

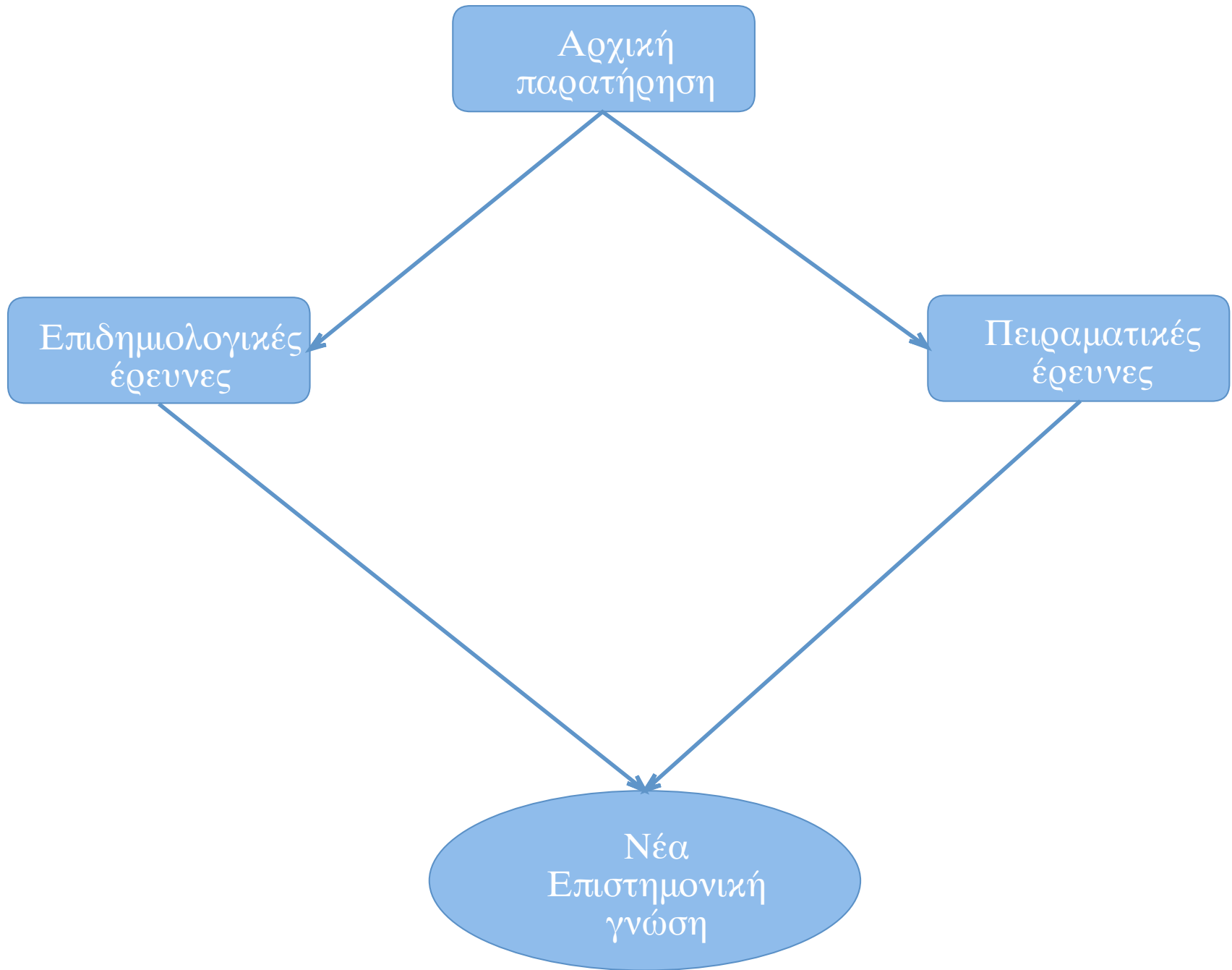
6^η Σύνοδος

της ΕΛΛΗΝΙΚΗΣ ΕΤΑΙΡΕΙΑΣ ΕΡΕΥΝΑΣ ΚΑΙ ΑΝΤΙΜΕΤΩΠΙΣΗΣ ΤΟΥ ΙΟΥ
ΤΩΝ ΘΗΛΩΜΑΤΩΝ (HPV) [ΕΛΛΗΝΙΚΗΣ HPV ΕΤΑΙΡΕΙΑΣ]



Υπάρχει συσχέτιση μεταξύ HPV λοίμωξης και μαιευτικών επιπλοκών; (πρόωρου τοκετού, πρόωρης ρήξης υμένων, προεκλαμψίας, πλακουντιακής ανεπάρκειας)

Κίμων Χατζησταματίου
Μαιευτήρας – Γυναικολόγος
Επιστημονικός Συνεργάτης Β' Μαιευτικής και Γυναικολογικής
Κλινικής Α.Π.Θ.



