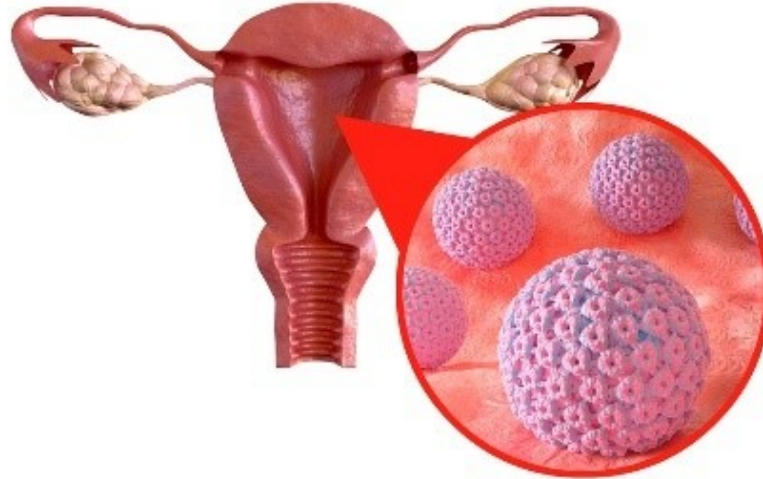


“TUMORI FEMMINILI E L’HPV: E’ CAMBIATO QUALCOSA NEL NUOVO MILLENNIO?”

HUMAN PAPILLOMAVIRUS

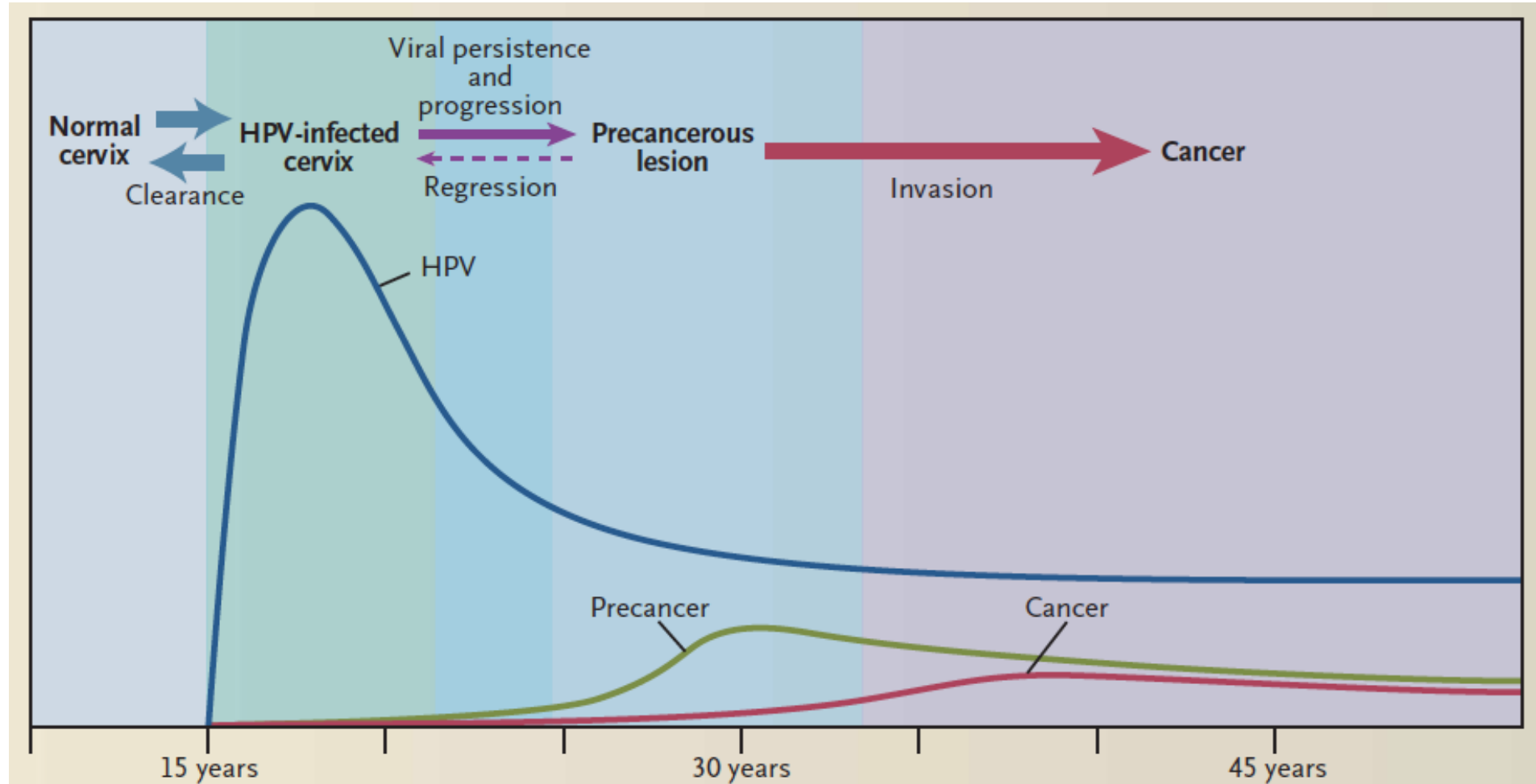


L’HPV nelle diverse età della donna

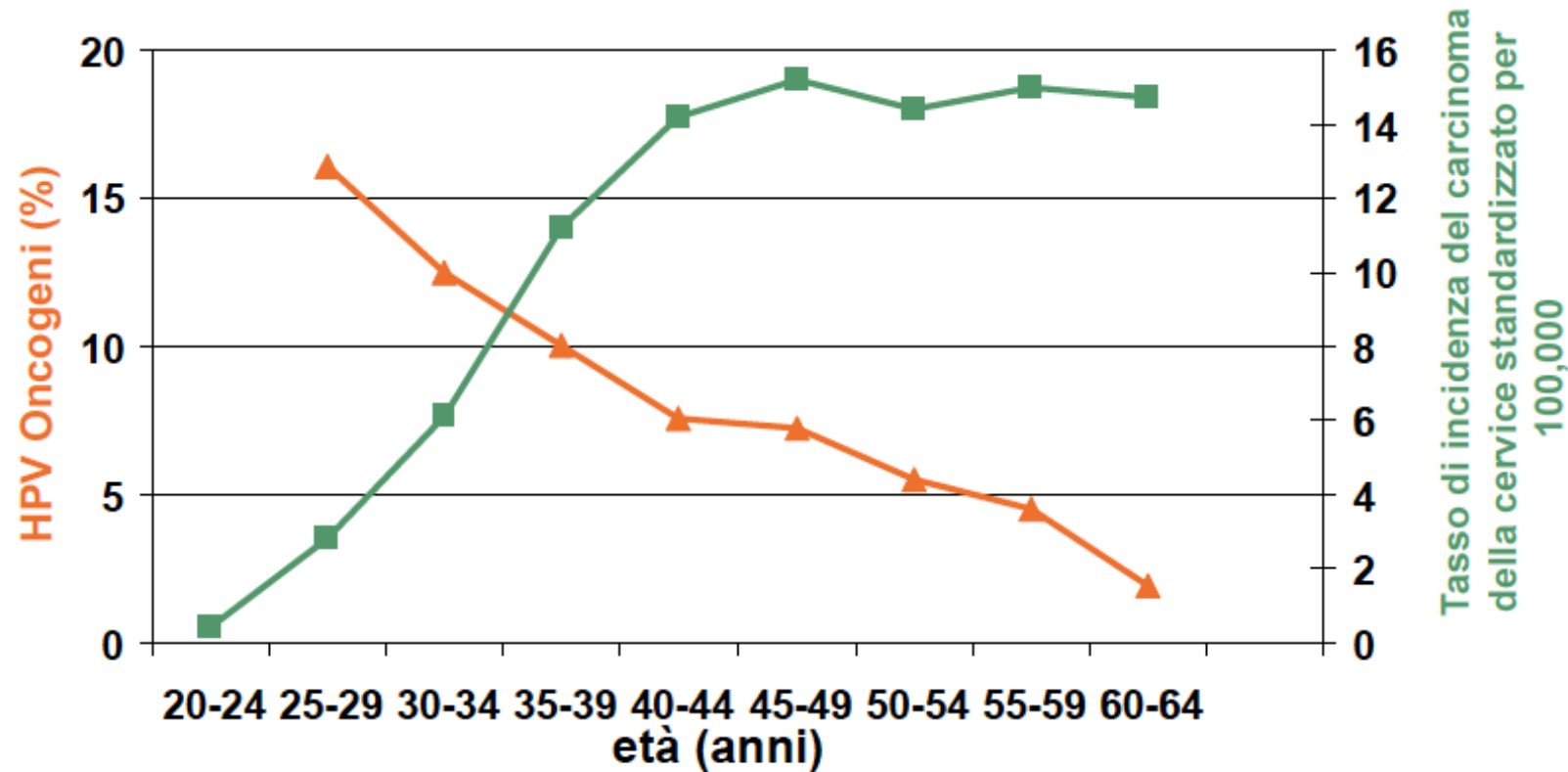
M. Della Martina

Udine 20 settembre 2024

L'HPV nelle diverse età della donna

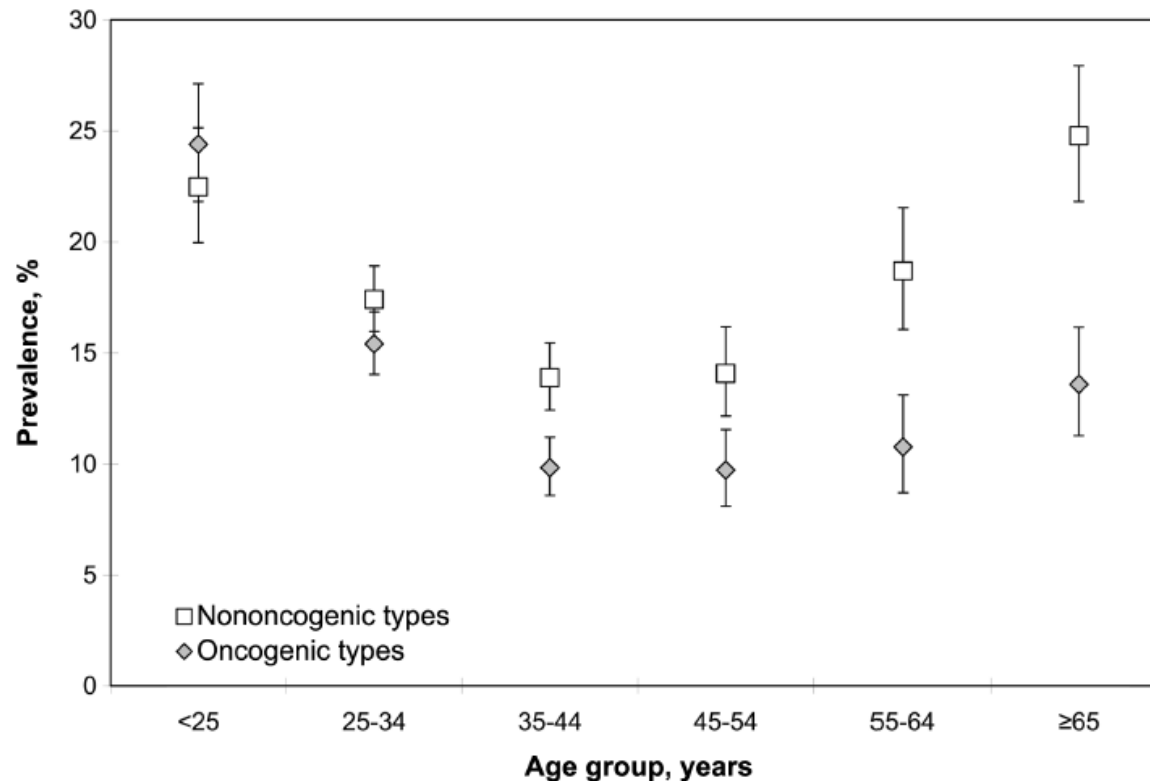


L'HPV nelle diverse età della donna: Incidenza età specifica C.C e prevalenza HPV in Italia



Epidemiologic Profile of Type-Specific Human Papillomavirus Infection and Cervical Neoplasia in Guanacaste, Costa Rica

Rolando Herrero,^{1,a} Philip E. Castle,^{2,a} Mark Schiffman,² M. Concepción Bratti,¹ Allan Hildesheim,² Jorge Morales,¹ Mario Alfaro,¹ Mark E. Sherman,² Sholom Wacholder,² Sabrina Chen,³ Ana C. Rodriguez,¹ and Robert D. Burk⁴



Human papillomavirus infection rate, distribution characteristics, and risk of age in pre- and postmenopausal women

