

評価対象論文リスト(要因:ヒトパピローマウイルスの感染・HPVワクチン、アウトカム:子宮頸がん)

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(ヒトパピローマウイルスの感染)

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(HPVワクチン)

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(HPV感染と子宮頸がん:コホート研究)

Reference		Study subjects							Category	Number among cases	Relative risk (95%CI or p)	P for trend	Confounding variables considered	Magnitude of association						
Author	Title	Year	Study period	Number of subjects	Source of subjects	Event followed	Number of incident cases or	Participant's race												
Yokoyama M et al.	Prognostic factors associated with the clinical outcome of cervical intraepithelial neoplasia: a cohort study in Japan	2003	1996-1999 (28.5 months)	185	9 hospitals of the Japan Study Group of HPV and cervical cancer	progression	19	Japanese	HR for progression				age and CIN grade.							
									HPV test positive	18	3.84(0.48-30.9)	↑ ↑								
									HPV test negative	1	1.00 (Reference)									
									Type											
									High-risk HPV*	15	9.94(1.27-77.6)	↑ ↑ ↑								
									Intermediate-risk HPV	1	1.00 (Reference)									
									Low-risk HPV	2	1.94(0.17-21.6)	↑								
									Negative	1	1.49(0.09-25.1)	-								
									HPV(-) or other type	11	1.00 (Reference)									
									HPV16	6	6.78 (2.31-20.0)	↑ ↑ ↑								
									*High-risk HPV DNA...16, 18, 33, 52, 58											
									HR for disease regression											
									HPV test positive	65	0.53(0.33-0.85)	↓ ↓								
									HPV test negative	30	1.00 (Reference)									
Type																				
High-risk HPV	23	0.56(0.31-1.01)	↓																	
Intermediate-risk HPV	23	1.00 (Reference)																		
Low-risk HPV	19	0.98(0.53-1.80)	-																	
Negative	30	1.43(0.80-2.56)	-																	
HPV(-) or other type	88	1.00 (Reference)																		
HPV16	7	1.02(0.47-2.21)	-																	
Matsumoto K et al.	Predicting the progression of cervical precursor lesions by human papillomavirus genotyping: a prospective cohort study	2010	1998-2004 (39.1 months)	570	Japan HPV And Cervical Cancer (JHACC) Study	progression	disease persistence	Japanese	LSIL regression with 2years				age and CIN grade.							
									HPV genotype											
									High-risk HPV*	189	0.47(0.35-0.65)	↓ ↓ ↓								
									HPVs 16	30	0.56(0.36-0.88)	↓ ↓ ↓								
									HPVs 18	8	0.49(0.23-1.08)	-								
									High-risk HPV*=16/18/31/33/35/45/52/58											
									LSIL regression with 5years											
									HPV genotype											
									High-risk HPV*	22	7.94(1.07-59.2)	↑ ↑ ↑								
									HPVs 16	6	7.63(0.90-64.6)	-								
HPVs 18	0	NA	-																	

(HPV感染と子宮頸がん:症例対照研究)