Επιπλοκές κύησης

Αυτόματη
έκτρωση

Προεκλαμψί
α

Καθυστέρηση ενδομήτριας
αύξησης

Πρώιμη πρόωρη ρήξη εμβρυικών
υμένων

Πρόωρος
τοκετός

Επιπλοκές κύησης

**Αυτόματη
έκτρωση**

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α

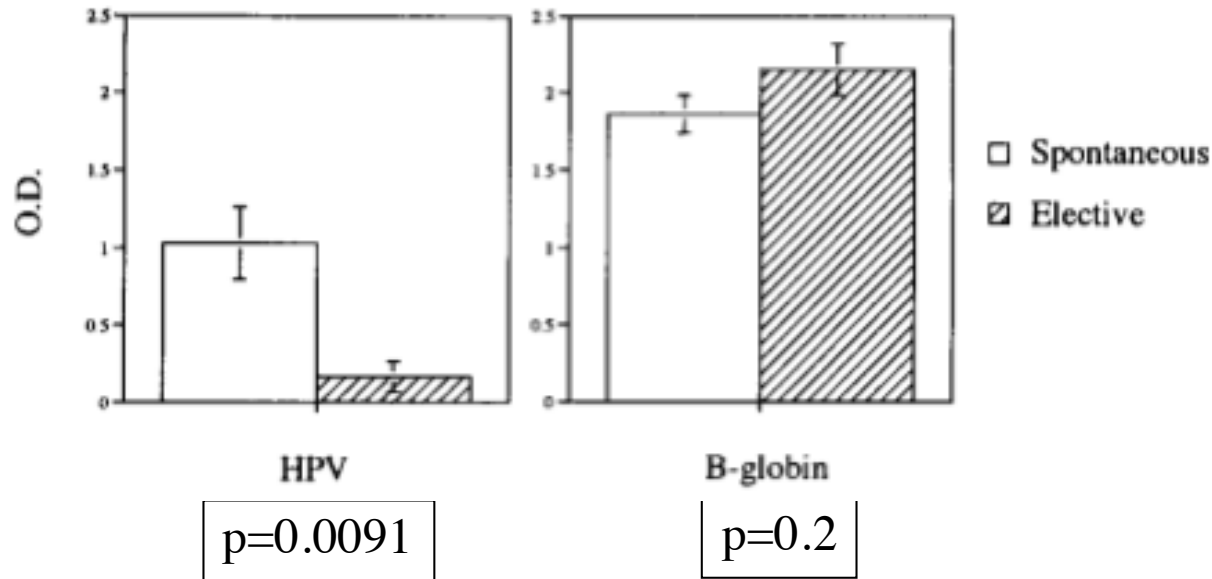
Καθυστέρηση ενδομήτριας
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Πρώιμη πρόωρη ρήξη εμβρυικών
υμένων

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τοκετός

HPV ↔ Αυτόματες εκτρώσεις

Η ανίχνευση HPV DNA σε ιστικά δείγματα αυτόματων εκτρώσεων είναι στατιστικώς μεγαλύτερη σε σύγκριση με αυτή σε δείγματα τεχνητών εκτρώσεων



Virus Genes. 1997;14(1):13-7.

Human papillomavirus is more prevalent in first trimester spontaneously aborted products of conception compared to elective specimens.

Hermonat PL, Han L, Wendel PJ, Quirk JG, Stern S, Lowery CL, Rechtin TM.

HPV ↔ Αυτόματες εκτροώσεις

**Στο 70% (18/26) δειγμάτων από αυτόματες
εκτροώσεις
ανιχνεύθηκε HPV DNA**

J Gen Virol. 1997 Aug;78 (Pt 8):1957-62.

Human genital tissues containing DNA of adeno-associated virus lack DNA sequences of the helper viruses adenovirus, herpes simplex virus or cytomegalovirus but frequently contain human papillomavirus DNA.

Malhomme O, Dutheil N, Rabreau M, Armbruster-Moraes E, Schlehofer JR, Dupressoir T.

**Στο 18% περιστατικών υδατιδώδους μύλης καθώς
και στο 50% χοριοκαρκινώματος ανιχνεύθηκε
HPV 18**

Int J Cancer. 1995 Nov 15;63(4):505-9.

Human papillomavirus type 18 DNA in gestational trophoblastic tissues and choriocarcinomas.

Pao CC, Hor JJ, Wu CJ, Shi YF, Xie X, Lu SM.

HPV ↔ Αυτόματες εκτροώσεις

Bivariate analysis of the variables associated with spontaneous abortion.

Variables	Cases	Controls	Odds ratio	p value
HPV infection				
HPV+	34	21	OR = 1.80 (0.95 < OR < 3.45)	p = 0.0538
HPV-	105	117		
Total: 277				
HPV infection (only Torch negative cases)				
HPV+	15	21	OR = 2.14 (0.94 < OR < 4.86)	p = 0.04498
HPV-	39	117		
Total: 192				

Eur J Obstet Gynecol Reprod Biol. 2013 Oct;170(2):468-73

Human papillomavirus infection and spontaneous abortion: a case-control study performed in Mexico.

Conde-Ferrález L, Chan May Ade A, Carrillo-Martínez JR, Ayora-Talavera G, González-Losa Mdel R.

Επιπλοκές κύησης

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αύξησης

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τοκετός

HPV ↔ Προεκλαμψία

TABLE 2
Obstetric outcomes of study participants

Variable	Exposed (HR-HPV) group n = 314	Unexposed group (normal pap) n = 628	P value
Gestational age at delivery, wks	39.14 (38–40)	39.14 (38.14–39.86)	.95
Birthweight, g	3295 (3012–3614)	3285 (3005–3580)	.91
Preeclampsia	32 (10.19)	31 (4.94)	.004
Severe preeclampsia	16 (5.1)	17 (2.71)	.09
Gestational age at onset of preeclampsia, wks	37.14 (35.86–39)	36.86 (34.57–39.57)	.88
GDM	17 (5.41)	45 (7.17)	.37
IUGR	7 (2.23)	9 (1.43)	.53
Cesarean delivery	75 (32.05)	191 (38.82)	.08

Data are presented as median (interquartile range) or n (%).

GDM, gestational diabetes mellitus; *HR-HPV*, high-risk human papillomavirus; *IUGR*, intrauterine growth restriction; *pap*, Papanicolaou.

McDonnold. HPV and preeclampsia. Am J Obstet Gynecol 2014.

Am J Obstet Gynecol. 2014 Feb;210(2):138.

High risk human papillomavirus at entry to prenatal care and risk of preeclampsia.

McDonnold M, Dunn H, Hester A, Pacheco LD, Hankins GD, Saade GR, Costantine MM.

HPV ↔ Προεκλαμψία

Table III. HPV L1 sequences detected in extravillous trophoblast region of placentas from cases and controls

Group	HPV present	HPV absent	<i>P</i> -value ¹
Controls (<i>n</i> = 30)	6 ²	24	—
Severe pre-eclampsia (<i>n</i> = 48)	8 ³	40	0.71
Spontaneous preterm delivery (<i>n</i> = 30)	15 ⁴	15	0.03

¹Chi-square, compared with controls.

²Low-risk HPV strains (6, 11) = 4; high-risk HPV strains (16, 18) = 2.

³Low-risk HPV strains (6, 11) = 3; high-risk HPV strains (16, 18) = 5.

⁴Low-risk HPV strains (6, 11) = 6; high-risk HPV strains (16, 18) = 9.

