Supplementary Material

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Supplementary Data

Supplementary Data S1. Search strategy

MEDLINE:

((("papillomaviridae"[MeSH Terms] OR "papillomaviridae"[Title/Abstract]) OR "human papilloma virus"[Title/Abstract]) OR "human papillomavirus"[Title/Abstract] OR "hpv"[Title/Abstract] OR "Human papillomaviruses"[Title/Abstract]) AND ("Anal Canal"[MeSH Terms] OR "anus"[Title/Abstract] OR "anal"[Title/Abstract] OR "perianal"[Title/Abstract]) AND ("Incidence"[MeSH Terms] OR "Cohort Studies"[MeSH Terms] OR "Natural History"[MeSH Terms] OR "Longitudinal Studies"[MeSH Terms] OR "Prospective Studies"[MeSH Terms] OR "inciden*"[Title/Abstract] OR "acqui*"[Title/Abstract] OR "clear*"[Title/Abstract] OR "persist*"[Title/Abstract] OR "Natural History"[Title/Abstract] OR "longitudinal"[Title/Abstract] OR "prospective"[Title/Abstract] OR "cohort"[Title/Abstract])

Embase:

1) 'Papillomaviridae'/exp OR 'papillomaviridae':ti,ab,kw OR ‘human papilloma virus infection':ti,ab,kw OR 'human papillomavirus infection':ti,ab,kw OR hpv:ti,ab,kw OR 'Human papillomaviruses':ti,ab,kw

2) 'anal Canal'/exp OR 'anal canal':ti,ab,kw OR 'anus':ti,ab,kw OR 'anal':ti,ab,kw OR 'perianal':ti,ab,kw

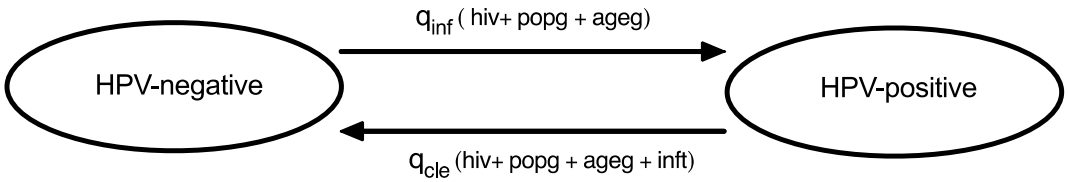
3) 'Incidence'/exp OR 'Cohort Studies'/exp OR cohort:ti,ab,kw OR 'Natural History'/exp OR 'Longitudinal Studies'/exp OR 'Prospective Studies'/exp OR 'inciden*':ti,ab,kw OR 'acqui*':ti,ab,kw OR 'clear*':ti,ab,kw OR 'persist*':ti,ab,kw OR 'Natural History':ti,ab,kw OR 'longitudinal':ti,ab,kw OR 'prospective':ti,ab,kw OR 'cohort':ti,ab,kw

4) 1 AND 2 AND 3

Supplementary Data S2. Continuous-time Markov model (CTMM) description

We collected longitudinal data on type-specific anal HPV status of individuals at different visits. The time of the visit is of limited information when estimating incidence and clearance rates since it does not give the exact time of incidence and clearance of an infection. This means that HPV status is interval censored. Furthermore, the current study is a collaborative pooled analyses in which we included different studies with heterogeneous visit intervals. CTMM is well fitted to analyse this type of data since they handle interval censored observation and allows inclusion of constant and time-varying variables acting on incidence and clearance rates.

The following co-variables were considered in the two-state CTMM: 1) HIV status (hiv, including negative and positive), 2) population group (popg, including MSM, women, and MSW), 3) age group (ageg, including <25, 25-34, 35-44, 45-54, and ⩾55 years); and 4) infection type (inft), including prevalent infection (for continuous positive test since baseline) and incident infection (for any positive test after at least one negative test has been observed). In the model, HIV status, population group, and age group were considered constant over time, and infection type was included as a time-changing variable. The schematic representation of the two-state CTMM was showed as below:



The model was run separately for each hrHPV type.

At a time t the individual is in the state $S(t)$ (HPV-Positive or HPV-Negative) and a person can switch between two states using a transition intensity distribution. At any point in time an individual can switch state according to a transition intensity qrs(t,z(t). The transition intensity distribution $q_{rs}(t, z(t))$ represents the instantaneous risk of moving from state r to state s. This transition rate can depend on an individual-specific covariable (that is allowed to change over time t) indicated with $z(t)$.

$$q_{rs}(t, z(t)) = \lim_{\delta t \to 0} P(S(t + \delta t) = s | S(t) = r)/\delta t$$

where $P(S(t + \delta t) = s|S(t) = r)$ represents the probability to be in state s at time $t + \delta t$ knowing that the individual was in state r at time t.

