>, Renske D. M. Steenbergen<sup>7</sup> and Alex Vorsters<sup>1</sup>

RESEARCH Open Access

**Concentration strategies for spiked and naturally present biomarkers in non-invasively collected first-void urine**

Laura Téblick<sup>1</sup>, Marijana Lipovac<sup>1</sup>, F. Ricardo Burdler<sup>1</sup>, Annemie De Smet<sup>1</sup>, Margo Bell<sup>1</sup>, Eef van den Borst<sup>1,2</sup>, Veerle Matheussen<sup>3,4,5</sup> and Alex Vorsters<sup>1</sup>

OPEN

**Triage of human papillomavirus infected women by methylation analysis in first-void urine**

Severien Van Keer<sup>1,2</sup>, Annina P. van Splunter<sup>3</sup>, Jade Pattyn<sup>1</sup>, Annemie De Smet<sup>1</sup>, Sereina A. Herzog<sup>4</sup>, Xaveer Van Ostade<sup>5</sup>, Wiebren A. A. Tjalma<sup>6,7</sup>, Margareta Ieven<sup>8</sup>, Pierre Van Damme<sup>1</sup>, Renske D. M. Steenbergen<sup>9</sup> & Alex Vorsters<sup>1</sup>

Analytical and clinical performance of extended HPV genotyping with BD Onclarity HPV Assay in home-collected first-void urine: A diagnostic test accuracy study

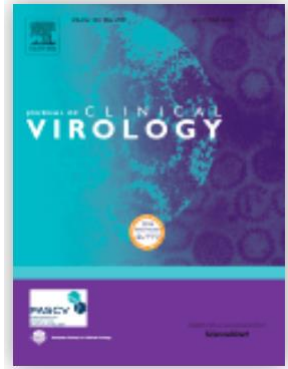
Severien Van Keer<sup>1,2</sup>, Ardashesh Latsuzbsia<sup>3</sup>, Davy Vanden Broeck<sup>4,5,6</sup>, Philippe De Sutter<sup>7</sup>, Gilbert Donders<sup>8,9</sup>, Jenn Doyen<sup>10</sup>, Wiebren A.A. Tjalma<sup>11</sup>, Steven Weyers<sup>12</sup>, Marc Arbyn<sup>13</sup>, Alex Vorsters<sup>14</sup>

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

Mario Poljak<sup>1</sup>, Kate Cuschieri<sup>2</sup>, Laia Alemany<sup>3,4</sup> and Alex Vorsters<sup>5</sup>

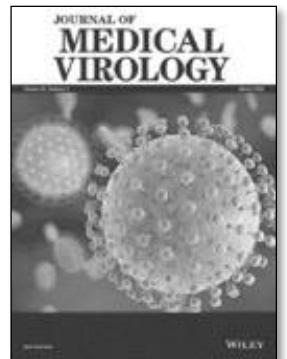
# First-void urine as a non-invasive liquid biopsy source to detect vaccine-induced human papillomavirus antibodies originating from cervicovaginal secretions

Severien Van Keer, Martina Willhauck-Fleckenstein, Jade Pattyn, Julia Butt, Wiebren A A Tjalma, Xaveer Van Ostade, Niel Hens, Pierre Van Damme, Tim Waterboer, Alex Vorsters. (2019)



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

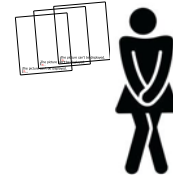
Pattyn J., Panicker G., Willhauck-Fleckenstein M., Van Keer S., Téblick L., Pieters Z., Tjalma W., Matheeußen V., Van Damme P., Waterboer T., Unger E., Vorsters A. (2020)



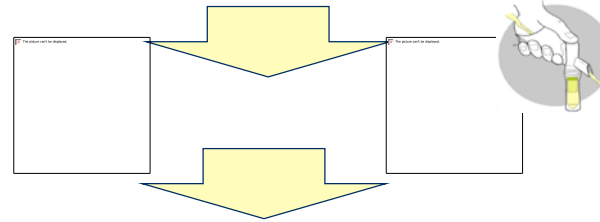


N=19

Median age 22y  
(IQR: 20-24y)



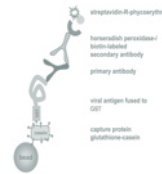
N=36



Vaccine type:  
N= 31/36 (4vHPV)  
N= 4/36 (2vHPV)  
N=1 (2v/4vHPV)



