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Supplementary appendix

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Supplement to: Lin C, Franceschi S, Clifford G M. Human papillomavirus types from infection to cancer in the anus, according to sex and HIV status: a systematic review and meta-analysis. *Lancet Infect Dis* 2017; published online Nov 17. http://dx.doi.org/10.1016/S1473-3099(17)30653-9.

Supplementary appendix

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Supplementary appendix

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Search strategy

MEDLINE

("papillomaviridae"[All Fields] OR "papillomavirus"[All Fields] OR "HPV"[All Fields]) AND (("anal"[All Fields] AND "canal"[All Fields]) OR "anal canal"[All Fields] OR "anus"[All Fields] OR "anal"[All Fields]))

EMBASE

('papillomaviridae':ta,ab,kw,ti OR 'papillomavirus':ta,ab,kw,ti OR 'hpv':ta,ab,kw,ti OR 'human papillomavirus':ta,ab,kw,ti) AND ('anal':ta,ab,kw,ti AND 'canal':ta,ab,kw,ti OR 'anal':ta,ab,kw,ti OR 'canal':ta,ab,kw,ti OR 'anus':ta,ab,kw,ti OR 'anal canal':ta,ab,kw,ti) AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND [humans]/lim AND [embase]/lim

Cochrane

("papillomaviridae" or "papillomavirus" or "HPV" or "human papillomavirus") and (("anal" and "canal") or ("anal" or "canal") or "anal" or "anus" or "anal canal")

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Appendix Tables

Appendix Table 1: Description of included studies

First author	Journal/conference	Year	Country/region	Sample	Primer	HIV	Gender	Normal	Low-grade*	High-grade†	Cancer
North America											
Hui Y	Am J Surg Pathol	2017	USA	Biopsy	Other	Positive	Men			11	1
						Negative	Men			11	2
						Positive	Women			1	
						Negative	Women			25	4
Hagensee M	IPV conference abstract	2017	USA	Cells	PGMY09/11	Positive	Men	61	87	13	
						Positive	Women	33	44	3	
Keglovitz K	LGBT Health	2016	USA	Cells	cobas	Positive	Men	9	35		
						Negative	Men	4	6		
Cronin B	Gynecol Oncol	2016	USA	Cells	Other	Negative	Women			7	1
Herfs M	J Pathol	2016	USA	Biopsy	Other	Positive	Men				4
						Negative	Men				19
						Negative	Women				27
Chung JH	Ann Oncol	2016	USA	Biopsy	Other	Unknown	Men				22
						Unknown	Women				48
D'Souza G	J Acquir Immune Defic Syndr	2016	USA	Cells	PGMY09/11	Positive	Men	411	244	31	
						Negative	Men	561	165	24	
Sambursky J	IANS conference abstract	2016	USA	Cells	cobas	Positive	Men	65	139	40	
						Negative	Men	101	190	49	
						Negative	Women	7	8	2	
Alemany L	Int J Cancer	2015	USA	Biopsy	SPF10	Unknown	Men				39
						Unknown	Women				57
Hood JE	Int J STD AIDS	2015	USA	Cells	MY09/11	Positive	Men	113	161	11	
Hessol NA	Aids	2013	USA	Cells	MY09/11; HMB01	Positive	Women	283	88	36	
						Negative	Women	147	12	2	
Meyer JE	J Gastrointest Cancer	2013	USA	Biopsy	SPF10	Positive	Men				10
						Negative	Men				13
						Positive	Women				2
						Negative	Women				17
Ouhoummane N	Cancer Epidemiol	2013	Canada	Biopsy	PGMY09/11	Positive	Men				3
						Negative	Men				22
						Negative	Women				42
						Unknown	Men				8

						Unknown	Women				21
Sahasrabuddhe VV	J Infect Dis	2013	USA	Cells	PGMY09/11	Positive	Men		99	104	
Steinau M	J Low Genit Tract Dis	2013	USA	Biopsy	PGMY09/11; SPF10	Unknown	Men				48
						Unknown	Women				85
Lowe B	Diagn Mol Pathol	2012	USA	Cells	GP5+/6+	Positive	Men	42	70	7	
						Negative	Men	74	68	3	
						Positive	Women		1		
						Negative	Women	6	1		
Schlecht NF	PLoS One	2012	USA	Cells	MY09/11	Negative	Women	168	27		
Gilbert M	Sex Transm Dis	2011	Canada	Cells	PGMY09/11	Positive	Men	13	10	13	
						Negative	Men	54	17	9	
Conley L	J Infect Dis	2010	USA	Cells	PGMY09/11	Positive	Men	239	182	49	
						Positive	Women	97	45	8	
Park IU	Gynecol Oncol	2009	USA	Cells	MY09/11	Negative	Women	79	6	2	
Salit IE	Cancer Epidemiol Biomarkers Prev	2009	Canada	Cells	PGMY09/11; MY09/11	Positive	Men			74	
Berry JM	Dis Colon Rectum	2009	USA	Cells	MY09/11	Positive	Men		5	15	
						Negative	Men		8	20	
Gohy L	J Acquir Immune Defic Syndr	2008	Canada	Biopsy	PGMY09/11	Positive	Men		60	62	
Coutlee F	J Clin Microbiol	2006	Canada	Cells	PGMY09/11	Positive	Men		67	66	
Daling JR	Cancer	2004	USA	Biopsy	MY09/11	Unknown	Men				51
						Unknown	Women				99
Moscicki AB	Aids	2003	USA	Cells	MYO9/11; HMB01	Positive	Men	25	40	19	
						Negative	Men	29	8		
						Positive	Women	156	63	14	
						Negative	Women	111	11	2	
Critchlow CW	Aids	1998	USA	Cells	MY09/11	Positive	Men	133	234	26	
						Negative	Men	221	112	8	
Shroyer KR	Am J Clin Pathol	1995	USA	Biopsy	MY09/11	Unknown	Men				2
						Unknown	Women				8
Zaki SR	Am J Pathol	1992	USA	Biopsy	Other	Positive	Men				1
						Unknown	Men				1
						Unknown	Women				6
Subtotal								**3242**	**2313**	**767**	**663**
<u>Europe</u>											
Lorincz AT	Oncotarget	2017	UK	Biopsy	Other	Positive	Men		32	44	3
						Negative	Men		8	5	1

						Positive	Women			7	
						Negative	Women		3	8	1
Schofield AM	Aids	2016	UK	Cells	cobas; PapilloCheck	Positive	Men	33	95	63	3
						Negative	Men	28	28	24	
Padilla-Espana L	Enferm Infecc Microbiol Clin	2016	Spain	Cells	CLART2HPV	Positive	Men	3	30	21	
						Negative	Men	1	14	7	
						Positive	Women		2	1	
						Negative	Women	2	7	4	
Fuchs M	Br J Dermatol	2016	Germany	Cells	A6/A8	Positive	Men	180	232	71	
Herfs M	J Pathol	2016	Belgium	Biopsy	Other	Positive	Men				9
						Negative	Men				35
						Positive	Women				1
						Negative	Women				54
Barroca HM	Porto Biomed J	2016	Portugal	Cells	cobas	Positive	Men	25	34	4	
Burgos J	Aids	2015	Spain	Cells	CLART2HPV	Positive	Men	189	266	16	
Alemany L	Int J Cancer	2015	Bosnia-Herzegovina, Czech Republic, France, Germany, Poland, Portugal, Slovenia, Spain, and UK	Biopsy	SPF10	Unknown	Men				54
						Unknown	Women				111
Arana R	Colorectal Dis	2015	France	Biopsy	SPF10	Positive	Men			10	9
						Negative	Men			2	3
						Positive	Women				1
						Negative	Women			5	4
Baricevic I	Eur J Cancer	2015	UK	Biopsy	E6/E7, L1 or L1/L2	Positive	Men				5
Borghetti A	J Infect	2015	Italy	Cells	PapilloCheck	Positive	Men	79	14		2
						Positive	Women	18	1		
Garbuglia AR	J Clin Virol	2015	Italy	Cells	MY09/11	Positive	Men	104	33	12	
						Negative	Men	6	2		
Heard I	Clin Infect Dis	2015	France	Cells	PGMY09/11	Positive	Women	98	25	28	1
Hidalgo-Tenorio C	PLoS One	2015	Spain	Cells	Other	Positive	Men	75	112	9	
Gosens K	IANS conference abstract	2015	Netherlands	Biopsy	SPF10	Positive	Men				20
Alexandrou A	Acta Gastroenterol Belg	2014	Greece	Biopsy	CLART2HPV	Negative	Men				5
						Negative	Women				6
Casadei Gardini A	PLoS One	2014	Italy	Biopsy	GP5+/6+	Positive	Men				6
Richel O	J Infect Dis	2014	Netherlands	Biopsy	SPF10	Positive	Men			21	
Darwich L	Dis Colon Rectum	2013	Spain	Cells	F-HPV	Positive	Men	297	139	69	
Garcia-Espinosa B	Diagn Pathol	2013	Spain	Biopsy	GP5+/6+	Positive	Men				1
Kim S	Ann Oncol	2013	France	Biopsy	SPF10	Negative	Men				2