At population/study level, the matrix of transition intensity $Q(z(t))$ is estimated with a proportional hazard model:

$$Q(z(t)) = \begin{pmatrix} -q_{01}(z(t)) & q_{01}(z(t)) \\ q_{10}(z(t)) & -q_{10}(z(t)) \end{pmatrix}$$

where $q_{01}(z(t))$ is the transition intensity from HPV-negative to HPV-positive state (incidence rate) and $q_{10}(z(t))$ is the transition intensity from HPV-positive to HPV-negative state (clearance rate) for an individual with the $z(t)$ characteristics at time t. More specifically,

$$q_{01}(z(t)) = q_{01}^{(0)} \exp(\beta_{hiv}\, hiv + \beta_{popg}\, popg + \beta_{ageg}\, ageg)$$

$$q_{10}(z(t)) = q_{10}^{(0)} \exp(\beta_{hiv}\, hiv + \beta_{popg}\, popg + \beta_{ageg} ageg + \beta_{inft}\, inft(t))$$

where $q_{01}^{(0)}$ and $q_{10}^{(0)}$ are the baseline infection and clearance intensities, hiv indicates HIV status (negative and positive), popg indicates the population group (MSM, women, and MSW), ageg indicates the age group (<25, 25-35, 35-44, 45-54, and ⩾ 55 years) and inft(t) indicates the infection type (incident and prevalent infection) of the individual at time t.

The transition probability matrix $P(t, z(t))$ using the above-described transition intensity can be defined as:

$$P(t, z(t)) = \begin{pmatrix} p_{00}(t, z(t)) & p_{01}(t, z(t)) \\ p_{10}(t, z(t)) & p_{11}(t, z(t)) \end{pmatrix} = \mathrm{Exp}(tQ(z(t)))$$

The model is optimized using likelihood function $L(Q(z(t)))$ which is the product of all the terms $L_{i,j}(z(t))$ over all the individuals and all the transitions. Final model coefficients are estimated by maximisation of $L(Q(z(t)))$.

Our dataset is composed of a total of I individuals i. Everyone has been tested a total of J_i and each individual test is indicated with j.

The likelihood $L_{i,j}(z(t))$ of two consecutive tests $S_i(t_j)$ and $S_i(t_{j+1})$ at time j and $j+1$ is defined as:

$$L_{i,j}(z(t)) = p_{S_i(t_j)S_i(t_{j+1})}(t_{j+1} - t_j)$$

Supplementary Tables

Supplementary Table S1. Characteristics of included studies.

Study	Country	Study period	Visit interval	MSMLWH	HIV-neg MSM	WLWH	HIV-neg women	MSWLWH	HIV-neg MSW
Goodman et al (2008)[1]	USA	1999.07–2009.12	4 months	0	0	3	1384	0	0
de Pokomandy et al (2009)[2]	Canada	2002.01–2007.11	6 months	224	0	0	0	0	0
Beachler et al (2013)[3]	USA	2006.03–2008.11	6 months	53	0	117	0	109	0
Mullins et al (2013)[4]	USA	1996.02–2000.11	12 months	0	0	205	92	0	0
Phanuphak et al (2013)[5]	Thailand	2009.12–2012.03	6 months	96	75	0	0	0	0
Wiley et al (2013)[6]	USA	2010.04–2015.08	6 months	583	637	0	0	9	11
Hessol et al (2013)[7]	USA	2001.10–2006.03	6 months	0	0	443	175	0	0
Moscicki et al (2014)[8]	USA	2009.08–2015.01	4 months	0	0	8	111	0	0
Burgos et al (2015)[9]	Spain	2004.10–2018.04	12 months	427	0	0	0	0	0
Zou et al (2015)[10]	Australia	2010.09–2013.08	3 months	0	186	0	0	0	0
Donà et al (2016)[11]	Italy	2009.08–2015.01	6 months	0	155	0	0	0	0
Geskus et al (2016)[12]	Spain	2007.05–2013.05	12 months	604	0	0	0	0	0
Schofield et al (2016)[13]	UK	2013.03–2015.05	6 months	143	63	7	4	0	0
de Pokomandy et al (2017)[14]	Canada	2012.01–2017.03	6 months	0	0	125	0	0	0
Hidalgo-Tenorio et al (2018)[15]	Spain	2012.05–2016.12	…	0	0	53	0	0	0
Ong et al (2018)[16]	Australia	2012.12–2016.05	24 months	188	0	0	0	0	0
Chikandiwa et al (2019)[17]	South Africa	2012.09–2016.11	18 months	11	0	0	0	144	0
Hidalgo-Tenorio et al (2019)[18]	Spain	2010.04–2018.12	…	230	0	0	0	0	0
Marra et al (2019)[19]	Netherlands	2010.07–2013.07	6 months	309	443	0	0	0	0

