Current status of urine samples to monitor HPV vaccination status.

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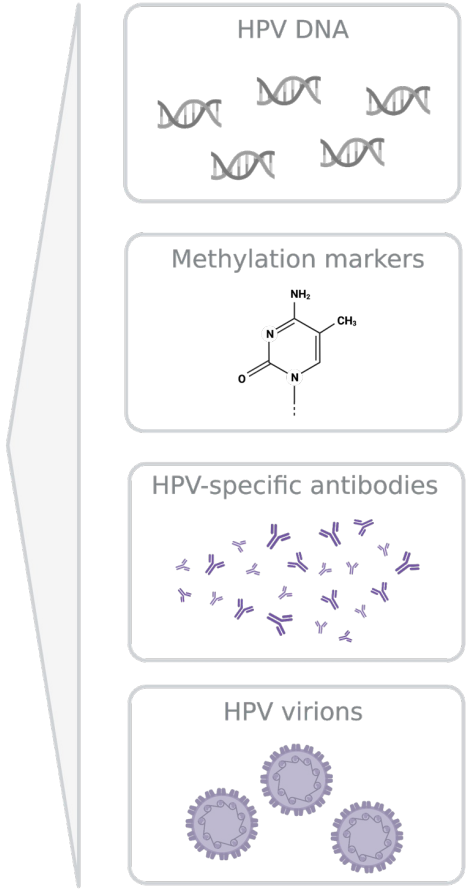
Why first-void urine (FVU)?

First-void urine



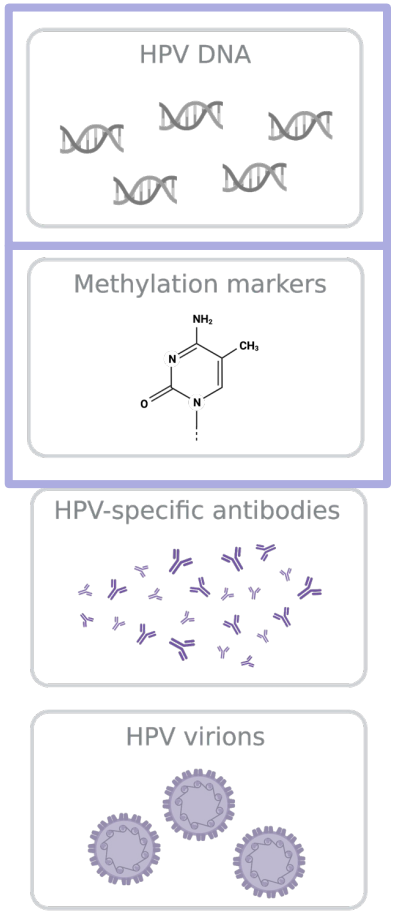
Initial stream of urine

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**
✓ **Likely preferred**
✓ **Home-based**
✓ **Reaches screening/follow-up non-participants**

Pattyn, J. et al. Front. Immunol. (2020); Pattyn, J. et al. Expert Review of Anti-Infective Therapy (2019).

First-void urine



Article

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

Alex Vorsters [1,*], Severien Van Keer [1], Samantha Biesmans [1], Annick Hens [1], Ilse De Coster [1], Herman Goossens [2,3], Margareta Ieven [2,3] and Pierre Van Damme [1]

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[a,*], E. Peeters[a], I. Benoy[b,c,d], D. Vanden Broeck[b,c,d,e], J. Bogers[b,c,d,e], P. De Sutter[f], G. Donders[g,h,i], W. Tjalma[j,k], S. Weyers[l], K. Cuschieri[m], M. Poljak[n], J. Bonde[o], C. Cocuzza[p], F.H. Zhao[q], S. Van Keer[r], A. Vorsters[r]

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[1], M. Chantal Umulisa[2], Ugyen Tshomo[3], Tarik Gheit[1], Iacopo Baussano[1], Vanessa Tenet[1], Tshokey Tshokey[4], Maurice Gatera[2], Fidele Ngabo[2], Pierre Van Damme[5], Peter J.F. Snijders[6], Massimo Tommasino[1], Alex Vorsters[5] and Gary M. Clifford[1]

