

Antiretroviral therapy, anal high-risk human papillomavirus and anal intraepithelial neoplasia: a systematic review and meta-analysis

Supplementary information

The search strategy in MEDLINE and EMBASE on 30 October 2019

ANAL HPV STUDIES:

HPV [Title/Abstract] OR Human papillomavirus[Title/Abstract] AND anal OR anal canal [MeSH Terms] OR anogenital OR anogenital tract [MeSH Terms] AND Antiretroviral therapy [Title/Abstract] OR ART [Title/Abstract] OR Antiretroviral therapy, highly active [MeSH Terms] OR HIV [Title/Abstract] or Human immunodeficiency virus [MeSH Terms]

ANAL LESION STUDIES:

Intraepithelial neoplasia [Title/Abstract] OR Squamous intraepithelial neoplasia [Title/Abstract] OR Neoplasms [MeSH Terms] OR Precancer [MeSH Terms] OR Cancer [Title/Abstract] OR malignant neoplasm [MeSH Terms] OR Intraepithelial lesion [Title/Abstract] OR anus tumor [MeSH Terms] OR anus carcinoma [MeSH Terms] OR Precursor lesions [Title/Abstract] OR Anal intraepithelial lesion [Title/Abstract] OR anus disease [MeSH Terms] OR dysplasia [MeSH Terms] OR anus cancer [MeSH Terms] OR Anal dysplasia [Title/Abstract] AND anal [Title/Abstract] OR anal canal [MeSH Terms] OR anogenital [Title/Abstract] OR anogenital tract [Title/Abstract] AND Antiretroviral therapy [Title/Abstract] OR ART [Title/Abstract] OR Antiretroviral therapy, highly active [MeSH Terms] OR HIV [Title/Abstract] or Human immunodeficiency virus [MeSH Terms]

Search strategies

This appendix provides full details of all search strings used for bibliographic databases, with dates and number of references returned and notes explaining any unusual search techniques or syntax. EndNote X9 referencing system was used. We conducted the original search on 1 December 2017 and repeated the search at three later dates (25 September 2018, 18 April 2019 and 30 October 2019) during the development of the review manuscript to ensure that the review was up to date at time of publication.

Ovid MEDLINE

Database name	Medline
Database platform	OvidSP
Dates of database coverage	1946 to October 29, 2019
Date searched	30 October 2017 25 September 2018 (updated search with limit set to yr="2017 -Current") 18 April 2019 ((updated search with limit set to yr="2019 -Current") 30 October 2019 (updated search with limit set to yr="2019 -Current")
Searched by	HK
Number of results (cumulative from all 4 searches)	1078

Search strategy and number of articles retrieved* on 01 December 2017

- 1 HPV (33601)
- 2 Human papillomavirus (31061)
- 3 Antiretroviral Therapy, Highly Active/ or antiretroviral therapy (20840)
- 4 ART (74013)
- 5 Antiretroviral therapy (42337)
- 6 1 or 2 (40699)
- 7 3 or 4 or 5 (106911)
- 8 6 and 7 (394)
- 9 anal (41873)
- 10 anogenital (3806)
- 11 anogenital tract (158)
- 12 9 or 10 or 11 (44980)
- 13 6 and 7 and 12 (141)
- 14 human immunodeficiency virus.mp. or HIV/ (100719)
- 15 6 and 12 and 14 (246)
- 16 13 or 15 (335)**
- 17 Intraepithelial neoplasia (18013)
- 18 squamous intraepithelial neoplasia (160)
- 19 Neoplasms/ (2582979)
- 20 precancer (1377)
- 21 cancer (1362430)
- 22 intraepithelial lesion (1931)

- 23 Carcinoma, Squamous Cell/ (128504)
- 24 Anus Neoplasms/ or anus carcinoma.mp. (5913)
- 25 precursor lesion (2720)
- 26 Anal intraepithelial lesion (2)
- 27 anal dysplasia (158)
- 28 or/17-27 (2830969)
- 29 12 and 28 (12050)
- 30 7 and 29 (295)
- 31 14 and 29 (345)
- 32 30 or 31 (555)**

***results for 16 and 32 retrieved for screening**

Ovid Embase Classic + Embase

Database name	Embase Classic + Embase
Database platfor	OvidSP
Dates of database coverage	1947 to October 29, 2019
Date searched	30 October 2017 25 September 2018 (updated search with limit set to yr="2017 -Current") 18 April 2019 ((updated search with limit set to yr="2019 -Current") 30 October 2019 (updated search with limit set to yr="2019 -Current")
Searched by	HK
Number of results (cumulative from all 4 searches)	5699