Total Human IgG

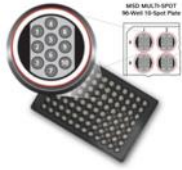


GST-L1



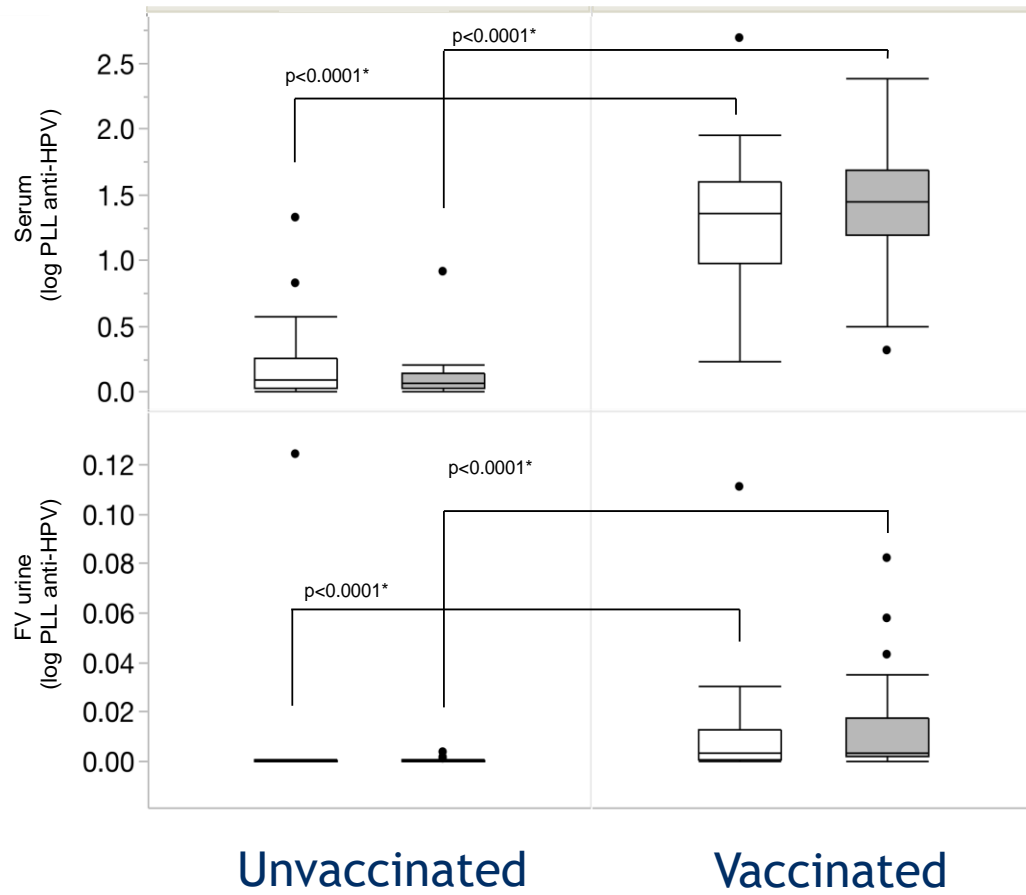
M4ELISA

Test results from **53 paired first-void urine and serum samples** included for statistical analysis

