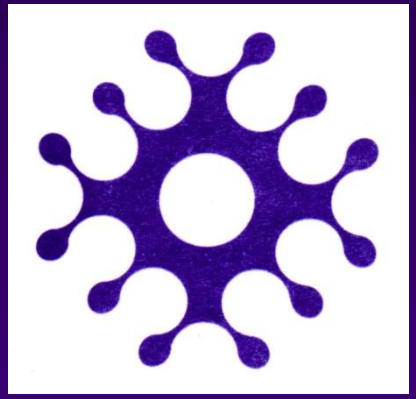
Triaža žensk s pozitivnim izvidom presejalnega testa HPV

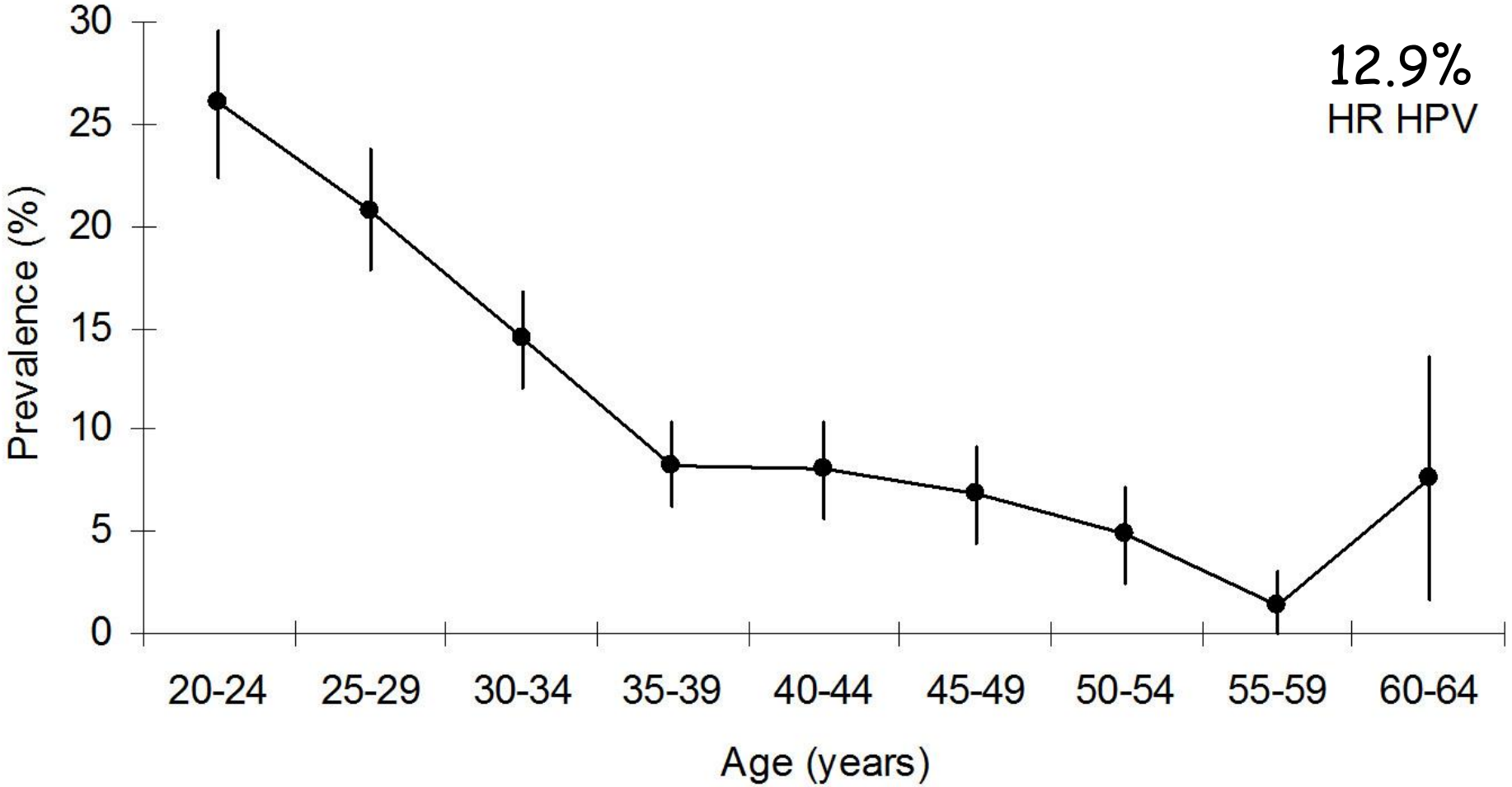
- genotipizacija HPV -



Mario Poljak

Institute of Microbiology and Immunology
Faculty of Medicine, University of Ljubljana, Slovenia