Search strategy and number of articles retrieved* on 01 December 2017

- 1 HPV (47714)
- 2 Human papillomavirus (40860)
- 3 highly active antiretroviral therapy/ (36089)
- 4 ART (150810)
- 5 Antiretroviral therapy/ (3851)
- 6 1 or 2 (56877)
- 7 3 or 4 or 5 (185004)
- 8 6 and 7 (722)
- 9 anal.mp. or anal canal/ (54718)
- 10 anogenital (5276)
- 11 anogenital tract (216)
- 12 9 or 10 or 11 (59276)
- 13 6 and 7 and 12 (251)
- 14 HIV.mp or human immunodeficiency virus/ (370482)
- 15 6 and 12 and 14 (1359)
- 16 13 or 15 (1383)**
- 17 Intraepithelial neoplasia (19020)

- 18 squamous cell carcinoma.mp. or squamous cell carcinoma/ (120146)
- 19 Neoplasm/ (471117)
- 20 precancer (22180)
- 21 cancer.mp. or malignant neoplasm/ (3035162)
- 22 intraepithelial lesion (3631)
- 23 anus tumor/ or anus carcinoma/ (4770)
- 24 precursor lesion.mp. (3876)
- 25 anal intraepithelial lesion (9)
- 26 anus disease/ or dysplasia/ or anus cancer/ or Anal dysplasia (36731)
- 27 or/17-26 (3263296)
- 28 12 and 27 (17610)
- 29 7 and 28 (482)
- 30 14 and 28 (2043)
- 31 29 or 30 (2127)**

***results for 16 and 31 retrieved for screening**

Newcastle-Ottawa scale (adapted version)

A. Selection

1) Representativeness of the exposed cohort, details in Table below.

Analysis	Exposed group	Outcome	Score "1"	Score "0"
ART vs. ART-naive (Analysis 1)	ART users ("effective" ART)	HR-HPV, ASCUS- AIN1+ and HSIL- AIN2+ prevalence	Proportion of ART users with suppressed or undetectable HIV PVL is $\geq 70\%$ OR If HIV PVL not stratified by ART use, then assume that majority of those with undetectable PVL are all on ART and therefore allow proportion of all participants enrolled with suppressed or undetectable HIV PVL to be $\geq 60\%$	Proportion of ART users with suppressed or undetectable HIV PVL is $< 70\%$, or no information given
		Anal cancer incidence	studies conducted in the combination ART era (i.e. 1996 onwards)	studies for which duration of follow-up includes the pre-combination ART era (i.e. includes the period before 1996)
Undetectable vs. detectable HIV PVL (Analysis 2)	Individuals with undetectable HIV PVL	HR-HPV, ASCUS- AIN1+ and HSIL- AIN2+ prevalence	Individuals with undetectable (or suppressed) HIV PVL should be representative of effective ART users Score "1" if analysis mostly conducted among ART users (% ART $> 80\%$), with high median CD4+ (> 500 cells/ μ l) and with high adherence	Analysis conducted among all participants when % ART users is $< 80\%$, or no information given
		Anal cancer incidence	studies conducted in the combination ART era (i.e. 1996 onwards)	studies for which duration of follow-up includes the pre-combination ART era (i.e. includes the period before 1996)
Nadir CD4+ ≥ 200 vs. < 200 cells/ μ l (Analysis 3)	Individuals with nadir CD4+ ≥ 200	All	Studies included in this analysis were more likely to be conducted when guidelines for initiation recommended initiation at ≤ 350 , so that individuals with nadir < 200 were representative of general population of PLHIV initiating ART at that time in that setting Score "1" if recruitment in recent ART era (> 2008)	Recruitment in early ART era when nadir CD4 might be lower (earlier than 2008)
Current CD4+ ≥ 500 vs. < 500 cells/ μ l (Analysis 3)	Individuals with current CD4+ ≥ 500	All	The majority of studies in this analysis included a high proportion of ART users ($> 90\%$) and with undetectable PVL ($> 80\%$). score 1 if controlling HIV, i.e. most ART users with undetectable PVL Participants with current CD4+ < 500 could therefore be by mix of ART users and ART-naïve, few studies provide this data	High proportion ART users but low proportion with undetectable PVL Or mostly ART naïve with low proportion undetectable PVL, or no information on ART or PVL detection