Study	Country	Study period	Visit interval	MSMLWH	HIV-neg MSM	WLWH	HIV-neg women	MSWLWH	HIV-neg MSW
Nowak et al (2019)[20]	Nigeria	2013.04–2017.08	3 months	146	106	0	0	0	0
Nyitray et al (2019)[21]	USA, Mexico, Brazil	2005.06–2016.03	6 months	8	356	0	0	1	1071
Viciana et al (2019)[22]	Spain	2008.01–2019.04	16 months	642	0	0	0	3	0
Phanuphak et al (2020)[23]	Thailand, Vietnam	2013.06–2017.06	12 months	0	0	85	87	0	0
Alberts et al (2020)[24]	France	2014.12–2018.06	12 months	438	0	0	0	0	0
Fan et al (2020)[25]	China	2018.11–2021.05	12 months	0	200	0	0	0	0
Gatechompol et al (2020)[26]	Thailand, Vietnam	2013.06–2017.06	12 months	7	15	0	0	37	23
Wei et al (2020)[27]	China	2014.05–2016.03	6 months	0	3	0	2024	0	1586
Yunihastuti et al (2020)[28]	Indonesia, Malaysia, Thailand	2011.03–2015.12	6 months	143	93	0	0	0	0
Cotte et al (2021)[29]	France	2012.12–2016.06	6 months	0	139	0	0	0	0
Liu et al (2021)[30]	China	2016.04–2019.12	6 months	0	482	0	0	0	0
Poynten et al (2021)[31]	Australia	2010.09–2018.04	12 months	186	324	0	0	0	0
Squillace et al (2021)[32]	Italy	2010.02–2019.02	…	89	0	16	0	27	0
Donà et al (2022)[33]	Italy	2009.11–2020.01	6 months	204	0	0	0	0	0
Zhou et al (2022)[34]	China	2017.01–2018.11	12 months	14	182	0	0	0	0
Overall	…	…	…	4745	3459	1062	3877	330	2691

Abbreviations: MSM, men who have sex with men; MSMLWH, MSM living with HIV; WLWH, women living with HIV; MSW, men who have sex with women; MSWLWH, MSW living with HIV; HIV-neg, HIV negative. Studies are ranked in ascending order of the year of publication.

Supplementary Table S2. Characteristics of included individuals in six risk groups.

	MSMLWH	HIV-neg MSM	WLWH	HIV-neg women	MSWLWH	HIV-neg MSW	Overall
No. at baseline	**4745**	**3459**	**1062**	**3877**	**330**	**2691**	**16 164**
Age (years) (n=16 164)							
Median (IQR)	42 (33, 51)	35 (26, 48)	37 (19, 46)	32 (23, 44)	42 (34, 48)	37 (28, 45)	37 (27, 47)
Lifetime number of sexual partners (n=12 402)*							
Low	1678 (63.1%)	1542 (68.8%)	181 (22.8%)	2540 (67.9%)	46 (16.2%)	1894 (72.4%)	7881 (63.5%)
High	980 (36.9%)	767 (33.2%)	614 (77.2%)	1199 (32.1%)	238 (83.8%)	723 (27.6%)	4521 (36.5%)
Ever having receptive anal sex (n=8342)							
No	336 (11.2%)	462 (16.5%)	535 (67.4%)	1161 (66.7%)	…	…	2494 (29.9%)
Yes	2673 (88.8%)	2336 (83.5%)	259 (32.6%)	580 (33.3%)	…	…	5848 (70.1%)
Lifetime number of anal sexual partners (n=4890)†							
Low	642 (52.3%)	768 (68.1%)	535 (67.4%)	1161 (66.7%)	…	…	3106 (63.5%)
High	585 (47.7%)	360 (31.9%)	259 (32.6%)	580 (33.3%)	…	…	1784 (36.5%)
Current smoking (n=8259)							
No	2490 (63.0%)	1923 (82.0%)	355 (48.0%)	176 (60.7%)	152 (98.7%)	5 (100%)	5746 (69.6%)
Yes	1463 (37.0%)	422 (18.0%)	385 (52.0%)	114 (39.3%)	2 (1.3%)	0 (0%)	2513 (30.4%)
Presence of anal HSIL at baseline (n=5105)							
No	2569 (82.7%)	1003 (84.8%)	451 (94.4%)	174 (98.3%)	152 (98.7%)	5 (100%)	4354 (85.3%)
Yes	539 (17.3%)	180 (15.2%)	27 (5.6%)	3 (1.7%)	2 (1.3%)	0 (0%)	751 (14.7%)