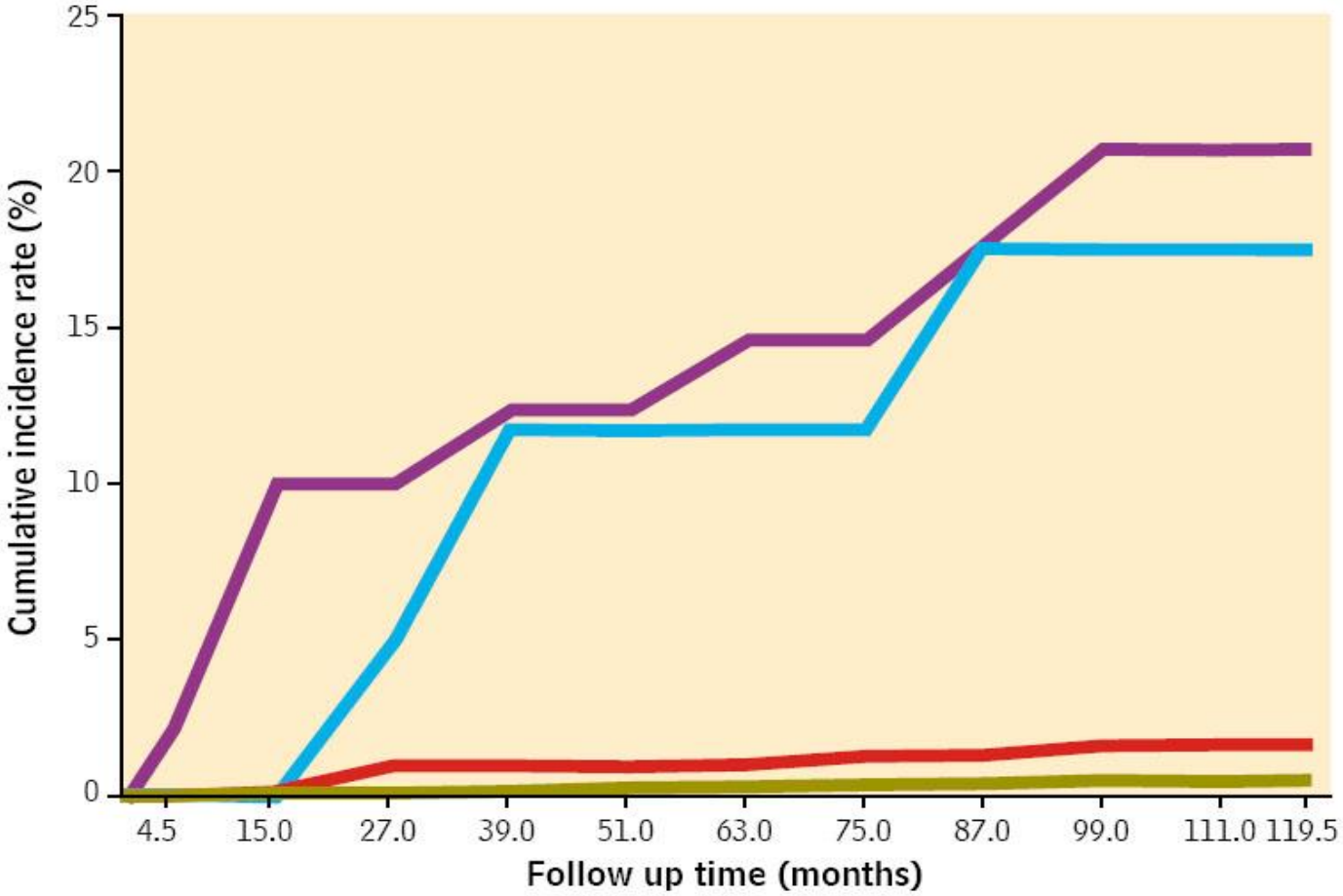
Prevalence of infection with 14 hr-HPV types with 95% confidence intervals according to age among 4,431 women screened for cervical cancer, Slovenia, 2010



Vaccine 2012; 30: 116-120.