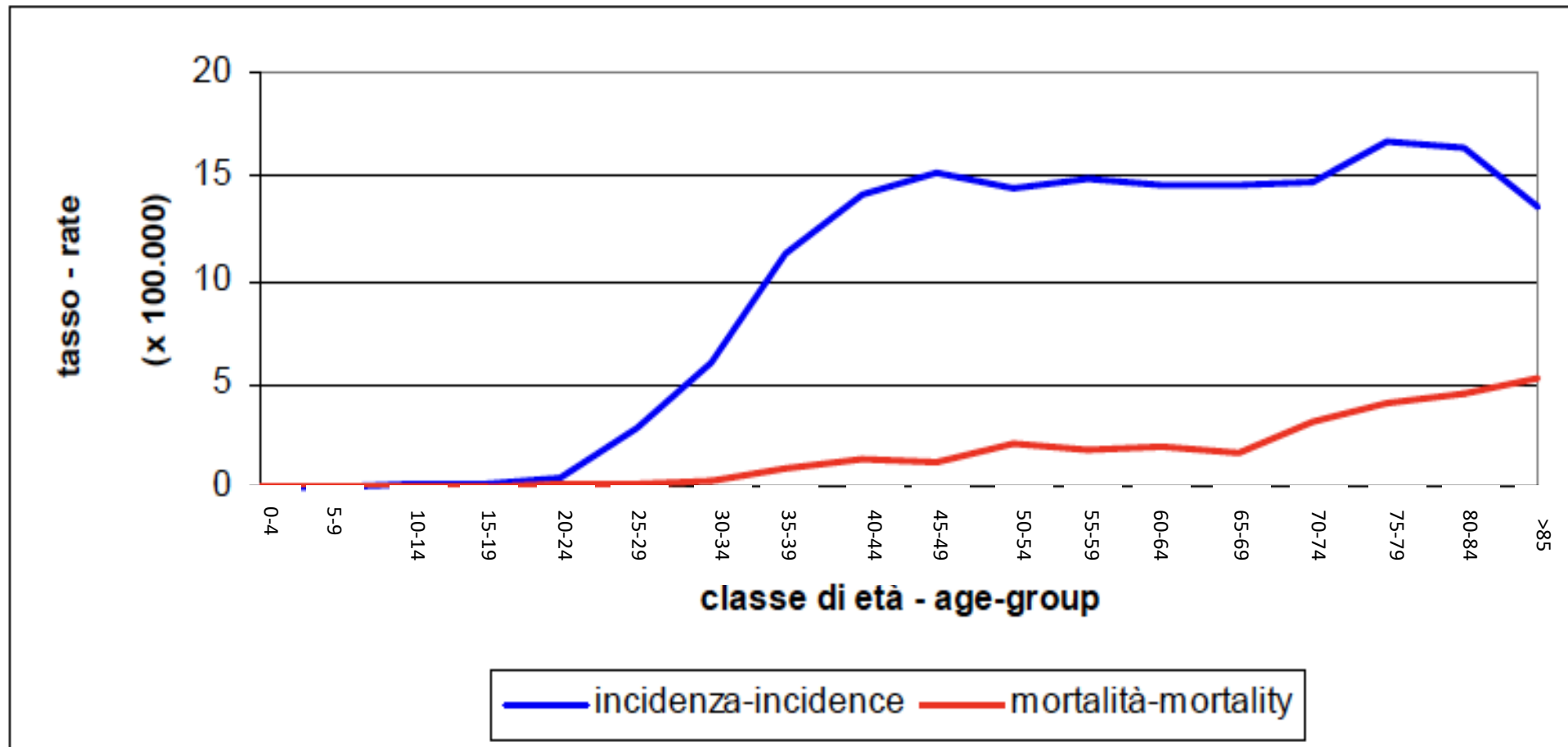
Table 4 The influence of h-rHPV infection in different age groups

Age	n/N	Percentage (+)	P	95% CI
≤ 30	50/401	12.47	0.443	1.146 (0.808, 1.626)
30–40	117/1310	8.93	0.080	0.789 (0.605, 1.029)
40 to menopause	105/1264	8.31	0.023	0.729 (0.555, 0.957)
Postmenopause	126/1140	11.05	–	1
Menopause to 65	106/987	10.74	–	1
≥ 65*	20/153	13.07	0.393	0.800 (0.480, 1.334)

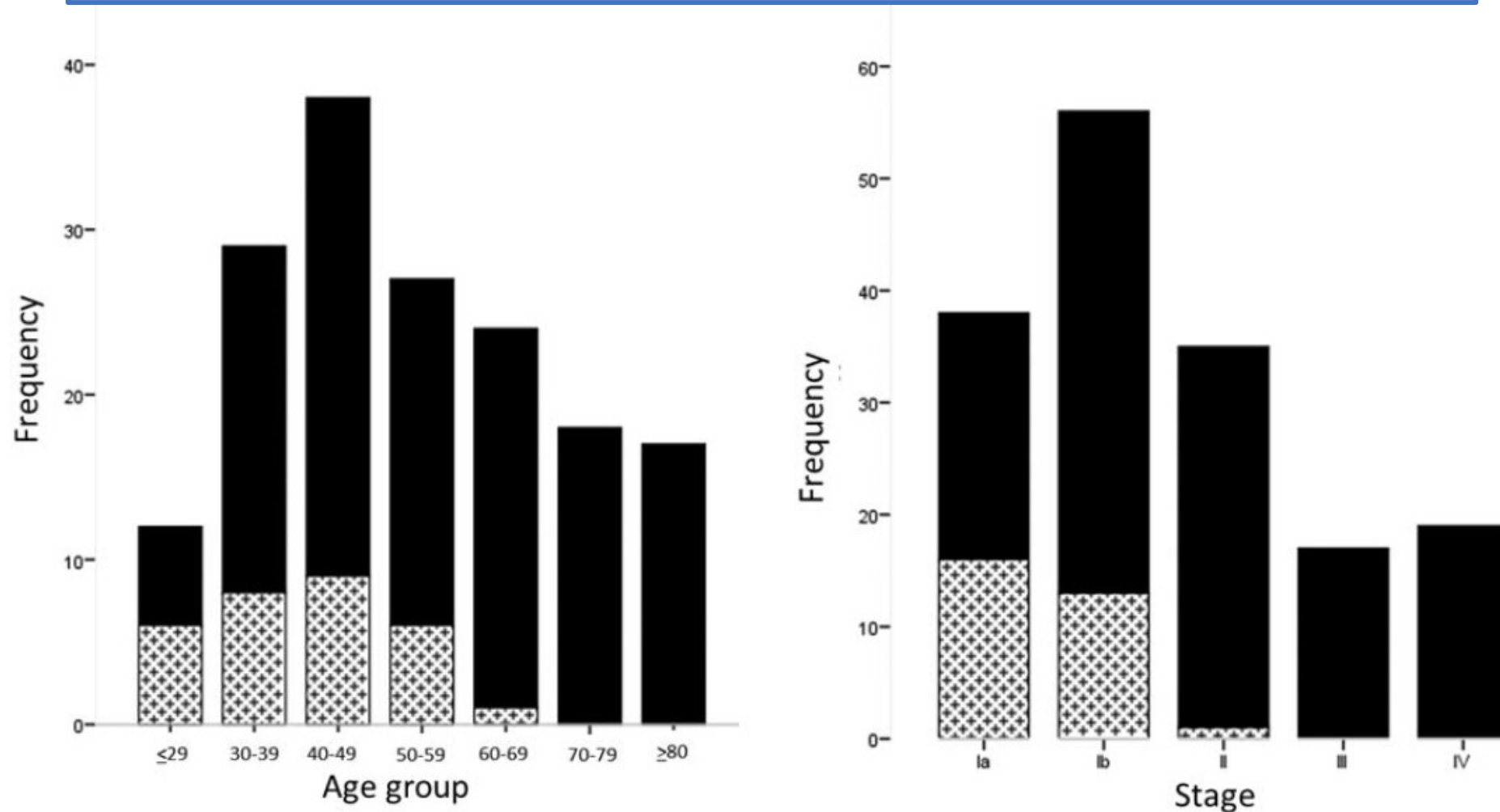
*Compared to menopausal to 65 years old

L'HPV nelle diverse età della donna:

Tassi di incidenza e mortalità per classi di età del CC



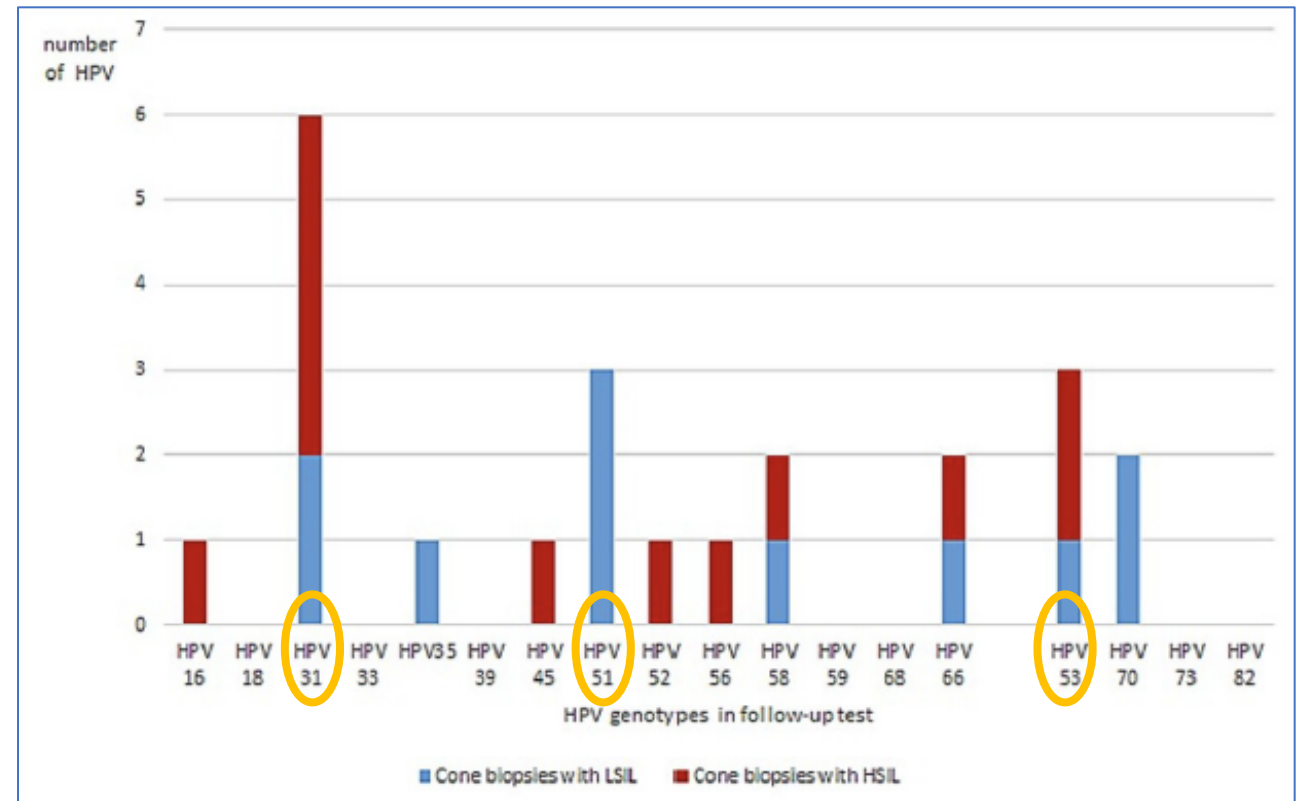
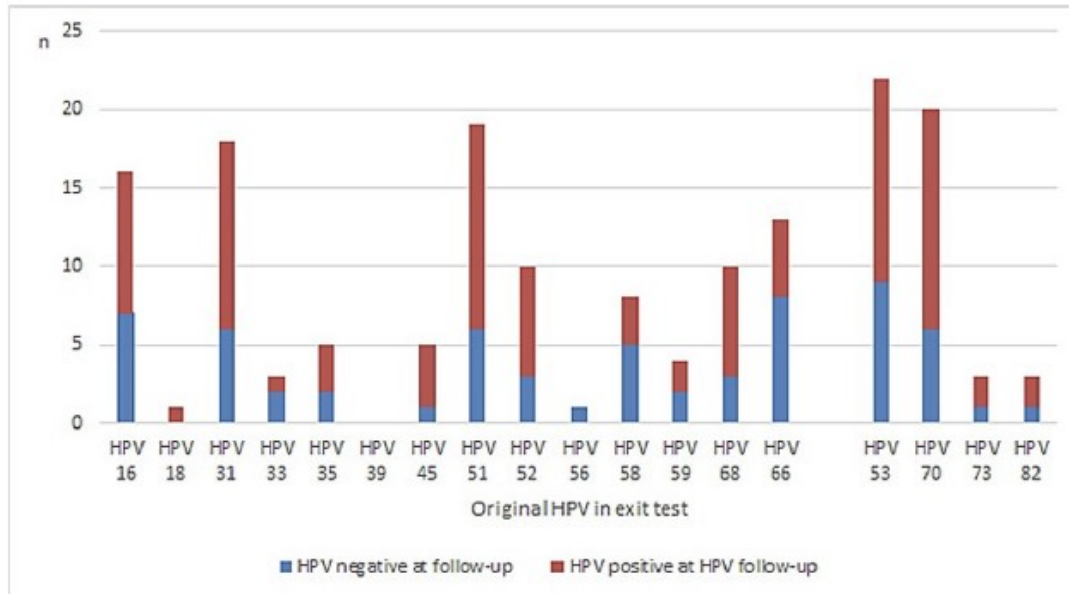
Elderly Women Above Screening Age Diagnosed with Cervical Cancer Have a Worse Prognosis



L'HPV nelle diverse età della donna

HPV-based screening for cervical cancer among women 55-59 years of age

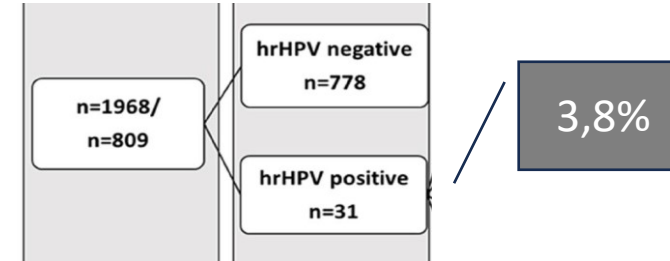
Lovisa Bergengren^{1*}, Gabriella Lillsunde-Larsson², Gisela Helenius³, Mats G. Karlsson³