						Negative	Women				4
Marchetti G	J Sex Transm Dis	2013	Italy	Cells	MY09/11; PU-1M/PU-2R	Positive	Men	84	72	11	
Torres M	J Clin Microbiol	2013	Spain	Cells	PGMY09/11	Positive	Men	441	465	44	
Valmary-Degano S	Hum Pathol	2013	France	Biopsy	SPF10	Unknown	Men				23
						Unknown	Women				50
D'Hauwers KW	Eur J Obstet Gynecol Repred Biol	2012	Belgium	Cells	E6/E7	Negative	Women	83	10		
Pierangeli A	J Infect	2012	Italy	Cells	Other	Negative	Women	71	34		
Dona MG	BMC Cance	2012	Italy	Cells	PGMY09/11	Negative	Men	210	89		
Etienney I	Cancer	2012	France	Cells	MY09/11; PGMY09/11	Positive	Men		3	3	
						Negative	Men	95	17	5	
						Positive	Women		2		
						Negative	Women	91	28	9	
Lanoix JP	AIDS Patient Care STDS	2012	France	Cells	SPF10	Positive	Men	12	3		
Abramowitz L	Int J Cancer	2011	France	Biopsy	SPF10	Positive	Men				45
						Negative	Men				13
						Positive	Women				5
						Negative	Women				33
						Unknown	Men				79
						Unknown	Women				187
Komlos KF	Acta Dermatovenerol Alp Pannonica Adriat	2011	Slovenia	Biopsy	SPF10	Unknown	Men				8
						Unknown	Women				9
Yaghoobi M	Colorectal Dis	2011	France	Biopsy	Other	Positive	Men				4
						Negative	Women				1
Damay A	J Med Virol	2010	France	Cells	PapilloCheck	Positive	Men	34	29	3	
Kreuter A	Br J Dermatol	2010	Germany	Biopsy	A5/A10; A6/A8	Positive	Men				9
Orlando G	Vaccine	2009	Italy	Cells	MY09/11	Positive	Men	31	176	32	3
						Negative	Men	4	14	2	
Tachezy R	APMIS	2007	Czech Republic	Biopsy	GP5+/6+	Unknown	Men				4
						Unknown	Women				18
Hampl M	JCRCO	2007	Germany	Biopsy	GP5+/6+; MY09/11	Negative	Women		1	22	
Varnai AD	Int J Colorectal Dis	2006	Germany	Biopsy	GP5+/6+; MY09/11	Unknown	Men				13
						Unknown	Women				34
Kreuter A	J Am Acad Dermatol	2005	Germany	Cells	A5/A10; A6/A8	Positive	Men		4	16	
Piketty C	Ann Intern Med	2003	France	Cells	MY09/11	Positive	Men	7	32	8	
Indinnimeo M	Tech Coloproctol	1999	Italy	Biopsy	TS	Unknown	Men				2
						Unknown	Women				12

Frisch M	N Engl J Med	1997	Denmark and Sweden	Biopsy	GP5+/6+	Unknown	Men				304
						Unknown	Women				84
Heselmeyer K	Br J Cancer	1997	Sweden	Biopsy	MY09/11	Unknown	Men				5
						Unknown	Women				11
Vincent-Salomon A	Mod Pathol	1996	France	Biopsy	TS	Unknown	Men				8
						Unknown	Women				19
Subtotal								**2301**	**2056**	**586**	**1324**
Latin America											
Limia CM	Infect Agent Cancer	2017	Cuba	Cells	LCR/E6/E7	Positive	Men	3	48	5	
Scapulatempo-Neto C	Oncol Lett	2017	Brazil	Biopsy	TS	Unknown	Men				22
						Unknown	Women				48
Ortiz AP	Galenus	2017	Puerto Rico	Cells	cobas	Positive	Men	18	64	89	
						Negative	Men	8	13	7	
						Positive	Women	9	33	47	
						Negative	Women	4	8	11	
Beachler DC	J Natl Cancer Inst	2016	Costa Rica	Cells	SPF10	Negative	Women	883	67	8	
Nicol AF	J Acquir Immune Defic Syndr	2016	Brazil	Biopsy	L1; GP5+/6+	Positive	Men		11	8	
						Positive	Women		6	9	
Alemany L	Int J Cancer	2015	Chile, Colombia, Ecuador, Guatemala, Honduras, Mexico, Paraguay	Biopsy	SPF10	Unknown	Men				31
						Unknown	Women				121
Cambou MC	AIDS Patient Care STDS	2015	Brazil	Cells	PapilloCheck	Positive	Women	551	188	42	
Tso FK	Genet Mol Res	2015	Brazil	Cells	cobas; PapilloCheck	Positive	Women	21	13	8	
						Negative	Women	38	16	2	
Melo VH	J Low Genit Tract Dis	2014	Brazil	Cells	MY09/11	Positive	Men	237	119	24	
Maia LB	Indian J Sex Transm Dis	2013	Brazil	Cells	PapilloCheck	Positive	Men	11	10	2	
						Positive	Women	7	3		
Heraclio S	Acta Cytol	2011	Brazil	Cells	MY09/11; GP5+/6+	Positive	Women		5	8	1
						Negative	Women		70	50	2
Subtotal								**1790**	**674**	**320**	**225**
Asia and Oceania											
Yaegashi H	J Infect Chemother	2017	Japan	Cells	Other	Positive	Men	23	92	7	
Machalek DA	Cancer Epidemiol Biomarkers Prev	2016	Australia	Cells	PGMY09/11	Positive	Men	45	57	113	
						Negative	Men	121	93	160	
Ruanpeng D	PLoS One	2016	Thailand	Cells	PGMY09/11	Positive	Men	10	36	2	
						Negative	Men	74	36		

Shwe MM	Acta Med Okayama	2016	Japan	Biopsy	pU-1M/pU-2R	Unknown	Women				5
Lee CH	PLoS One	2016	Korea	Cells	Other	Positive	Men	131	69	1	
Simpson S Jr	Cancer Epidemiol	2016	Australia	Cells	PGMY09/11	Negative	Women	74	14	35	
Alemany L	Int J Cancer	2015	Australia, Bangladesh, India, and Korea	Biopsy	SPF10	Unknown	Men				21
						Unknown	Women				31
Cheng SH	Int J Clin Oncol	2015	Taiwan	Cells	PGMY09/11	Positive	Men	412	119	11	1
Phanuphak N	PLoS One	2013	Thailand	Cells	PGMY09/11	Positive	Men	101	13		
						Negative	Men	104	14	3	
Yang Y	PLoS One	2012	China	Cells	Other	Positive	Men	55	19		
Yhim HY	Int J Cancer	2011	Korea	Biopsy	Other	Negative	Men				22
						Negative	Women				25
Tsai TF	Sex Transm Dis	2008	China	Biopsy	MY09/GP6+; GP5+/6+	Negative	Men				7
						Negative	Women				5
Kagawa R	Surg Today	2006	Japan	Biopsy	Other	Unknown	Men				2
						Unknown	Women				4
Subtotal								**1150**	**562**	**332**	**123**
Africa											
Mbulawa Z	Am J Clin Pathol	2017	South Africa	Cells	Xpert	Positive	Women	51	125	19	
Mpunga T	AORTIC conference abstract	2017	Rwanda	Biopsy	GP5+/6+	Positive	Women				2
Alemany L	Int J Cancer	2015	Mali, Nigeria, and Senegal	Biopsy	SPF10	Unknown	Men				12
						Unknown	Women				9
Subtotal								**51**	**125**	**19**	**23**
Total								**8534**	**5730**	**2024**	**2358**

*Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1.
†High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.