Urine testing for HPV: rationale for using first void

Alex Vorsters *researcher*[1], Pierre Van Damme *professor*[1], Gary Clifford *cancer epidemiologist*[2]

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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 [a,*], Eliana Peeters [b], Davy Vanden Broeck [c,d,e,f], Philippe De Sutter [g], Gilbert Donders [h,i,j], Jean Doyen [k], Wiebren A.A. Tjalma [l,m], Steven Weyers [n], Alex Vorsters [a], Marc Arbyn [b]

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 Matheeussen [3,4,5], Renee Mandersloot [6], Arno Floore [6], Chris J. L. M. Meijer [6,7], Renske D. M. Steenbergen [7] and Alex Vorsters [1]

Impact of Human Papillomavirus Vaccination, Rwanda and Bhutan

acopo 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

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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[a,*], Severien Van Keer[a], Samantha Biesmans[a], Margareta Ieven[a,c], Charlotte Vanderborght[a], Koen Beyers[b], Vanessa Vankerckhoven[a,b], Robin Bruyndonckx[c,d], Pierre Van Damme[a], Alex Vorsters[a]

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

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 [1] · Wiebren A. A. Tjalma [2,3] · Jade Pattyn [1] · Samantha Biesmans [1] · Zoë Pieters [4,5] · Xaveer Van Ostade [6] · Margareta Ieven [7] · Pierre Van Damme [1] · Alex Vorsters [1]

First-void urine

HPV DNA

Methylation markers

HPV-specific antibodies

HPV virions

Contents lists available at ScienceDirect

Journal of Clinical Virology

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

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[b], Jade Pattyn[a], Julia Butt[b], Wiebren A.A. Tjalma[c,d], Xaveer Van Ostade[e], Niel Hens[f,g], Pierre Van Damme[a], Tim Waterboer[b], 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[1] | Gitika Panicker[2] | Martina Willhauck-Fleckenstein[3] | Severien Van Keer[1] | Laura Téblick[1] | Zoë Pieters[4,5] | Wiebren A. A. Tjalma[6,7] | Veerle Matheeussen[8,9,10] | Pierre Van Damme[1] | Tim Waterboer[3] | Elizabeth R. Unger[2] | Alex Vorsters[1]

Contents lists available at ScienceDirect

Papillomavirus Research

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

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

Jade Pattyn[a,*], Severien Van Keer[a], Wiebren Tjalma[b], Veerle Matheeussen[c], Pierre Van Damme[a], Alex Vorsters[a]

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

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

Faculty of Medicine and Health Sciences, Centre for the Evaluation of Vaccination, Vaccine and Infectious Disease Institute (VAXINFECTIO), 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