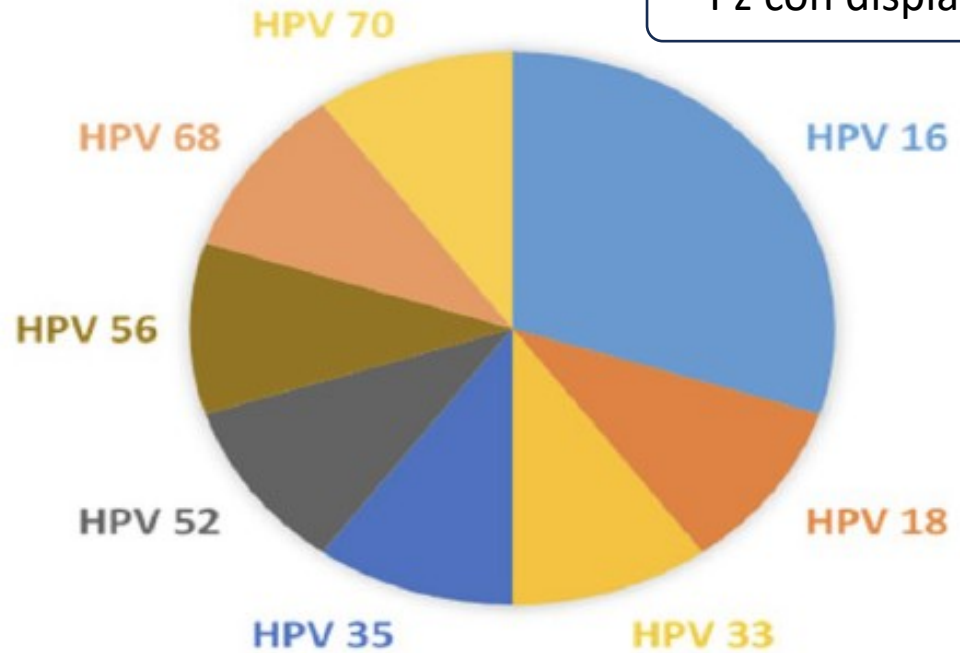
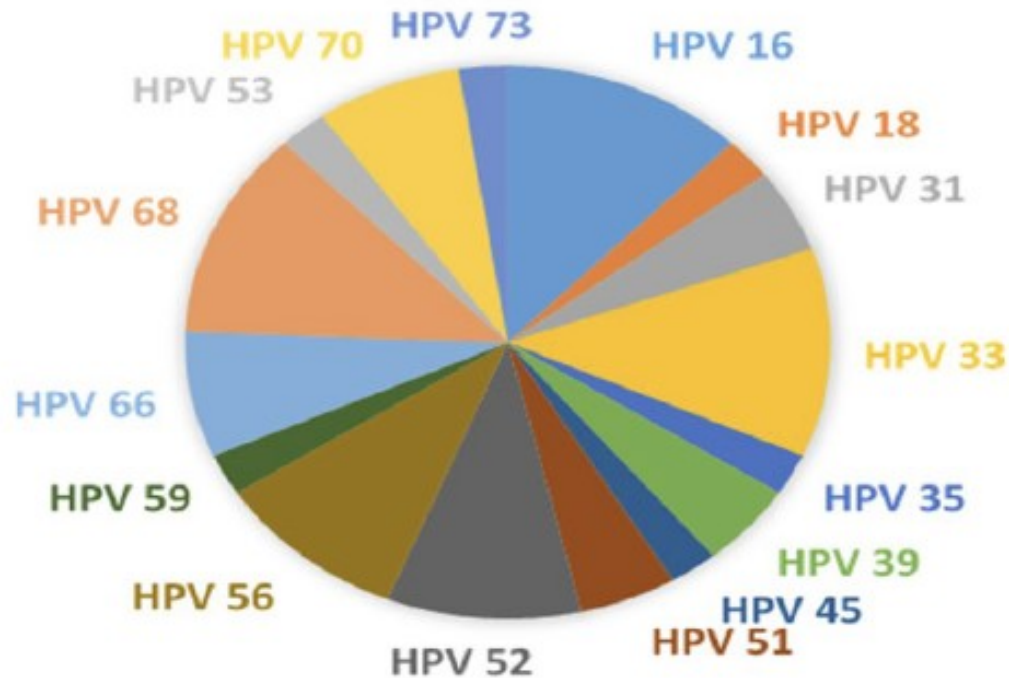
L'HPV nelle diverse età della donna

Prevalence of HPV and pathological changes among women 70 years of age, 10 years after exclusion from the Swedish cervical cancer screening program

Lovisa Bergengren¹ · Mats G. Karlsson² · Gisela Helenius²



Pz con displasia



L'HPV nelle diverse età della donna



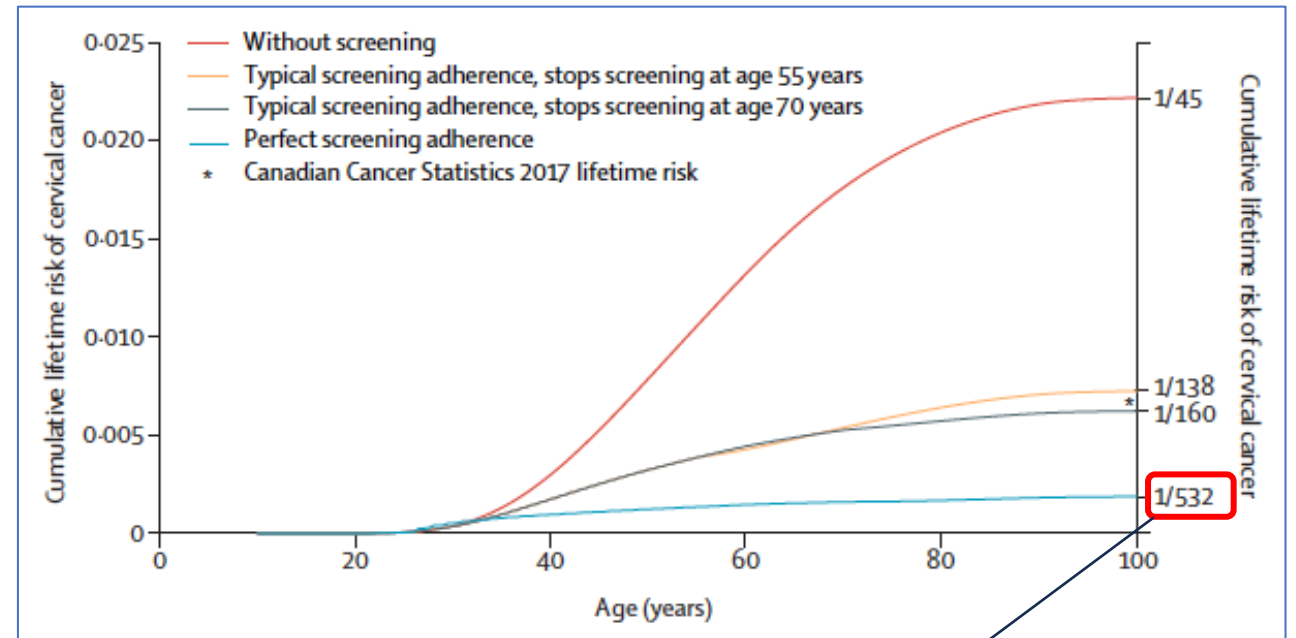
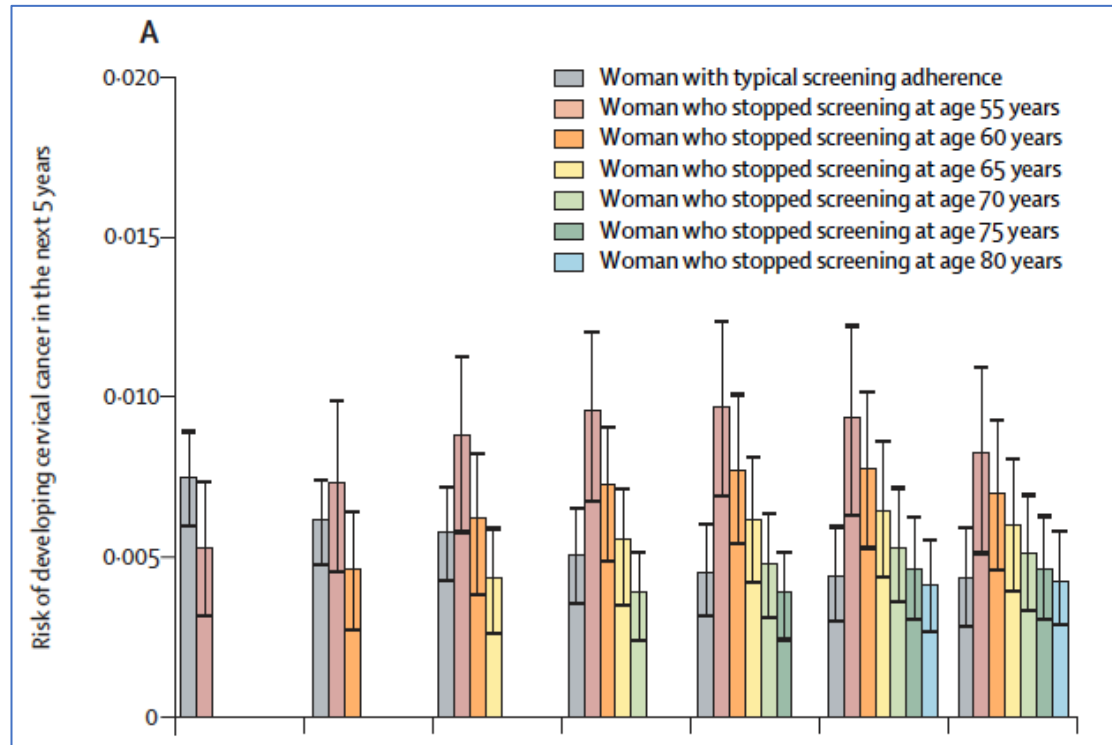
Screening HPV fino a che età?

L'HPV nelle diverse età della donna

Age at last screening and remaining lifetime risk of cervical cancer in older, unvaccinated, HPV-negative women: a modelling study

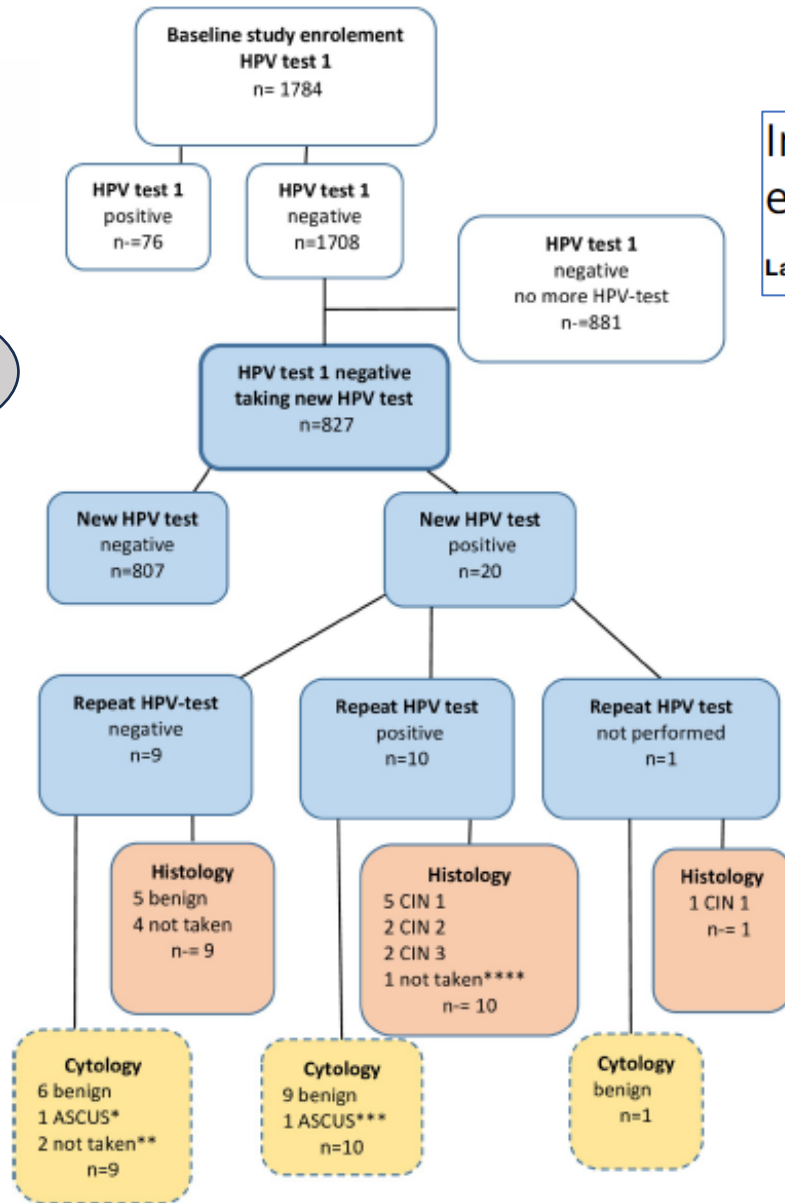
Talía Malagón, Shalini Kulasingam, Marie-Hélène Mayrand, Gina Ogilvie, Leah Smith, Céline Bouchard, Walter Gotlieb, Eduardo L Franco

THE LANCET
Oncology



1/532

60-90
anni



* Follow up with 4 negative HPV test
** Histology benign
*** Cytology ASCUS, histology CIN I
**** Lost to follow up

Incidence of HPV and HPV related dysplasia in elderly women in Sweden
Lars Lannér¹, Annika Kristina Lindström^{1,2*}

1/3 dei cancri cervicali > 60 anni

L'incidenza dell'HPV nelle donne anziane con HPV negativo a 60 anni è bassa , ma il VPP per displasia istologica è alto nelle donne HPV positive alla ripetizione del test. Il tempo di sviluppo di lesione ad alto grado è relativamente breve.
Difficile sapere se infezione nuova o latente.

Necessità di studi focalizzati sull'età di termine dello screening nelle donne anziane per prevenire l'insorgenza di cancro cervicale

Step by step instructions how to perform the self-sampling



1

- Wash your hands!
- Pick up the sampling card.
- Place the card on a dry surface
- Open the card by lifting the protecting flap.



2

- Remove the sampling tool from its package by the blue handle. Do not touch the bristles.



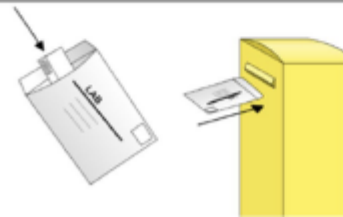
3

- Assume a relaxed position (or lie down).
- Insert the sampling tool into the vagina until you feel a resistance (7-10 cm).
- Turn the brush once and remove.



4

- Press the bristles at the card and rotate against the coloured area on the right side.
- Dispose off the sampling tool.
- The sample will make the card change colour.
- Let the card air dry for 10-20 minutes.
- Fold back the protective flap over the card.