Appendix Table 2: Prevalence of single and multiple infections of human papillomavirus (HPV) types* in HPV-positive anal cancer by HIV status (sensitivity analysis showing known HIV-negative and HIV-unknown anal cancers separately)

HPV type	HIV-negative				HIV-unknown				HIV-positive			
	N	Prevalence %	Single %	Multiple %	N	Prevalence %	Single %	Multiple %	N	Prevalence %	Single %	Multiple %
HPV16	320	89·7%	81·3%	8·4%	1234	84·8%	77·5%	7·3%	144	66·7%	43·8%	22·9%
HPV33	196	2·0%	1·5%	0·5%	1173	3·4%	2·5%	0·9%	130	9·2%	2·3%	6·9%
HPV18	320	4·1%	2·8%	1·3%	1234	4·3%	2·3%	2·0%	144	14·6%	2·1%	12·5%
HPV6	192	4·1%	1·0%	3·1%	1223	3·8%	2·2%	1·6%	124	6·4%	2·4%	4·0%
HPV58	195	3·6%	3·1%	0·5%	1003	1·6%	1·2%	0·4%	123	0·8%	0·0%	0·8%
HPV35	195	0·5%	0·5%	0·0%	1137	1·0%	0·9%	0·1%	123	0·0%	0·0%	0·0%
HPV11	192	2·6%	0·0%	2·6%	1223	2·6%	0·8%	1·8%	124	8·1%	0·8%	7·3%
HPV31	196	1·0%	1·0%	0·0%	1142	1·5%	0·8%	0·7%	129	4·7%	1·6%	3·1%
HPV52	195	3·6%	1·0%	2·6%	1003	1·4%	0·7%	0·7%	123	9·7%	1·6%	8·1%
HPV45	195	0·5%	0·0%	0·5%	1134	0·8%	0·5%	0·3%	125	6·4%	2·4%	4·0%
HPV39	195	0·0%	0·0%	0·0%	995	0·7%	0·2%	0·5%	123	6·5%	0·8%	5·7%
HPV56	195	1·5%	1·0%	0·5%	995	0·3%	0·2%	0·1%	123	0·8%	0·0%	0·8%
HPV68	195	0·0%	0·0%	0·0%	995	0·4%	0·2%	0·2%	123	8·1%	0·0%	8·1%
HPV59	195	0·0%	0·0%	0·0%	995	0·2%	0·1%	0·1%	123	4·1%	0·0%	4·1%
HPV51	195	1·0%	0·0%	1·0%	995	0·9%	0·0%	0·9%	123	6·5%	0·8%	5·7%
Any HPV	196	100·0%	87·8%	12·2%	1234	99·5%	89·7%	9·8%	130	98·4%	56·9%	41·5%
HPV16/18	191	89·6%	81·2%†	8·4%‡	438	86·9%	78·5%†	8·4%‡	118	73·8%	49·2%†	24·6%‡
HPV6/11/16/18	191	91·1%	86·9%†	4·2%‡	438	92·4%	85·6%†	6·8%‡	118	77·1%	55·9%†	21·2%‡
HPV6/11/16/18/31/33/45/52/58	191	97·9%	96·3%†	1·6%‡	438	98·4%	94·7%†	3·7%‡	118	92·3%	75·4%†	16·9%‡

*In order of prevalence of single infection in HIV-unknown anal cancer.
†Single = in the absence of any other any other HPV type(s).
‡Multiple = in the presence of any other HPV type(s).

Appendix Table 3: Prevalence of human papillomavirus (HPV) types in HPV-positive men by anal diagnosis and HIV status

HPV type	HIV	Normal N (%)	Low-grade* N (%)	High-grade† N (%)	Cancer‡ N (%)
HPV6	Negative	727 (11·4%)	402 (27·1%)	75 (22·7%)	687 (5·1%)
	Positive	2500 (17·9%)	2779 (28·6%)	800 (20·4%)	122 (9·0%)
HPV11	Negative	727 (6·6%)	402 (15·2%)	75 (13·3%)	687 (3·2%)
	Positive	2500 (11·8%)	2779 (21·2%)	800 (15·1%)	122 (6·6%)
HPV16	Negative	972 (20·6%)	707 (27·4%)	317 (46·7%)	780 (81·8%)
	Positive	2860 (26·4%)	3454 (36·8%)	1129 (50·5%)	136 (66·9%)
HPV18	Negative	972 (6·1%)	700 (10·6%)	303 (16·5%)	780 (5·1%)
	Positive	2860 (12·3%)	3449 (18·3%)	1115 (19·6%)	136 (14·0%)
HPV31	Negative	800 (5·5%)	480 (7·3%)	242 (11·2%)	668 (1·3%)
	Positive	2661 (10·3%)	2984 (14·0%)	945 (17·9%)	122 (4·9%)
HPV33	Negative	800 (4·1%)	480 (6·0%)	242 (11·6%)	674 (4·6%)
	Positive	2661 (8·9%)	2984 (11·3%)	945 (16·2%)	123 (8·9%)
HPV35	Negative	800 (2·9%)	480 (3·8%)	242 (5·4%)	384 (0·5%)
	Positive	2579 (7·7%)	2934 (11·2%)	940 (12·0%)	111 (0·0%)
HPV39	Negative	806 (6·2%)	488 (10·2%)	242 (11·2%)	338 (0·3%)
	Positive	2586 (9·2%)	2969 (12·6%)	957 (10·9%)	111 (7·2%)
HPV45	Negative	931 (6·4%)	584 (9·8%)	250 (14·4%)	384 (1·3%)
	Positive	2777 (11·3%)	3247 (14·9%)	988 (13·3%)	118 (5·9%)
HPV51	Negative	806 (9·3%)	488 (11·7%)	242 (15·3%)	338 (1·2%)
	Positive	2586 (12·3%)	2969 (15·2%)	957 (17·0%)	111 (7·2%)
HPV52	Negative	806 (12·7%)	488 (14·5%)	242 (14·0%)	340 (3·8%)
	Positive	2586 (17·0%)	2969 (17·9%)	957 (16·4%)	116 (9·5%)
HPV56	Negative	806 (4·2%)	488 (7·4%)	242 (5·0%)	338 (1·5%)
	Positive	2586 (6·9%)	2969 (8·4%)	957 (8·6%)	111 (0·9%)
HPV58	Negative	806 (7·1%)	488 (8·4%)	242 (10·3%)	340 (1·5%)
	Positive	2589 (14·3%)	3005 (14·7%)	962 (20·1%)	116 (1·7%)
HPV59	Negative	800 (6·9%)	480 (7·9%)	242 (14·9%)	338 (0·3%)
	Positive	2579 (12·0%)	2934 (14·9%)	940 (13·3%)	111 (3·6%)
HPV68	Negative	800 (6·8%)	480 (5·8%)	242 (7·9%)	338 (0·9%)
	Positive	2579 (9·2%)	2934 (10·7%)	878 (10·5%)	110 (8·2%)

*****Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1.
†High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.
‡Anal cancers of unknown HIV status are assumed to be HIV-negative.

Appendix Table 4: Prevalence of human papillomavirus (HPV) types in HPV-positive women by anal diagnosis and HIV status

HPV type	HIV	Normal N (%)	Low-grade* N (%)	High-grade† N (%)	Cancer‡ N (%)
HPV6	Negative	576 (6·3%)	173 (27·7%)	117 (17·9%)	961 (2·4%)
	Positive	503 (10·7%)	305 (23·9%)	110 (18·2%)	12 (0·0%)
HPV11	Negative	576 (1·2%)	173 (8·7%)	117 (0·9%)	961 (1·5%)
	Positive	503 (2·4%)	305 (11·8%)	110 (5·5%)	12 (16·7%)
HPV16	Negative	743 (13·9%)	218 (19·7%)	160 (56·3%)	1149 (88·1%)
	Positive	788 (17·0%)	511 (25·2%)	216 (36·1%)	13 (69·2%)
HPV18	Negative	743 (5·8%)	218 (7·3%)	160 (5·6%)	1149 (4·4%)
	Positive	771 (6·9%)	463 (17·3%)	202 (17·8%)	13 (15·4%)
HPV31	Negative	719 (7·6%)	205 (7·8%)	142 (12·0%)	903 (1·3%)
	Positive	711 (8·6%)	389 (9·0%)	145 (11·7%)	12 (0·0%)
HPV33	Negative	719 (3·1%)	205 (5·9%)	142 (10·6%)	928 (3·7%)
	Positive	711 (4·8%)	389 (10·3%)	145 (12·4%)	12 (8·3%)
HPV35	Negative	719 (3·1%)	205 (2·9%)	142 (2·1%)	841 (1·0%)
	Positive	693 (4·6%)	388 (7·2%)	145 (9·7%)	12 (0·0%)
HPV39	Negative	740 (7·6%)	209 (7·2%)	144 (2·1%)	745 (0·4%)
	Positive	749 (5·9%)	437 (11·0%)	157 (10·8%)	12 (0·0%)
HPV45	Negative	740 (3·2%)	209 (3·8%)	144 (3·5%)	838 (0·5%)
	Positive	767 (7·6%)	438 (11·6%)	157 (10·8%)	12 (8·3%)
HPV51	Negative	740 (12·0%)	209 (10·0%)	144 (9·0%)	745 (0·9%)
	Positive	749 (8·5%)	437 (11·0%)	157 (10·8%)	12 (8·3%)
HPV52	Negative	740 (9·6%)	209 (6·7%)	144 (4·2%)	751 (1·1%)
	Positive	749 (6·8%)	437 (13·5%)	157 (11·5%)	12 (8·3%)
HPV56	Negative	740 (6·2%)	209 (4·8%)	144 (1·4%)	745 (0·1%)
	Positive	749 (7·5%)	437 (12·1%)	157 (8·9%)	12 (0·0%)
HPV58	Negative	740 (5·7%)	209 (4·8%)	144 (4·9%)	751 (1·9%)
	Positive	749 (9·3%)	437 (13·3%)	157 (22·3%)	12 (0·0%)
HPV59	Negative	719 (3·6%)	205 (2·9%)	142 (4·2%)	745 (0·1%)
	Positive	693 (6·2%)	388 (8·8%)	145 (6·2%)	12 (8·3%)
HPV68	Negative	651 (5·4%)	194 (2·1%)	140 (1·4%)	745 (0·1%)
	Positive	485 (12·6%)	304 (13·5%)	111 (11·7%)	12 (8·3%)