Επιπλοκές κύησης

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α

**Καθυστέρηση ενδομήτριας
αύξησης**

Πρώιμη πρόωρη ρήξη εμβρυικών
υμένων

Πρόωρος
τοκετός

HP ↔ Καθυστέρηση ενδομήτριας V αύξησης

Μοντέλο λογιστικής παλινδρόμησης όπου φαίνεται στατιστική σημαντικότητα του θετικού Παπ τεστ της μητέρας όσον αφορά τη γέννηση SGA παιδιού (<3 Εκατοστιαία Θέση)

Key variables in the equations determined by logistic regression analysis.

Factor	B	S.E.	Wald	Df	Significance	Exp (B)
<i>A: Risk of birth of SGA babies with birth weight less than 3rd percentile</i>						
Education	-1.403	0.707	3.938	1	0.047	0.246
Winter conception	-1.201	0.687	3.059	1	0.080	0.301
Abnormal pap smear	-2.170	0.791	7.534	1	0.006	0.114
<i>B: Risk of birth of SGA babies with birth weight less than 10th percentile</i>						
Overseas Travel in month of conception	-2.652	1.049	6.390	1	0.011	0.071
Not taking vitamins 5 days each week	2.077	1.036	4.017	1	0.045	7.983

Early Hum Dev. 2011 Dec;87(12):785-9

Preconception risk factors and SGA babies: Papilloma virus, omega 3 and fat soluble vitamin deficiencies.

Ford JH.

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**Πρώιμη πρόωρη ρήξη εμβρυικών
υμένων**

Πρόωρος
τοκετός

HPV ↔ Πρώιμη ρήξη εμβρυικών υμένων

Table 3 Odds ratios (OR) of HR-HPV infection and demographic variables for PROM

	Unadjusted OR (95% CI)	Adjusted OR ^a (95% CI)
HR-HPV infection	2.260 (1.071-4.770)	2.318 (1.079-4.980)
Age	0.980 (0.910-1.054)	0.986 (0.908-1.072)
Parity	0.918 (0.583-1.446)	0.737 (0.416-1.307)
Number of abortions	1.113 (0.850-1.457)	1.168 (0.872-1.538)
BMI	1.029 (0.944-1.121)	1.047 (0.956-1.146)
Gestational age at delivery	0.960 (0.894-1.030)	0.941 (0.870-1.017)
History of preterm birth	2.435 (0.720-8.239)	1.466 (0.278-7.728)
History of PROM	3.155 (0.888-11.213)	2.977 (0.555-15.965)

PROM: Premature rupture of the membranes, OR: Odds ratio, CI: Confidence interval, HR-HPV: High risk human papillomavirus, BMI: Body mass index.

^a The model is adjusted for variables in the table.

BMC Pregnancy Childbirth. 2013 Sep 6;13:173

High-risk human papillomavirus infection is associated with premature rupture of membranes.

Cho G, Min KJ, Hong HR, Kim S, Hong JH, Lee JK, Oh MJ, Kim H.

Επιπλοκές κύησης

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**Πρόωρος
τοκετός**

HPV ↔ Πρόωρος τοκετός

Table III. HPV L1 sequences detected in extravillous trophoblast region of placentas from cases and controls

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HPV ↔ Πρόωρος τοκετός

TABLE 3
Rates of preterm delivery of study participants

Variable	Exposed (HR-HPV) group n = 314	Unexposed group (normal pap) n = 628	P value	OR (95% CI)
Any PTD <37 wks	31 (9.8)	41 (6.5)	.09	1.57 (0.96–2.55)
Spontaneous PTD <37 wks	23 (7.3)	26 (4.1)	.04	1.83 (1.03–3.26)
Any PTD <35 wks	15 (4.8)	12 (1.9)	.02	2.58 (1.19–5.37)
Spontaneous PTD <35 wks	10 (3.2)	3 (0.5)	< .001	6.85 (1.87–25.09)

Data are reported as n (%). Any PTD indicates PTD that is indicated or spontaneous. Spontaneous PTD indicates preterm delivery because of preterm labor or preterm premature rupture of membranes.

CI, confidence interval; OR, odds ratio; HR-HPV, high-risk human papillomavirus; pap, Papanicolaou; PTD, preterm delivery.

McDonnold. HPV and preeclampsia. *Am J Obstet Gynecol* 2014.

Am J Obstet Gynecol. 2014 Feb;210(2):138.e1-5

High risk human papillomavirus at entry to prenatal care and risk of preeclampsia.

McDonnold M, Dunn H, Hester A, Pacheco LD, Hankins GD, Saade GR, Costantine MM.

HPV ↔ Πρόωρος τοκετός

Associations Among Cervical Cytologic Findings, Placental Abnormalities, and Preterm Birth

Cervical Cytologic Finding	No. (%) of Placental Abnormalities	OR (95% CI)	<i>P</i>	Preterm Births	OR (95% CI)	<i>P</i>
Normal (n = 715)	175 (24.5)			116 (16.2)		
AGUS (n = 29)	16 (55)	3.80 (1.79-8.05)	<.001	11 (38)	3.16 (1.45-6.86)	.005
ASCUS (n = 290)	133 (45.9)	2.61 (1.96-3.48)	<.001	66 (22.8)	1.52 (1.08-2.14)	.018
HSIL (n = 103)	44 (42.7)	2.30 (1.50-3.52)	<.001	24 (23.3)	1.57 (0.95-2.58)	.051
LSIL (n = 161)	69 (42.9)	2.31 (1.62-3.30)	<.001	32 (19.9)	1.28 (0.83-1.98)	.208
Reactive changes (n = 1,182)	482 (40.8)	2.12 (1.73-2.61)	<.001	278 (23.5)	1.59 (1.25-2.02)	<.001
<i>Trichomonas</i> (n = 187)	96 (51.3)	3.26 (2.33-4.54)	<.001	63 (33.7)	2.62 (1.83-3.77)	<.001
<i>Candida</i> (n = 476)	193 (40.5)	2.10 (1.64-2.70)	<.001	100 (21.0)	1.37 (1.02-1.85)	.043

AGUS, atypical glandular cells of undetermined significance; ASCUS, atypical squamous cells of undetermined significance; CI, confidence interval; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; OR, odds ratio.