	MSMLWH	HIV-neg MSM	WLWH	HIV-neg women	MSWLWH	HIV-neg MSW	Overall
No. at all visits	**15 792**	**12 904**	**4991**	**14 349**	**871**	**7141**	**56 048**
Visit number (n=56 048)							
Median (IQR)	3.0 (2.0, 4.0)	4.0 (2.0, 5.0)	4.0 (3.0, 7.0)	3.0 (3.0, 4.0)	2.0 (2.0, 3.0)	2.0 (2.0, 3.0)	3.0 (2.0, 4.0)
Follow-up time (years) (n=56 048)							
Median (IQR)	2.1 (1.2, 3.2)	2.0 (1.0, 2.5)	2.5 (1.8, 3.5)	1.0 (1.0, 1.3)	1.5 (1.3, 2.0)	1.0 (0.5, 1.1)	1.4 (1.0, 2.5)
Recent number of sexual partners (n=31 180)‡							
Low	3687 (74.7%)	3829 (71.9%)	3301 (90.0%)	8837 (90.8%)	367 (79.3%)	6128 (86.8%)	26 149 (83.9%)
High	1251 (25.3%)	1494 (28.1%)	366 (10.0%)	893 (9.2%)	96 (20.7%)	931 (13.2%)	5031 (16.1%)
Recent number of anal sexual partners (n=21 611)§							
Low	4442 (70.8%)	4890 (72.9%)	1991 (89.1%)	5687 (88.9%)	…	…	17 010 (78.7%)
High	1831 (29.2%)	1816 (27.1%)	243 (10.9%)	711 (11.1%)	…	…	4601 (21.3%)
Current CD4 count (cells per µl) (n=19 865)							
>500	8969 (60.2%)	…	2140 (47.6%)	…	231 (49.3%)	…	11 340 (57.1%)
350-500	3381 (22.7%)	…	955 (21.3%)	…	113 (24.1%)	…	4449 (22.4%)
<350	2553 (17.1%)	…	1398 (31.1%)	…	125 (26.7%)	…	4076 (20.5%)
Current HIV viral load (copies per ml) (n=19 374)							
<50	9339 (64.6%)	…	1907 (43.0%)	…	304 (64.8%)	…	11 550 (59.6%)
50-10 000	1824 (12.6%)	…	1479 (33.3%)	…	63 (13.4%)	…	3366 (17.4%)
>10 000	3304 (22.8%)	…	1052 (23.7%)	…	102 (21.7%)	…	4458 (23.0%)

Abbreviations: MSM, men who have sex with men; MSMLWH, MSM living with HIV; WLWH, women living with HIV; MSW, men who have sex with women; MSWLWH, MSW living with HIV; HIV-neg, HIV negative; HSIL, high-grade squamous intraepithelial lesions; IQR, interquartile range.

The categories of (lifetime or recent) number of (anal) sexual partners were defined by the combination of median value for each population and the availability of categorical variables from contributed studies. *MSM (low: ≤200; high: >200), women (low: ≤3; high: >3). †MSM (low: ≤5; high: >5), women (low: ≤1; high: >1). ‡MSM (low: ≤50; high: >50), women (low: 0; high: >0). §MSM (low: ≤3; high: >3), women (low: 0; high: >0).