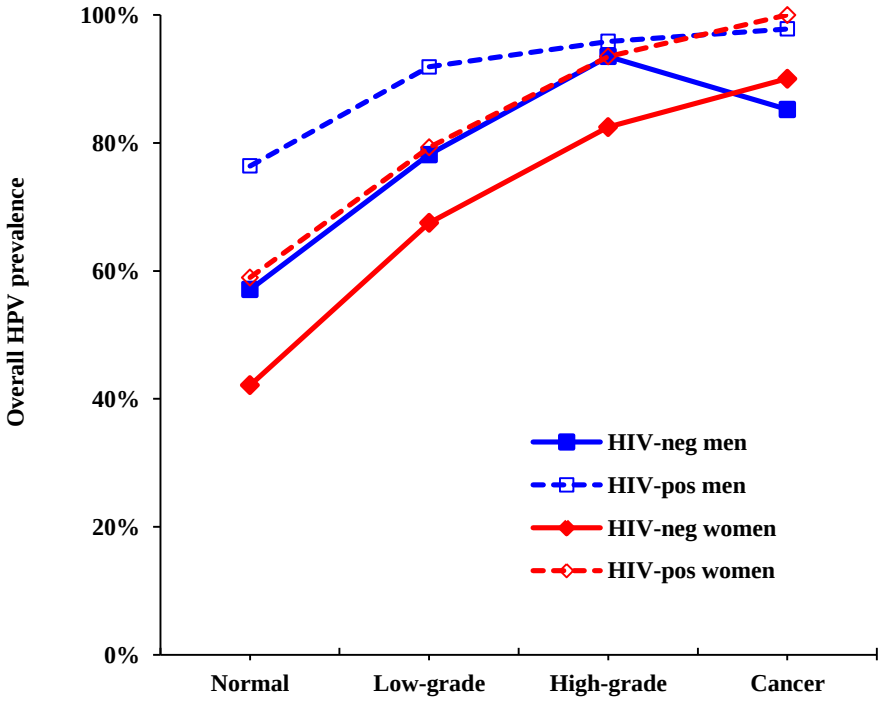
*Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1.

†High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.

‡Anal cancers of unknown HIV status are assumed to be HIV-negative.

Appendix Figures

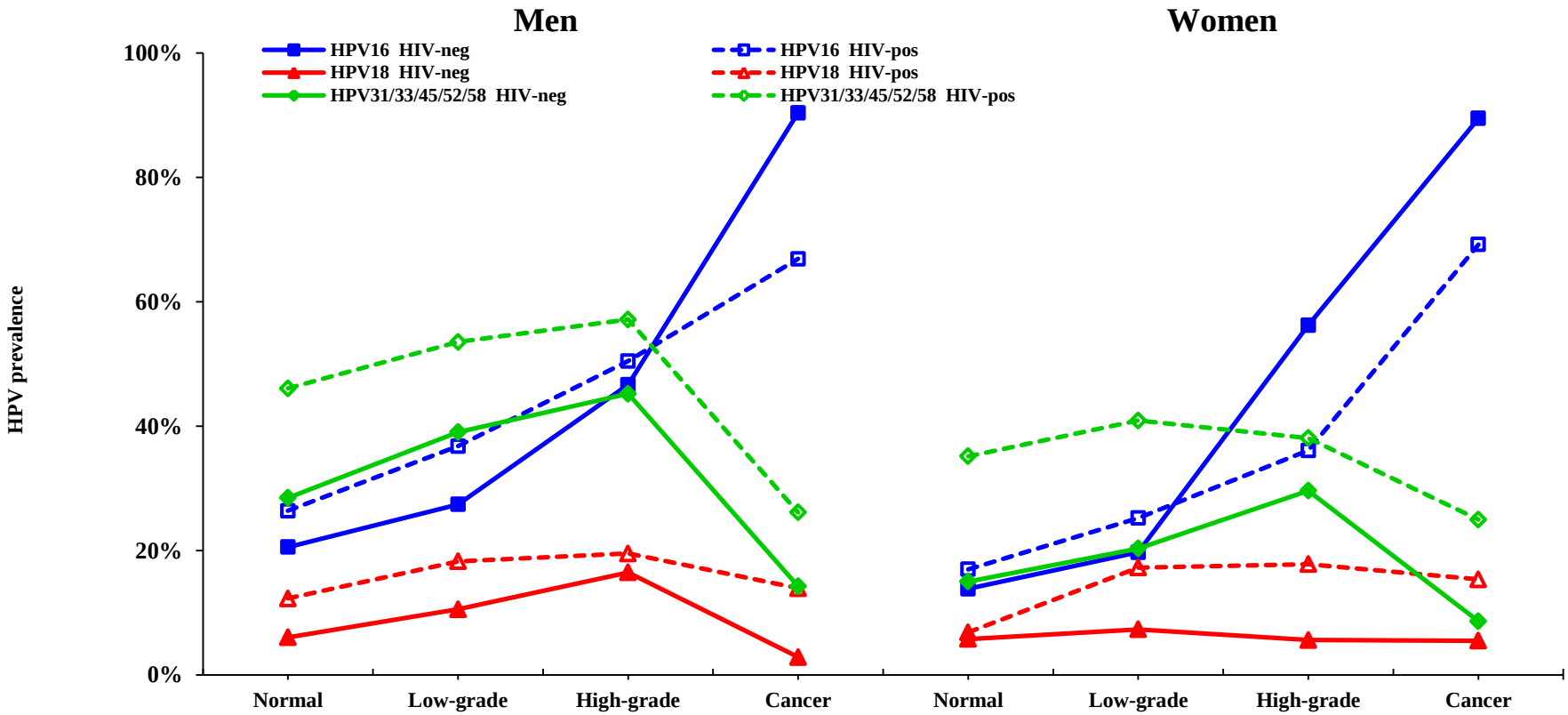
Appendix Figure 1: Overall human papillomavirus (HPV) prevalence by gender, anal diagnosis* and HIV status (sensitivity analysis including known HIV-negative anal cancers only)



Population	N (%)	N (%)	N (%)	N (%)
HIV-neg men	1685 (57·1%)	894 (78·2%)	339 (93·5%)	122 (85·2%)
HIV-pos men	3459 (76·4%)	3633 (91·9%)	1161 (95·9%)	137 (97·8%)
HIV-neg women	1764 (42·1%)	323 (67·5%)	194 (82·5%)	201 (90·0%)
HIV-pos women	1306 (59·0%)	643 (79·3%)	231 (93·5%)	13 (100·0%)

*Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1; High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.

Appendix Figure 2: Prevalence of human papillomavirus 16 (HPV16), HPV18, HPV31/33/45/52/58 and prevalence ratio (PR) by anal diagnosis* and HIV status, in HPV-positive men and women (sensitivity analysis including known HIV-negative anal cancers only)