5

- Put the card in the envelope.
- Seal the envelope.
- Send in the card to the lab by regular mail.

Fig. 1 Information supplied to the women on how to perform self-sampling using the Rovers Viba-brush and the FTA card

L'HPV nelle diverse età della donna

Elderly women's experiences of self-sampling for HPV testing

Ruth S. Hermansson^{1,2*}, Matts Olovsson¹, Catharina Gustavsson^{3,4,5} and Annika Kristina Lindström^{1,3,2}

Table 2 Answers by age group on how easy or difficult it had been to perform self-sampling

Age group years (n)	Very easy n (%)	Easy n (%)	Not easy n (%)	No answer n (%)
60 (227)	121 (53.3)	101 (44.5)	2 (0.9)	3 (1.3)
65 (233)	124 (53.2)	103 (44.2)	4 (1.7)	2 (0.9)
70 (218)	105 (48.2)	100 (45.9)	6 (2.8)	7 (3.2)
75 (190)	77 (40.5)	102 (53.7)	6 (3.2)	5 (2.6)
Total (868)	427 (49.2)	406 (46.8)	18 (2.0)	17 (2.0)

*There were no significant differences in the answers between age groups ($p = 0.104$)

Table 3 Answers by age group about sampling preference

Age group years (n)	Prefer self-sampling n (%)	Prefer health-care provider n (%)	Uncertain n (%)	No answer n (%)
60 (227)	124 (54.6)	41 (18.0)	61 (26.9)	1 (0.4)
65 (233)	142 (60.9)	34 (14.6)	56 (24.0)	1 (0.4)
70 (218)	118 (54.1)	43 (19.7)	55 (25.2)	2 (0.9)
75 (190)	127 (66.8)	25 (13.2)	34 (17.9)	4 (2.1)
Total (868)	511 (58.9)	143 (16.5)	206 (23.7)	8 (0.9)

*There were no significant differences in the answers between age groups ($p = 0.085$)

L'HPV e infiammazione

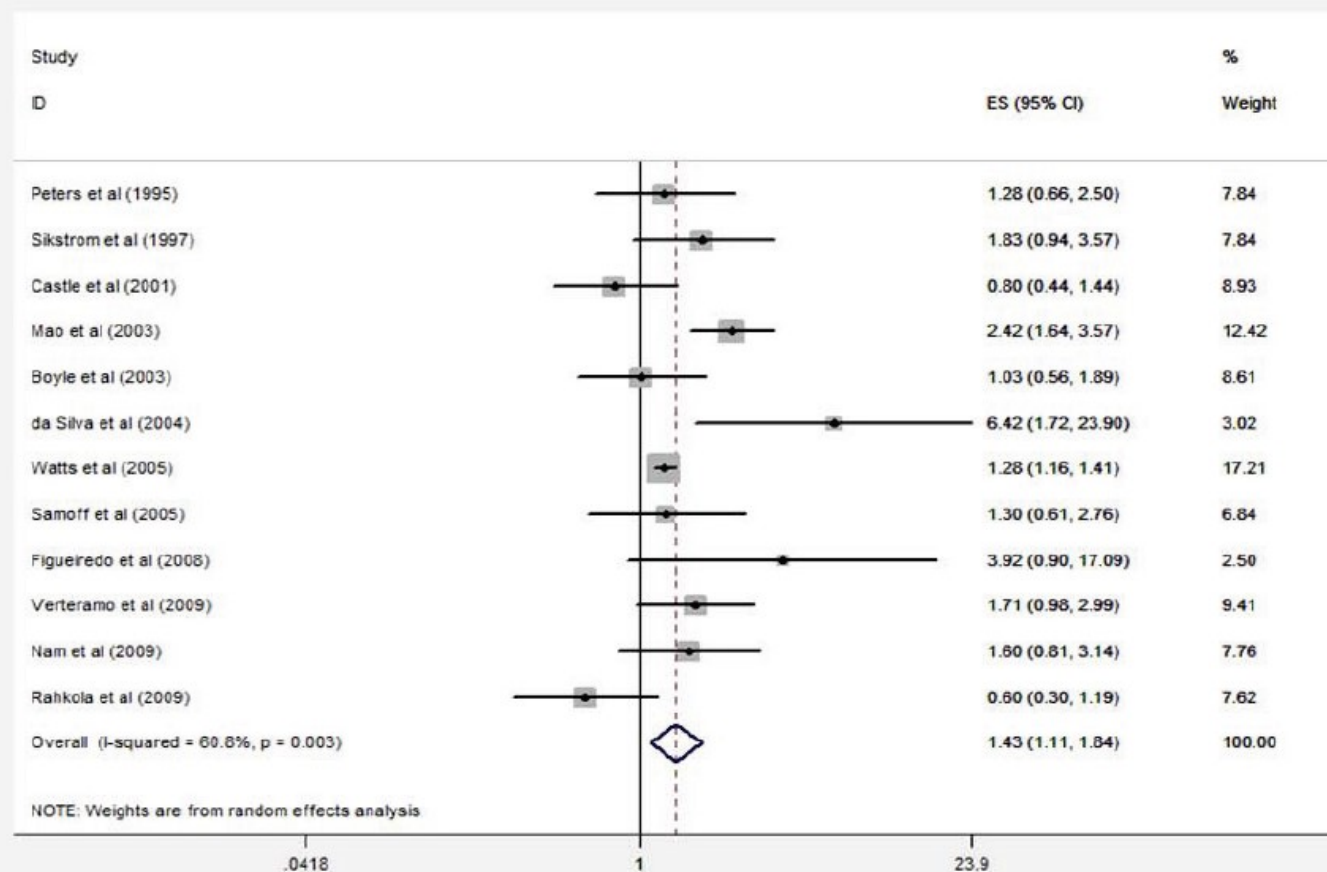
Human papillomavirus infection rate, distribution characteristics, and risk of age in pre- and postmenopausal women

Table 2 Comparison of HPV infection rate between women with and without inflammation

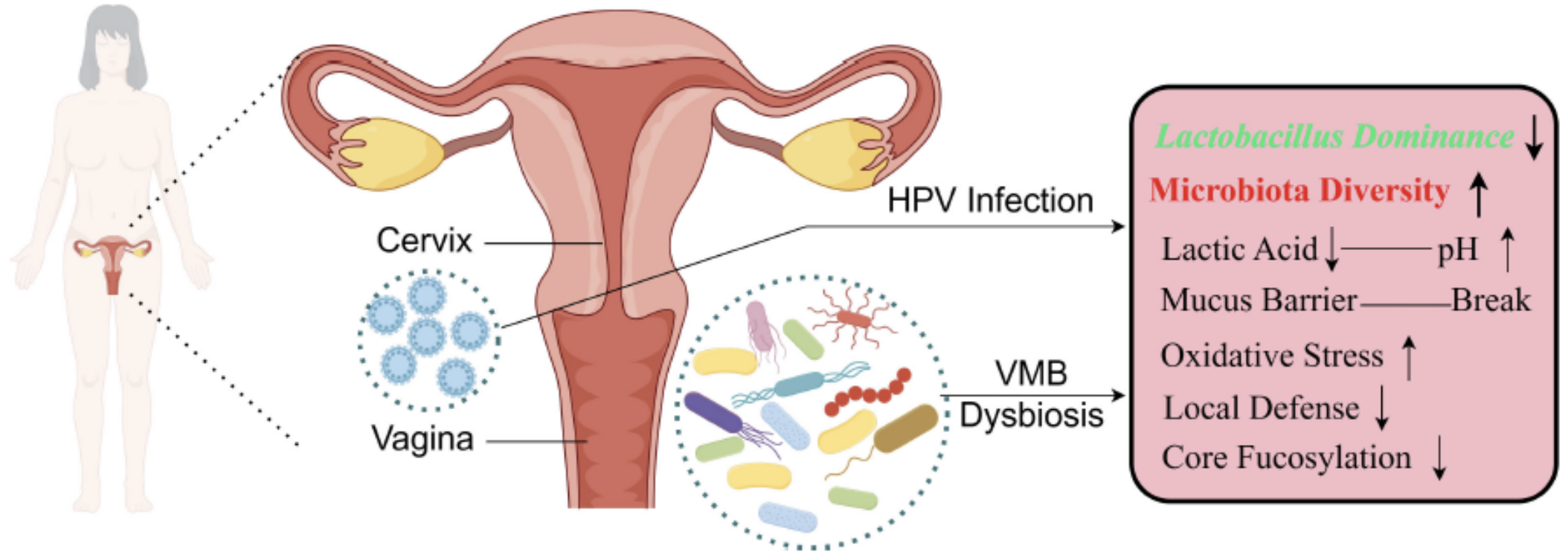
Inflammatory state	Total		HPV(+)		Percentage (%)		P	95% CI
	Pre-postmenopause		Pre-postmenopause		Pre-postmenopause			
No inflammation	2003	739	211	83	10.53	11.23	0.000	1.911 (1.416, 2.580)
Inflammation	367	132	63	21	17.17	15.91		

Bacterial vaginosis is associated with uterine cervical human papillomavirus infection: a meta-analysis

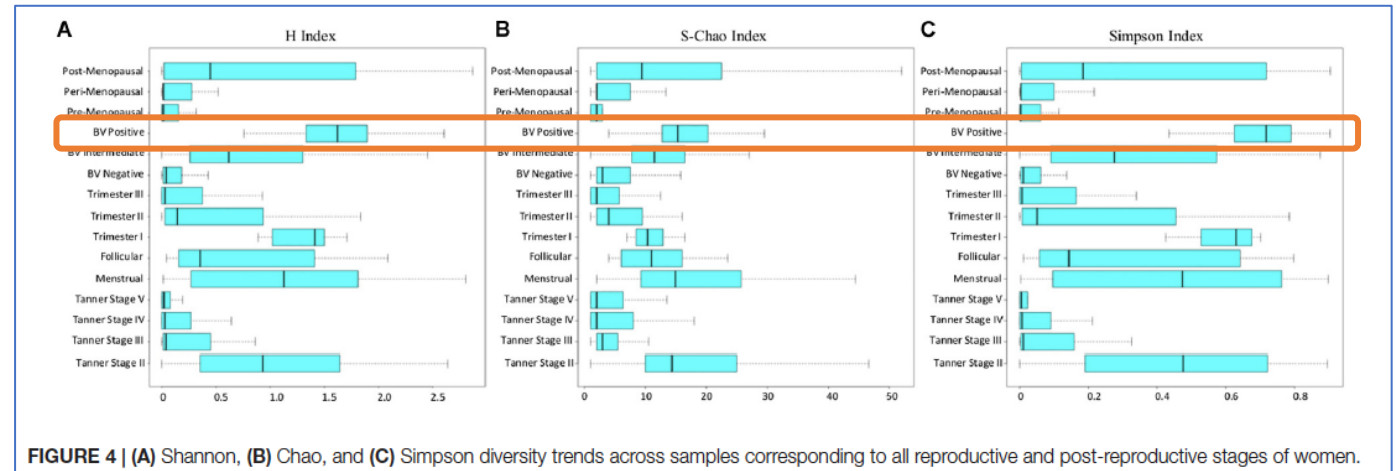
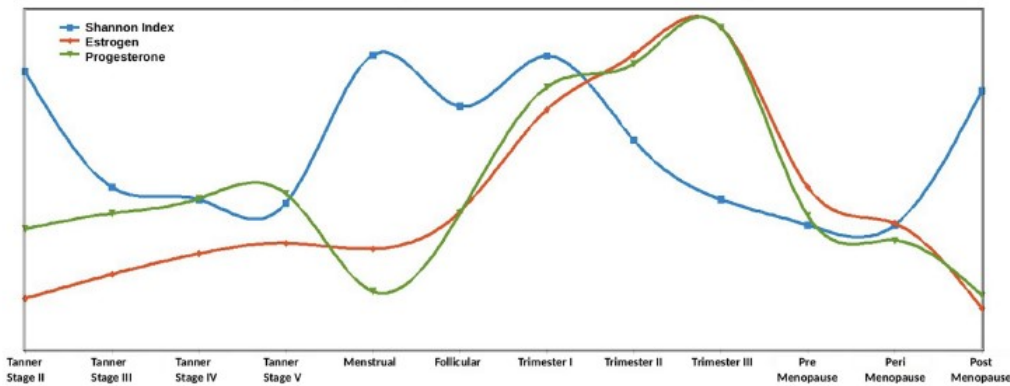
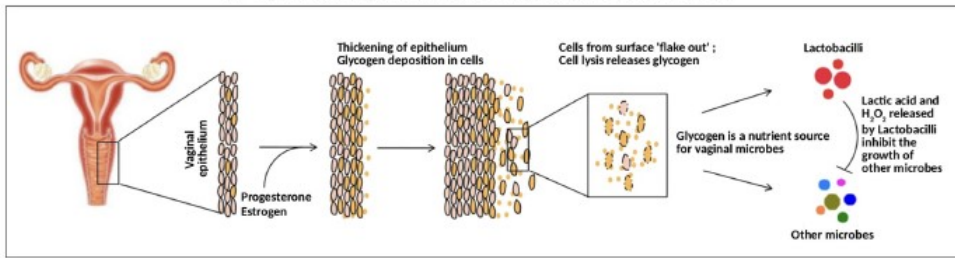
Evy Gillet^{1,2}, Joris FA Meys³, Hans Verstraelen⁴, Carolyn Bosire¹, Philippe De Sutter², Marleen Temmerman¹, Davy Vanden Broeck^{1*}