Major presence of IgG in female genital tract

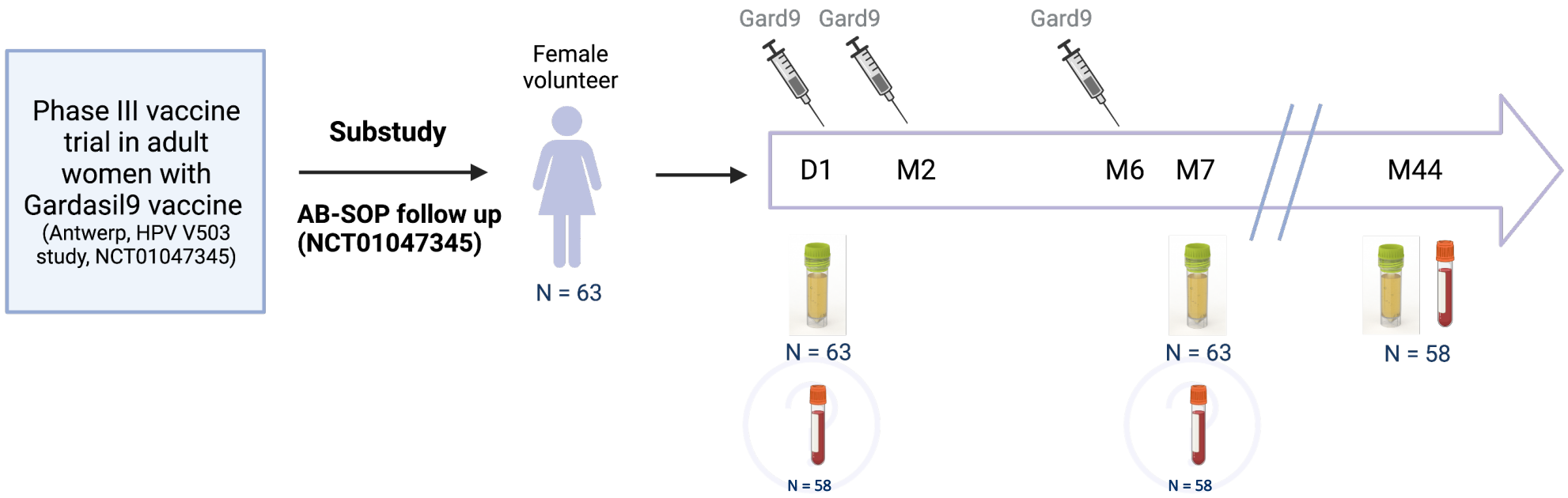
- 90% reduction of total IgG in genital tract secretions after total hysterectomy

Ab transport mechanism blood → FVU

- Exudation
- Transudation
- Receptor mediated: FcRn receptor

AB-SOP follow-up study / 2018-2022

NCT03542227



Samples
1 (3) serum + 3 FVU

Mean age at inclusion
35y (IQR: 28 - 41)

Vaccine type:
100% 9vHPV

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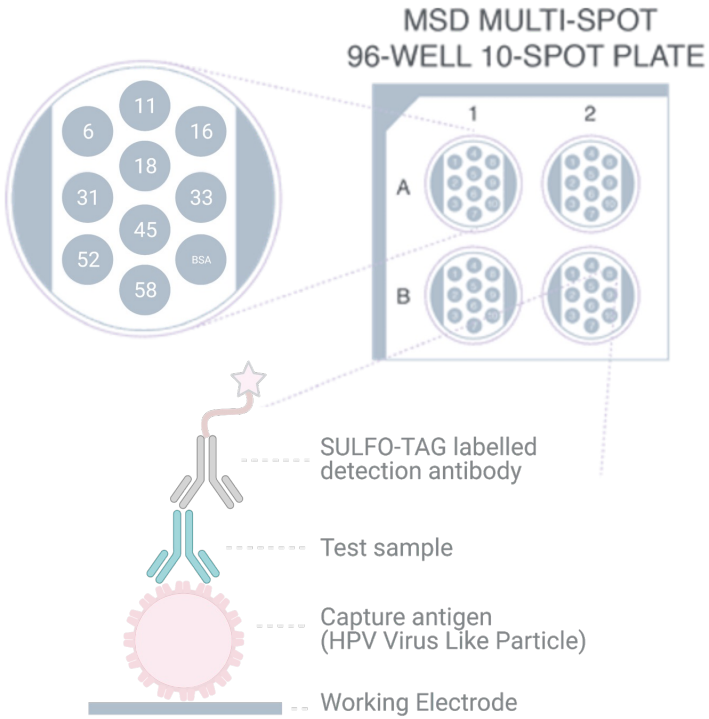
NCT03542227

HPV-specific antibody detection

- M9ELISA at CDC
- Multiplex VLP based IgG assay for HPV types included in the nonavalent HPV-vaccine
- Multiarray plates: spotted at Meso Scale Discovery
- Concentrations calculated using
  → Parallel line (PLL) method
- International and arbitrary units (IU/ml and AU/ml)



HPV DNA Detection

1. **All FVU samples:** Roche Cobas 6800 (HPV16/18/otherHrHPV)
2. **Cobas 6800 positive samples:** Riatol qPCR HPV genotyping assay (HPV6/11/16/18/31/33/35/39/45/51/52/53/56/58/59/66/68/67)

Panicker, G. *et al. J. Immunol. Methods* (2015).