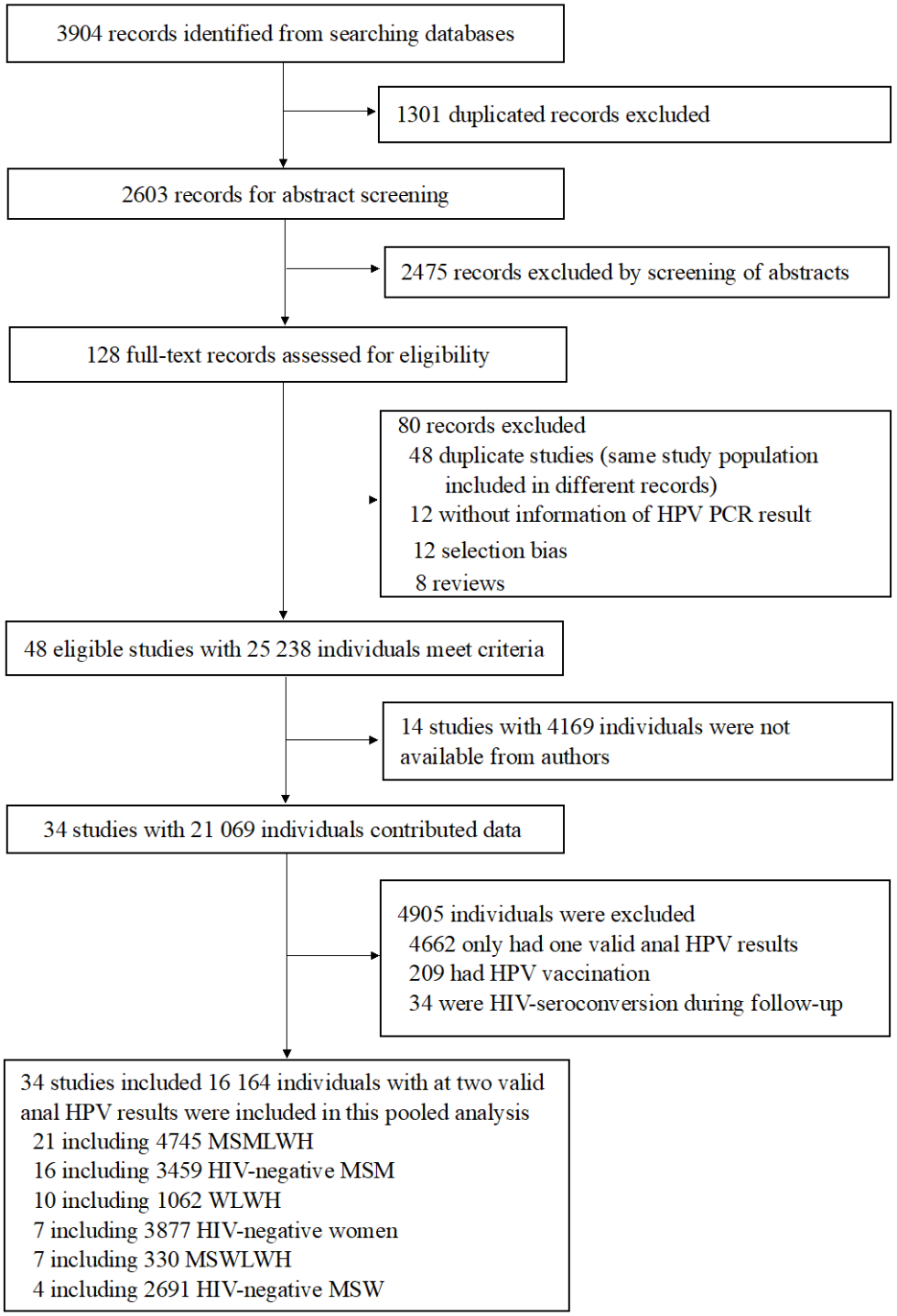
Supplementary Table S3. Hazard ratios of anal HPV16 incidence and clearance by population.

	aHR (95%CI) of MSW versus MSM	aHR (95%CI) of women versus MSM
Incidence	0.22 (0.14–0.34)	0.54 (0.47–0.62)
Clearance of prevalent infection	3.51 (2.53–4.87)	1.59 (1.34–1.89)
Clearance of incident infection	2.25 (1.31–3.84)	1.93 (1.58–2.35)

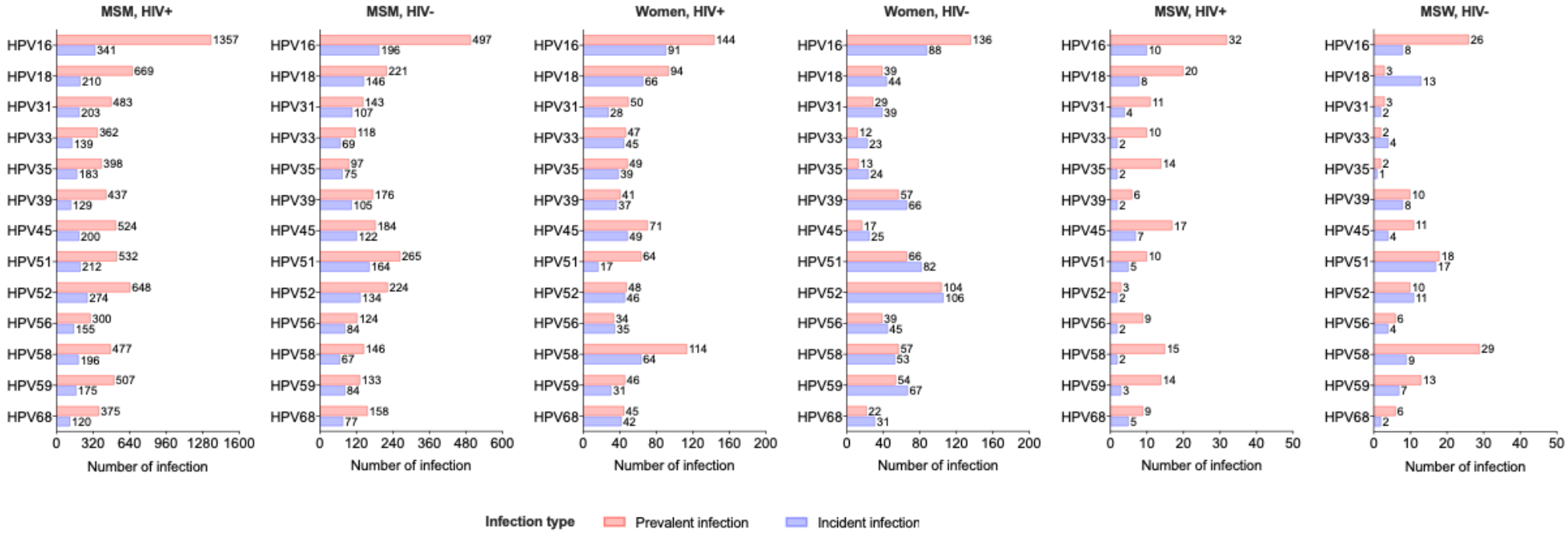
Hazard ratios (aHR) were adjusted by age group and HIV status. Abbreviations: HPV, human papillomavirus; MSM, men who have sex with men; MSW, men who have sex with women.