Reference			Study subjects					Category	Relative risk (95%CI or p)	Confounding variables considered	Magnitude of association				
Author	Title	Year	Study period	Type and source	Definition	Number of cases	Number of controls								
Yoshikawa H et al.	Human papillomavirus infection and other risk factors for cervical intraepithelial neoplasia in Japan	1999	1995-1996	Hospital-based	Cases: histologically diagnosed	167	167	HPV test	1.00 (Reference)						
					Negative			30.0 (9.5-94.8)				↑ ↑ ↑			
					Positive			109.6 (9.1-1320)				↑ ↑ ↑			
					High-risk HPVs*			19.8 (6.1-64.4)				↑ ↑ ↑			
					Intermediate-risk HPVs			41.5 (6.1-283.6)				↑ ↑ ↑			
Low-risk HPVs															
*HPV DNA...16, 18															
Sasagawa T et al.	High-risk and multiple human papillomavirus infections associated with cervical abnormalities in Japanese women	2001	1995-1999	Hospital-basedcervical cancer-screeningprogram (Fukuoka, Ishikawa,and Toyama prefectures)	Cases: cytologically abnormal	366	1,562	HPV genotype	1.00 (Reference)						
					Controls: randomly chose from the same population			145				Negative	7.6 (3.7-16.0)	↑ ↑ ↑	
								137				16	2.0 (0.9-6.4)	↑ ↑ ↑	
								137				18	HSIL(high-grade squamous intraepithelial lesions)	43 (24-75)	↑ ↑ ↑
								72				16	1.5 (0.44-5.1)	↑	
								72				18	SCC(squamous cell carcinoma)	69 (36-131)	↑ ↑ ↑
								12				16	5.0 (1.84-14)	↑ ↑ ↑	
								12				18	ADCA(cervical adenocarcinoma)	15 (3.2-75)	↑ ↑ ↑
								12				16	94 (28-317)	↑ ↑ ↑	
								12				18			
Matsumoto K et al.	IgG antibodies to human papillomavirus 16, 52, 58, and 6 L1 capsids: case-control study of cervical intraepithelial neoplasia in Japan	2003	1995-1996	Hospital-based	Cases: histologically diagnosed	141	109	HPV DNA	1.00 (Reference)	age					
					Controls:mached one-to one with case on age and selected from subject who were found to have normal cervical cytology.			36				93	Negative	17.9 (9.5-36.0)	↑ ↑ ↑
								105				16	Positive		
								65				76	HPV antibodies*	1.00 (Reference)	age
								76				33	Negative	2.7 (1.6-4.6)	↑ ↑ ↑
			Positive												
*IgG antibodies to any type of HPV16/52/58 LI-															
Asato T et al.	A large case-control study of cervical cancer risk associated with human papillomavirus infection in Japan, by nucleotide sequencing-based genotyping	2004	1993-2000	Hospital-based	Cases: histologically diagnosed	311	333	HPV genotype	1.00 (Reference)						
					Controls: both women who had consulted Ryukyu University Hospitaland the participantsin cervical cancer screenings.			-93 years c				24-89 years old	Negative	534.6 (294.2-970.8)	↑ ↑ ↑
													High-risk HPVs	259.2 (101.1-664.8)	↑ ↑ ↑
			16												
			18												
Onuki Y et al.	Human papillomavirus infections among Japanese women: age-related prevalence and type-	2009	1999-2007	Hospital-based cervical cancer-screening	Cases: histologically diagnosed	765	1,517	HPV genotype	1.00 (Reference)						
					Controls: normal cytology			-84 years old				Normal cytology			

specific risk for cervical cancer

(University of Tsukuba Hospital et al.)

CIN(cervical intraepithelial neoplasia) grade 2-3 +ICC(invasive cervical cancer)

HPVs 16 144.5 (86.3-251.3)
HPVs 18 128.6 (68.0-254.6)

↑ ↑ ↑
↑ ↑ ↑

(RCT : HPVワクチン)

Reference		Year	Study period	Study subjects		Category	Vaccine Efficacy						
Author	Title			Type and source	Definition		N	No. cases persistent infection	Incidence rate (/100 person-years at risk)	Reduction %	(95% CI) Lower Upper		P-value
Yoshikawa, H et al.	Efficacy of quadrivalent human papillomavirus (types 6, 11, 16 and 18) vaccine (GARDASIL) in Japanese women aged 18-26 years	2013	median follow up vaccine ; 22.7 months placebo; 22.8 months	human papillomavirus (types 6, 11, 16 and 18) women aged 18-26 years (n=1,030)	HPV; quadrivalent HPV(types 6/11/16/18) L1 virus-like particle vaccine (n=509) placebo control (n=512)	HPV 6/11/16/18							
						HPV vaccine	419	3	0.4	87.6	59.2	97.6	<0.001
						Placebo	422	24	3.1				
						HPV 16/18							
						HPV vaccine	415	1	0.1	94.5	65.2	99.9	<0.001
						Placebo	417	18	2.4				
Konno, R et al.	Efficacy of the human papillomavirus (HPV)-16/18 AS04-adjuvanted vaccine against cervical intraepithelial neoplasia and cervical infection in young Japanese women	2014	4-years Initial study: 2 years (M0-M24); Extended follow-up study: 2 years (M25-M48);	human papillomavirus type 16/18 AS04-adjuvanted vaccine in Japanese women aged 20-25	HPV; 16/18 AS04-adjuvanted vaccine (n=519) Control; hepatitis A vaccine (n=521)	HPV 16/18							
						Incident infection							
						HPV vaccine	358	7	2.48	80.4	54.7	92.7	
						Control	355	32	12.66				
						persistent infection							
						HPV vaccine	276	0	0	100.0	64.2	100.0	
						Control	259	11	4.69				
						ASC-US+							
						HPV vaccine	358	3	1.05	78.5	21.7	96.1	
						Control	355	13	4.88				
						CIN1+							
						HPV vaccine	358	0	0	100.0	34.1	100.0	
Control	355	7	2.52										
CIN2+													
HPV vaccine	358	0	0	100.0	19.4	100.0							
Control	355	6	2.16										