AB-SOP follow-up study / 2018-2022

NCT03542227

M9ELISA

	FIRST-VOID URINE		
	Month 0	Month 7	Month 44
HPV type	Uropositivity (positive/total (%))	Uropositivity (positive/total (%))	Uropositivity (positive/total (%))
6	11/63 (17%)	62/63 (98%)	57/58 (98%)
11	6/63 (10%)	63/63 (100%)	57/58 (98%)
16	8/63 (13%)	63/63 (100%)	58/58 (100%)
18	8/63 (13%)	61/63 (97%)	52/58 (90%)
31	6/63 (10%)	63/63 (100%)	55/58 (95%)
33	4/63 (6%)	63/63 (100%)	56/58 (97%)
45	2/63 (3%)	60/63 (95%)	52/58 (90%)
52	0/63 (0%)	62/63 (98%)	49/58 (84%)
58	5/63 (8%)	63/63 (100%)	53/58 (91%)

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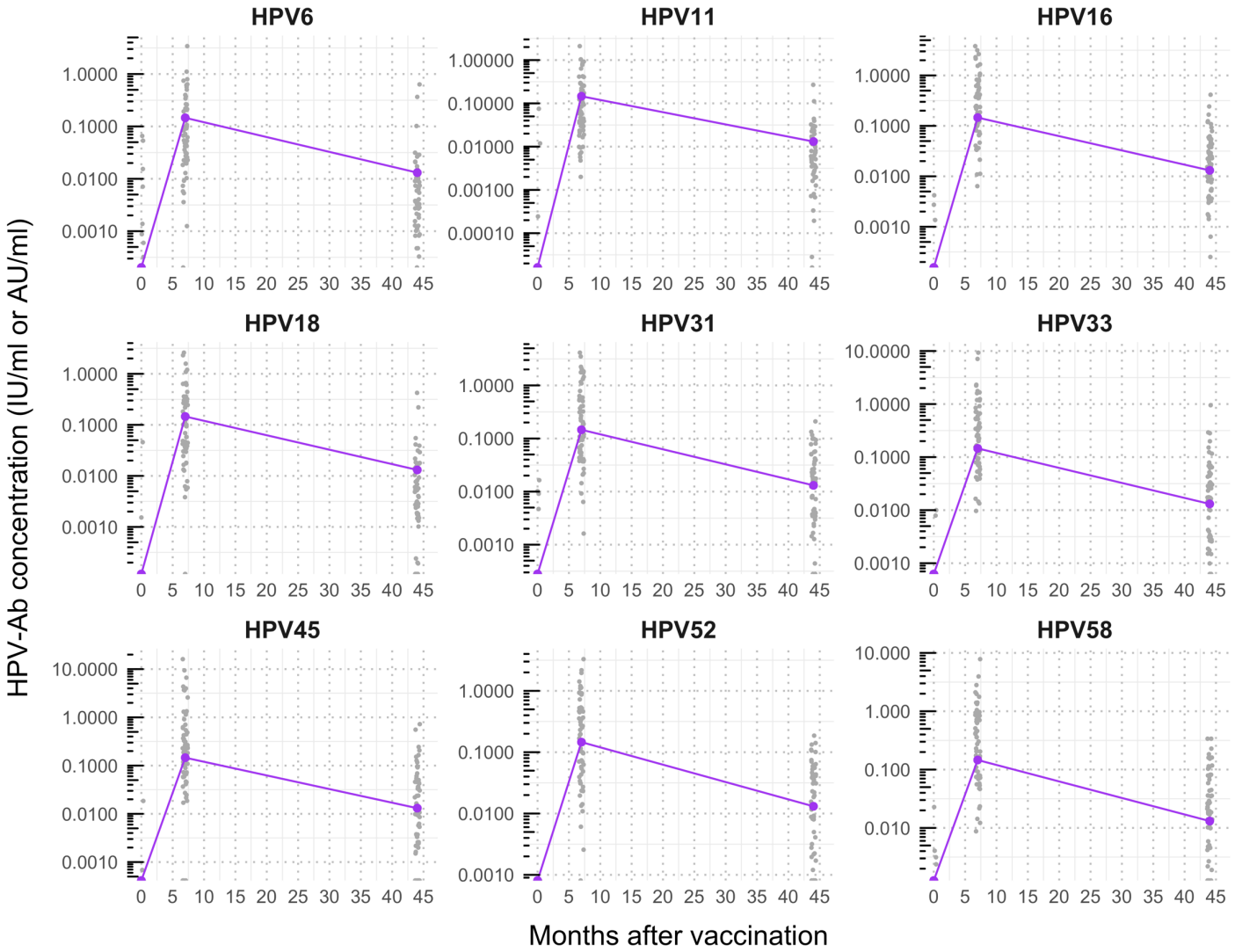
M9ELISA