High-risk alpha HPV genotypes

HPV-16, -18, -31, -33, -35, -39, -45, -51, -52, -56, -58, -59

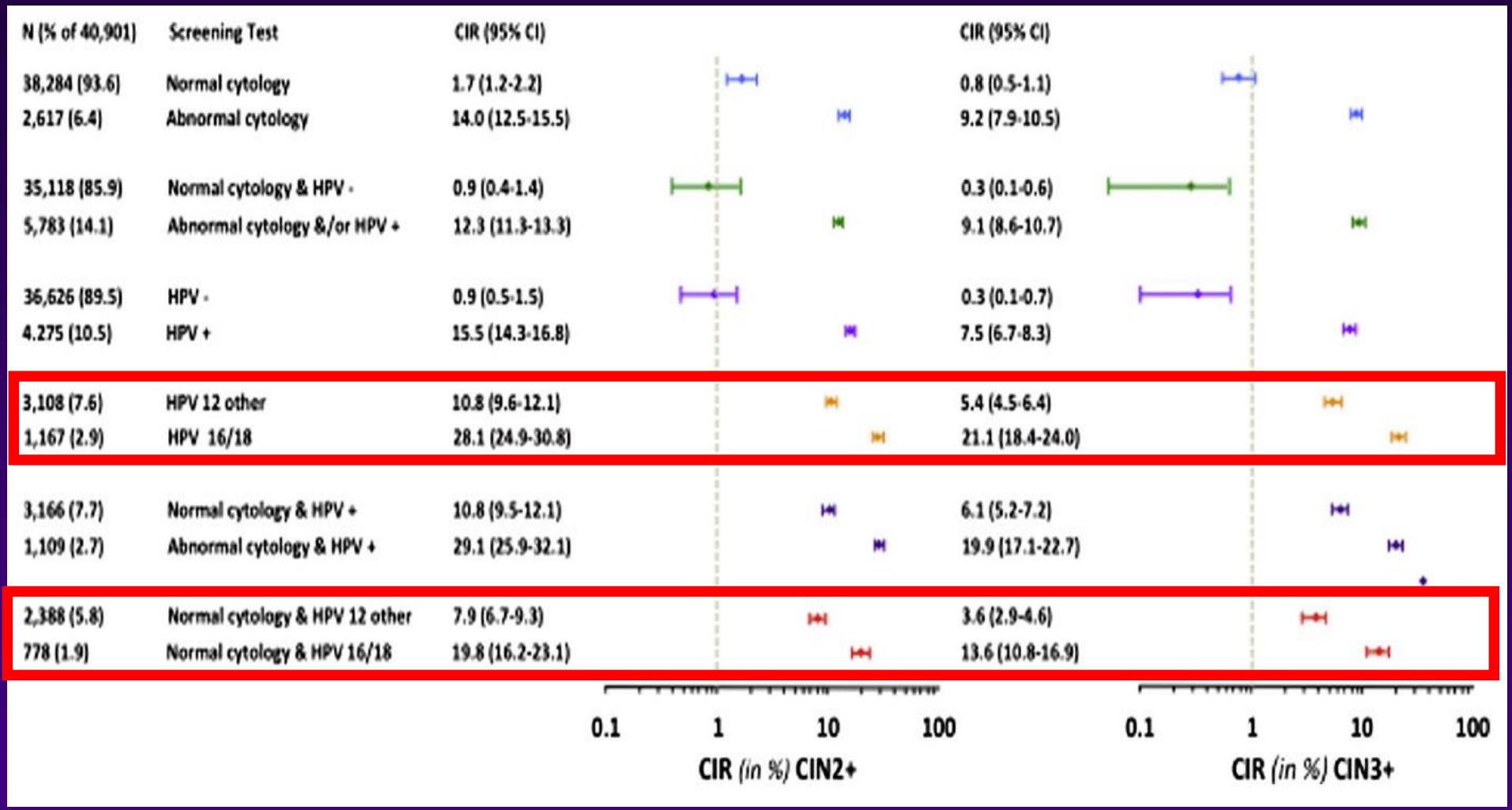


No.of women seen during follow-up interval

HPV-16+	93	50	39	38	36	39	28	28	27	11	1
HPV-18+	38	18	20	14	15	12	9	15	11	3	0
HC2+	890	498	463	419	370	353	310	276	288	127	7
HC2-	11741	6763	6231	5784	5369	4923	4619	4281	4140	2051	133

Khan MJ et al. J Natl Cancer Inst 2005; 97: 1072-9

Verification bias-adjusted 3-year cumulative incidence rates of consensus pathology CIN2+ and CIN3+ stratified by different combinations of baseline cervical cytology and HPV results (ATHENA - end of study results)