L'HPV e il microbiota vaginale






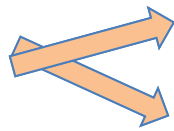

L'HPV e il microbiota vaginale



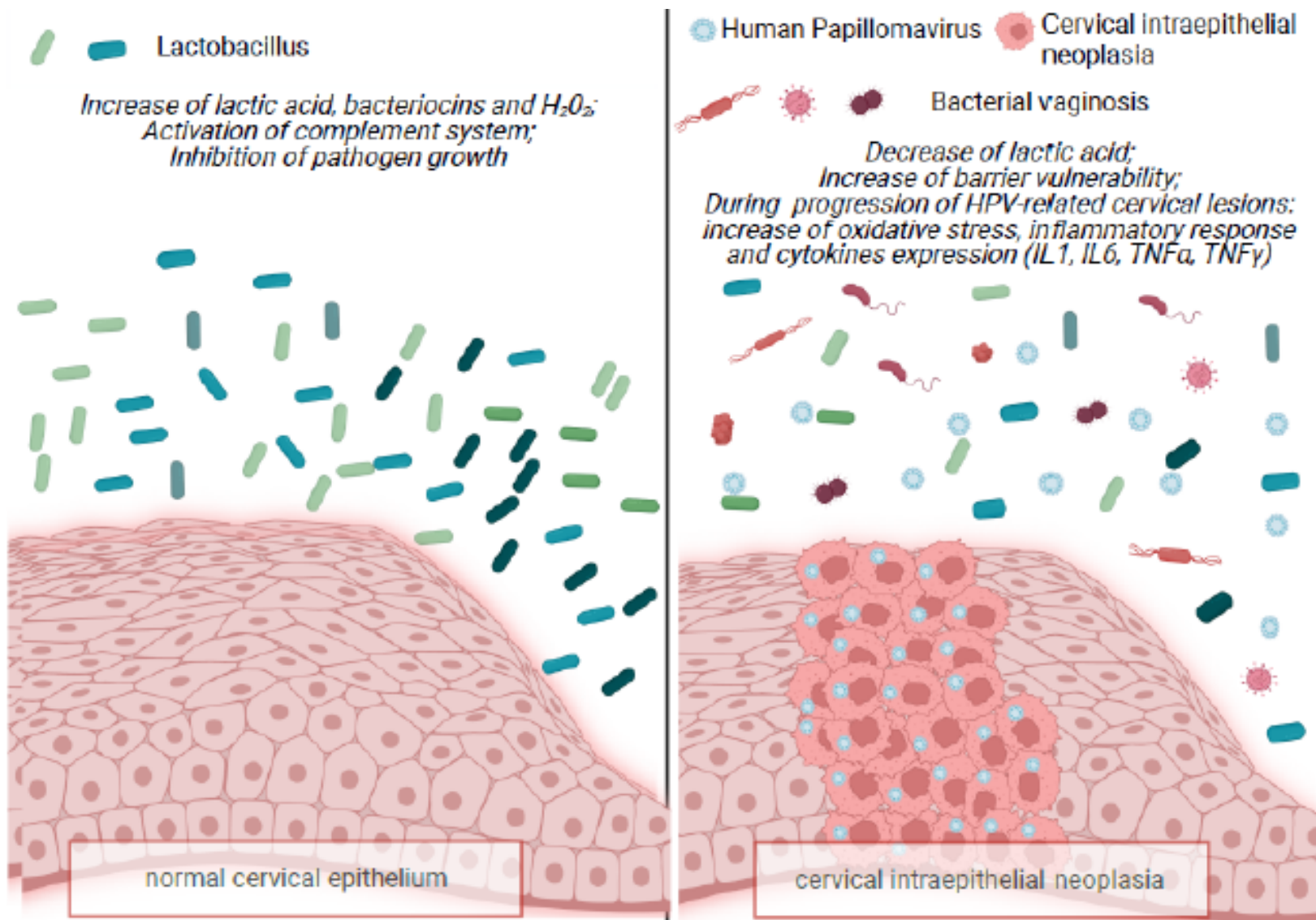
Gli stati ormonali di maggior diversità del microbioma correlano con una condizione di positività alla vaginosi batterica (VB)

MICROBIOMA VAGINALE

5 CST (Community State Types)

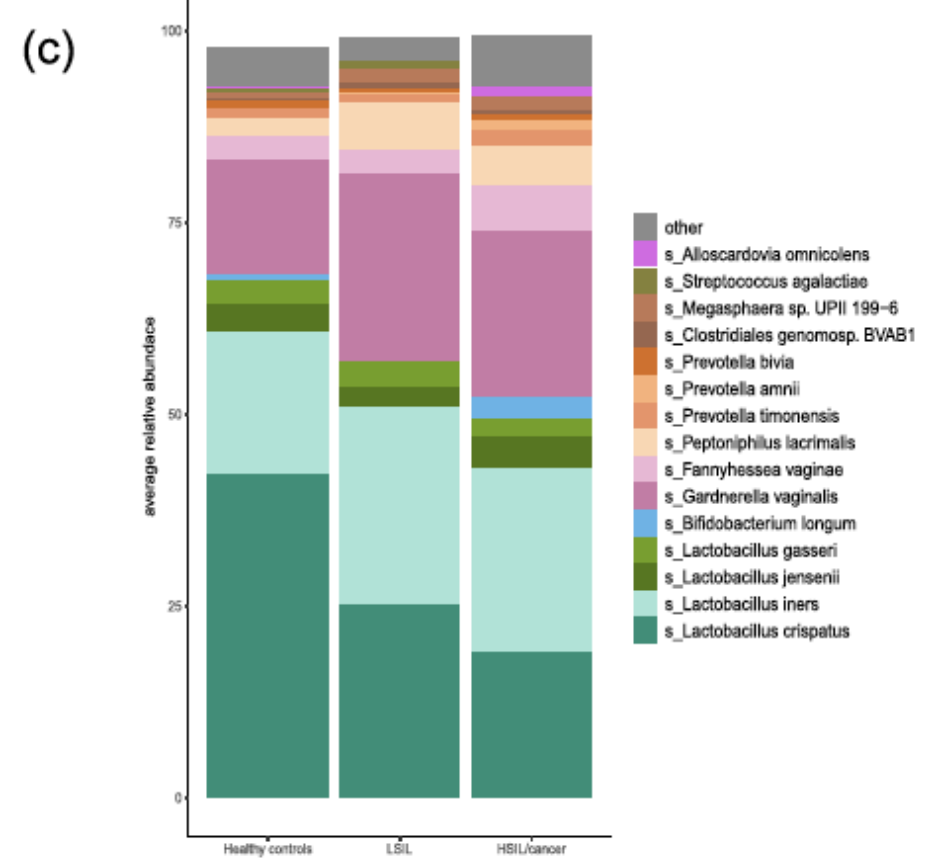
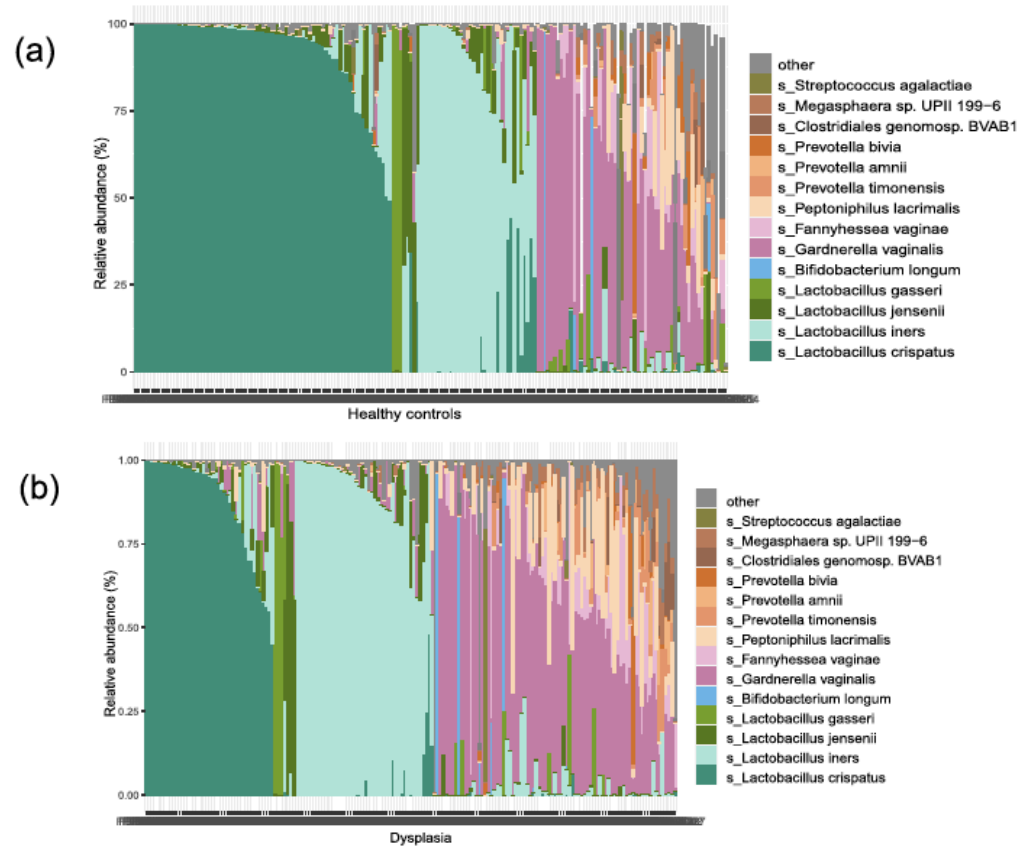
- CST I  *L. crispatus*
- CST II  *L. gasseri*
- CST III  *L. iners*
- CST IV  IVA specie anaerobie (*Anaerococcus*, *Peptoniphilus*,
Prevotella, *Streptococcus*)
IVB *Atopobium* e *Megasphaera*
- CST V  *L. jenseii*

L'HPV e il microbiota vaginale



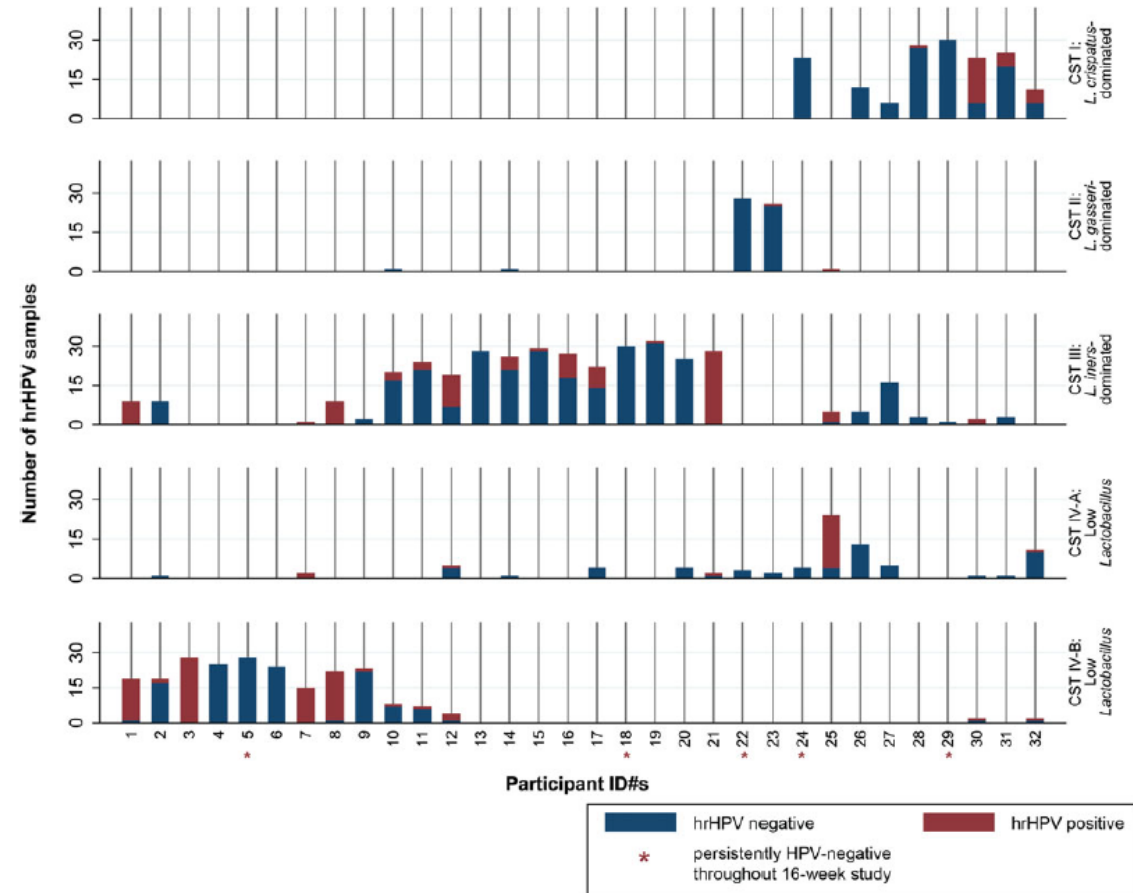
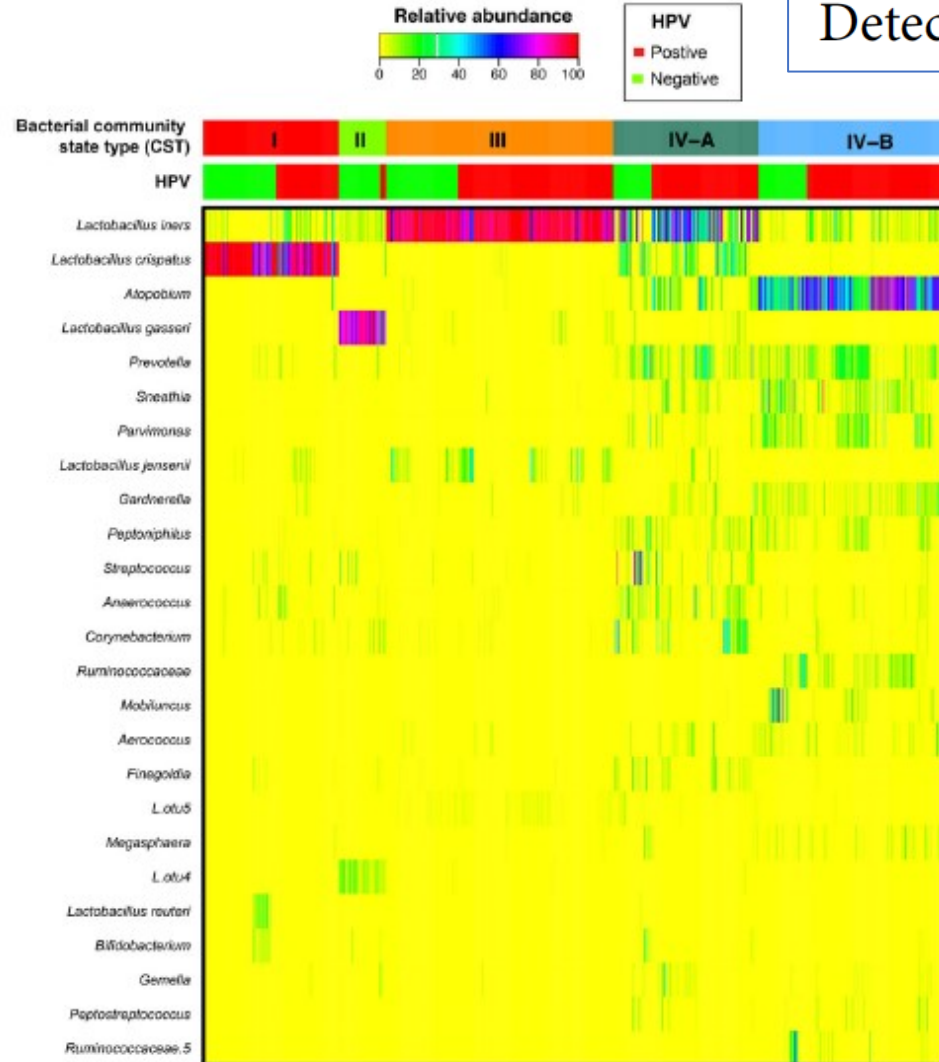
Compositional and functional differences of the vaginal microbiota of women with and without cervical dysplasia