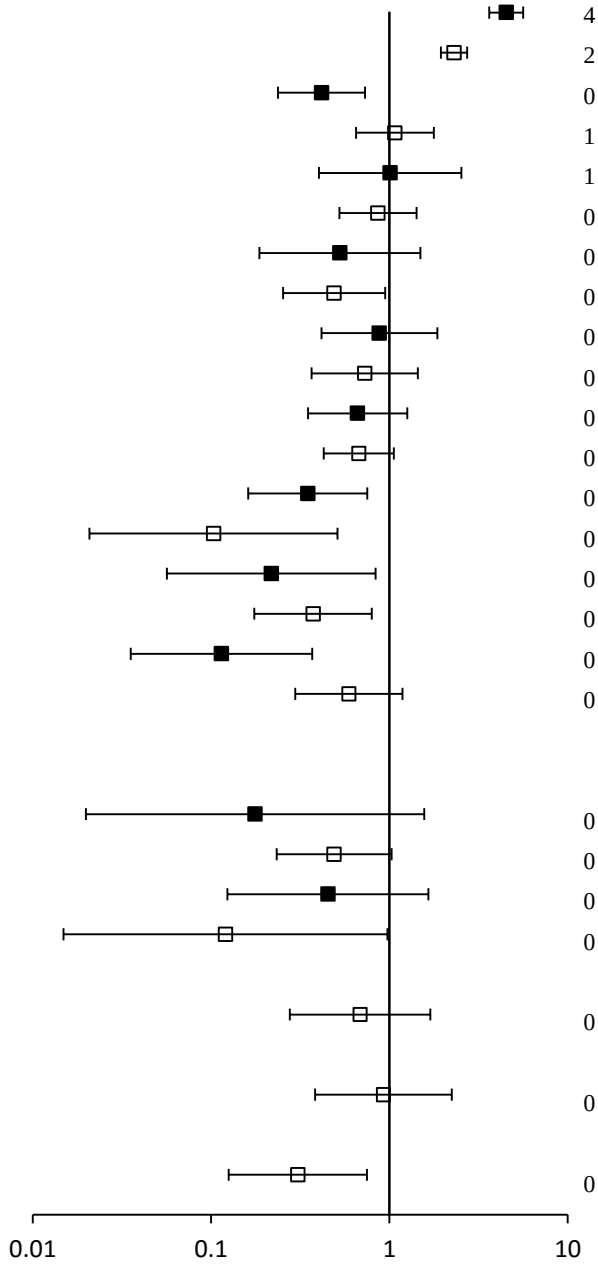


Population	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
HPV16 HIV-neg	972 (20·6%)	707 (27·4%)	317 (46·7%)	104 (90·4%)	743 (13·9%)	218 (19·7%)	160 (56·3%)	181 (89·5%)
HPV16 HIV-pos	2860 (26·4%)	3454 (36·8%)	1129 (50·5%)	136 (66·9%)	788 (17·0%)	511 (25·2%)	216 (36·1%)	13 (69·2%)
PR (95% CI) HIV+ vs HIV-	**1·3 (1·0–1·6)**	**1·3 (1·2–1·6)**	**1·1 (1·0–1·2)**	**0·7 (0·6–0·8)**	**1·2 (0·8–1·8)**	**1·3 (1·0–1·7)**	**0·6 (0·5–0·9)**	**0·8 (0·6–1·0)**
HPV18 HIV-neg	972 (6·1%)	700 (10·6%)	303 (16·5%)	104 (2·9%)	743 (5·8%)	218 (7·3%)	160 (5·6%)	181 (5·5%)
HPV18 HIV-pos	2860 (12·3%)	3449 (18·3%)	1115 (19·6%)	136 (14·0%)	771 (6·9%)	463 (17·3%)	202 (17·8%)	13 (15·4%)
PR (95% CI) HIV+ vs HIV-	**2·0 (1·6–2·6)**	**1·7 (1·3–2·3)**	**1·2 (1·0–1·4)**	**4·8 (1·5–15·6)**	**1·2 (0·7–1·9)**	**2·4 (1·1–5·0)**	**3·2 (1·7–5·9)**	**2·8 (0·6–13·3)**
HPV31/33/45/52/58 HIV-neg	572 (28·5%)	361 (39·1%)	230 (45·2%)	56 (14·3%)	153 (15·0%)	118 (20·3%)	135 (29·6%)	104 (8·7%)
HPV31/33/45/52/58 HIV-pos	1252 (46·1%)	1408 (53·6%)	474 (57·2%)	107 (26·2%)	91 (35·2%)	88 (40·9%)	63 (38·1%)	12 (25·0%)
PR (95% CI) HIV+ vs HIV-	**1·6 (1·5–1·8)**	**1·4 (1·1–1·7)**	**1·3 (1·1–1·5)**	**1·8 (1·1–2·9)**	**2·3 (1·8–3·1)**	**2·0 (1·1–3·5)**	**1·3 (0·7–2·4)**	**2·9 (0·9–9·6)**

* Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1; High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.

Appendix Figure 3: Cancer:normal prevalence ratio (PR) in human papillomavirus (HPV)-positive samples of HPV types by HIV status (sensitivity analysis including known HIV-negative anal cancers only)

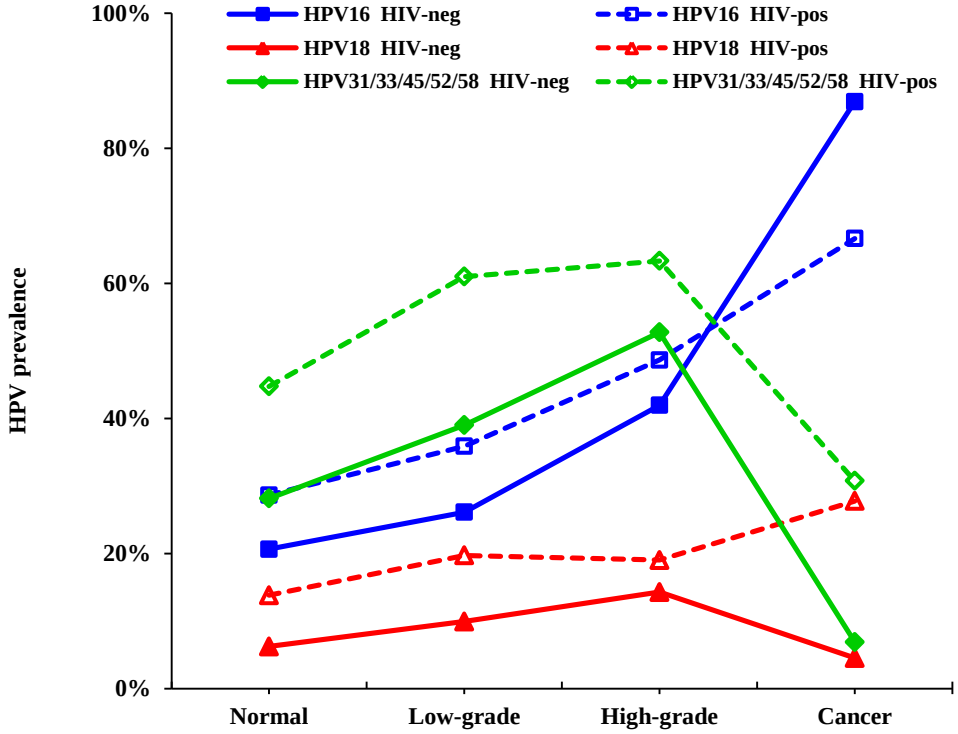
HPV type	HIV	Normal N (%)	Cancer N (%)	PR (95% CI)*
HPV16	Neg	1715 (17·7%)	320 (89·7%)	4·5 (3·6–5·6)
	Pos	3648 (24·4%)	149 (67·1%)	2·3 (1·9–2·7)
HPV18	Neg	1715 (5·9%)	320 (4·1%)	0·4 (0·2–0·7)
	Pos	3631 (11·2%)	149 (14·1%)	1·1 (0·6–1·8)
HPV33	Neg	1519 (3·6%)	196 (2·0%)	1·0 (0·4–2·5)
	Pos	3372 (8·1%)	135 (8·9%)	0·9 (0·5–1·4)
HPV6	Neg	1303 (9·1%)	192 (4·2%)	0·5 (0·2–1·5)
	Pos	3003 (16·7%)	134 (8·2%)	0·5 (0·3–0·9)
HPV11	Neg	1303 (4·2%)	192 (2·6%)	0·9 (0·4–1·9)
	Pos	3003 (10·3%)	134 (7·5%)	0·7 (0·4–1·4)
HPV52	Neg	1546 (11·2%)	195 (3·6%)	0·7 (0·3–1·3)
	Pos	3335 (14·7%)	128 (9·4%)	0·7 (0·4–1·1)
HPV58	Neg	1546 (6·4%)	195 (3·6%)	0·3 (0·2–0·8)
	Pos	3338 (13·2%)	128 (1·6%)	0·1 (0·0–0·5)
HPV31	Neg	1519 (6·5%)	196 (1·0%)	0·2 (0·1–0·8)
	Pos	3372 (9·9%)	134 (4·5%)	0·4 (0·2–0·8)
HPV51	Neg	1546 (10·6%)	195 (1·0%)	0·1 (0·0–0·4)
	Pos	3335 (11·4%)	123 (7·3%)	0·6 (0·3–1·2)
HPV35	Neg	1519 (3·0%)	195 (0·5%)	0·0
	Pos	3272 (7·0%)	123 (0·0%)	0·0
HPV45	Neg	1671 (5·0%)	195 (0·5%)	0·2 (0·0–1·6)
	Pos	3544 (10·5%)	130 (6·2%)	0·5 (0·2–1·0)
HPV56	Neg	1546 (5·2%)	195 (1·5%)	0·5 (0·1–1·7)
	Pos	3335 (7·0%)	123 (0·8%)	0·1 (0·0–1·0)
HPV39	Neg	1546 (6·9%)	195 (0·0%)	0·0
	Pos	3335 (8·5%)	123 (6·5%)	0·7 (0·3–1·7)
HPV68	Neg	1451 (6·1%)	195 (0·0%)	0·0
	Pos	3064 (9·8%)	122 (8·2%)	0·9 (0·4–2·2)
HPV59	Neg	1519 (5·3%)	195 (0·0%)	0·0
	Pos	3272 (10·8%)	123 (4·1%)	0·3 (0·1–0·7)



■ **HIV-negative**
□ **HIV-positive**

*Adjusted by gender and region.