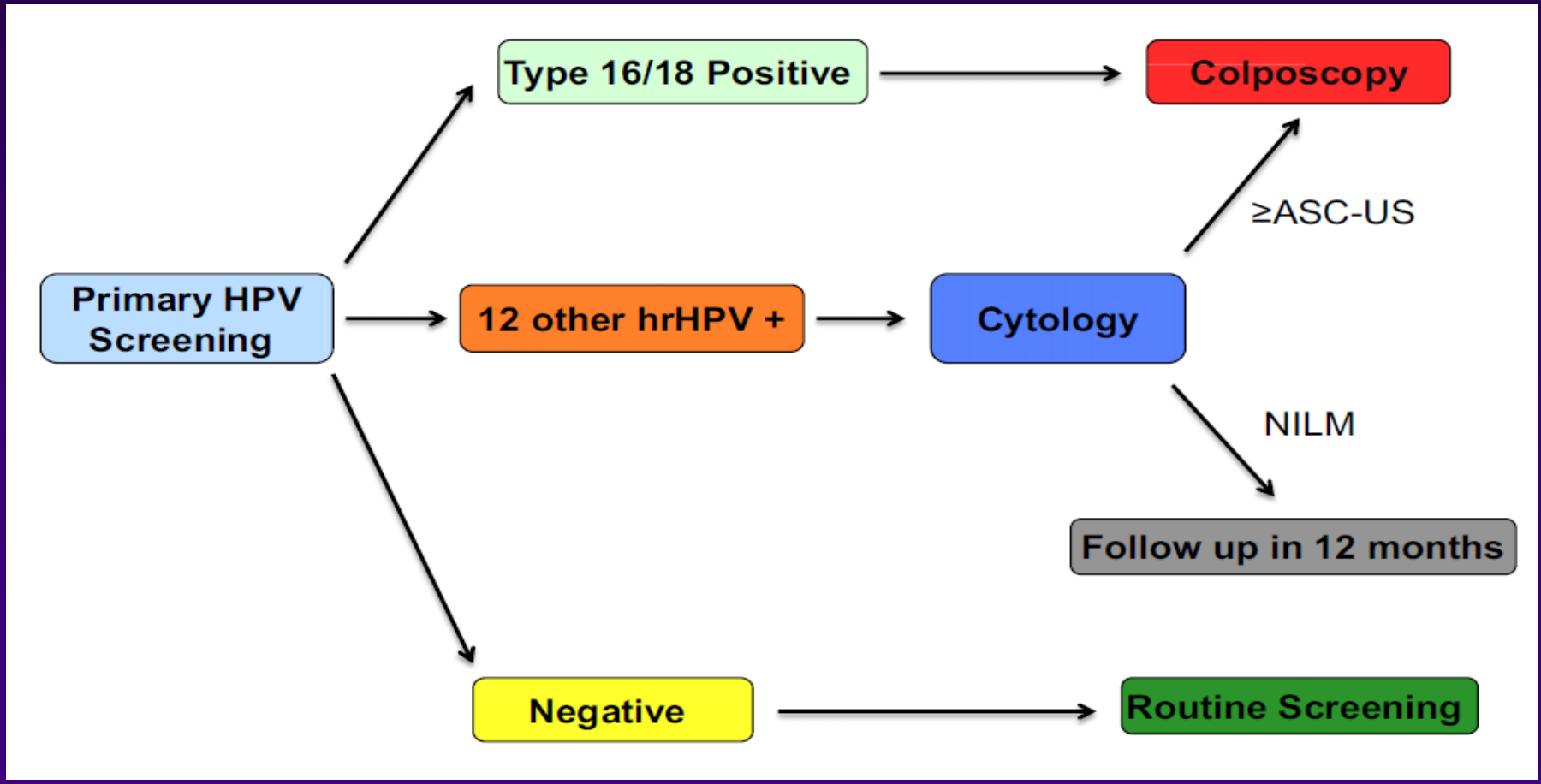
Wright TC et al. Gynecol Oncol 2015; 136: 189-97.