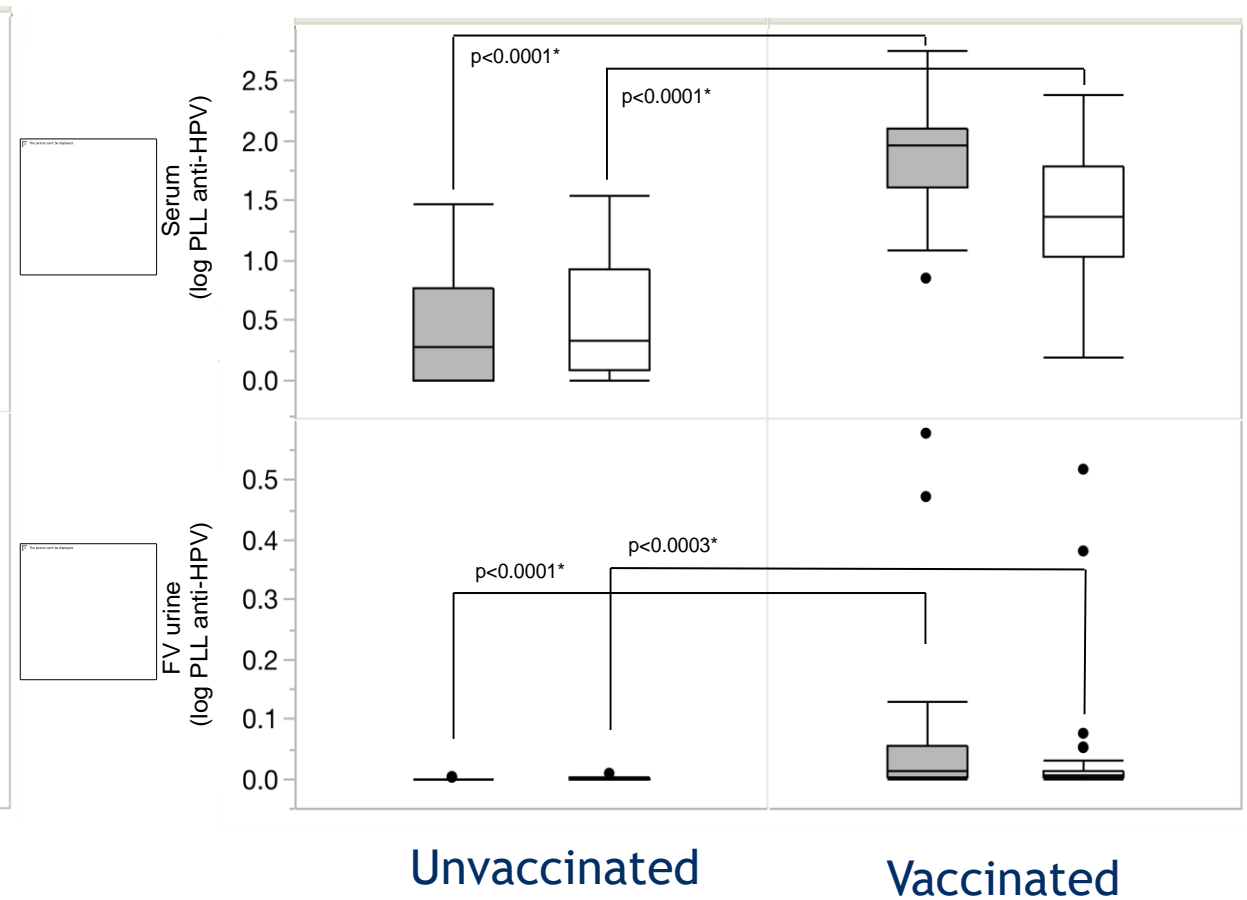


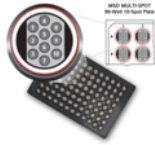
# M4ELISA measured HPV antibody levels

□ HPV6  
■ HPV11



■ HPV16  
□ HPV18



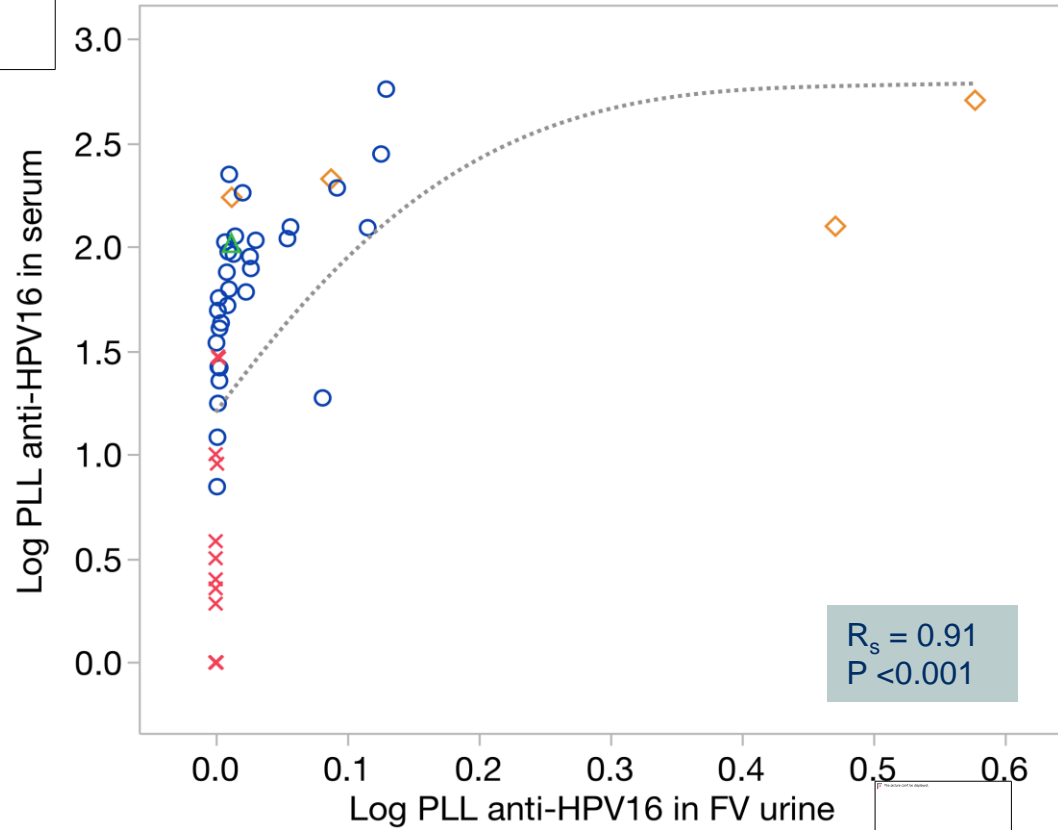


# M4ELISA comparison between FV urine and serum



HPV16

(C) HPV16



- 4vHPV vaccine
- ◇ 2vHPV vaccine
- △ 2v- and 4vHPV vaccine
- × Unvaccinated

HPV6 -  $R_s = 0.85$   
HPV11 -  $R_s = 0.86$   
HPV18 -  $R_s = 0.79$

# What do we know about HPV-specific antibodies in first-void urine?

*Hypothesis antibodies in first-void urine*

*Detection of HPV-specific antibodies*

*First-void urine vs. mid-stream urine*

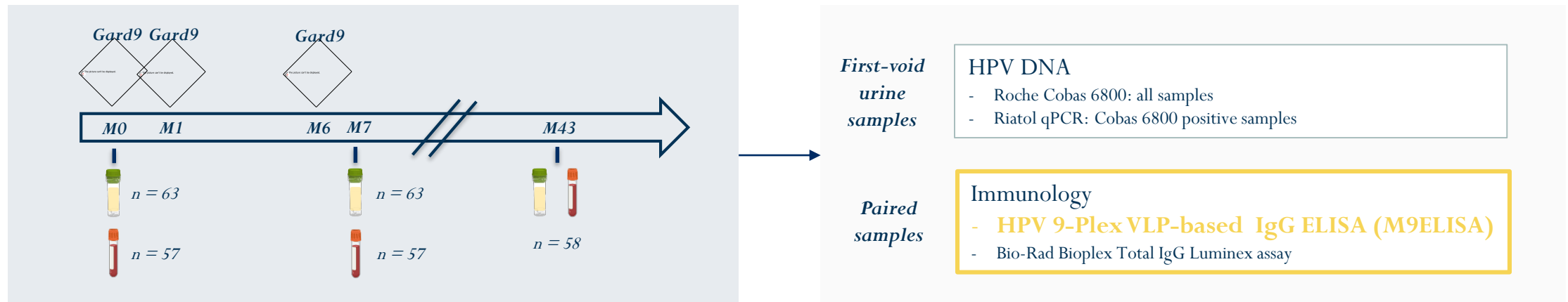
*Long-term detection of HPV-specific antibodies*