2) Selection of the non-exposed cohort

Analysis	Non-exposed groups	Outcome	Score "1"	Score "0"
ART vs. ART-naive (Analysis 1)	ART naïve	HR-HPV, ASCUS-AIN1+ and HSIL-AIN2+ prevalence only	Drawn from same source as ART users, And /or if median CD4+ not stratified by ART status and there is a high proportion of ART users, then median CD4+ among all participants should be ≥ 400 cells/ μ l If study includes a large proportion of ART naïve ($>70\%$), then median CD4 >500 is acceptable	Drawn from different source as ART users, or Median CD4+ count of ART-naïve individuals is <500 cells/ μ l, or no information given
Undetectable vs. detectable HIV PVL (Analysis 2)	Individuals with detectable HIV PVL	HR-HPV, ASCUS-AIN1+ and HSIL-AIN2+ prevalence only	This analysis is mostly conducted among individuals taking ART; therefore individuals taking ART but with detectable HIV PVL should report low adherence, and have lower median CD4+ count. This information is unavailable in the included studies, so the following applies: The unexposed should come from same pool as exposed	no information given
Nadir CD4+ ≥ 200 vs. <200 cells/ μ l	Individuals with nadir CD4+ ≥ 200	HR-HPV, ASCUS-AIN1+ and HSIL-AIN2+ prevalence only	Median nadir is <350 cells/ μ l among ART users as most studies were conducted in period when guidelines recommended ART initiation at <350 cells/ μ l or The unexposed should come from same pool as exposed	No information given
Current CD4+ ≥ 500 vs. <500 cells/ μ l	Individuals with current CD4+ ≥ 500	HR-HPV, ASCUS-AIN1+ and HSIL-AIN2+ prevalence only	The unexposed should come from same pool as exposed	No information given

Note: this item is not used to assess risk of bias for anal cancer incidence studies

3) Ascertainment of exposure

Analysis	Exposure	Score "1"	Score "0"
ART vs. ART-naive (Analysis 1)	ART use	Clinic records	Self-report, no information, or unclear information (i.e participants completed questionnaire without clarifying if HIV related information was extracted from clinic records or through self report)
Undetectable vs. detectable HIV PVL (Analysis 2)	Undetectable HIV PVL	Lab test at time of outcome measure (at least one visit with HIV PVL <400 copies/ml), or clinic records in previous 6 months, or 'most recent' If authors state that data on HIV PVL obtained from national/regional HIV monitoring database, it is assumed that HIV PVL is biannual and measured in previous 6 months.	Obtained from clinic records >6 months prior to outcome measure, or does not indicate time obtained from clinic records, self reported or no information.
Nadir CD4+ ≥ 200 vs. <200 cells/ μ l	Nadir CD4+ count	Clinic records	No information
Current CD4+ ≥ 500 vs. <500 cells/ μ l	Current CD4+ count	Lab test at time of outcome measure, or clinic records in previous 6 months, or 'most recent'. If authors state that data on CD4+ count obtained from national/regional HIV monitoring database, it is assumed that CD4+ count is measured in previous 12 months.	Obtained from clinic records >6 months prior to outcome measure, or does not indicate time obtained from clinic records, self reported or no information.

4) Outcome of interest was not present at start of study (for anal cancer incidence studies only)

- Score of “1” if study reports exclusion of prevalent cancer cases identified at enrolment or before or within first 6 months of HIV diagnosis, or in the first 6 months of ART initiation
- Score of “0” if no information

B. Comparability

1) Study controls for factors strongly predictive of **prevalence of anal HR-HPV, ASCUS-AIN1+ and HSIL-AIN2+** :

- score of “2” if study adjusts for any of: receptive anal intercourse, ART use, ART duration, HIV PVL, nadir or current CD4+ count
- score of “1” if adjusts for sociodemographic or behavioural factors, but not receptive anal intercourse, ART use, ART duration, HIV PVL, nadir or current CD4+ count
- score of “0” if estimate is unadjusted for potential confounders (i.e. raw data used to estimate crude effect estimate, or original authors present crude effect estimate in univariate risk factor analysis)

2) Study controls for factors strongly predictive of **anal cancer incidence**:

- score of “2” if study adjusts for any of: ART use, ART duration, HIV PVL, nadir or current CD4+ count AND duration of HIV infection
- score of “1” if study adjusts for any of: ART use, ART duration, HIV PVL, nadir or current CD4+ count
- score of “0” if estimate is adjusted for sociodemographic or behavioural factors, or is unadjusted for potential confounders (i.e. raw data used to estimate crude effect estimate, or original authors present crude effect estimate in univariate risk factor analysis)