Clinical Commentary

Use of primary high-risk human papillomavirus testing for cervical cancer screening: Interim clinical guidance ☆

Gynecol Oncol 2015; 136:178-82

Warner K. Huh [a,*], Kevin A. Ault [b], David Chelmow [c], Diane D. Davey [d], Robert A. Goulart [e], Francisco A.R. Garcia [f], Walter K. Kinney [g], L. Stewart Massad [h], Edward J. Mayeaux [i], Debbie Saslow [j], Mark Schiffman [k,1], Nicolas Wentzensen [k,1], Herschel W. Lawson [l], Mark H. Einstein [m]



Five-Year Cervical (Pre)Cancer Risk of Women Screened by HPV and Cytology Testing

Margot H. Uijterwaal[1], Nicole J. Polman[1], Folkert J. Van Kemenade[2], Sander Van Den Haselkamp[1], Birgit I. Witte[3], Dorien Rijkaart[1], Johannes Berkhof[3], Peter J.F. Snijders[1], and Chris J.L.M. Meijer[1]

Cancer Prev Res (Phila) 2015;8:502-8

Table 2. Five-year cumulative incidences for CIN3+ and CIN2+ in HPV-positive women with normal cytology triaged with different triage strategies

			CIN3+			CIN2+		
Baseline	**Repeat cytology (after 12 months)**	***n***	***n***	**Cumulative incidence**	**95% CI**	***n***	**cumulative incidence**	**95% CI**
HPV-positive, normal cytology	—	905	72	7.9%	4.4%–10.1%	114	12.9%	9.6%–16.0%
HPV-positive, normal cytology	Normal cytology	407	15	4.1%	0.44%–5.9%	25	7.0%	3.3%–9.2%
HPV-positive, normal cytology	≥BMD	72	23	31.1%	19.5%–40.9%	38	53.2%	39.3%–66.8%
HPV 16/18-positive, normal cytology	—	259	48	18.1%	9.4%–33.9%	62	24.6%	16.7%–30.2%
HPV 16/18-positive, normal cytology	Normal cytology	104	10	11.3%	0.00%–19.2%	12	13.4%	2.8%–21.0%
HPV 16/18-positive, normal cytology	≥BMD	32	14	40.9%	22.3%–59.1%	22	69.6%	50.3%–87.5%
HPV-non 16/18-positive, normal cytology	—	646	24	3.5%	1.7%–5.3%	52	7.9%	5.7%–10.4%
HPV-non 16/18-positive, normal cytology	Normal cytology	303	5	0.42%	0.00%–1.4%	13	3.5%	0.00%–6.2%
HPV-non 16/18-positive, normal cytology	≥BMD	40	9	23.3%	10.3%–38.7%	16	41.3%	23.1%–58.6%

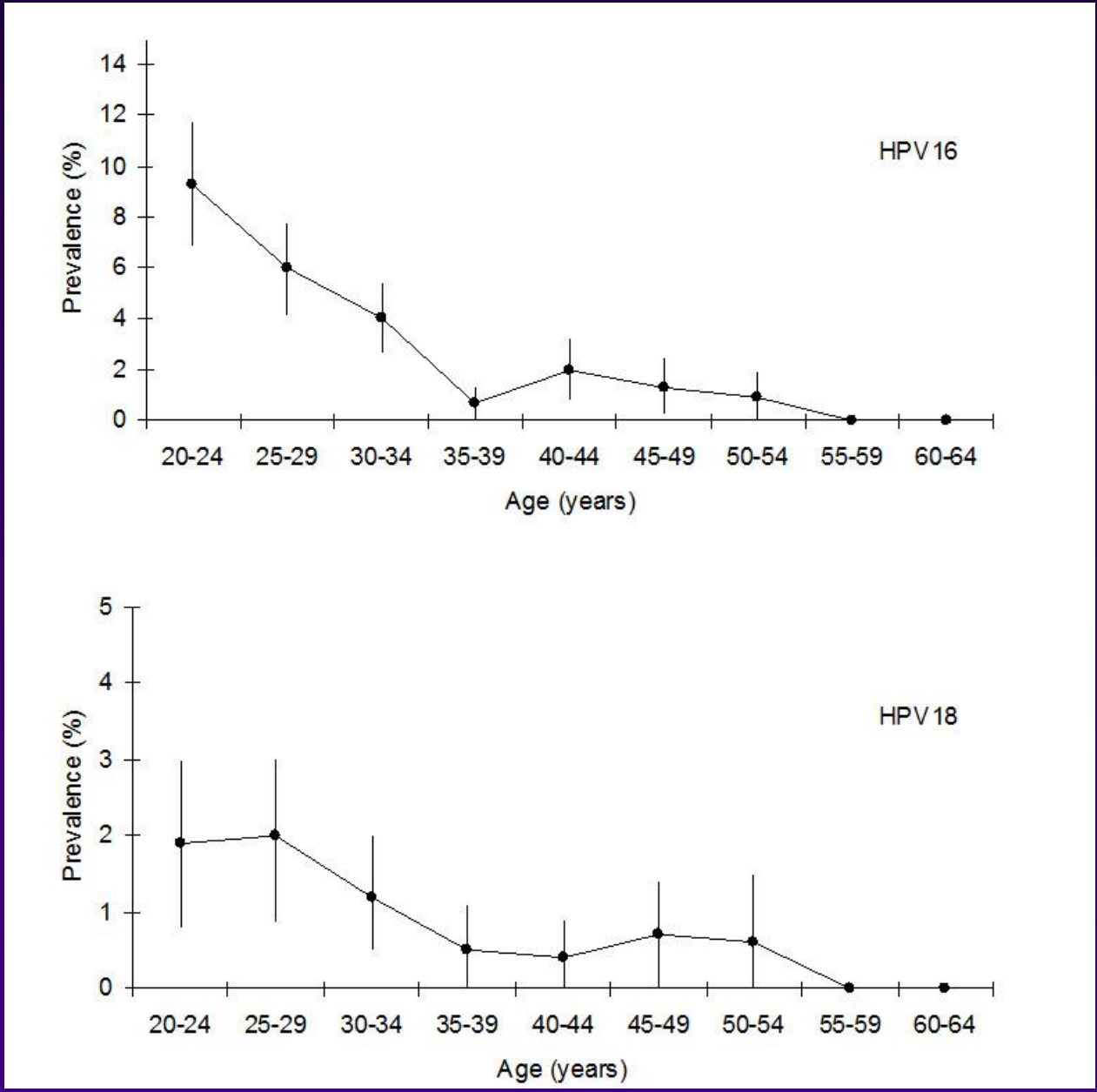
n = number of women.