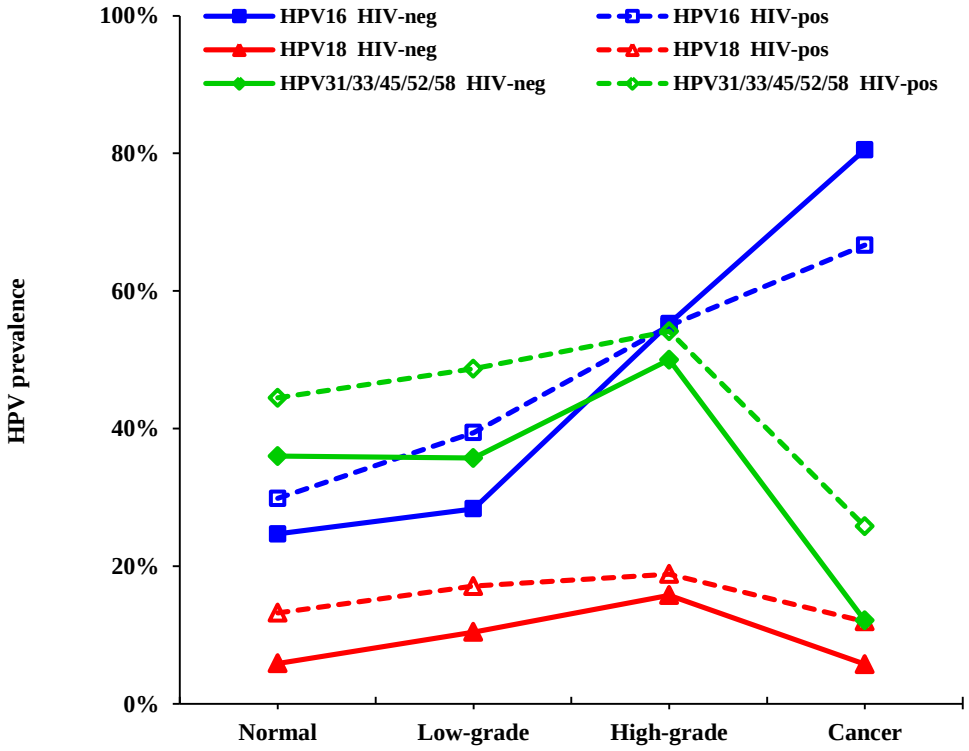
Appendix Figure 4: Prevalence of human papillomavirus 16 (HPV16), HPV18, HPV31/33/45/52/58 and prevalence ratio (PR) in HPV-positive men by anal diagnosis* and HIV status: in North America only



Population	N (%)	N (%)	N (%)	N (%)
HPV16 HIV-neg	625 (20·6%)	440 (26·1%)	112 (42·0%)	199 (86·9%)†
HPV16 HIV-pos	890 (28·7%)	1318 (35·9%)	450 (48·7%)	18 (66·7%)
PR (95% CI) HIV+ vs HIV-	**1·4 (1·0–1·9)**	**1·4 (1·1–1·8)**	**1·2 (0·9–1·5)**	**0·8 (0·6–0·9)**
HPV18 HIV-neg	625 (6·2%)	433 (9·9%)	98 (14·3%)	199 (4·5%)†
HPV18 HIV-pos	890 (13·8%)	1313 (19·7%)	436 (19·0%)	18 (27·8%)
PR (95% CI) HIV+ vs HIV-	**2·2 (1·7–3·0)**	**2·0 (1·3–3·1)**	**1·3 (1·0–1·8)**	**6·1 (2·6–14·3)**
HPV31/33/45/52/58 HIV-neg	426 (28·2%)	205 (39·0%)	36 (52·8%)	116 (6·9%)†
HPV31/33/45/52/58 HIV-pos	438 (44·7%)	372 (61·0%)	60 (63·3%)	13 (30·8%)
PR (95% CI) HIV+ vs HIV-	**1·6 (1·5–1·7)**	**1·6 (1·2–2·0)**	**1·2 (1·0–1·4)**	**4·5 (1·9–10·7)**

*Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1; High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.
†Anal cancers of unknown HIV status are assumed to be HIV-negative.

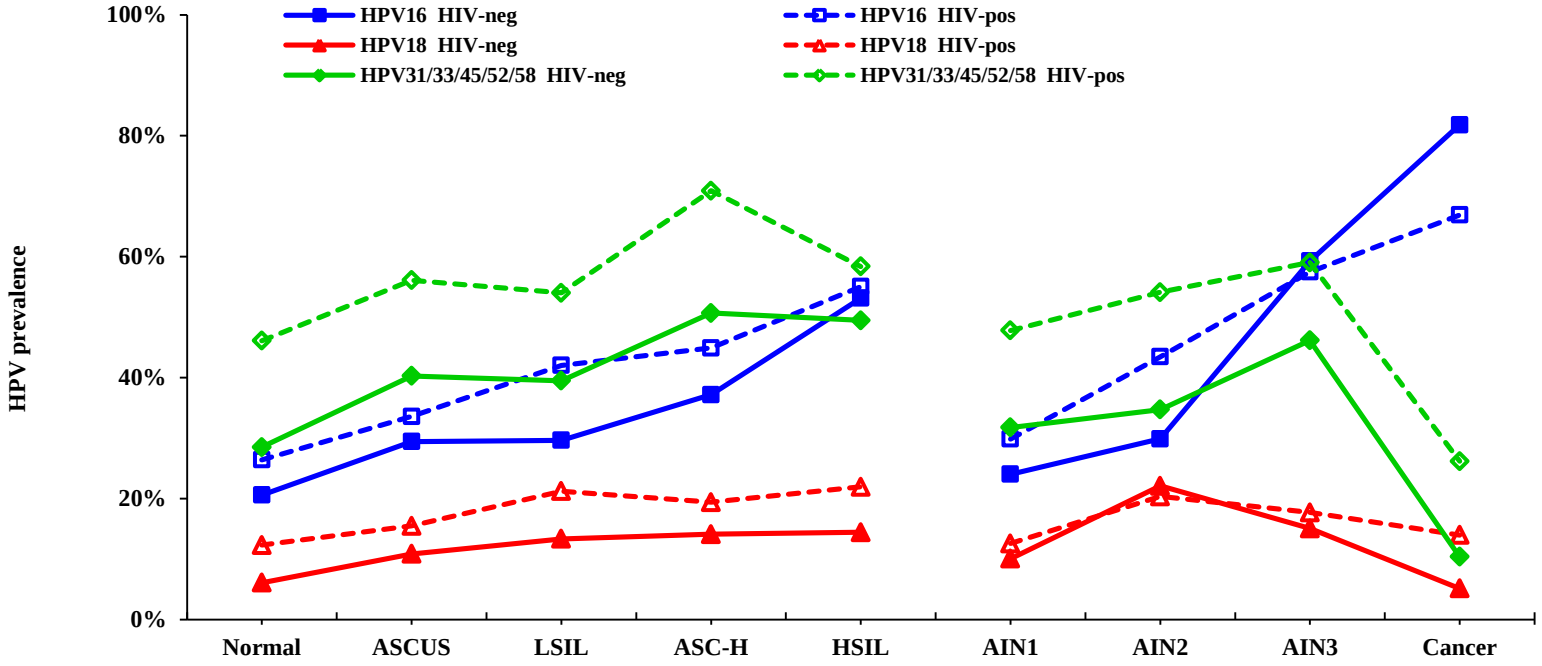
Appendix Figure 5: Prevalence of human papillomavirus 16 (HPV16), HPV18, HPV31/33/45/52/58 and prevalence ratio (PR) in HPV-positive men by anal diagnosis* and HIV status: in Europe only



Population	N (%)	N (%)	N (%)	N (%)
HPV16 HIV-neg	170 (24·7%)	134 (28·4%)	38 (55·3%)	505 (80·2%)†
HPV16 HIV-pos	1241 (30·1%)	1553 (39·5%)	428 (55·1%)	117 (66·7%)
PR (95% CI) HIV+ vs HIV-	**1·2 (1·0–1·5)**	**1·4 (1·2–1·7)**	**1·0 (0·8–1·2)**	**0·8 (0·7–0·9)**
HPV18 HIV-neg	170 (5·9%)	134 (10·4%)	38 (15·8%)	505 (5·7%)†
HPV18 HIV-pos	1241 (13·1%)	1553 (17·3%)	428 (18·9%)	117 (12·0%)
PR (95% CI) HIV+ vs HIV-	**2·2 (1·5–3·4)**	**1·7 (0·8–3·6)**	**1·2 (0·6–2·5)**	**2·1 (1·4–3·1)**
HPV31/33/45/52/58 HIV-neg	25 (36·0%)	42 (35·7%)	36 (50·0%)	165 (12·1%)†
HPV31/33/45/52/58 HIV-pos	416 (44·5%)	735 (48·7%)	277 (54·2%)	93 (25·8%)
PR (95% CI) HIV+ vs HIV-	**1·2 (0·6–2·4)**	**1·4 (1·1–1·8)**	**1·1 (0·9–1·3)**	**2·1 (1·0–4·7)**

*Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1; High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.
†Anal cancers of unknown HIV status are assumed to be HIV-negative.