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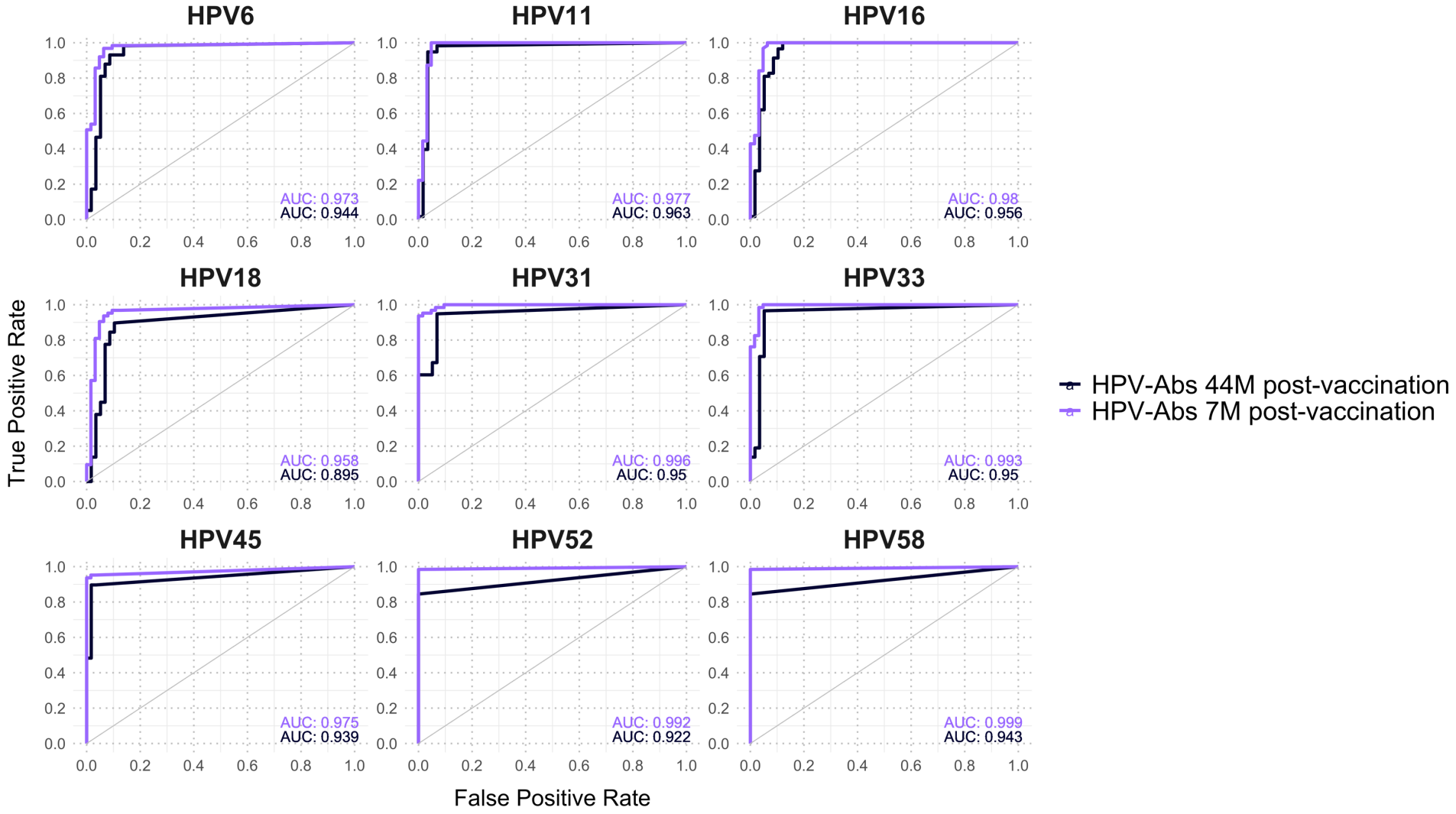
NCT03542227