Association of Cervical High-Risk HPV DNA Status With Placental Abnormalities and Preterm Birth

HPV DNA Status	No. (%) of Preterm Births	<i>P</i>	No. (%) of Placental Abnormalities	<i>P</i>
Negative (n = 227)	23 (10.1)		86 (37.9)	
Positive (n = 160)	47 (29.4)	<.001	78 (48.8)	.023

HPV, human papillomavirus.

Am J Clin Pathol. 2011 Aug;136(2):260-5

Association of cervical cytology and HPV DNA status during pregnancy with placental abnormalities and preterm birth.

Zuo Z, Goel S, Carter JE.

**Πώς ερμηνεύονται τα παραπάνω
αποτελέσματα;**

Best Pract Res Clin Obstet Gynaecol. 2011 Jun;25(3):313-27

Placental bed disorders in preterm labor, preterm PROM, spontaneous abortion and abruptio placentae.

Romero R, Kusanovic JP, Chaiworapongsa T, Hassan SS.

Παθοφυσιολογί α

Table III. The number (percent) of patients who had failure of physiologic transformation of the spiral arteries in normal pregnant women at term and patients with preeclampsia and preterm PROM

	<i>Normal pregnancy at term</i>	<i>Preeclampsia</i>	<i>P value</i>	<i>Preterm PROM</i>	<i>P^a value</i>	<i>P^b value</i>
Myometrial segment of the spiral arteries						
Total No. of patients	59	23		31		
Completely transformed in all vessels	31 (52.5%)	1 (4.3%)		9 (29%)		
Partially transformed or mixed transformed and nontransformed vessels	24 (40.7%)	10 (43.5%)		16 (51.6%)		
Nontransformed in all vessels	4 (6.8%)	12 (52.2%)	<.0001*	6 (19.4%)	.016*	.003*
Decidual segment of the spiral arteries in the basal plate						
Total No. of patients	52	22		30		
Completely transformed in all vessels	44 (84.6%)	8 (36.4%)		25 (83.3%)		
Partially transformed or mixed transformed and nontransformed vessels	8 (15.4%)	13 (59.1%)		5 (16.7%)		
Nontransformed in all vessels	0	1 (4.5%)	<.0001*	0	NS	.001*

The *P* values for pairwise comparisons between diagnostic groups derived from the comparisons of shift in proportions of patients in each classification using Spearman rank correlation. *P* = Comparison between preeclampsia and normal pregnancy at term. *P^a* = Comparison between preterm PROM and normal pregnancy at term. *P^b* = Comparison between pre-eclampsia and preterm PROM. NS, Not significant.

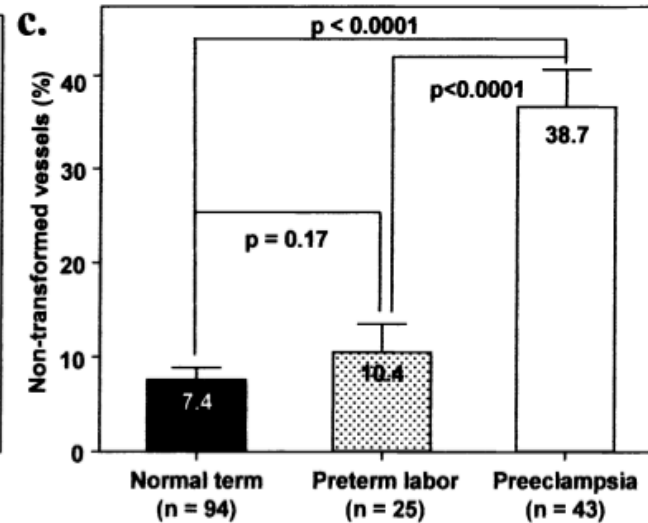
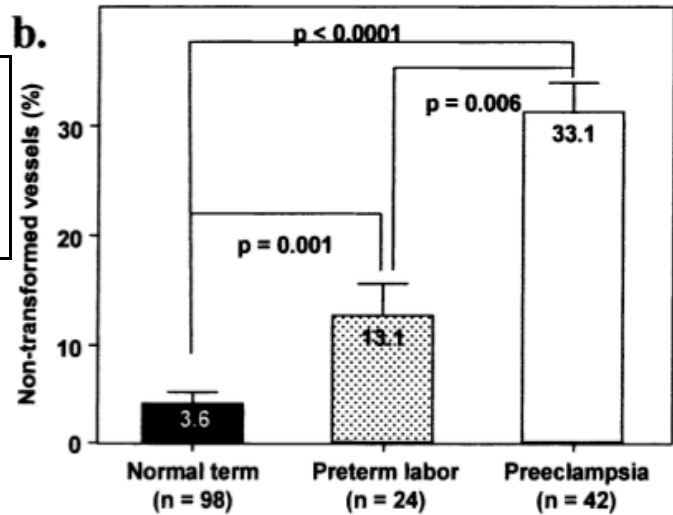
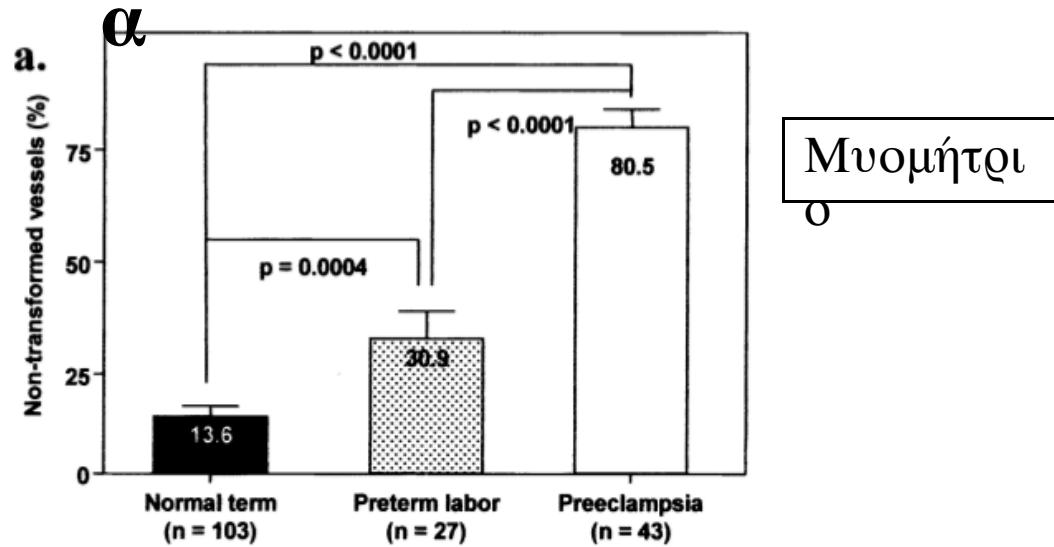
**P* < .05.