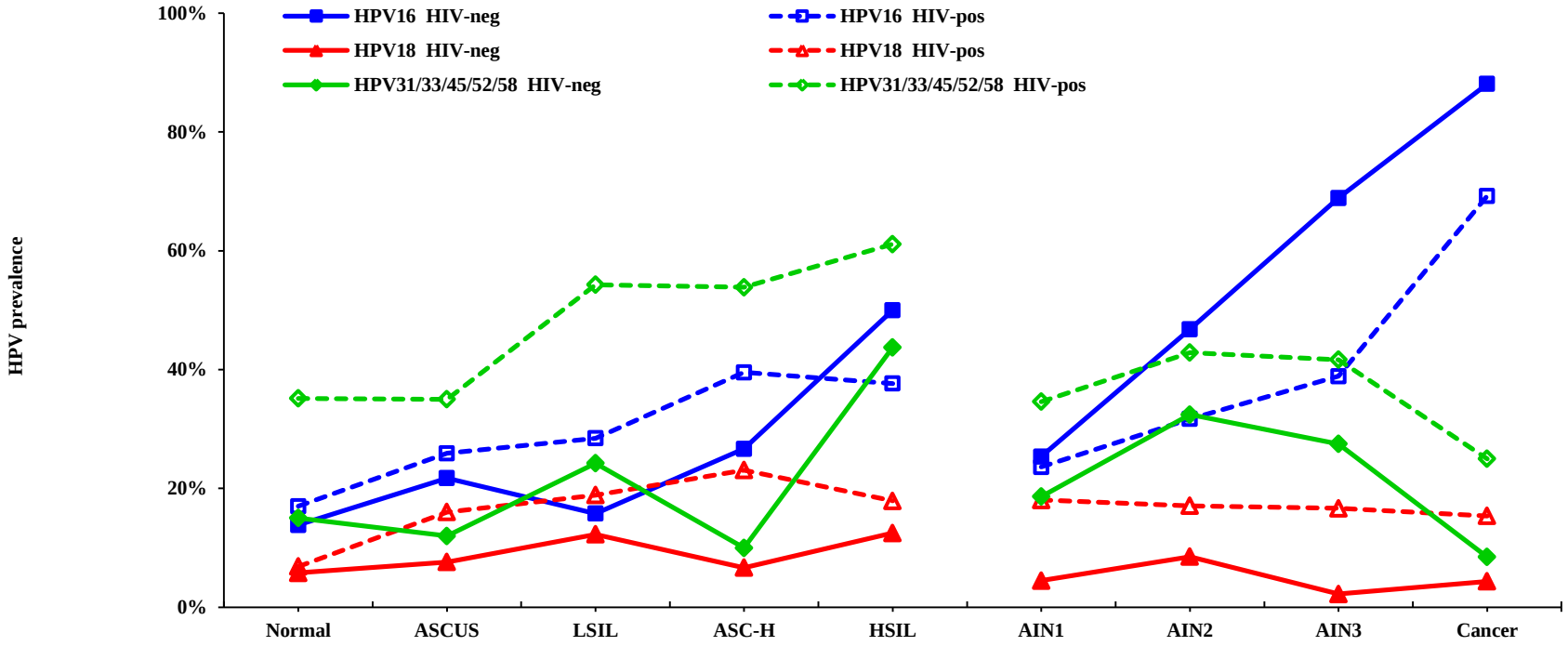
Appendix Figure 6: Prevalence of human papillomavirus 16 (HPV16), HPV18, HPV31/33/45/52/58 and prevalence ratio (PR) in HPV-positive men by nine grades of cytological and histological anal diagnosis and HIV status



Population	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
HPV16 HIV-neg	972 (20·6%)	452 (29·4%)	270 (29·6%)	78 (37·2%)	111 (53·2%)	179 (24·0%)	77 (29·9%)	113 (59·3%)	778 (82·0%)*
HPV16 HIV-pos	2860 (26·4%)	1254 (33·6%)	2032 (42·0%)	98 (44·9%)	447 (55·0%)	764 (29·8%)	290 (43·4%)	294 (57·5%)	136 (66·9%)
PR (95% CI) HIV+ vs HIV-	**1·3 (1·0–1·6)**	**1·1 (1·0–1·4)**	**1·4 (1·2–1·7)**	**1·2 (0·9–1·6)**	**1·0 (0·8–1·3)**	**1·2 (1·0–1·6)**	**1·5 (1·1–1·9)**	**1·0 (0·8–1·1)**	**0·8 (0·7–0·9)**
HPV18 HIV-neg	972 (6·1%)	452 (10·8%)	270 (13·3%)	78 (14·1%)	111 (14·4%)	179 (10·1%)	77 (22·1%)	113 (15·0%)	778 (5·1%)*
HPV18 HIV-pos	2860 (12·3%)	1254 (15·5%)	2032 (21·2%)	98 (19·4%)	447 (21·9%)	764 (12·6%)	290 (20·3%)	294 (17·7%)	136 (14·0%)
PR (95% CI) HIV+ vs HIV-	**2·0 (1·6–2·6)**	**1·4 (1·0–2·1)**	**1·6 (1·2–2·2)**	**1·4 (1·0–1·8)**	**1·5 (1·1–2·1)**	**1·2 (0·9–1·8)**	**0·9 (0·5–1·7)**	**1·2 (0·8–1·6)**	**2·7 (1·7–4·3)**
HPV31/33/45/52/58 HIV-neg	572 (28·5%)	226 (40·3%)	114 (39·5%)	73 (50·7%)	93 (49·5%)	148 (31·8%)	72 (34·7%)	104 (46·2%)	338 (10·4%)*
HPV31/33/45/52/58 HIV-pos	1252 (46·1%)	599 (56·1%)	783 (54·0%)	55 (70·9%)	221 (58·4%)	341 (47·8%)	170 (54·1%)	188 (59·0%)	107 (26·2%)
PR (95% CI) HIV+ vs HIV-	**1·6 (1·5–1·8)**	**1·4 (1·2–1·7)**	**1·4 (1·0–1·9)**	**1·4 (1·2–1·6)**	**1·2 (1·0–1·5)**	**1·5 (1·1–2·1)**	**1·6 (1·1–2·1)**	**1·3 (1·1–1·5)**	**2·5 (1·5–4·3)**

ASCUS=atypical squamous cells of undetermined significance. LSIL=low-grade squamous intraepithelial lesion. ASC-H=atypical squamous cells-cannot exclude HSIL.
HSIL= high-grade squamous intraepithelial lesion. AIN=anal intraepithelial neoplasia.
*Anal cancers of unknown HIV status are assumed to be HIV-negative.

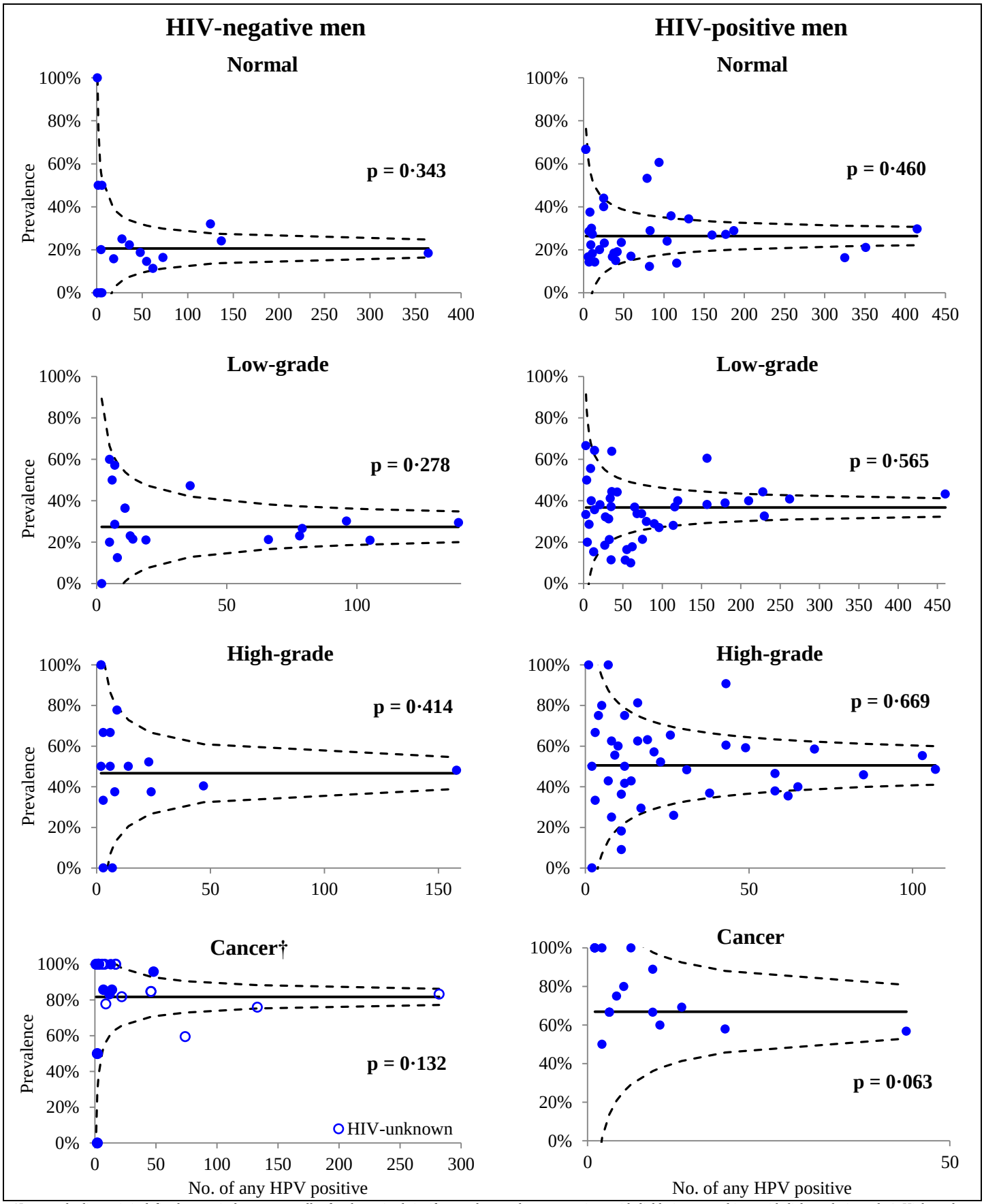
Appendix Figure 7: Prevalence of human papillomavirus 16 (HPV16), HPV18, HPV31/33/45/52/58 and prevalence ratio (PR) in HPV-positive women by nine grades of cytological and histological anal diagnosis and HIV status