M9ELISA



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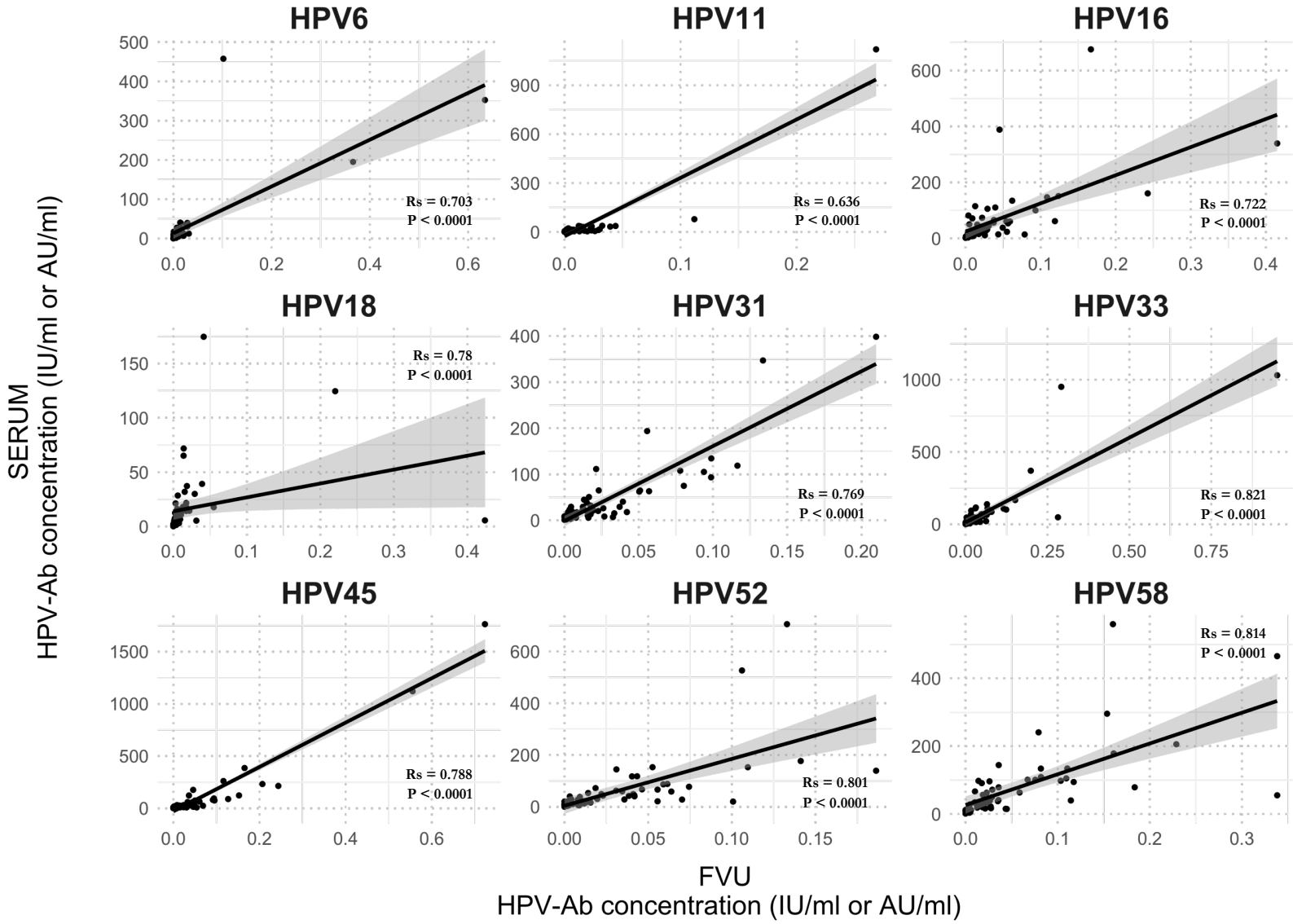
M9ELISA