**Are HPV-specific antibodies still detectable in first-void urine on the long-term?**

*Phase III vaccine trial in adult women with Gardasil9 vaccine*

Substudy  
AB-SOP  
follow-up

*N = 63  
Median age = 35*



# What do we know about HPV-specific antibodies in first-void urine?

*Hypothesis antibodies in first-void urine*

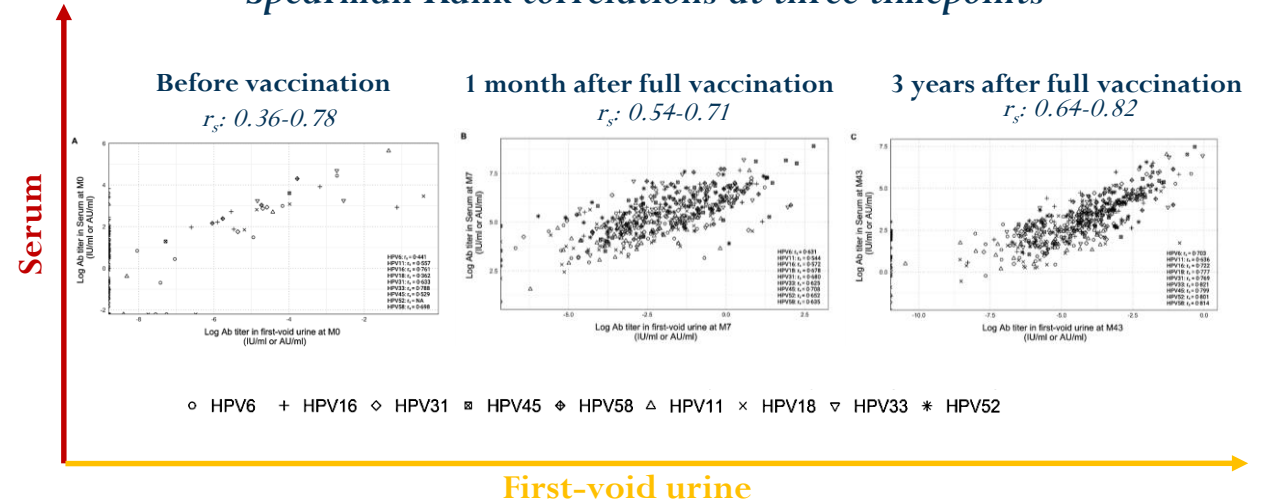
*Detection of HPV-specific antibodies*

*First-void urine vs. mid-stream urine*

*Long-term detection of HPV-specific antibodies*

Type	Months	First-void urine		Serum	
		Antibody detection	Antibody concentration (AU-IU/ml or µg/ml)	Antibody detection	Antibody concentration (AU-IU/mL or µg/mL)
HPV6	0	9/58 (16%)	0.000 (0.000–0.000)	21/57 (37%)	0.000 (0.000–0.380)
	7	57/58 (98%)	0.057 (0.022–0.203)	57/57 (100%)	92.60 (56.30–137.00)
	43	57/58 (98%)	0.006 (0.002–0.013)	58/58 (100%)	10.01 (4.89–18.13)
HPV11	0	4/58 (7%)	0.000 (0.000–0.000)	7/57 (12%)	0.000 (0.000–0.000)
	7	58/58 (100%)	0.058 (0.029–0.199)	57/57 (100%)	106.0 (56.60–158.0)
	43	57/58 (98%)	0.007 (0.003–0.016)	58/58 (100%)	10.72 (5.24–17.93)
HPV16	0	7/58 (12%)	0.000 (0.000–0.000)	10/57 (18%)	0.000 (0.000–0.000)
	7	58/58 (100%)	0.184 (0.077–0.552)	57/57 (100%)	291.0 (178.0–468.0)
	43	58/58 (100%)	0.019 (0.008–0.045)	58/58 (100%)	32.17 (13.32–64.67)
HPV18	0	6/58 (10%)	0.000 (0.000–0.000)	21/57 (37%)	0.000 (0.000–0.440)
	7	56/58 (97%)	0.058 (0.031–0.274)	57/57 (100%)	102.0 (44.00–210.0)
	43	52/58 (90%)	0.005 (0.002–0.015)	58/58 (100%)	6.54 (2.07–17.35)
HPV31	0	4/58 (7%)	0.000 (0.000–0.000)	8/57 (14%)	0.000 (0.000–0.000)
	7	58/58 (100%)	0.145 (0.050–0.573)	57/57 (100%)	195.0 (118.0–541.0)
	43	55/58 (95%)	0.016 (0.004–0.036)	58/58 (100%)	21.28 (10.48–49.17)
HPV33	0	3/58 (5%)	0.000 (0.000–0.000)	5/57 (9%)	0.000 (0.000–0.000)
	7	58/58 (100%)	0.238 (0.078–0.573)	57/57 (100%)	322.0 (197.0–677.0)
	43	56/58 (97%)	0.020 (0.004–0.051)	58/58 (100%)	31.92 (13.36–69.07)
HPV45	0	2/58 (3%)	0.000 (0.000–0.000)	7/57 (12%)	0.000 (0.000–0.000)
	7	55/58 (95%)	0.202 (0.061–0.586)	57/57 (100%)	336.0 (140.0–562.0)
	43	52/58 (90%)	0.016 (0.003–0.050)	58/58 (100%)	16.37 (8.63–63.59)
HPV52	0	0/58 (0%)	0.000 (0.000–0.000)	11/57 (12%)	0.000 (0.000–0.000)
	7	57/58 (98%)	0.110 (0.035–0.507)	57/57 (100%)	297.0 (151.0–600.0)
	43	49/58 (84%)	0.017 (0.003–0.046)	57/58 (98%)	28.27 (11.45–65.31)
HPV58	0	4/58 (7%)	0.000 (0.000–0.000)	9/57 (16%)	0.000 (0.000–0.000)
	7	58/58 (100%)	0.359 (0.079–0.849)	57/57 (100%)	365.0 (222.0–790.0)
	43	53/58 (91%)	0.026 (0.010–0.078)	58/58 (100%)	39.81 (15.65–97.34)