Am J Obstet Gynecol. 2002 Nov;187(5):1137-42.

Failure of physiologic transformation of the spiral arteries in the placental bed in preterm premature rupture of membranes.

Kim YM, Chaiworapongsa T, Gomez R, Bujold E, Yoon BH, Rotmensch S, Thaler HT, Romero R.

Παθοφυσιολογί



Εγγύς
τμήμα
βασικού
φθαρτού

Βασικός
φθαρτού

Am J Obstet Gynecol. 2003 Oct;189(4):1063-9.

Failure of physiologic transformation of the spiral arteries in patients with preterm labor and intact membranes.

Kim YM, Bujold E, Chaiworapongsa T, Gomez R, Yoon BH, Thaler HT, Rotmensch S, Romero R.

**Πώς σχετίζεται ο HPV με την
ατελή διείσδυση της
τροφοβλάστης;**

In vivo ανίχνευση HPV DNA σε υλικό από βιοψία χοριακών λαχνών

(11η -13η Εβδ. κύησης)

Table 1. HPV) Polymerase Chain Reaction Results Obtained for the HPV-Positive Chorionic Villous Sampling

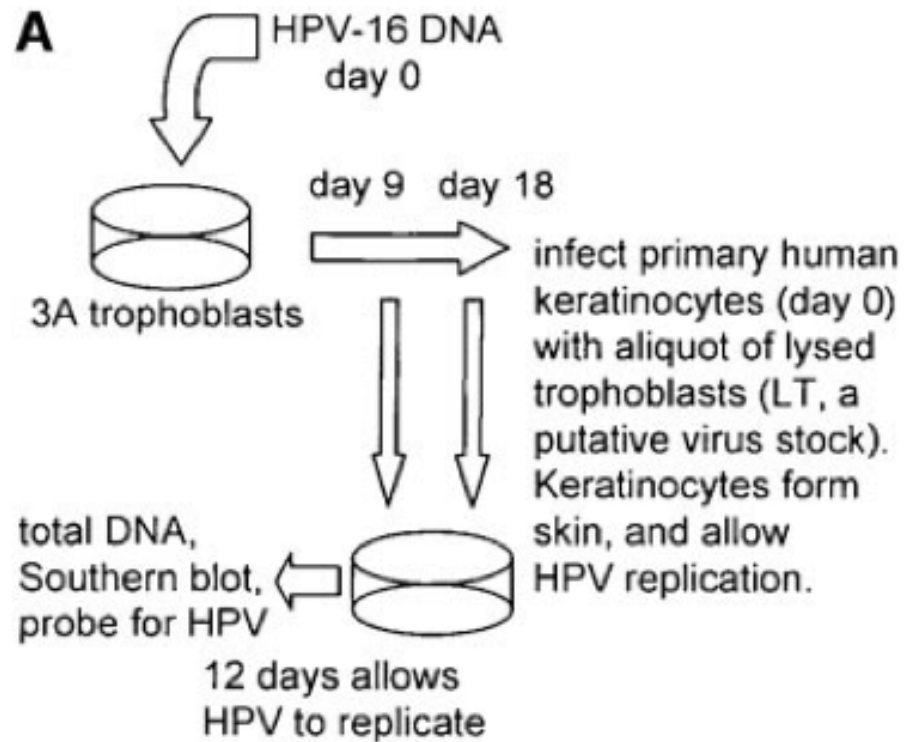
Results	Sample 1	Sample 2
L1 region:PGMY09/11 and GP5+/6+ (Sequencing)	HPV-16	HPV-62
L1 region:PGMY09/11 and SPF10 (INNO-LiPA)	HPV-16	undefined
E6/E7 region:pU (Sequencing)	HPV-16	undefined

NOTE. The genotyping method is mentioned in brackets.

J Infect Dis. 2011 Feb 1;203(3):341-3

Evidence of human papillomavirus in the placenta.

Weyn C, Thomas D, Jani J, Guizani M, Donner C, Van Rysselberge M, Hans C, Bossens M, Englert Y, Fontaine V.



Τα σχηματιζόμενα
ικά σωματία έχουν
λοιμογόνο δράση σε
καλλιέργειες
κερατινοκυττάρων

Virology. 2001 Nov 10;290(1):99-105.

Display of complete life cycle of human papillomavirus type 16 in cultured placental trophoblasts.

Liu Y, You H, Chiriva-Internati M, Korourian S, Lowery CL, Carey MJ, Smith CV, Hermonat PL.