Johanna Norenhag^{1,4}, Gabriella Edfeldt^{2,4}, Karin Stålberg¹, Fabricio Garcia², Luisa Warchavchik Hugerth³, Lars Engstrand², Emma Fransson^{1,2}, Juan Du², Ina Schuppe-Koistinen² & Matts Olovsson¹

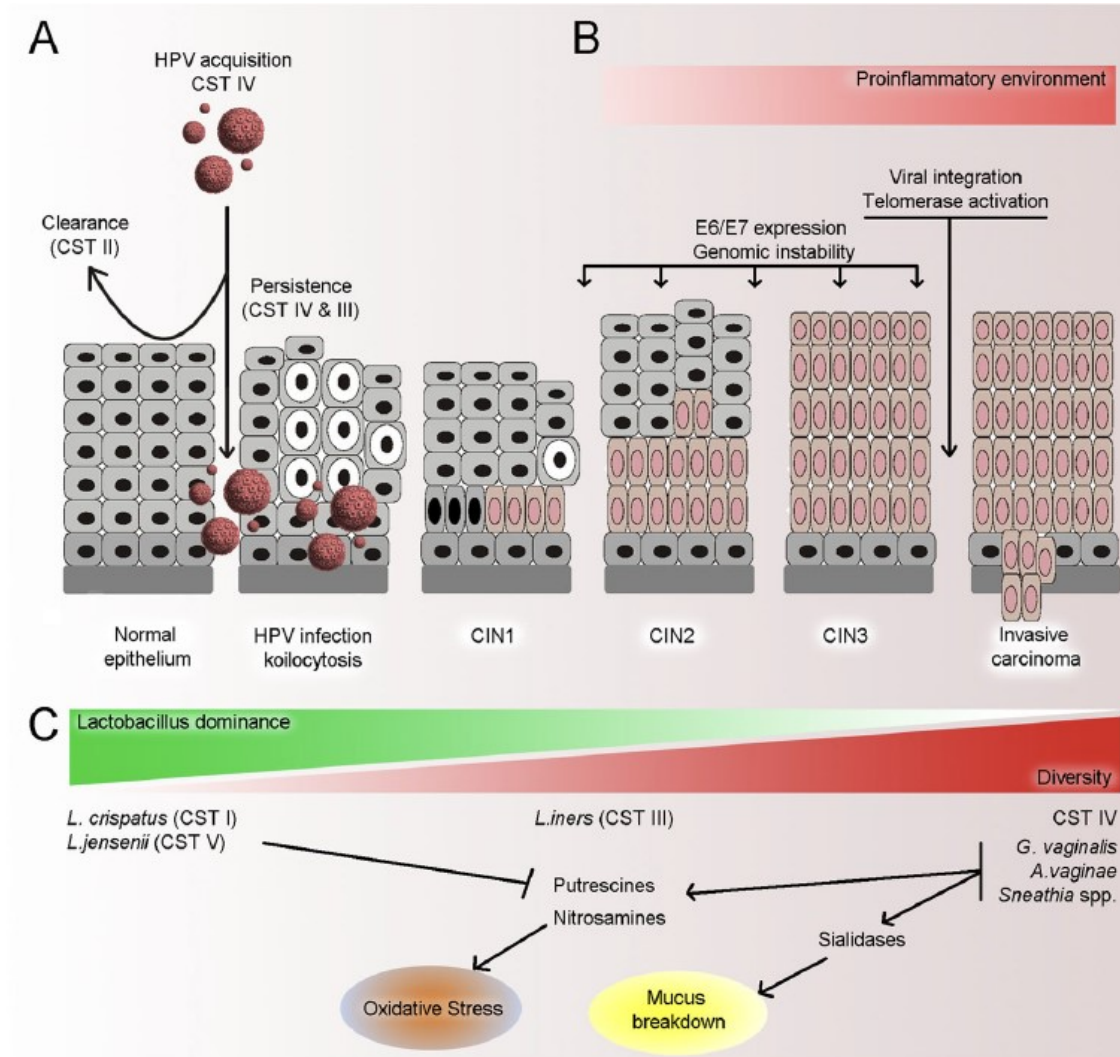


L'HPV e il microbiota vaginale

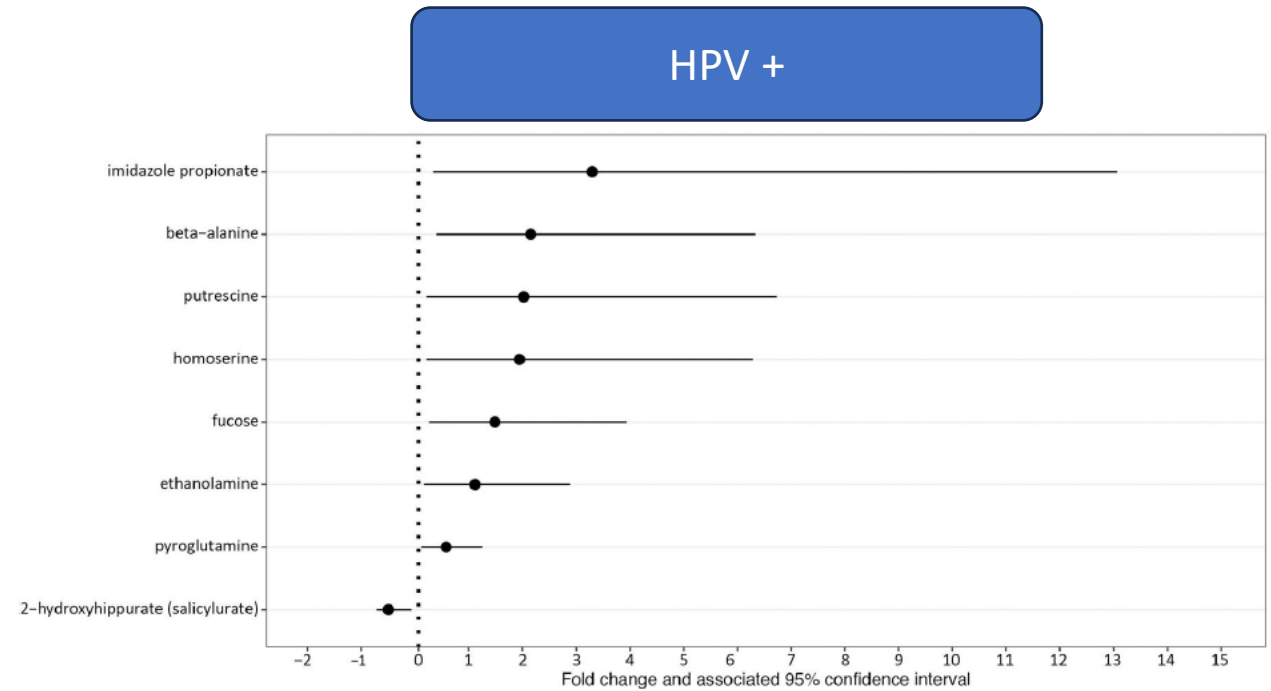
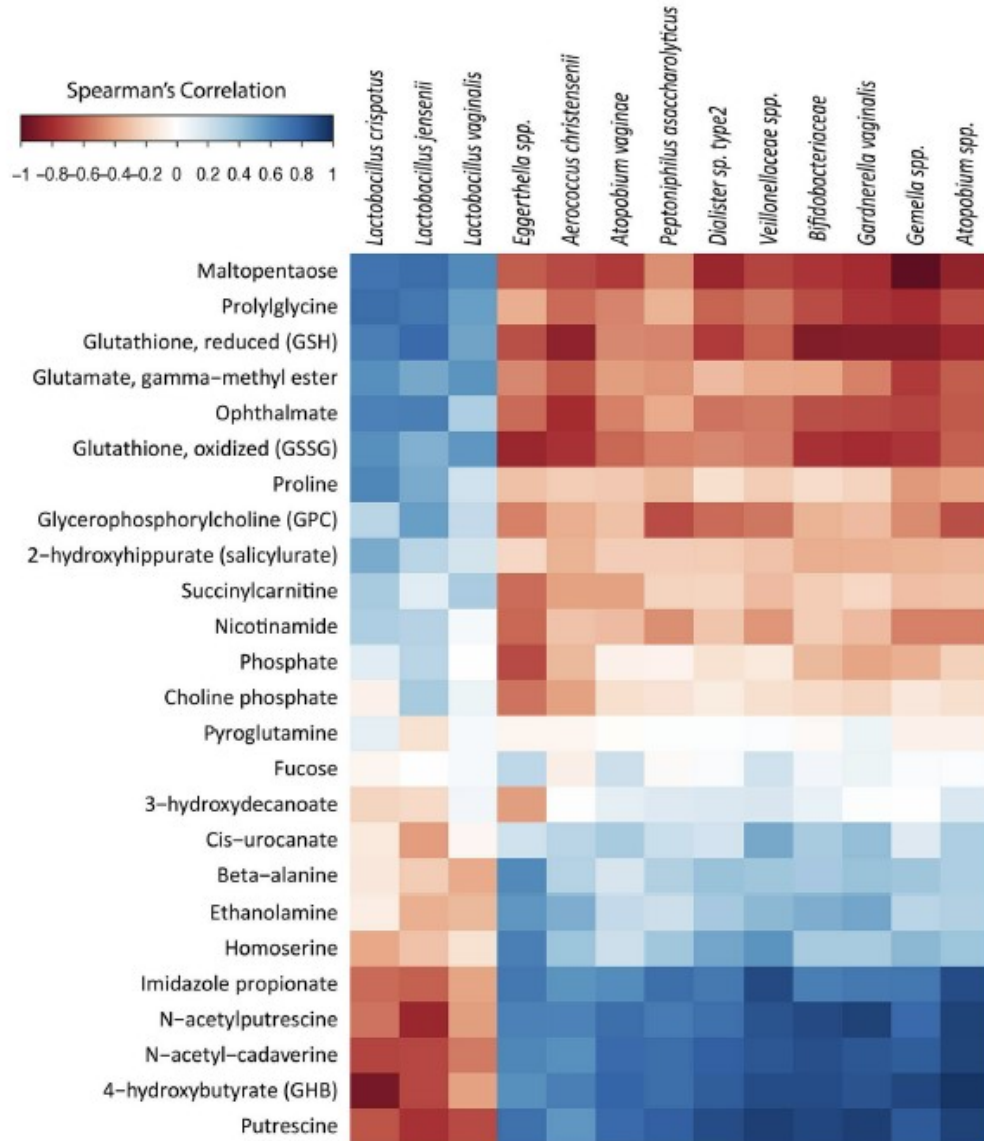
Interplay Between the Temporal Dynamics of the Vaginal Microbiota and Human Papillomavirus Detection



L'HPV e il microbiota vaginale



L'HPV e il microbiota vaginale



Association between the vaginal microbiota, menopause status, and signs of vulvovaginal atrophy

Rebecca M. Brotman, PhD, MPH,^{1,2} Michelle D. Shardell, PhD,² Pawel Gajer, PhD,¹ Doug Fadrosh, MS,¹ Kathryn Chang, RN,³ Michelle I. Silver, ScM,³ Raphael P. Viscidi, MD,⁴ Anne E. Burke, MD, MPH,⁵ Jacques Ravel, PhD,^{1,6} and Patti E. Gravitt, PhD, MS³

Menopause 2014

Associazione tra menopausa e CST

	Premenopause	Perimenopause	Postmenopause
CST (dominant bacterial species) ^b			
CST I (<i>Lactobacillus crispatus</i>)	14 (46.7)	6 (20.7)	7 (25.0)
CST II (<i>Lactobacillus gasseri</i>)	1 (3.3)	6 (20.7)	1 (3.6)
CST III (<i>Lactobacillus iners</i>)	10 (33.3)	11 (37.9)	5 (17.9)
CST IV-A (low <i>Lactobacillus</i>)	0 (0.0)	2 (6.9)	8 (28.6)
CST IV-B (low <i>Lactobacillus</i>)	5 (16.7)	3 (10.3)	5 (17.9)
CST V (<i>Lactobacillus jensenii</i>)	0 (0.0)	1 (3.5)	2 (7.1)
Signs of vulvovaginal atrophy			
None	27 (93.1)	21 (87.5)	12 (46.2)
Mild	2 (6.9)	2 (8.3)	9 (34.6)
Moderate	0 (0.0)	1 (4.2)	5 (19.2)