Supplementary Figures

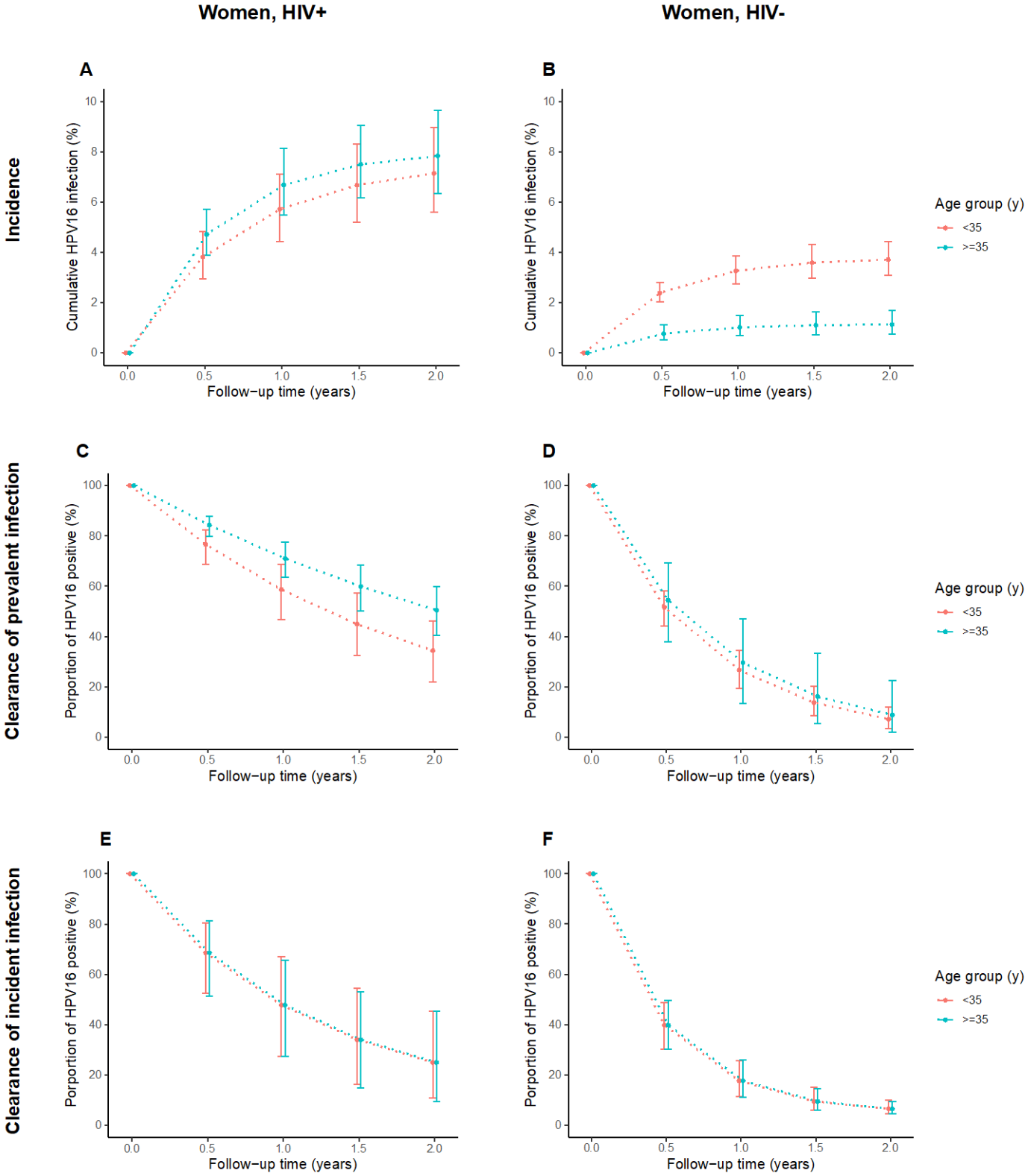
Supplementary Figure S1. Flow chart.
Abbreviations: HPV, human papillomavirus; MSM, men who have sex with men; MSMLWH, MSM living with HIV; WLWH, women living with HIV; MSW, men who have sex with women; MSWLWH, MSW living with HIV.