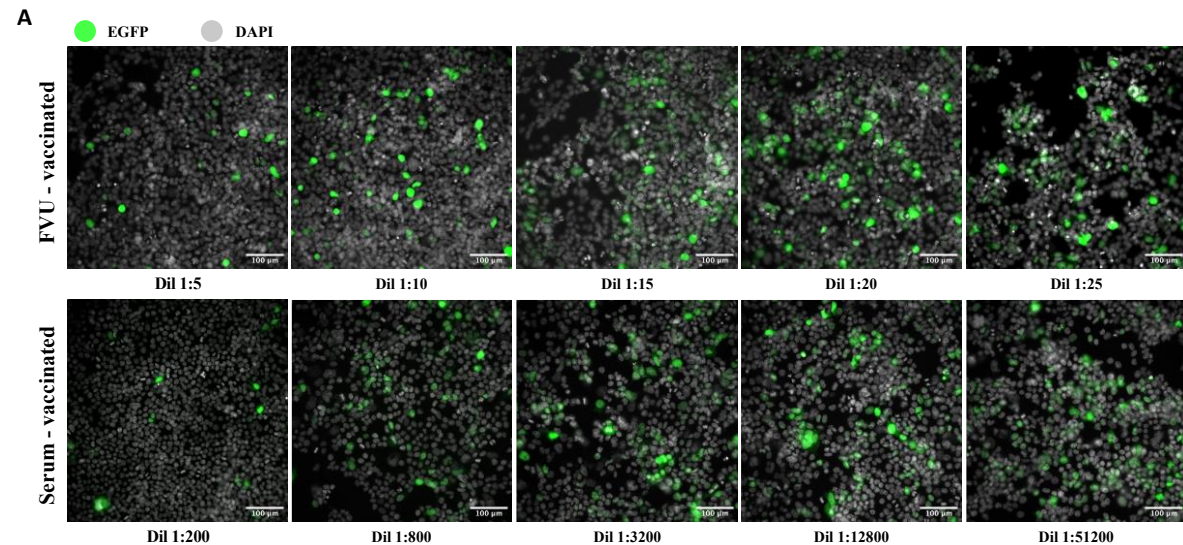
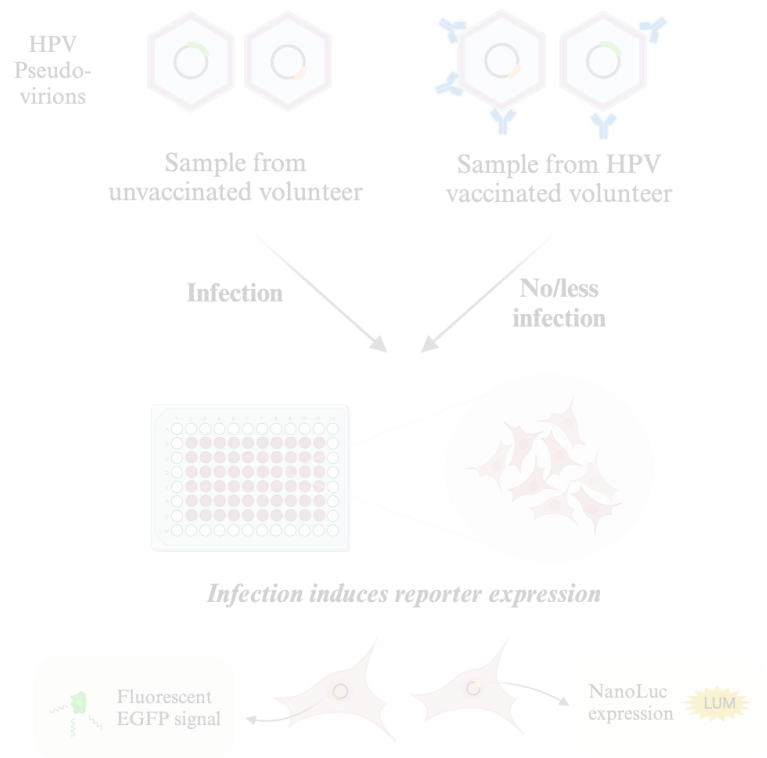
## Spearman Rank correlations at three timepoints



**HPV-specific antibodies are still detectable in first-void urine after a longer period of time.**

# What do we know about HPV neutralization in first-void urine?

*Are HPV-specific antibodies still neutralizing pseudovirions in first-void urine?*



Assay	Outcome	Vaccinated	
		FVU	Serum
EGFP PBNA	Positive (%)	8/25 (32%)	25/25 (100%)
	HPV16-nAbs EC <sub>50</sub>	0.00 (0.00-6.04)	1573 (774-4887)
Nluc PBNA	Positive (%)	18/25 (72%)	25/25 (100%)
	HPV16-Abs EC <sub>50</sub>	5.69 (0.00-18.69)	1616 (520-6981)

**Antibodies are still neutralizing in FVU**

**Assay optimization for FVU is required due to low concentrations**

# Primary prevention – OUTPUT

*Detection of HPV DNA  
and methylation markers*

*Detection of HPV-  
specific total antibodies*

*Functionality of local  
immune markers*

Perspective

HPV vaccination: Are we overlooking additional opportunities to control HPV infection and transmission?