(コホート研究: HPVワクチン)

Reference		Study period		Study subjects		Category		Vaccine Efficacy			Magnitude of association	
Author	Title	year		Type and source	Definition		rate (%)	Relative Risk**	(95% CI)		P-value	
							HSIL+		LL	UL		
Konno, R et al.	Effectiveness of HPV vaccination against high grade cervical lesions in Japan	2018	2015	22,743 women 20-29 years Population-based screening program (parts of national cervical cancer screening program of FY [fiscal year] 2015, the Japan Cancer Society).	women who vaccinated at age of 16 years (birth year 1994),							
						HPV vaccination (-)	20,774	136 (0.66)	1.00 (ref)			
						HPV vaccination	1,969	4 (0.20)	0.31	0.11	0.83	0.013
						*HSIL+; high grade precursor lesions of cervical cancer						
						** The crude relative risk estimate was 0.31 (95% CI: 0.11–0.83; p-value = 0.013) by normal approximation.						
Matsumoto, K et al.	Reduction in HPV16/18 prevalence among young women with high-grade cervical lesions following the Japanese HPV vaccination program	2019	2012-2017	7,709 women; aged 16-39 years (age at registration) Hospitals-based; 21 hospitals which rank highly for the number of ICC cases registered with the Japan Society of Obstetrics and Gynecology (JSOG) Oncology; MINT Study	women were newly diagnosed with ICC, CIN, or AIS, without a history of treatment for cervical diseases	All birth cohorts;						
						HPV-16/18	n	No. cases (prevalence)	P-value	*CIN1; cervical intraepithelial neoplasia grade 1		
						P-value calculated using Fisher's exact probability test.						
						*CIN2-3/AIS; cervical intraepithelial neoplasia grade 2-3 or adenocarcinoma in situ (AIS)						
						HPV vaccination (-)	543	106 (19.5)	0.14			
						HPV vaccination	29	2 (6.9)				
						*ICC: invasive cervical cancer						
						HPV vaccination (-)	3,213	1535 (47.8)	0.003			
						HPV vaccination	106	35 (33.0)				
						Birth year; 1973-1993						
							n	No. cases (prevalence)	P-value			
						CIN1						
						HPV vaccination (-)	538	105 (19.5)	0.33			
						catch-up HPV vaccination (+)	16	1 (6.3)				
						CIN2-3/AIS						
						HPV vaccination (-)	3,190	1525 (47.8)	0.04			
						catch-up HPV vaccination (+)	90	33 (36.7)				
						ICC						
						HPV vaccination (-)	1,097	855 (77.9)	0.29			
						HPV vaccination	21	14 (66.7)				
						Birth year; 1994-1996						
							n	No. cases (prevalence)	P-value			
						CIN1						
						HPV vaccination (-)	5	1 (20.0)	0.49			
						catch-up HPV vaccination (+)	13	1 (7.7)				
						CIN2-3/AIS						
						HPV vaccination (-)	23	10 (43.5)	0.08			
						catch-up HPV vaccination (+)	16	2 (12.5)				
						ICC						
						HPV vaccination (-)	2	2 (100.0)	1.00			
						HPV vaccination	1	1 (100.0)				
Karube, A et al.	Reduction in HPV 16/18 prevalence among	2019	2008-2017	1,342 women 18-49 years		Pre-vaccine (2008–2012)			routine HPV vaccination (2013–2017)			

young women following HPV vaccine introduction in a highly vaccinated district, Japan, 2008–2017