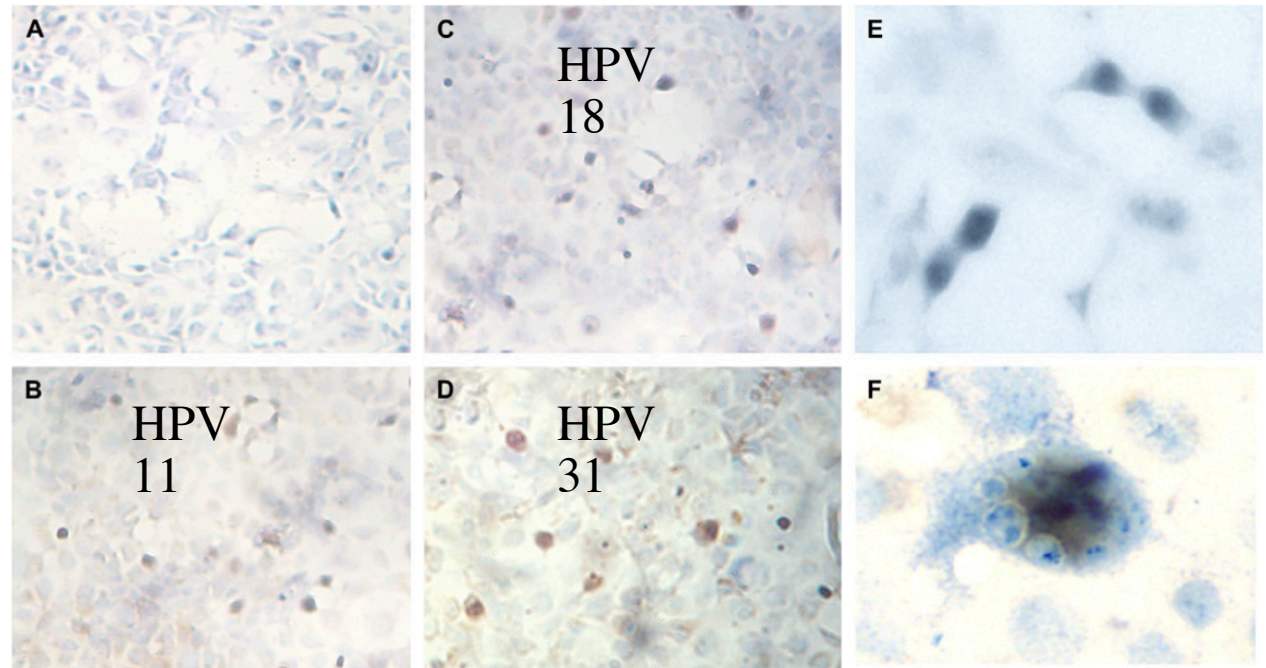
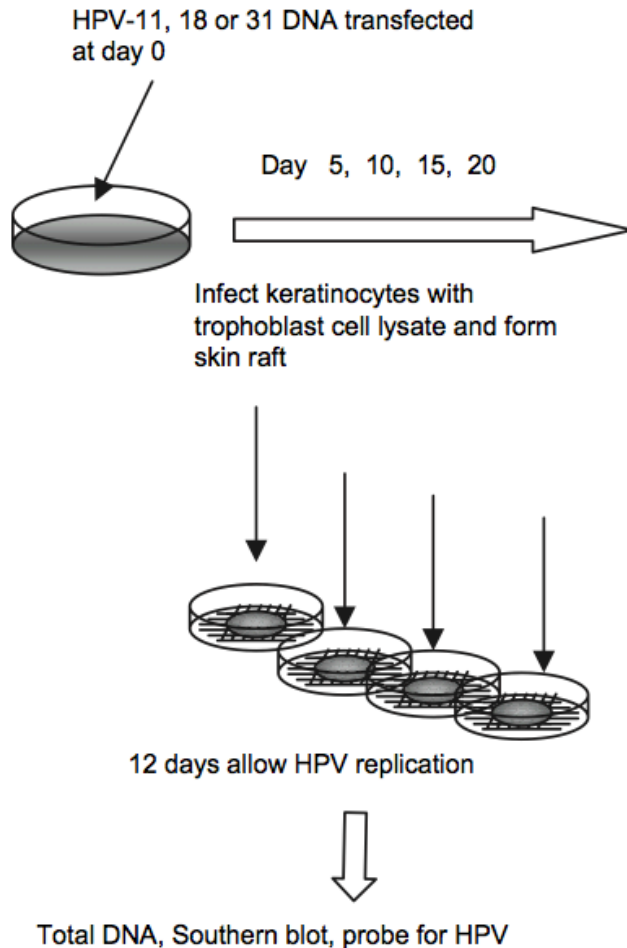


Fig. 3. Immunocytochemistry of L1 expression in trophoblast. Untransfected and HPV-11,18, or 31 transfected 3A trophoblasts were fixed and stained using the anti-L1 antibody at 15 days post-infection, as described in Section 2. A Shows uninfected 3A cells to be negative for L1 protein (negative control). B, C, D Shows HPV-11, 18, or 31 transfected 3A trophoblast to be L1-positive upon anti-L1 antibody staining (brown color). Most of the staining was observed in the nuclei of the cells, with a lower signal occurring in the cytoplasm. E, F Shows a higher power picture of the L1 signal in nuclei.