Alex Vorsters<sup>a,\*</sup>, Pierre Van Damme<sup>a</sup>, F. Xavier Bosch<sup>b,c</sup>

<sup>a</sup>Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute, Faculty of Medicine, University of Antwerp, Universiteitsplein 1, 2610 Antwerp, Belgium

<sup>b</sup>Cancer Epidemiology Research Programme (CERP), Catalan Institute of Oncology (ICO- IDIBELL), Avinguda de la Granvia de l'Hospitalet 199–203, 08908 L'Hospitalet de Llobregat, Barcelona, Spain

<sup>c</sup>Open University of Catalonia (UOC), Barcelona, Spain

RESEARCH

Open Access

Concentration strategies for spiked and naturally present biomarkers in non-invasively collected first-void urine



Laura Téblick<sup>1\*</sup>, Marijana Lipovac<sup>1</sup>, F. Ricardo Burdier<sup>1</sup>, Annemie De Smet<sup>1</sup>, Margo Bell<sup>1</sup>, Eef van den Borst<sup>1,2</sup>, Veerle Matheeußen<sup>3,4,5</sup> and Alex Vorsters<sup>1</sup>

RESEARCH ARTICLE

OPEN ACCESS



HPV-specific antibodies in female genital tract secretions captured via first-void urine retain their neutralizing capacity

Laura Téblick<sup>a</sup>, Marijana Lipovac<sup>a</sup>, Freya Molenberghs<sup>b</sup>, Peter Delpitte<sup>c</sup>, Winnok H. De Vos<sup>b,d,e</sup>, and Alex Vorsters<sup>a</sup>

<sup>a</sup>Centre for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, University of Antwerp, Antwerp, Belgium; <sup>b</sup>Laboratory of Cell Biology and Histology, University of Antwerp, Antwerp, Belgium; <sup>c</sup>Laboratory for Microbiology, Parasitology and Hygiene, University of Antwerp, Antwerp, Belgium; <sup>d</sup>Antwerp Centre for Advanced Microscopy, University of Antwerp, Antwerp, Belgium; <sup>e</sup>µNEURO Centre of Research Excellence, University of Antwerp, Antwerp, Belgium

# Future perspective: Non-invasive assessment of vaccine-induced HPV antibodies via first-void urine.

Pattyn J., Van Keer S., Teblich L., Van Damme P., and Vorsters A. (2020)



Focus on **urine** as sample to assess HPV DNA



- ✓ Less invasive than serum collection
- ✓ Does not require trained personnel
- ✓ Assessment of both HPV infection and immunogenicity simultaneously

→ FV urine could allow HPV **vaccine effectiveness data** to be reliably generated in different settings 1) where serum samples cannot be taken, 2) (self-collected) vaginal swabs are less preferred due to for example cultural reasons or a fear of discomfort and 3) limited data on vaccination status is available.

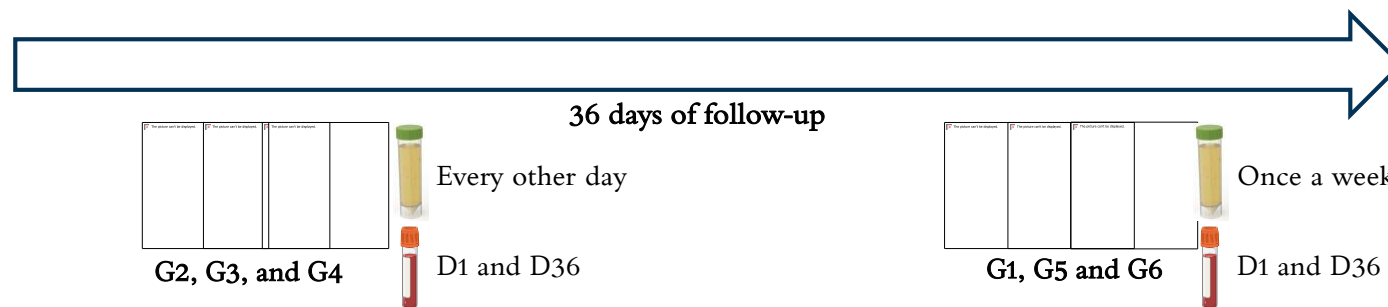
# URINORM

Can we normalize for intra- and inter-individual variability?

Recruitment ongoing - Clinicaltrials.gov: NCT06582654

G1: Pre-adolescent girls	G2: Women using contraceptives	G3: Women with IUD	G4: Women with natural cycle	G5: Post-menopausal women	G6: Men
<ul style="list-style-type: none"> <li>n = 25</li> <li>9-14 years</li> <li>Fully vaccinated</li> </ul>	<ul style="list-style-type: none"> <li>n = 25</li> <li>18-30 years</li> <li>Fully vaccinated</li> <li>Ovulation influencing contraceptive use</li> </ul>	<ul style="list-style-type: none"> <li>n = 25</li> <li>18-30 years</li> <li>Fully vaccinated</li> <li>Use of an hormonal or copper IUD</li> </ul>	<ul style="list-style-type: none"> <li>n = 25</li> <li>18-30 years</li> <li>Fully vaccinated</li> <li>No ovulation influencing contraceptive use</li> </ul>	<ul style="list-style-type: none"> <li>n = 25</li> <li>50-70 years</li> <li>Fully vaccinated</li> <li>No ovulation influencing contraceptive use</li> </ul>	<ul style="list-style-type: none"> <li>n = 25</li> <li>18-30 years</li> <li>Fully vaccinated</li> </ul>

- Within- and between-group differences?
- Differences between consecutive samples of same participant?
- Patterns in fluctuations and normalization markers to normalize for fluctuations?



# URINORM

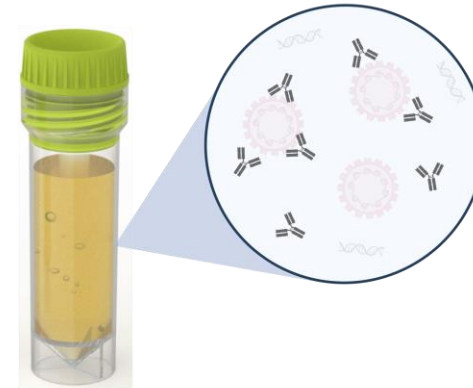
Can we normalize for intra- and inter-individual variability?