Associazione tra AVV e CST

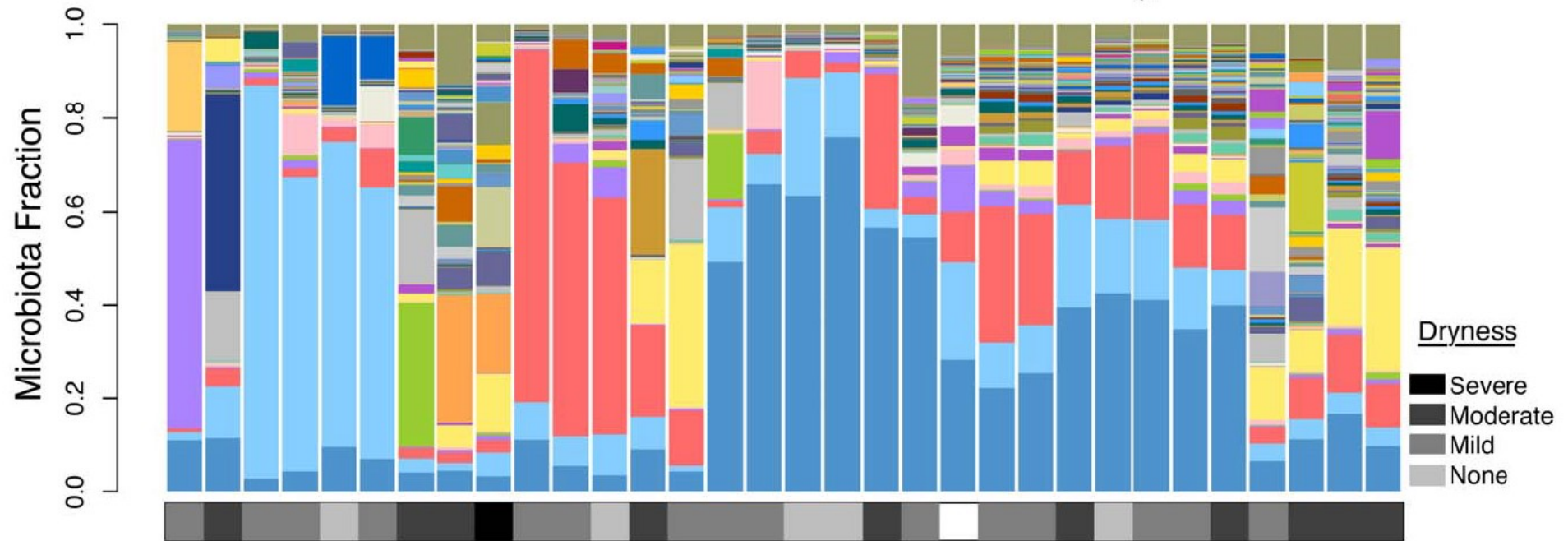
	CST I (<i>Lactobacillus crispatus</i>)	CST II (<i>Lactobacillus gasseri</i>)	CST III (<i>Lactobacillus iners</i>)	CST IV-A (low <i>Lactobacillus</i> , diverse)	CST IV-B (<i>Atopobium</i> , <i>Gardnerella</i>)	CST V (<i>Lactobacillus jensenii</i>)	P ^a
Vaginal atrophy							
None	21 (84.0)	6 (100.0)	21 (91.3)	2 (22.2)	8 (61.5)	2 (66.7)	0.002
Mild	3 (12.0)	0 (0.0)	2 (8.7)	3 (33.3)	4 (30.8)	1 (33.3)	
Moderate	1 (4.0)	0 (0.0)	0 (0.0)	4 (44.4)	1 (7.7)	0 (0.0)	

Vaginal Microbiome and Epithelial Gene Array in Post-Menopausal Women with Moderate to Severe Dryness

Ruben Hummelen^{1,2}, Jean M. Macklaim^{1,3}, Jordan E. Bisanz^{1,4}, Jo-Anne Hammond^{1,5}, Amy McMillan^{1,4}, Rebecca Vongsa⁶, David Koenig⁶, Gregory B. Gloor^{1,3}, Gregor Reid^{1,4*}

Studio del microbioma di 32 donne in postmenopausa

Plos One 2011



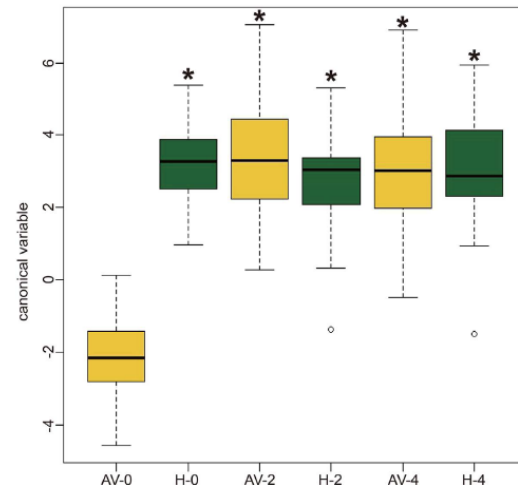
- Donne pauci-asintomatiche → minor diversità di specie
→ prevalenza di Lactobacilli
- Donne sintomatiche → riduzione di Lactobacilli
→ maggior diversità (*Prevotella*, *Porphiromonas*, *Peptoniphilus* e *Bacillus*)

Effects of low dose estrogen therapy on the vaginal microbiomes of women with atrophic vaginitis

Jian Shen^{1,2,6}, Ning Song^{1,2}, Christopher J. Williams^{3,5}, Celeste J. Brown^{4,5}, Zheng Yan⁷, Chen Xu^{1,2} & Larry J. Forney^{4,5}

Sci Rep 2016

VARIAZIONI MICROBIOMA NEI DUE GRUPPI



- Il microbioma al tempo 0 nei due gruppi è significativamente differente
- Il microbioma nel gruppo sintomatico si modifica con il trattamento

Phylotype	Week 0	Week 4	p^a
<i>Anaerococcus</i>	0.004 ± 0.008	0.019 ± 0.064	>0.05
<i>Atopobium</i>	0.048 ± 0.055	0.003 ± 0.012	<0.0001 ^b
<i>Gardnerella</i>	0.417 ± 0.310	0.096 ± 0.234	<0.0001 ^b
<i>Lactobacillus</i>	0.112 ± 0.164	0.710 ± 0.375	<0.0001 ^c
<i>Prevotella</i>	0.060 ± 0.103	0.007 ± 0.014	<0.01 ^b

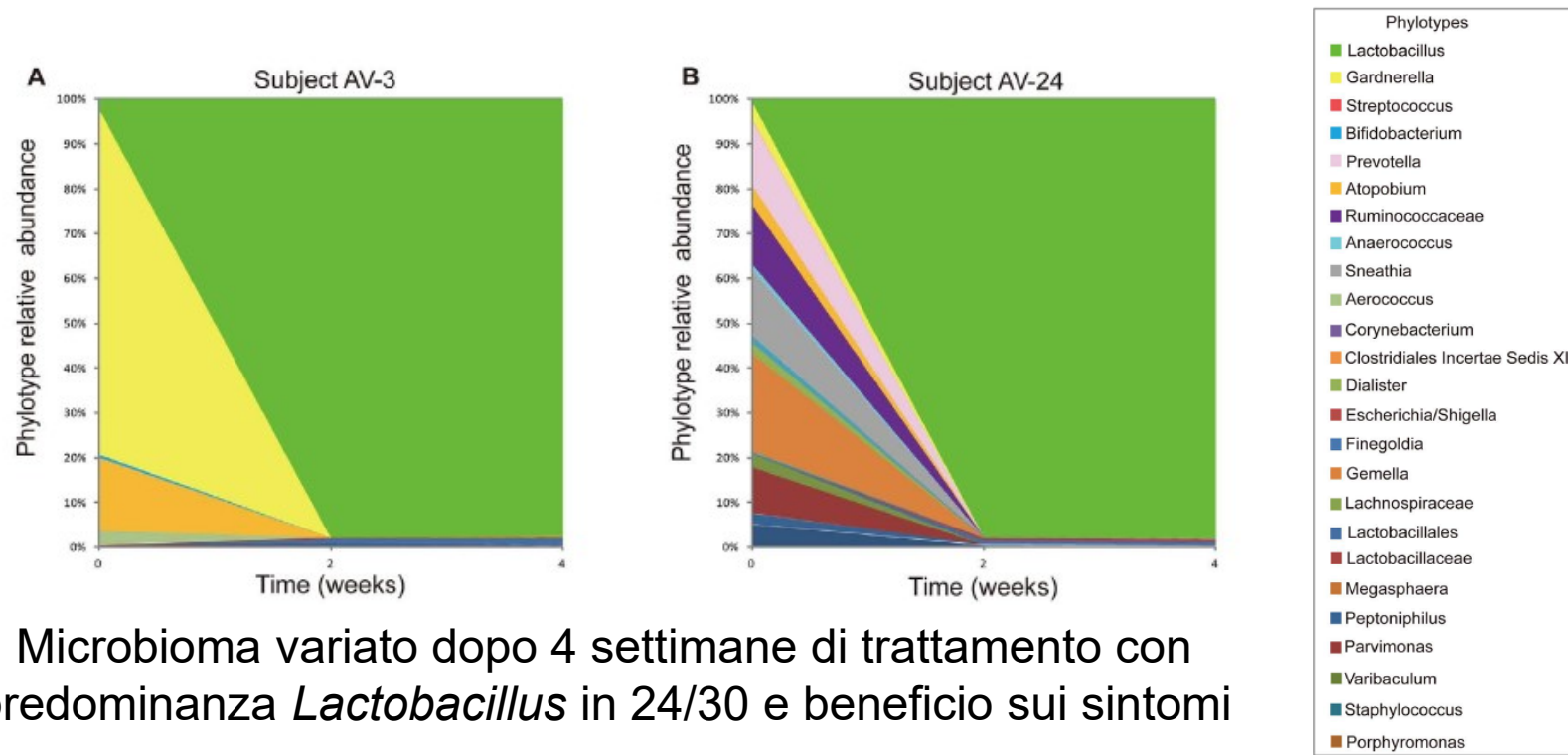
Clinical index	Week 0	Week 2	Week 4
Serum estradiol (pmol/L)	42.05 ± 7.68	168.07 ± 8.30 ^a	171.48 ± 6.98 ^b
Vaginal maturation index	28.07 ± 11.51	39.30 ± 10.75 ^a	55.37 ± 7.38 ^b
Symptom score	3.93 ± 0.25	1.50 ± 0.63 ^a	1.00 ± 0.00 ^b
Vaginal pH	6.64 ± 0.20	5.41 ± 0.35 ^a	4.95 ± 0.32 ^b

Effects of low dose estrogen therapy on the vaginal microbiomes of women with atrophic vaginitis

Sci Rep 2016

Jian Shen^{1,2,6}, Ning Song^{1,2}, Christopher J. Williams^{3,5}, Celeste J. Brown^{4,5}, Zheng Yan⁷, Chen Xu^{1,2} & Larry J. Forney^{4,5}

VARIAZIONI MICROBIOMA NELLE DONNE SINTOMATICHE TRATTATE



Microbioma variato dopo 4 settimane di trattamento con predominanza *Lactobacillus* in 24/30 e beneficio sui sintomi

La ripopolazione con *Lactobacillus* potrebbe essere uno dei segni di verifica trattamento AV insieme al livello estrogenico e VMI score

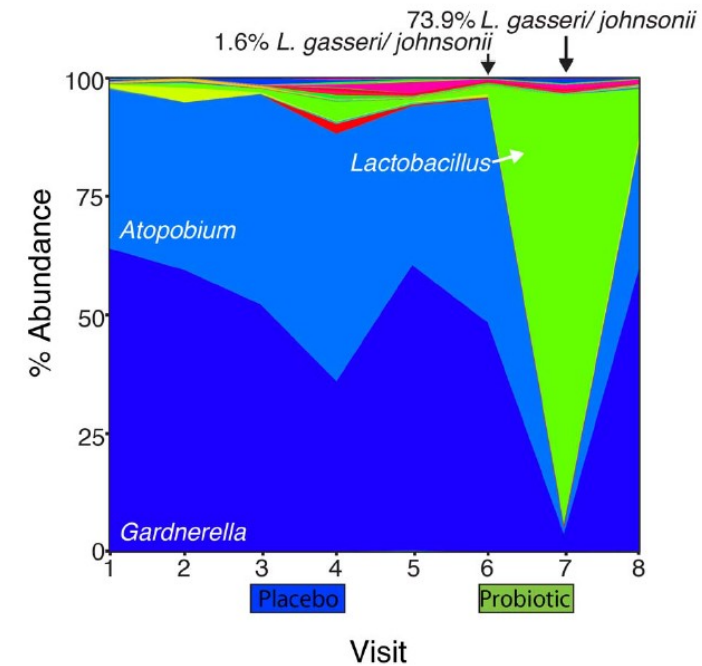
A Systems Biology Approach Investigating the Effect of Probiotics on the Vaginal Microbiome and Host Responses in a Double Blind, Placebo-Controlled Clinical Trial of Post-Menopausal Women

2014

Jordan E. Bisanz^{1,2}, Shannon Seney¹, Amy McMillan^{1,2}, Rebecca Vongsa³, David Koenig³, LungFai Wong³, Barbara Dvoracek³, Gregory B. Gloor^{1,4}, Mark Sumarah⁵, Brenda Ford⁶, Dorli Herman⁶, Jeremy P. Burton^{1,2,7,8}, Gregor Reid^{1,2,7*}

RISULTATI

- Non miglioramento del Nugent score dopo trattamento con probiotici rispetto placebo
- Aumento Lactobacilli con probiotici
- Riduzione Atopobium con probiotici
- Aumentata risposta immunomodulatoria con espressione genica di IL 18; CR1; TLR 2, caspasi 14
- Aumento IL-5 nel gruppo trattato