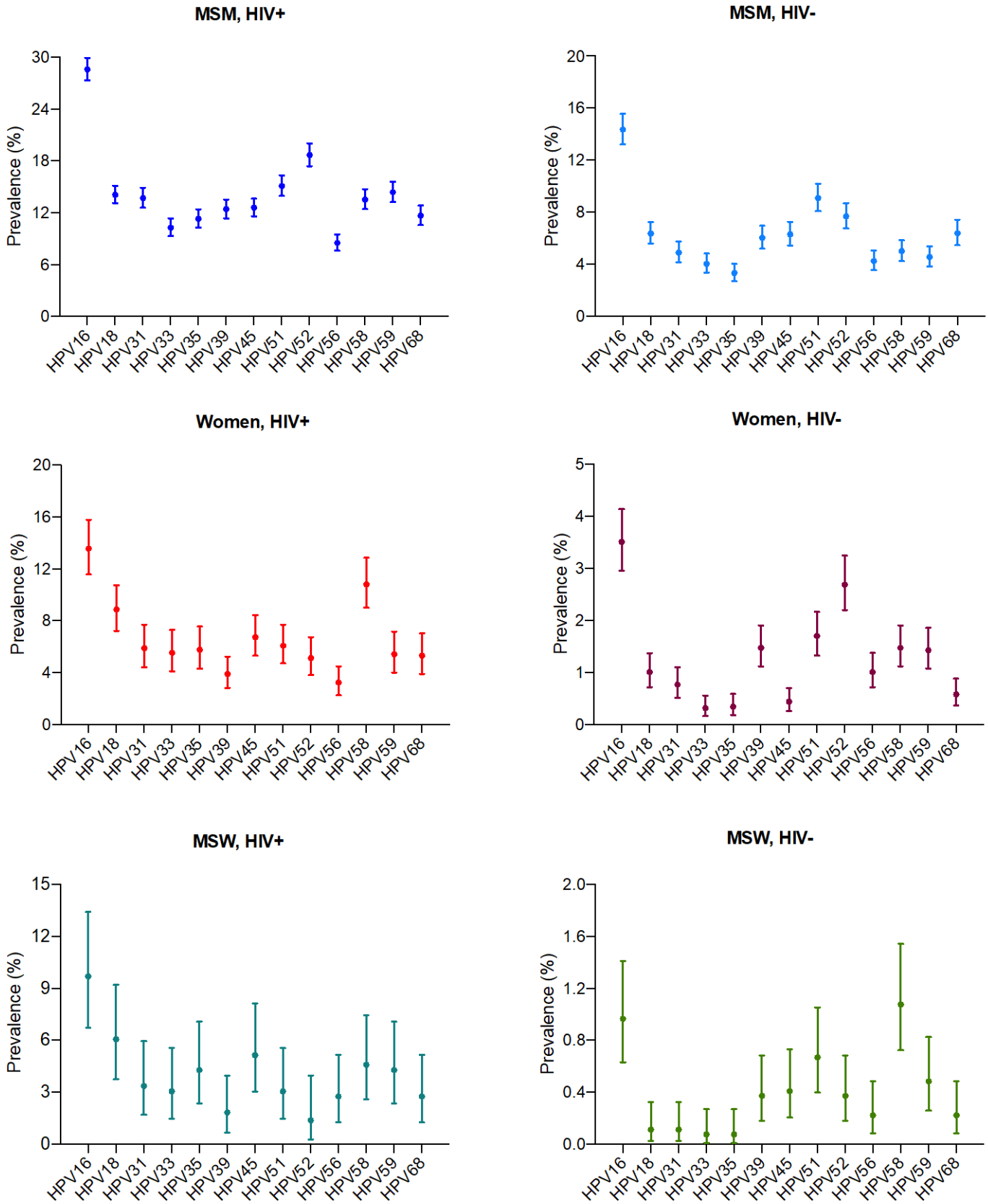
Supplementary Figure S2. Number of anal high-risk HPV prevalent and incident infection during the study period in six risk groups.
Abbreviations: HPV, human papillomavirus; HIV+, living with HIV; HIV-, HIV negative; MSM, men who have sex with men; MSW, men who have sex with women.