Risk at baseline and baseline plus future risk at 3 years for cervical intraepithelial neoplasia grade 2 or worse (CIN2+) and grade 3 or worse (CIN3+) with corresponding 95% confidence intervals (95% CI) for women with different baseline characteristics in the total study population

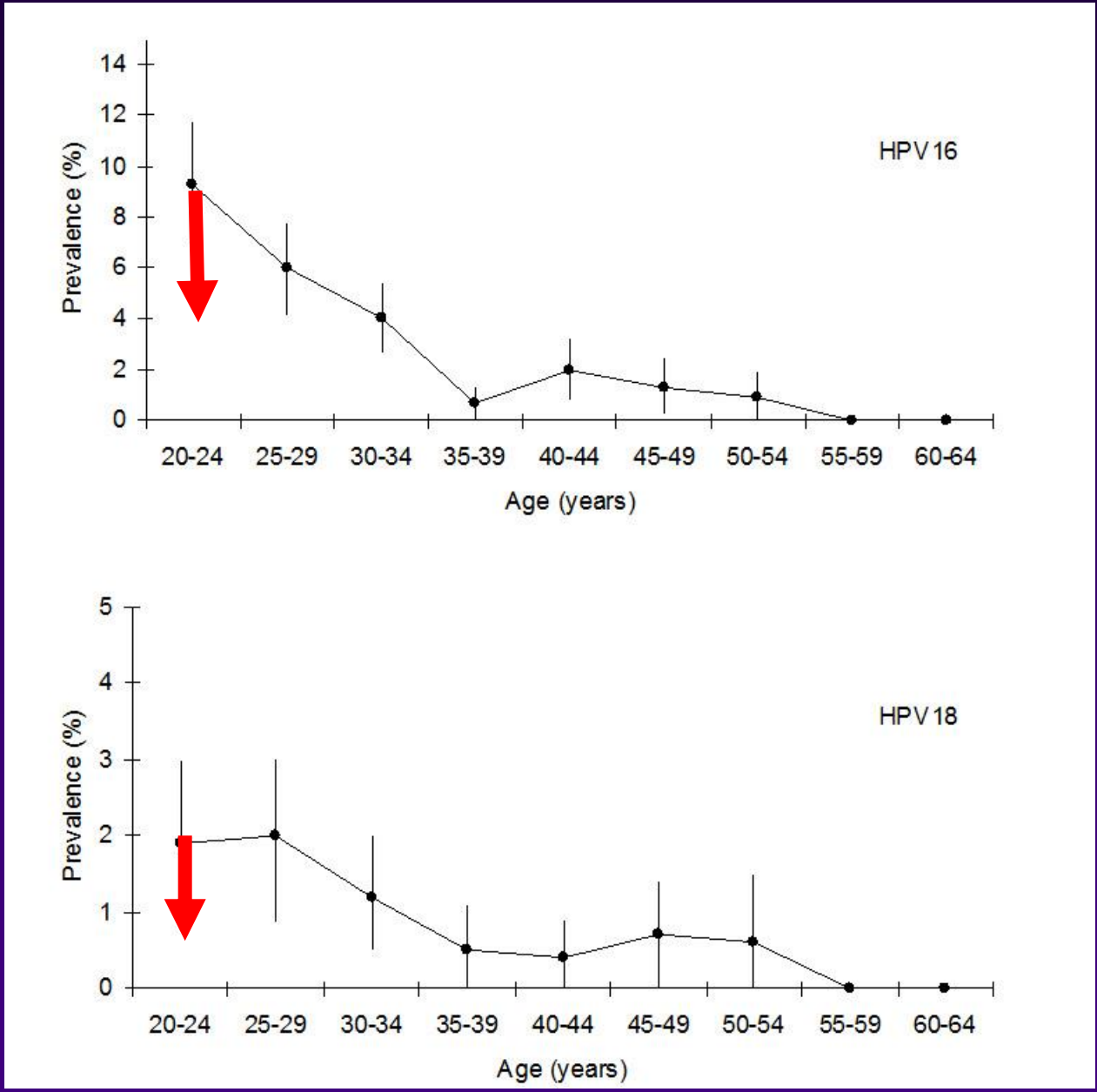
	CIN2+				CIN3+			
	Risk at baseline		Baseline plus future risk at 3 years		Risk at baseline		Baseline plus future risk at 3 years	
	n	% (95% CI)	*n*	% (95% CI)	*n*	% (95% CI)	*n*	% (95% CI)
HPV16-positive	35/160	21.9% (15.2–30.4%)	50/150	33.3% (24.7–44.0%)	17/160	10.6% (6.2–17.0%)	24/150	16.0% (10.3–23.8%)
HPV16/18-positive	41/201	20.4% (14.6–27.7%)	57/187	30.5% (23.1–39.5%)	20/201	10.0% (6.1–15.4%)	27/187	14.4% (9.5–21.0%)
non-16/18 hrHPV-positive	26/372	7.0% (4.6–10.2%)	43/327	13.2% (9.5–17.7%)	11/372	3.0% (1.5–5.3%)	22/327	6.7% (4.2–10.2%)
hrHPV-positive	67/573	11.7% (9.1–14.9%)	100/514	19.5% (15.8–23.7%)	31/573	5.4% (3.7–7.7%)	49/514	9.5% (7.1–12.6%)
hrHPV-negative	1/3,937	0.03% (0.00–0.14%)	4/3,474	0.12% (0.03–0.29%)	0/3,937	0.0%	0/3,474	0.0%

Poljak et al., J Clin Virol 2016;76 Suppl 1:S29-S39.

Prevalence of infection with HPV-16 and HPV-18 with 95% confidence intervals according to age among 4,431 women screened for cervical cancer, Slovenia, 2010



Prevalence of infection with HPV-16 and HPV-18 with 95% confidence intervals according to age among 4,431 women screened for cervical cancer, Slovenia, 2010



High-risk alpha HPV genotypes

HPV-16, -18, -31, -33, -35, -39, -45, -51, -52, -56, -58, -59

Contents lists available at ScienceDirect

Papillomavirus Research

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

Papillomavirus Research 2 (2016) 112–115

Cuzick and Wheeler

Need for expanded HPV genotyping for cervical screening ☆

Prevalence of HPV 16, 18, 31, 33 and positive predictive value (PPV) or relative risk (RR, where indicated) for CIN2+ and CIN3+ in different studies