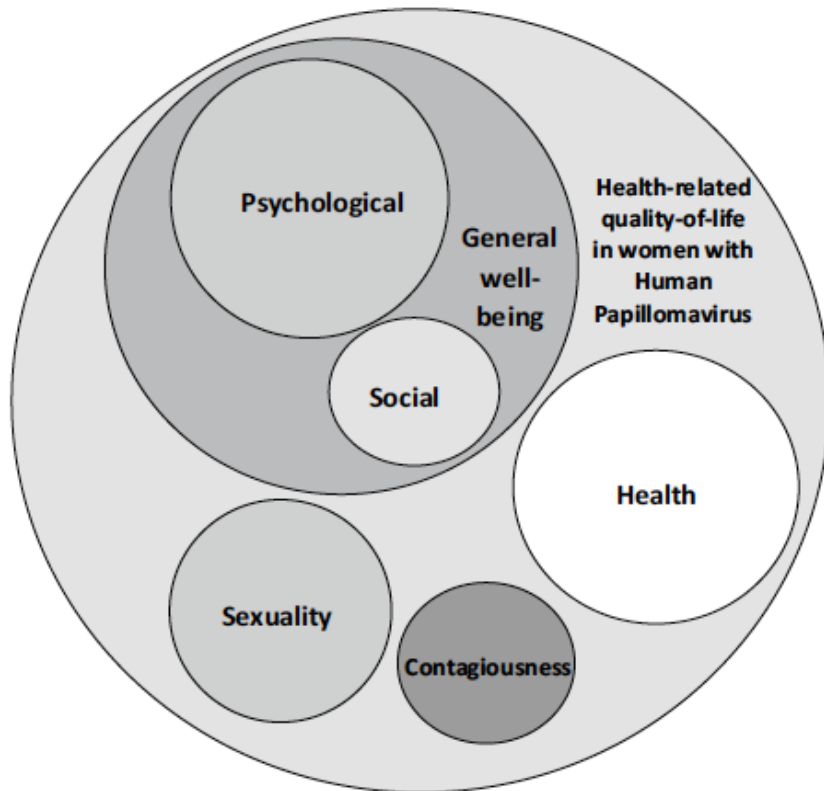


Il trattamento con probiotici anche se per breve tempo è in grado di aumentare i lattobacilli e modulare i markers infiammatori migliorando la funzione epiteliale di barriera

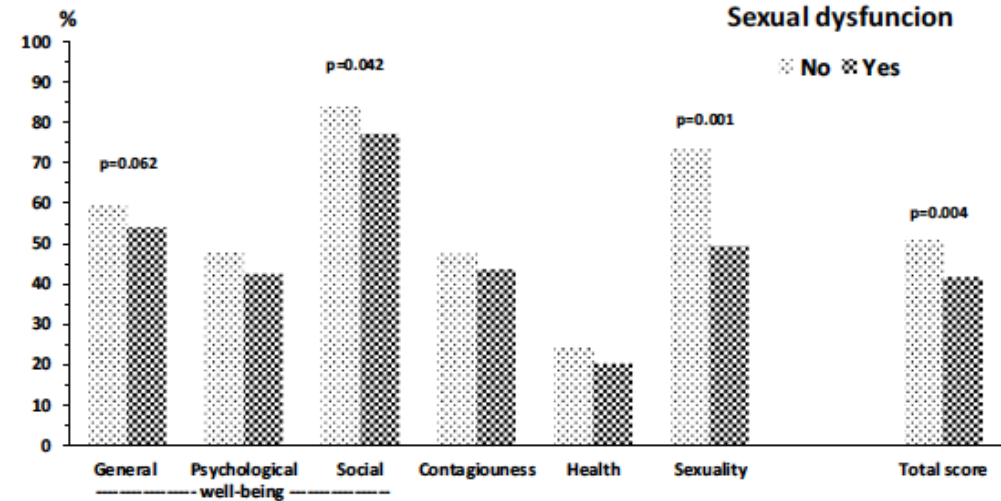
QUALITA' DI VITA: HPV-QoL

Development and psychometric properties of the human papillomavirus-quality of life (HPV-QoL) questionnaire to assess the impact of HPV on women health-related-quality-of-life

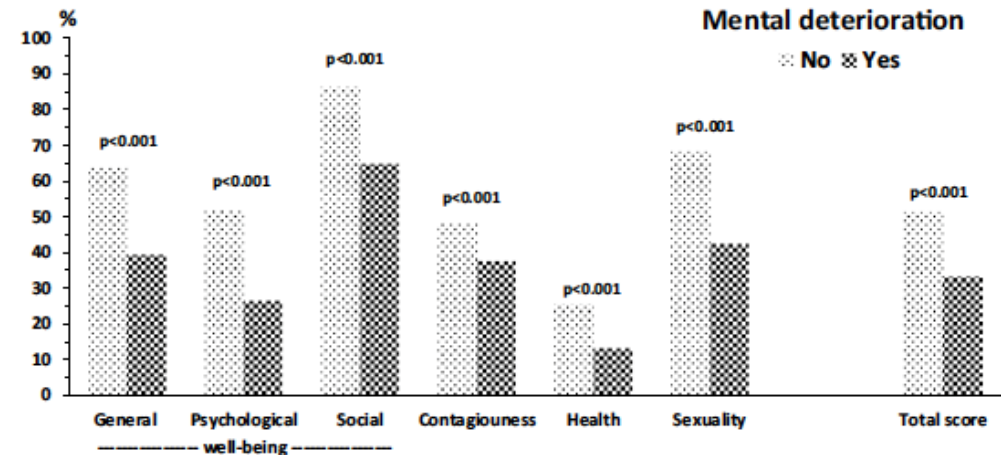
Pluvio J. Coronado¹ · Carmen González-Granados² · Mar Ramírez-Mena¹ · Javier Calvo¹ · María Fasero³ · Mónica Bellón¹ · Javier F. García-Santos¹ · Javier Rejas-Gutiérrez⁴



Graph a



Graph b



QUALITA' DI VITA: HPV-QoL

Development and psychometric properties of the human papillomavirus-quality of life (HPV-QoL) questionnaire to assess the impact of HPV on women health-related-quality-of-life

Pluvio J. Coronado¹ · Carmen González-Granados² · Mar Ramírez-Mena¹ · Javier Calvo¹ · María Fasero³ · Mónica Bellón¹ · Javier F. García-Santos¹ · Javier Rejas-Gutiérrez⁴

At the present time	Totally agree	Agree	Nor agree or disagree	Disagree	Totally disagree
1. I think having HPV infection has changed my life	1	2	3	4	5
2. I feel depressed since I know I have HPV infection	1	2	3	4	5
3. I feel nervous since I know I have HPV infection	1	2	3	4	5
4. I feel insecure since I know I have HPV infection	1	2	3	4	5
5. Knowing I have HPV infection interferes with my daily activities (house-keeping, working, studying, etc.)	1	2	3	4	5
6. Knowing I have HPV infection interferes with my social activities (partying, meeting friends, working, studying, leisure time etc.)	1	2	3	4	5
7. I feel worried about infecting my partner	1	2	3	4	5
8. I feel worried about infecting my partner those around me (children, family, friends)	1	2	3	4	5
9. I feel worried about if HPV can cause me cancer	1	2	3	4	5
10. I feel worried about if HPV does not disappear	1	2	3	4	5
11. I feel anxious to know if I could recover from HPV related lesions	1	2	3	4	5
12. I do not feel confident when having sexual intercourse because of the risk of infection	1	2	3	4	5
13. Since I know I have HPV infection my sexual desire has decreased (intercourse, affection, masturbation)	1	2	3	4	5
14. Since I know I have HPV infection; sexual intercourse bothers me	1	2	3	4	5
15. Since I know I have HPV infection; sexual intercourse is a less delightful experience	1	2	3	4	5

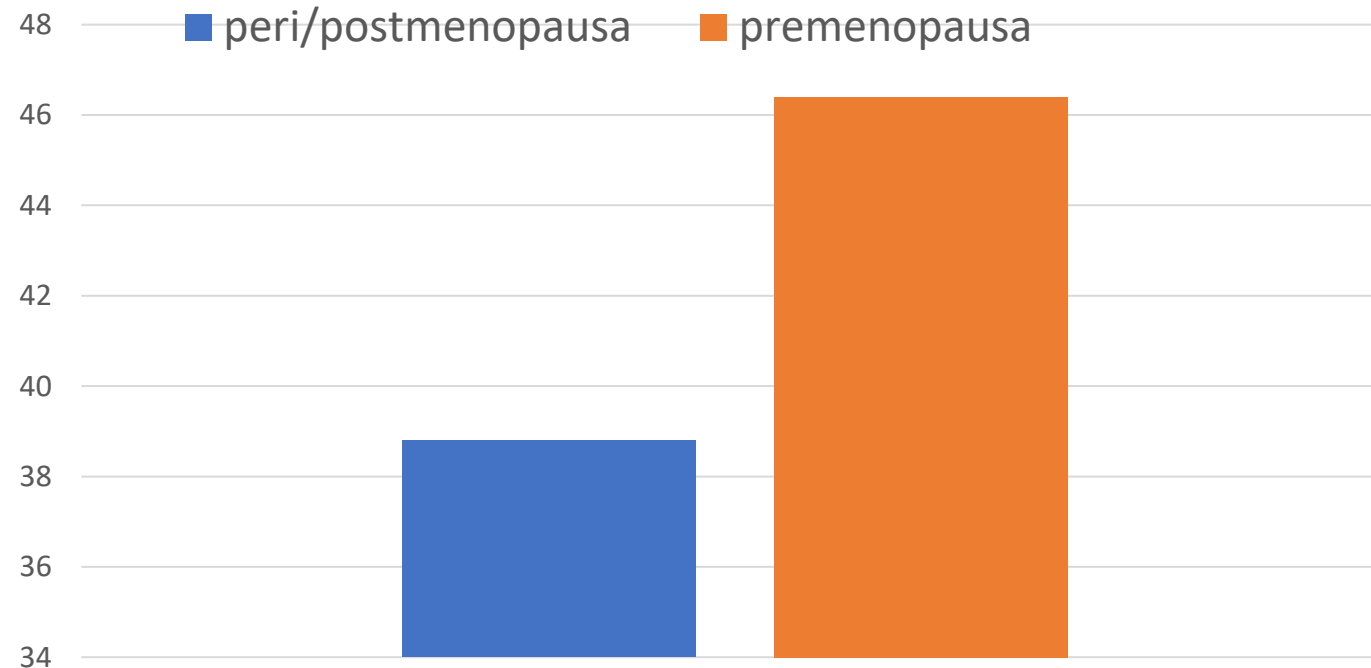
QUALITA' DI VITA: HPV-QoL

Menopause in adult women with human papillomavirus: health-related quality of life and determinants

Studio multicentrico
HPV-QoL premenopausa vs. peri/postmenopausa
1016 donne 18-80 aa (81.2% premenopausa; 18.8% peri/postmenopausa)



HPV-QoL score



L'HPV nelle diverse età della donna

TAKE HOME MESSAGE

HUMAN PAPILLOMAVIRUS



- HPV rilevante anche in post-menopausa e dopo i 65 anni (prolungamento screening?)
- Influenza microbioma vaginale su infezione HPV
- Individuare le pazienti a rischio in menopausa di infezione HPV
- Impatto dell'HPV sulla qualità di vita maggiore in postmenopausa



Grazie...

L'HPV nelle diverse età della donna

Incidence of oncogenic HPV and HPV-related dysplasia five years after a negative HPV test by self-sampling in elderly women

Ruth S. Hermansson^{1,2*}, Matts Olovsson¹, Inger Gustavsson³, Ulf Gyllensten³, Olga Lindkvist¹, Julia Hedlund Lindberg³, Gabriella Lillsunde-Larsson^{4,5} and Annika K. Lindström¹

Table 1 HPV incidence for the different age groups

Current age, years	HPV negative five years ago n	Self-sampling n (%)	HPV test 1 positive n (%)	HPV test 2 positive n (%)
65	210	196 (93.3)	7 (3.6)	3 (1.5)
70	219	162 (74.0)	3 (1.9)	2 (1.2)
75	197	159 (80.7)	4 (2.5)	1 (0.6)
80	178	115 (64.6)	4 (3.5)	2 (1.7)
Total	804	632 (78.6)	18 (2.8)	8 (1.3)

In total 804 women were eligible for and invited to this study and 632 women did send a sample. Of them 18 had a positive first HPV test and the second test ended up with 8 that were still HPV positive

Table 2 Data on HPV type and results for cytology and histology on samples from elderly women who were HPV positive (n = 18)

Current age	HPV test 1	HPV test 2	Cytology	Histology
70	31	31	Benign	Benign
65	51	51	Benign	Benign
70	51	51	LSIL	LSIL
75	51	51	Benign	LSIL
80	56	56	Benign	Benign
80	18/45	18/45	ASCUS	Benign
65	33/52/58	33/52/58	ASCUS	LSIL
65	33/52/58	33/52/58	ASCUS	LSIL
65	18/45	negative		
65	51	negative		
65	51	negative		
65	33/52/58	negative		
70	18/45	negative		
75	18/45	negative		
75	39	negative		
75	31	negative		
80	16	negative		
80	33/52/58	negative		

LSIL low grade squamous intraepithelial lesion; ASCUS atypical cells of undetermined significance

Article

The Impact of Diagnosis of Human Papillomavirus (HPV) Infection and Electrosurgical Excision Procedure (LEEP) for Cervical Intraepithelial Neoplasia 3 (CIN3) on Women's Sexual Lives

Maria Teresa Bruno ^{1,2,*}, Giuseppe Caruso ¹, Elena Torrisi ¹, Raffaella Grimaldi ¹, Biagio Abate ¹, Francesco Saverio Luciani ³, Susanna Basile ⁴ and Marco Marzio Panella ^{1,2}

Table 3. Qualitative and quantitative aspects of sexual function and experience of women with diagnoses of CIN3 after LEEP procedure.

Item	Worse <i>n</i> (%)	Unchanged <i>n</i> (%)	Better <i>n</i> (%)
Desire	81 (61.8)	36 (27.5)	14 (10.7)
Arousal	69 (52.7)	50 (38.1)	12 (9.2)
Lubrication	68 (51.9)	49 (37.4)	14 (10.7)
Orgasm	79 (60.3)	35 (26.7)	17 (13)
Satisfaction	89 (67.9)	31 (23.7)	11 (8.4)
Dyspareunia	91 (69.5)	34 (25.9)	6 (4.6)
Fear of sexual intercourse	82 (62.6)	39 (29.8)	10 (7.6)
Intimacy with the partner	85 (64.9)	35 (26.7)	11(8.4)

Hpv nelle varie età
HPV in postmenopausa
microbioma
microbioma rischio cancro
il cancro nelle over 60 HPV