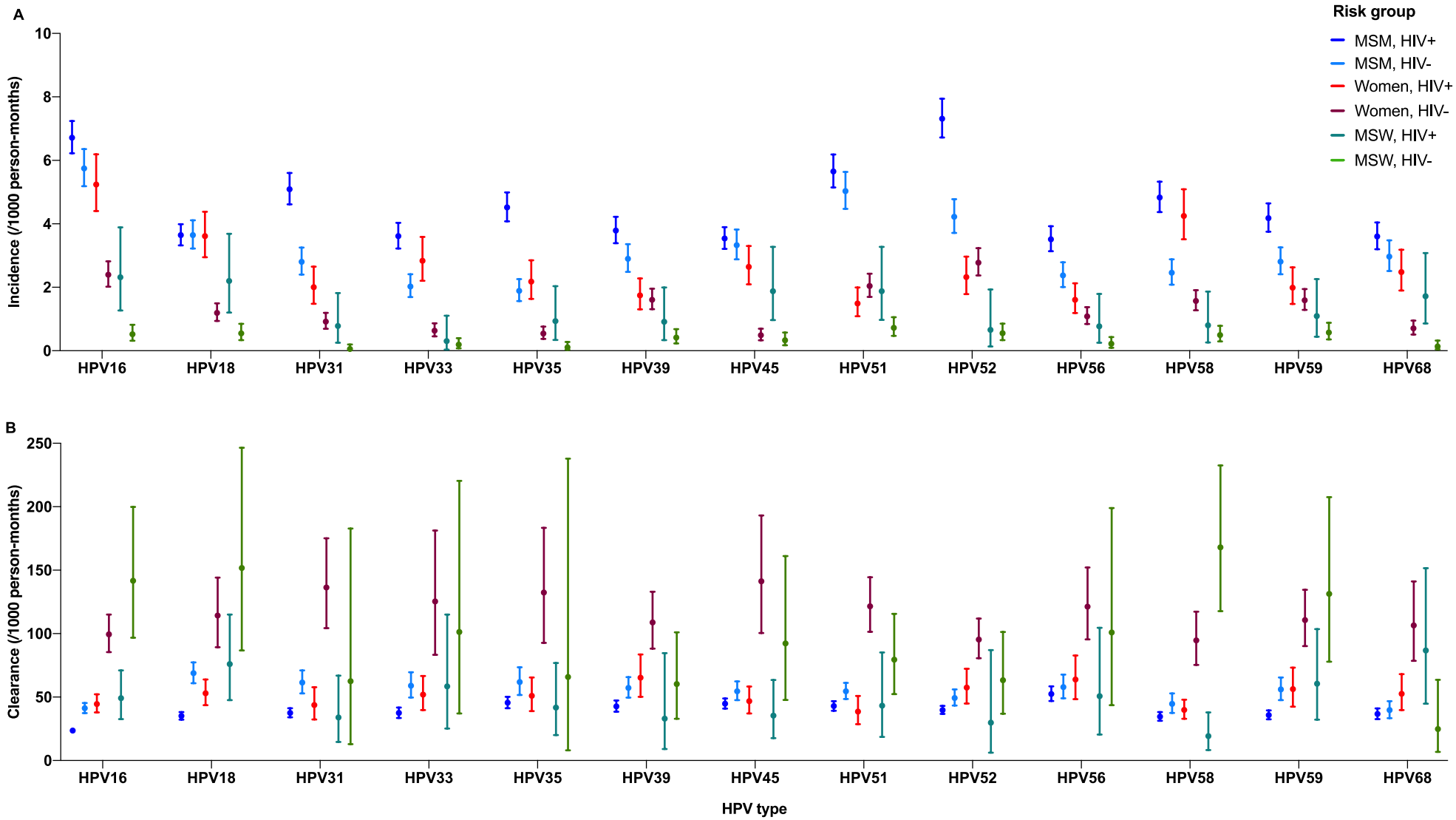
Supplementary Figure S3. Cumulative incidence and clearance of anal HPV16 infection in WLWH and HIV-negative women, by age group.
Error bar=95% CI. Abbreviations: HPV, human papillomavirus; HIV+, living with HIV; HIV-, HIV negative; WLWH, women living with HIV.



Supplementary Figure S4. Prevalence at baseline of anal type-specific high-risk HPV infection in six risk groups.
Error bar=95% CI. Abbreviations: HPV, human papillomavirus; HIV+, living with HIV; HIV-, HIV negative; MSM, men who have sex with men; MSW, men who have sex with women.



Supplementary Figure S5. Incidence and clearance of anal type-specific high-risk HPV infection in six risk groups by use of standard person-time approach.
Error bar=95% CI. Abbreviations: HPV, human papillomavirus; HIV+, HIV positive; HIV-, HIV negative; MSM, men who have sex with men; MSW, men who have sex with women. In standard person-time approach, incidence was defined as a positive HPV test result preceded by a negative HPV test. Time at risk for incidence started from the first HPV-negative visit of the HPV type under consideration, and it ended either at the midpoint between the last negative test and the first positive test, or at the date of the last HPV-negative sample (if the HPV outcome was not detected). Clearance was defined as the negative test result that was preceded by a positive test result. People entered the risk-set for clearance from the first HPV-positive visit, and they left the risk-set either at the midpoint between the last positive test and the first negative test or at the date of the last HPV-positive sample (if the HPV infection had not cleared).



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