Investigating naturally induced immune response

AB-SOP follow-up study / 2018-2022

NCT03542227

4/63 women had an infection of HPV type included in nonavalent vaccine = red

1. All samples: Roche Cobas 6800

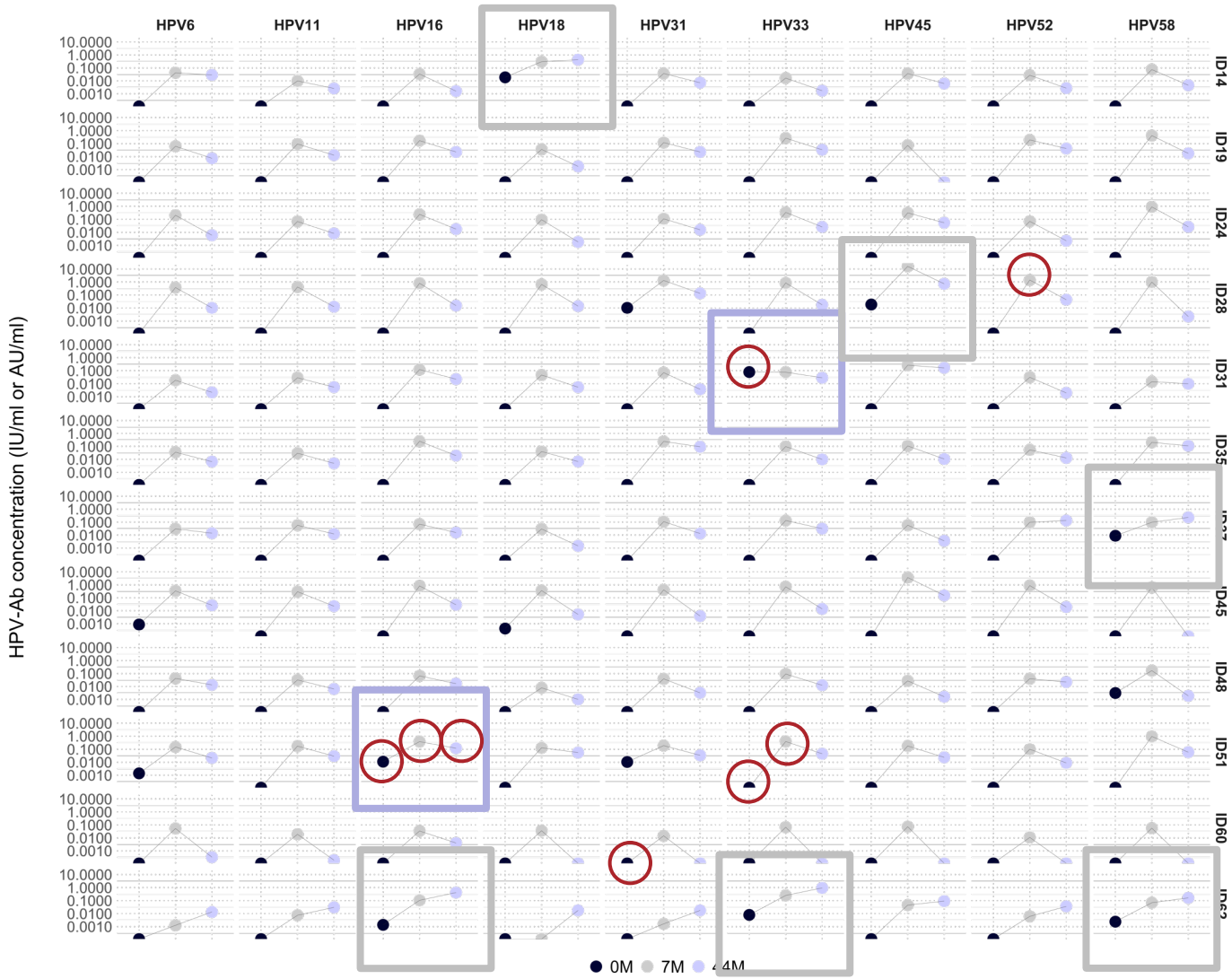
2. Riatol qPCR HPV genotyping assay

ID	Before vaccination	7M after 1st dose	44M after 1st dose
14	HPV59	HPV59	HPV other
19	None	None	/
24	/	HPV66	/
28	/	**HPV52**	/
31	**HPV33,** HPV59	/	/
35	HPV51	HPV51	/
37	HPV56	HPV56	/
45	/	/	HPV other
48	/	/	HPV other
51	**HPV16, HPV33,** HPV51	**HPV16, HPV33,** HPV51, HPV56, HPV66	**HPV16**, HPV other
60	**HPV31**, HPV51	HPV35, HPV51	/
62	HPV51	/	/

Investigating naturally induced immune response

AB-SOP follow-up study / 2018-2022

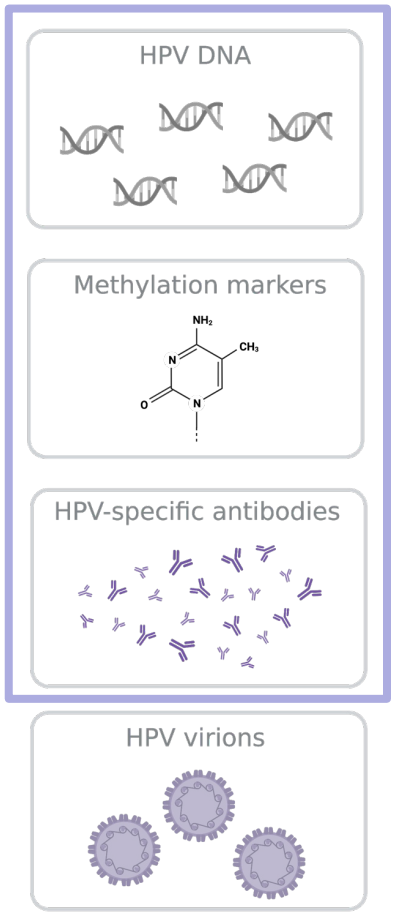
NCT03542227



4/63 women had an infection of HPV type included in nonavalent vaccine

= red

First-void urine



Concluding remarks

1. Follow-up of vaccination using FVU samples
   - Promising data
   - Normalisation is being investigated

2. Good correlation between HPV-specific antibody concentrations in FVU and serum

3. First-void urine has potential to become the **"golden sample"** for both detecting HPV infection and monitoring HPV vaccination

   (Also anti-HIV antibodies can be detected in urine)

University of Antwerp
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Vaccine and Infectious Disease Institute

UZA

Centers for Disease Control and Prevention

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Severien Van Keer, PhD; Jade Pattyn, PhD; Annemie De Smet; Prof. Alex Vorsters, PhD

Centers for Disease Control and Prevention (CDC):

Gitika Panicker, PhD; Prof. Elizabeth Ünger, MD, PhD

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Current status of urine samples to monitor HPV vaccination status.

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