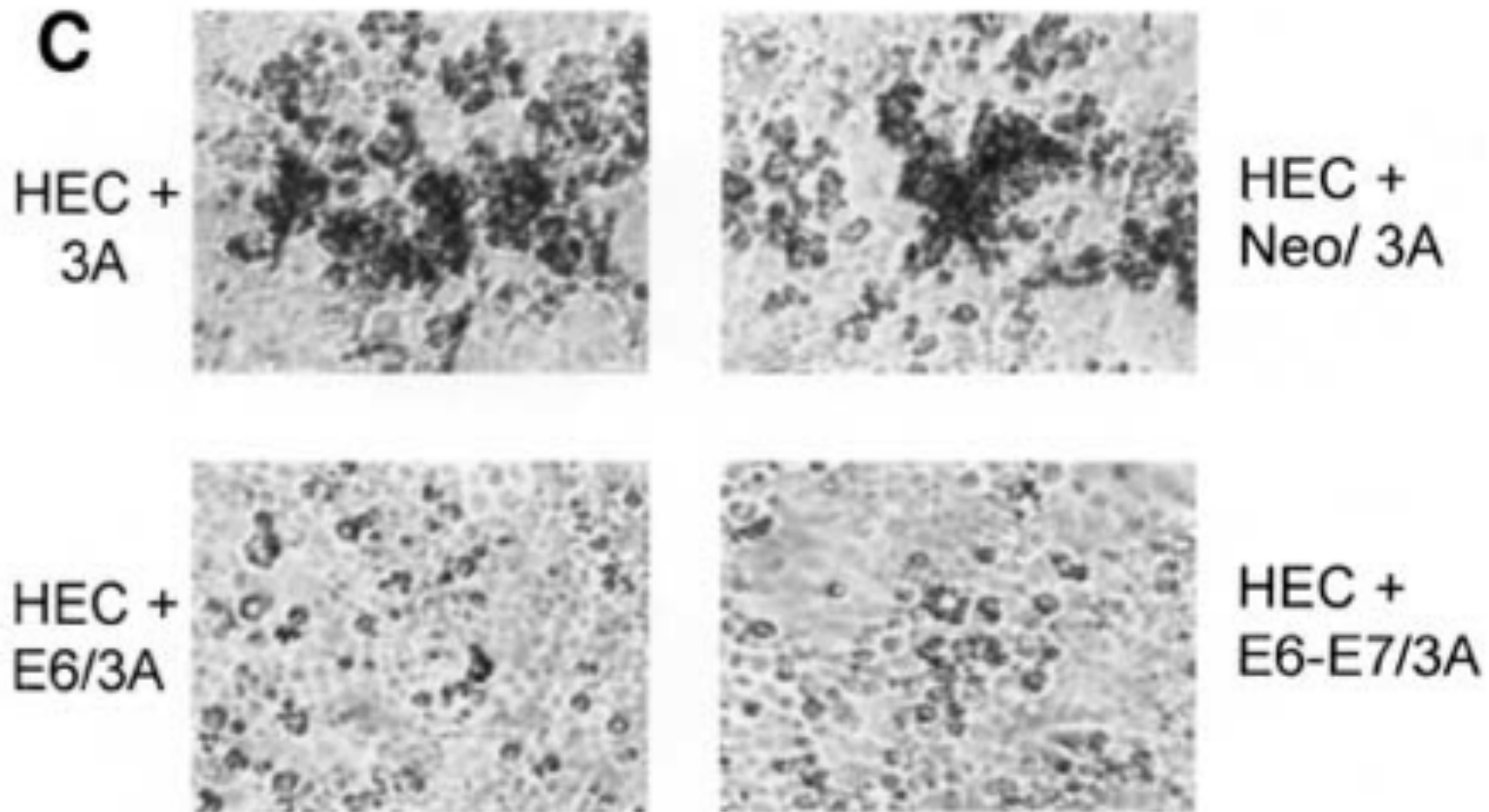
Αντίστοιχα με τον HPV 16, πλήρη αναπαραγωγικό κύκλο μπορούν να έχουν σε καλλιέργειες τροφοβλαστικών κυττάρων και άλλοι τύποι του HPV όπως ο 11, ο 18 και ο 31.

Placenta. 2008 Jan;29(1):30-8. Epub 2007 Oct 1.

Multiple human papillomavirus types replicate in 3A trophoblasts.

You H, Liu Y, Agrawal N, Prasad CK, Edwards JL, Osborne AF, Korourian S, Lowery CL, Hermonat PL.

ΕΛΑΤΤΩΜΑΤΙΚΗ ΠΡΟΣΔΕΣΗ ΤΡΟΦΟΒΛΑΣΤΙΚΩΝ ΚΥΤΤΑΡΩΝ ΣΕ ΚΑΛΛΙΕΡΓΕΙΕΣ ΚΥΤΤΑΡΩΝ ΕΝΔΟΜΗΤΡΙΟΥ

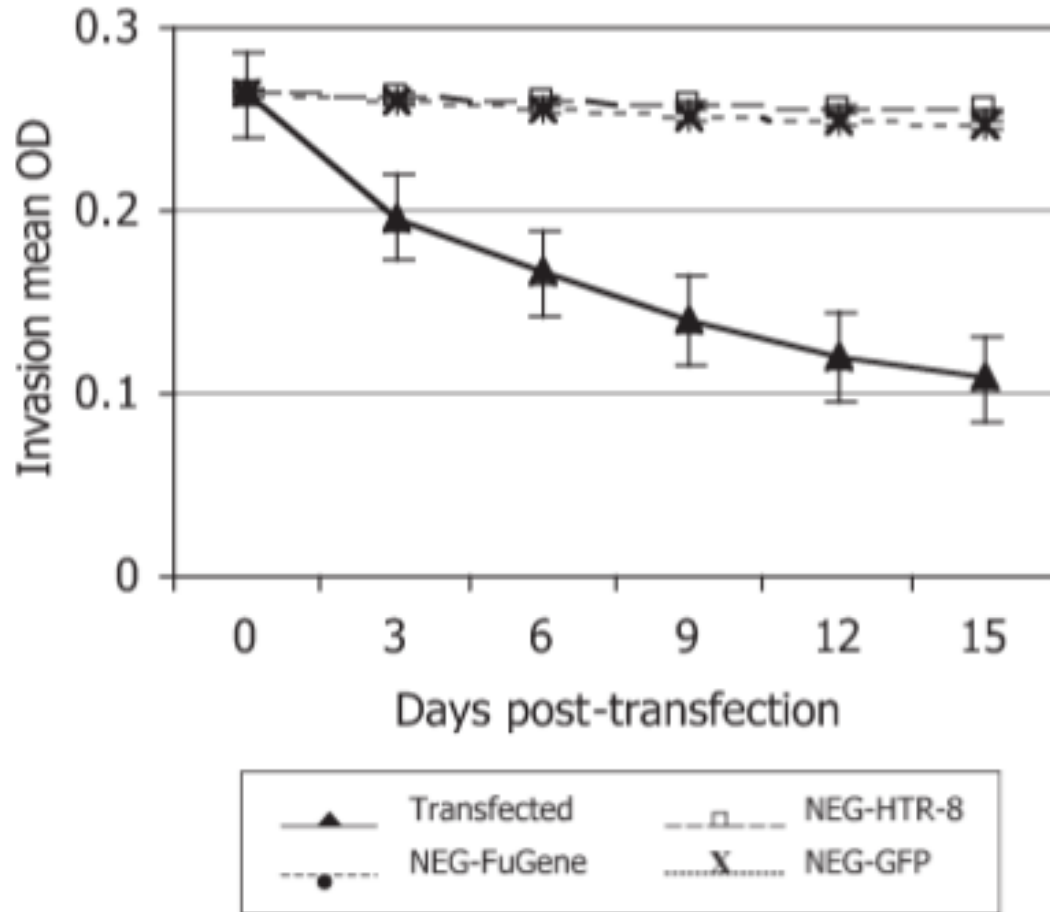


Mol Cancer Res. 2002 Nov;1(1):25-31.

Defective 3A trophoblast-endometrial cell adhesion and altered 3A growth and survival by human papillomavirus type 16 oncogenes.