Hospital-based

women who visited Yuri Kumiai General Hospital and underwent HPV genotype tests from June 2008 to December

Age group at diagnosis	Birth year	n	HPV16/18 positive case (prevalence)	Birth year	n	HPV16/18 positive case (prevalence)	P-value
≤24	1984–1994	49	18 (36.7)	1989–	52	3 (5.8)	0.00013
25–29	1979–1987	82	13 (15.9)	1984–	113	20 (17.7)	n.s.
30–34	1974–1982	93	13 (14.0)	1979–	176	30 (17.0)	n.s.
35–39	1969–1977	118	18 (15.3)	1974–	171	19 (11.1)	n.s.
40–44	1964–1972	115	12 (10.4)	1969–	148	8 (5.4)	n.s.
45–49	1959–1967	97	9 (9.3)	1964–	128	5 (3.9)	n.s.

(症例対照研究:HPVワクチン)

Reference			Study subjects				Category		Vaccine Efficacy			Magnitude of association			
Author	Title	year	Study period	Type and source	Definition	Number of cases	Number of controls	Controls	Cases	Reduction %	Odds ratio		(95% CI) Lower Upper		
Ikeda, S et al.	Human papillomavirus vaccine to prevent cervical intraepithelial neoplasia in Japan: A nationwide case-control study	2,020	2013.4-2017.3	nationwide case-control aged 20-24 Cervical cancer screening in 30 municipalities across	cases and controls (one-to-five matching) were eligible in 30 municipalities in Cases; women diagnosed as abnormal cytology Controls; women with normal cytology	12,296	2,483	abnormal cytology							
								HPV vaccination (-)	9,691	2,079		1.00 (ref)			
								HPV vaccination (+)	2,605	404	58.5	0.42	0.34	0.50	↓↓↓
								*CIN1+ = CIN1(including CIN2+)							
								HPV vaccination (-)	9,691	853		1.00 (ref)			
								HPV vaccination (+)	2,605	161	57.9	0.42	0.31	0.58	↓↓↓
								*CIN1+ = CIN1(including CIN2+)							
								HPV vaccination (-)	9,691	192		1.00 (ref)			
								HPV vaccination (+)	2,605	25	74.8	0.25	0.12	0.54	↓↓↓
								*CIN2+ = CIN2+CIN3+SCC/invasive CIN3+							
HPV vaccination (-)	9,691	49		1.00 (ref)											
HPV vaccination (+)	2,605	3	80.9	0.19	0.03	0.15	↓↓↓								
*CIN3+ = CIN3+SCC/invasive															

		n	NILM	HSIL		
aged 20 Cervical cancer screening in Matsuyama city Women who received cervical cancer screenings at age 20 from 2011 to 2016 (i.e., born between 1991 and 1996)	Women were examined cervical cytology, histology using data of cervical cancer screening at age 20 from 2011 to 2016 (i.e., born between 1991 and 1996).	Birth year; 1991-1993				
		Screening year at age 20; 2011- unvaccinated generatio	7,872	7,863	9 (0.11)	
		Birth year; 1994-1996				
		Screening year at age 20; 2014- vaccination generation	7,389	7,389	0	0.0042
		CIN1 or worse				
		Birth year; 1991-1993				
		Screening year at age 20; 2011- unvaccinated generatio	7,872	7,853	19 (0.24)	
		Birth year; 1994-1996				
		Screening year at age 20; 2014- vaccination generation	7,389	7,378	11 (0.15)	0.2000
		CIN3 or worse				
		Birth year; 1991-1993				
		Screening year at age 20; 2011- unvaccinated generatio	7,872	7,865	7 (0.09)	
Birth year; 1994-1996						
Screening year at age 20; 2014- vaccination generation	7,389	7,378	0	0.0160		