Population	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
HPV16 HIV-neg	743 (13·9%)	92 (21·7%)	57 (15·8%)	15 (26·7%)	24 (50·0%)	67 (25·4%)	47 (46·8%)	45 (68·9%)	1149 (88·1%)*
HPV16 HIV-pos	788 (17·0%)	216 (25·9%)	218 (28·4%)	43 (39·5%)	77 (37·7%)	72 (23·6%)	41 (31·7%)	54 (38·9%)	13 (69·2%)
PR (95% CI) HIV+ vs HIV-	**1·2 (0·8–1·8)**	**1·2 (0·8–1·7)**	**1·8 (1·1–3·0)**	**1·5 (0·6–3·7)**	**0·8 (0·4–1·4)**	**0·9 (0·6–1·4)**	**0·7 (0·3–1·5)**	**0·6 (0·3–0·9)**	**0·8 (0·6–1·0)**
HPV18 HIV-neg	743 (5·8%)	92 (7·6%)	57 (12·3%)	15 (6·7%)	24 (12·5%)	67 (4·5%)	47 (8·5%)	45 (2·2%)	1149 (4·4%)*
HPV18 HIV-pos	771 (6·9%)	206 (16·0%)	180 (18·9%)	39 (23·1%)	67 (17·9%)	72 (18·1%)	41 (17·1%)	54 (16·7%)	13 (15·4%)
PR (95% CI) HIV+ vs HIV-	**1·2 (0·7–1·9)**	**2·1 (0·8–5·4)**	**1·5 (0·6–3·8)**	**3·5 (0·4–31·6)**	**1·4 (0·5–4·5)**	**4·0 (1·3–12·7)**	**2·0 (0·8–5·0)**	**7·5 (1·7–32·4)**	**3·5 (0·9–14·0)**
HPV31/33/45/52/58 HIV-neg	153 (15·0%)	25 (12·0%)	33 (24·2%)	10 (10·0%)	16 (43·8%)	59 (18·6%)	37 (32·4%)	40 (27·5%)	745 (8·5%)*
HPV31/33/45/52/58 HIV-pos	91 (35·2%)	40 (35·0%)	35 (54·3%)	13 (53·8%)	18 (61·1%)	26 (34·6%)	7 (42·9%)	12 (41·7%)	12 (25·0%)
PR (95% CI) HIV+ vs HIV-	**2·3 (1·8–3·1)**	**2·9 (0·8–10·2)**	**2·2 (0·9–5·6)**	**5·4 (2·5–11·5)**	**1·4 (1·1–1·8)**	**1·9 (1·0–3·5)**	**1·3 (0·8–2·1)**	**1·5 (1·0–2·4)**	**3·0 (1·6–5·6)**

ASCUS=atypical squamous cells of undetermined significance. LSIL=low-grade squamous intraepithelial lesion. ASC-H=atypical squamous cells-cannot exclude HSIL.
HSIL=high-grade squamous intraepithelial lesion. AIN=anal intraepithelial neoplasia.
*Anal cancers of unknown HIV status are assumed to be HIV-negative.

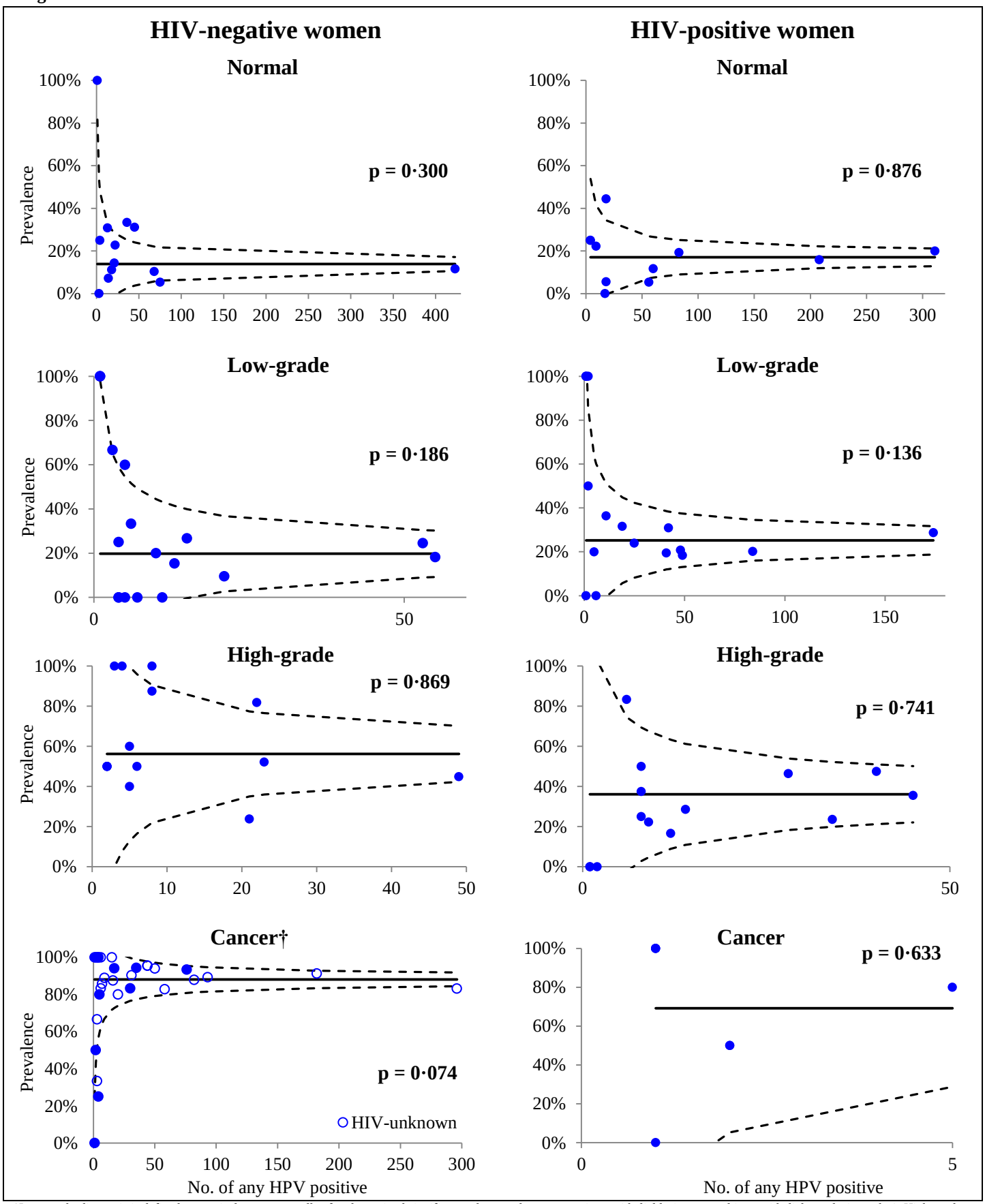
Appendix Figure 8: Funnel plots of human papillomavirus 16 (HPV16) prevalence in HPV-positive men by anal diagnosis* and HIV status



*Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1; High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.

†Anal cancers of unknown HIV status are assumed to be HIV-negative.

Appendix Figure 9: Funnel plots of human papillomavirus 16 (HPV16) prevalence in HPV-positive women by anal diagnosis* and HIV status



*Low-grade diagnosis is defined as atypical squamous cells of undetermined significance, low-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 1; High-grade diagnosis is defined as high-grade squamous intraepithelial lesion, atypical squamous cells-cannot exclude high-grade squamous intraepithelial lesion, or anal intraepithelial neoplasia grade 2 or 3.

†Anal cancers of unknown HIV status are assumed to be HIV-negative.