## Current status

	Included
Pre-adolescent girls:	25/25
Ovulation-influencing contraceptives group:	25/25
IUD group:	25/25
Natural cycle group:	25/25
Men:	20/25
Post-menopausal women:	7/25

> 2000 samples collected

## Experimental goals



1. LH surge
2. Erythrocytes
3. Anti-HPV antibodies
4. HPV DNA
5. Total IgG
6. Ig isotyping
7. GAPDH
8. Total protein
9. Estrogen/progesterone
10. ...

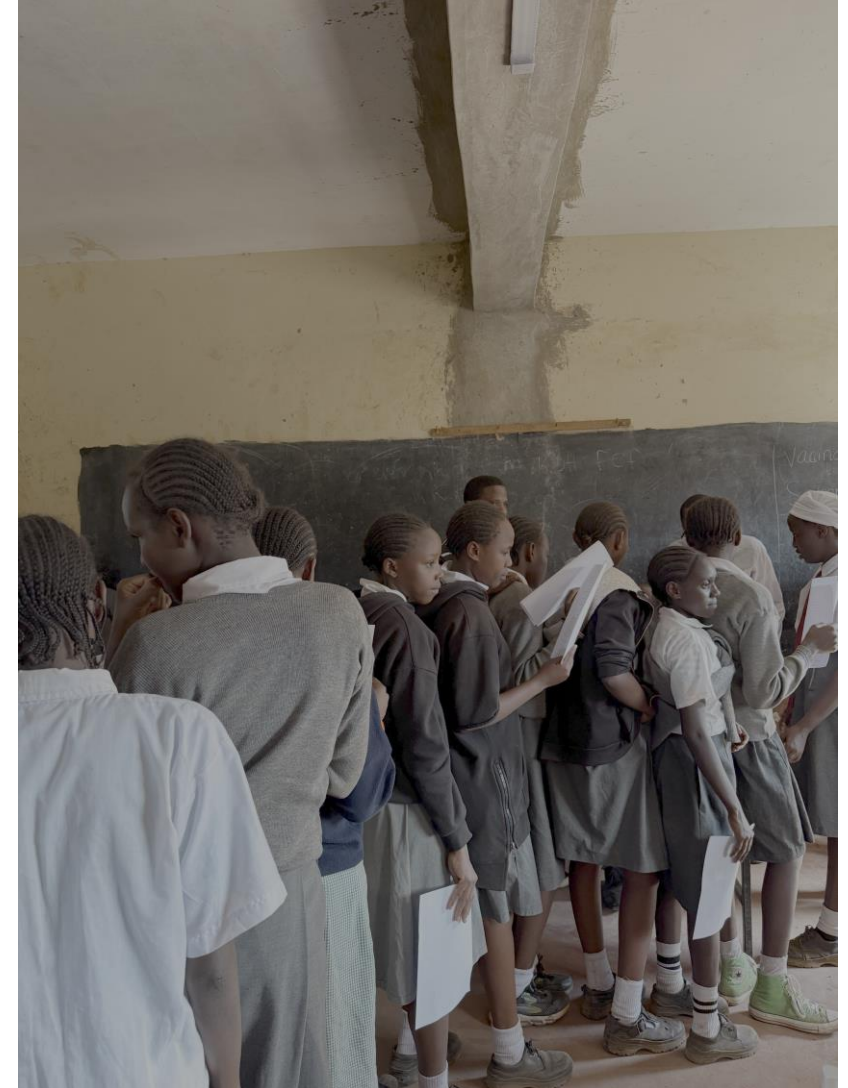
**Aimed outcome:** To find (the best combination of) biomarkers to normalize inter- and intra-individual variability in HPV-specific antibody levels in first-void urine samples.

# MISP-IMPACT-HPV study: Study Objectives

The overall objective of this study is to generate local data on HPV vaccine immune response and HPV infection prevalence in the Gavi demonstration cohort and young adolescents vaccinated as part of NIP, and to generate evidence on information on gaps and challenges related to HPV vaccination training among HCPs

## The research questions:

- Generate local data on HPV vaccine immune response and HPV infection prevalence.
- Generate evidence-based information on gaps and challenges related to HPV vaccination training among HCPs/ health workforce
- Assess the implementation feasibility of the study in various settings