You H, Liu Y, Carey MJ, Lowery CL, Hermonat PL.

HPV – ΠΡΩΡΟΣ ΤΟΚΕΤΟΣ



Μείωση της διεισδυτικής ικανότητας διαμολυνθέντων με HPV 16 τροφοβλαστικών κυττάρων στην εξωκυττάρια ουσία

Hum Reprod. 2008 Mar;23(3):709-15

Placental infection with human papillomavirus is associated with spontaneous preterm delivery.

Gomez LM, Ma Y, Ho C, McGrath CM, Nelson DB, Parry S.

Αυτόματες
εκτρώσεις

Προεκλαμψία

IUGR

PPROM

Πρόωρος
τοκετός

Ατελής
διείσδυση
τροφοβλάστης

HPV



Ο HPV συσχετίζεται με την καρδιαγγειακή νόσο,
ανεξάρτητα από άλλους παράγοντες κινδύνου!

Η δράση των ογκοπροτεϊνών E6 και E7 του HPV πιθανόν επιταχύνει την αθηρωμάτωση (συσχέτιση με προεκλαμψία όπου υπάρχει η λεγόμενη «οξεία αθηρωμάτωση»)

Table 3 Association Between Cardiovascular Disease and HPV

	Model 1		Model 2		Model 3		Model 4		Model 5	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Presence of HPV DNA										
Negative (reference)	1.0		1.0		1.0		1.0		1.0	
Positive	2.46 (1.42–4.27)	0.001	2.13 (1.21–3.74)	0.009	2.14 (1.21–3.79)	0.009	2.30 (1.27–4.16)	0.006	2.06 (1.14–3.74)	0.017
HPV genotypes										
Negative HPV (reference)	1.0		1.0		1.0		1.0		1.0	
Other HPV types	2.13 (1.12–4.06)	0.021	1.91 (0.99–3.69)	0.055	1.88 (0.97–3.67)	0.063	1.89 (0.94–3.78)	0.072	1.70 (0.84–3.43)	0.137
Cancer-associated HPV types	2.87 (1.52–5.43)	0.001	2.39 (1.24–4.61)	0.009	2.46 (1.27–4.77)	0.008	2.86 (1.43–5.70)	0.003	2.53 (1.27–5.01)	0.008

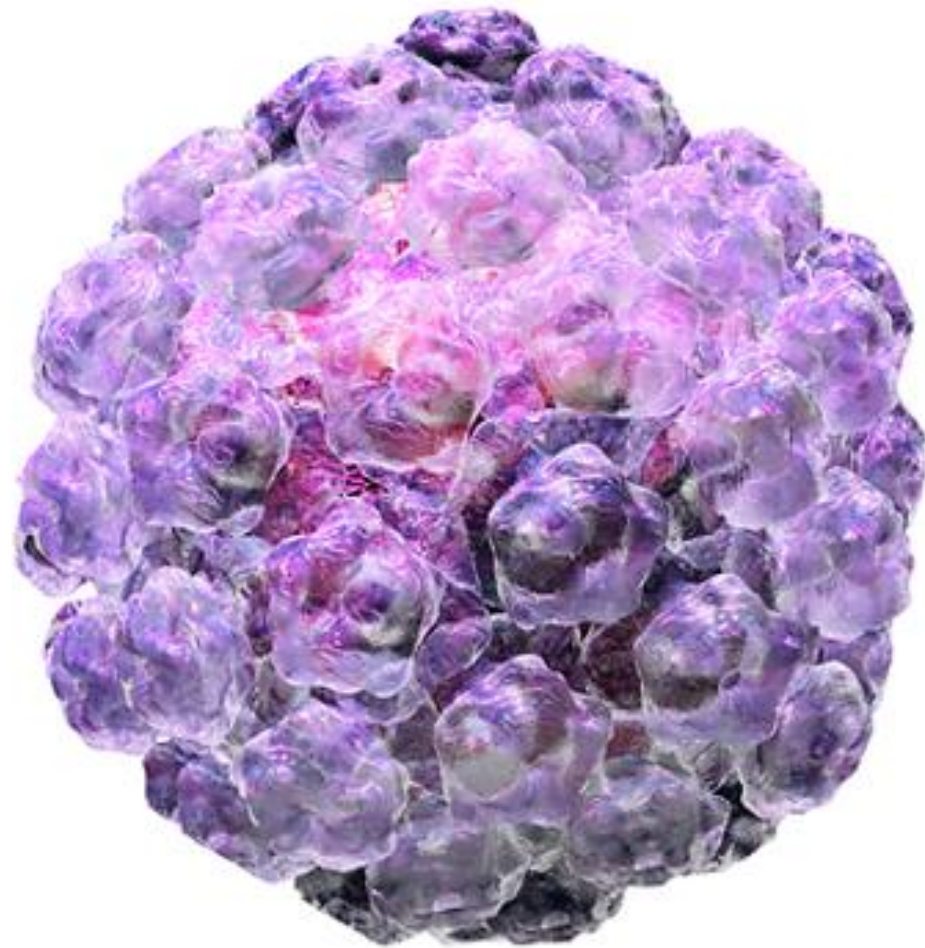
Adjusted covariates: Model 1 = Age and race. Model 2 = Model 1 + health behaviors (smoking and alcohol consumption) and sex behavior. Model 3 = Model 2 + medical comorbidities (lung disease, liver disease, thyroid disease, estimated glomerular filtration rate, sexually transmitted disease, history of cervical cancer, history of all other cancer). Model 4 = Model 3 + cardiovascular risk factors and management (hypertension, diabetes mellitus, waist circumference, triglycerides, high-density lipoprotein cholesterol, log-transformed levels of C-reactive protein and urinary albumin-to-creatinine ratio, use of antihypertensive agents or cholesterol-lowering medications). Model 5 = Model 3 + metabolic z-score, use of antihypertensive agents or cholesterol-lowering medications. Cancer-associated HPV (human papillomavirus) types = HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68.

CI = confidence interval; OR = odds ratio.

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Human papillomavirus and cardiovascular disease among U.S. women in the National Health and Nutrition Examination Survey, 2003 to 2006.

Kuo HK, Fujise K.



**... Ευχαριστώ για την προσοχή
σας.**