Study [ref]	HPV type	Population prevalence % (95% CI)	CIN2+		CIN3+	
			PPV (95% CI)	rank	PPV (95% CI)	rank
ATHENA (N=40 901) [[3], (Table 3)]	16	2.1 (1.9, 2.2)	19.5 (16.8, 22.3)	1	14.7(12.2, 17.3)	1
	18	.82 (.73, .91)	8.4 (5.64, 11.9)	4	6.9 (4.4, 10.2)	4
	31	1.0 (.92, 1.1)	15.2 (11.9, 19.0)	2	8.0 (5.5, 11.0)	2
	33	.28 (.23, .33)	9.7 (4.96, 16.8)	3	7.1 (3.1, 13.5)	3
NMHPVPR (N=47 617, 3y FU) [[13], Table 1; [14], Table 3]]	16	3.5 (3.3, 3.6)	10.9 (6.1, 12.7)	1.5	8.0 (6.5, 9.6)	1
	18	1.2 (1.1, 1.3)	5.7 (3.4, 7.9)	4	2.9 (1.5, 4.3)	4
	31	1.8 (1.7, 1.9)	7.3 (4.7, 9.9)	3	3.1 (1.9, 4.4)	3
	33	.50 (.43, .57)	10.9 (5.8, 16.0)	1.5	5.2 (1.8, 8.6)	2
FUTURE I (N=1694, 3y FU) [[15], Table 1]	16	13.9 (12.4, 15.5)	9.2 (6.0, 13.2)	2	1.7 (0.0, 3.8)	3
	18	5.8 (4.8, 6.9)	4.4 (1.4, 10.0)	4	0 (-)	–
	31	8.0 (6.8, 9.3)	8.9 (5.0, 14.5)	3	3.2 (0.0, 8.8)	2
	33	2.9 (2.2, 3.7)	14.0 (6.26, 25.8)	1	4.1 (0.0, 10.5)	1
KPNC (3y FU) (N=18 810, HPV+, cyto neg, >30y) [[6], Tables 2 and 3)]	16	14.7 (14.2, 15.2)	16.7 (15.5, 17.9)	1	10.6 (.89, 11.4)	1
	18	6.3 (6.0, 6.7)	9.4 (8.3, 10.7)	4	5.9 (5.2, 6.7)	2
	31	10.1 (9.7, 10.5)	10.2 (9.3, 11.3)	3	4.5 (4.1, 5.0)	4
	33	2.2 (2.0, 2.4)	8.9 (7.1, 11.0)	6	5.9 (4.8, 7.2)	3
			HPV 52-2nd; HPV35-5th			
Predictors 2 (referral) N=1067 [[4], Table 3 and new data[a]]	16	30.2 (27.4, 33.0)	57.8 (52.2, 63.2)	2	42.3 (37.0, 47.8)	1
	18	5.4 (4.1, 7.0)	29.3 (18.1, 42.8)	4	15.2 (6.34, 28.9)	6
	31	7.6 (6.1, 9.4)	39.5 (28.8, 51.0)	3	22.2 (13.7, 32.8)	3
	33	7.7 (6.2, 9.4)	59.8 (48.3, 70.4)	1	31.0 (20.5, 43.1)	2

Cuzick and Wheeler, Papillomavirus Research, 2016;2:112-5.

HPV-33 has a higher positive predictive value for CIN2+ and CIN3+ than HPV-18, for all studies, except in a study conducted in Kaiser Permanente Northern California where the risk was virtually equal

HPV-31 consistently stands out as being higher risk than other 'high risk HPV types' and has a higher risk than HPV-18

HPV-45 emerges in the top four HPV genotypes causing invasive cervical cancer

HPV-66 should be excluded from hr-HPV screening tests

- separate readouts: HPV-16, HPV-18, HPV-31 and HPV-33
- pool 1 – 'other high risk' types - HPV-35, HPV-45, HPV-51, HPV-52, HPV-58
- pool 2 - 'intermediate risk' types - HPV-39, HPV-56, HPV-59, HPV-68

Cuzick and Wheeler, Papillomavirus Research, 2016;2:112-5.

Balancing prevalence vs. risk for CIN3+ by HPV genotype:
Perspectives from the Onclarity clinical trial

Genotype	<CIN2	CIN3+	Absolute Risk
	N = 2,607	N = 162	
16	293 (11.2%)	83 (51.2%)	20% (16.5-24.0%)
31	274 (10.5%)	35 (21.6%)	9.9% (7.2-13.2%)
18	160 (6.1%)	10 (6.2%)	6.6% (3.6-10.3%)
33_58	278 (10.7%)	13 (8.0%)	4.7% (2.6-7.3%)
52	385 (14.8%)	20 (12.3%)	3.4% (1.8-5.6%)
45	192 (7.4%)	7 (4.3%)	2.4% (0.7-5.1%)
39_68_35	683 (26.2%)	22 (13.6%)	1.7% (0.8-2.9%)
51	223 (8.6%)	5 (3.1%)	1.6% (0.1-4.0%)
59_56_66	694 (26.6%)	18 (11.1%)	0.5% (0.1-1.4%)