# MISP-IMPACT-HPV study: Co-Investigators at the Country-level

## Kenya

**Prof. Nelly Mugo**

**Senior Principal Clinical Scientist - Kenya Medical Research Institute (*KEMRI*)**

## Senegal

**Prof. Tandakha Ndiaye Dieye**

**Immunology & vaccinology**

**Head of laboratories, Centre National de Transfusion Sanguine**

**Head of immunology unit, IRESSEF (Diamniadio)**

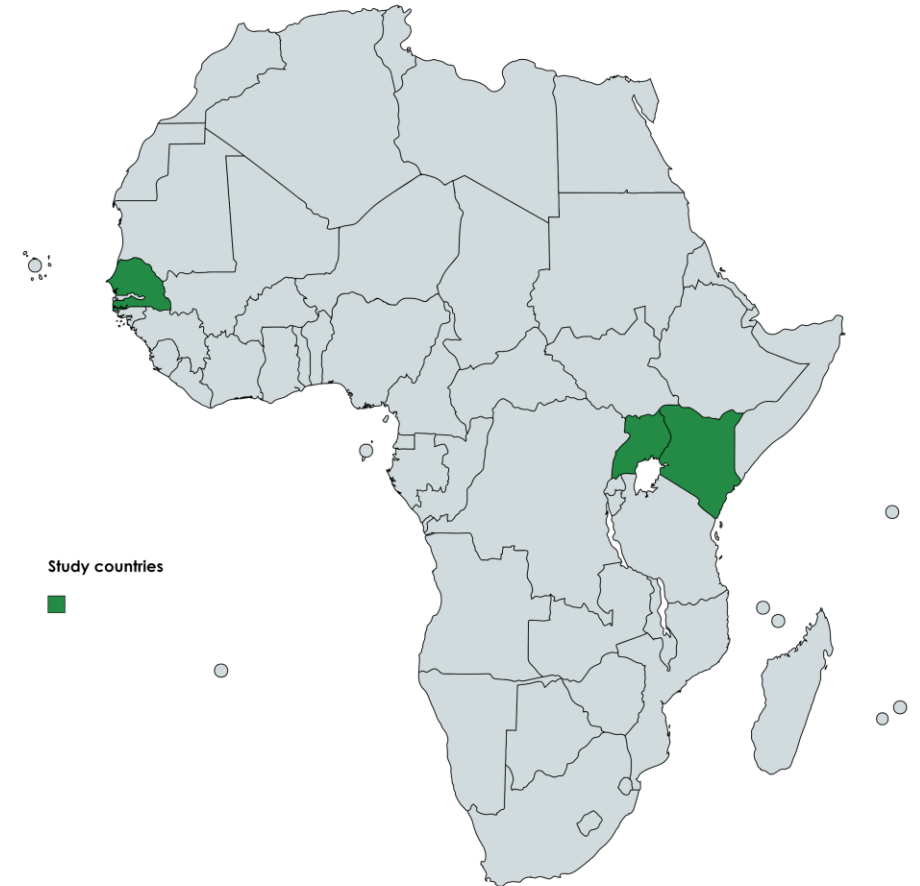
**President of the African Society for Immunodeficiencies (ASID)**

**Secretary General of the Society of AIDS in Africa (SAA)**

## Uganda

**Dr. Sabrina Bakeera-Kitaka & Dr. Joseph Rujumba**

**College of Health Sciences, School of Medicine, Department of Pediatrics and Child Health, Makerere University, Uganda**



Created with mapchart.net

**Study design:** Comparative cohort study measuring HPV immune response and infection prevalence between vaccinated and unvaccinated adolescent girls.

**Two cohorts per site:** Vaccinated (NIP or GAVI pilot) vs. unvaccinated — age-matched to ensure comparability across all sites.

## Study sites — Uganda & Kenya

### UG Uganda - Kampala

#### NIP cohort (from 2019)

- NIP-vaccinated cohort (school-based)
- Vaccinated vs. unvaccinated age-matched
- Recruited via health facilities & schools

### UG Uganda — Nakasongola

#### GAVI Pilot cohort (2009)

- Young women traced via facility and community
- Original pilot registers retrieved from health facilities
- Snowball sampling + Community Health Promoters

### KE Kenya — Kiambu

#### NIP cohort (from 2019)

- Girls <18 yrs; parental consent + child assent
- Schools with high & low vaccination coverage
- Community outreach in agricultural & slum areas

### KE Kenya — Kitui

#### GAVI Pilot cohort (2013–15)

- Young women traced via schools & community
- Original pilot registers retrieved from schools
- Snowball sampling + Community Health Promoters

Senegal sample collection ongoing

# Multicentric cohort study to compare efficacy of a single dose of 4-HPV vaccine compared to two & three doses in 10-18 yr old females in India

**Partha Basu MD, PhD**

Dty Head, Early Detection, Prevention & Infections Branch

International Agency  
for Research on Cancer



Study designed as a cluster RCT to compare 2 vs. 3 doses of 4-HPV vaccine in 10-18 year old unmarried girls initiated in Sept 2009

Study arm to receive 2 doses of 4-HPV at 0 & 6 months  
(Recruitment planned:10,000; Recruited: 9188)

Comparison arm to receive 3 doses of 4-HPV at 0, 2 & 6 months  
(Recruitment planned: 10,000; Recruited:8541)

*Loss of randomization due to order issued on **8 April 2010** by Ministry of Health to stop HPV vaccination in research studies with immediate effect*

Recipients of 3 doses  
as per protocol  
(N= 4,348)

Recipients of 2 doses  
as per protocol  
(N= 4,980)

Recipients of 2 doses by  
default at 0 & 2 months  
(N= 3,452)

Recipients of a single  
dose by default  
(N= 4,949)

- Yearly follow up
- Cervical specimen collection for HPV genotyping (Luminex™ assay) for 21 HPV types starting at 18 months after marriage or 6 months after first pregnancy yearly x 4 such

- Screening for cervical cancer using Hybrid Capture II™ (HC II) for married participants at 25 & 30 years of age
- HC II positive women tested for HPV 16/18/45 only using PS genotyping test (test used for triaging of HPV positives)
- HC II positive women undergo colposcopy (& biopsy)

Unvaccinated cohorts recruited post-hoc:

Age & site-matched first  
unvaccinated control group  
recruited during 2013-2015  
(N= 1,541)

Age & site-matched second  
unvaccinated control group  
(screening-only) recruited during  
2017-2019  
(N= 3,631)

# HPVplus team

**PI:** Prof. Alex Vorsters, PhD

- Margo Bell
- Ricardo Burdier
- Annemie De Smet
- Sakshi Jindal
- Marijana Lipovac
- Xenia Mikulla
- Tine Pinxteren
- Laura Téblick, PhD
- Anne Van Caesbroeck
- Eef van den Borst
- Prof. Severien Van Keer, PhD
- Dur-e-Nayab Waheed



**Wide network in HPV-field:**



COALITION to STRENGTHEN  
the HPV IMMUNIZATION  
COMMUNITY



Thank you for your  
attention