C. Outcome (adapted)

1) Ascertainment of outcome

Outcome	Score “2”	Score “1”	Score “0”
HR-HPV prevalence, incidence or persistence	Validated/commercial PCR or genotyping method; high risk defined using the current International Agency for Research on Cancer (IARC) classification ⁽¹⁾ ; ‘carcinogenic to humans’ (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59). The definition of HR can include ‘probable carcinogenic’ (HPV68), and HPV66 (targeted by some next generation HPV tests)	Definition of high risk includes “possible” carcinogenic types (26, 53, 66, 67, 70, 73, 82) or low risk types, or definition includes fewer than the 12 “carcinogenic” types	No information given
ASCUS-AIN1+ or HSIL-AIN2+ prevalence, incidence, recurrence or regression	Directed biopsy indicated by HRA and/or following positive screen test <u>in addition to</u> random biopsy of normal looking quadrants (considered highest quality) Or Biopsy indicated by HRA/cytology abnormality and biopsy rate $\geq 75\%$	Histological verification of tissue obtained through directed biopsy indicated by HRA following abnormal cytology or HR-HPV positive screen test; OR A composite diagnosis of cytology + histology following HRA guided biopsy (with or without knowledge of cytology); OR Histological verification of tissue obtained through directed Biopsy indicated by HRA without knowledge of cytology or HR-HPV test when biopsy rate $\geq 50\%$	Cytology or HRA only without histological verification (irrespective of whether there was independent verification of cytology or HRA) OR Histological verification of tissue obtained through directed Biopsy indicated by high resolution anoscopy (HRA) without knowledge of cytology or HR-HPV test when proportion of participants with biopsy $< 50\%$ as this represents a very limited number of verified endpoints
Anal cancer incidence	Histology confirmed, or ICD10 clinic records verified by histology	ICD10 clinic records	No information

- 2) Independent verification of outcome; Relevant for outcomes of ASCUS-AIN1+ or HSIL-AIN2+ prevalence, incidence, recurrence or regression only :
 - score “1” if outcome classification is independently verified by a second, or series of, pathologist(s) by consensus review (for histology measures only), or if p16 staining was used for grading of biopsies.
 - score “0” if outcome classification is not independently verified, or no information given
- 3) Duration of follow-up was long enough for outcomes to occur
 - Score “1” if median duration of follow-up was ≥ 3 months (HR-HPV incidence or persistence); ≥ 12 months (ASCUS-AIN1+ and HSIL-AIN2+ outcomes); ≥ 5 years (anal cancer incidence).
 - Score “0” if less than above, or if retrospective or case-control study
 -
- 4) Adequacy of follow up of cohorts (anal cancer incidence studies only)
 - score “1” if loss to follow up is $\leq 20\%$ and full description of participants lost to follow-up, either in flowchart, or in table of descriptive characteristics
 - score “0” if loss to follow up is $> 20\%$ or case-control study/retrospective study and/or no information given

Supplementary Table 1. Summary characteristics of studies included for each outcome

		All ¹		Any HPV prevalence		HR-HPV prevalence		HPV16 prevalence		ASCUS-SIL prevalence		HSIL-AIN2+ prevalence		Anal cancer incidence	
		N	N PLHIV	N	N	N	N	N	N	N	N PLHIV	N	N PLHIV	N	N PLHIV
		pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV
Gender and sexual orientation	All	130	417 006	13	2 968	29	7 750	9	2 539	37	8 790	23	8 400	17	380 231
	Women	25	5 221	4	550	5	732	2	354	10	2 813	5	1 177	0	-
	MSM	57	33 888	4	1 373	15	4 197	6	1 962	12	3 112	13	4 733	3	11 388
	MSW	7	1 084	2	400	0	-	0	-	4	636	0	-	0	-
	Combination men	16	82 164	1	119	6	1 944	0	-	7	1 542	1	147	3	78 623
Geographic region	Combination women and men	25	294 649	2	526	3	877	1	223	4	687	4	2 343	11	290 220
	Africa	4	930	2	426	1	200	0	-	1	304	1	200	0	-
	Asia	20	4 000	3	517	9	1 681	3	539	6	1 527	1	148	0	-
	Latin America	10	2 838	2	433	4	1 170	3	993	4	1 235	0	-	0	-
	Europe	41	224 135	0	-	9	3 219	3	1 007	14	3 502	9	3 718	6	212 593
Study design	North America	53	184 799	6	1 592	6	1 480	0	-	12	2 222	11	4 182	11	167 638
	Australia	2	304	0	-	0	-	0	-	0	-	1	152	0	-
	Randomised controlled trial ²	3	851	0	-	0	-	0	-	0	-	1	575	0	-
	Prospective cohort	25	289 783	0	-	0	-	0	-	0	-	0	-	11	287 055
	Cross-sectional ³	84	23 077	11	2 455	27	7 283	8	2 493	34	7 717	19	7 122	0	-
	Record linkage	2	15 901	0	-	0	-	0	-	0	-	0	-	2	15 901
	Retrospective cohort or chart review	11	86 060	0	-	0	-	0	-	3	1 073	3	703	3	76 921
	Case-control or convenience	5	1 334	2	513	2	467	1	46	0	-	0	-	1	354

		HR-HPV incidence		HR-HPV persistence		ASCUS-AIN1+ incidence		HSIL-AIN2+ incidence		HSIL-AIN2+ clearance following treatment		HSIL-AIN2+ recurrence following treatment		HSIL-AIN2+ spontaneous regression	
		N	N PLHIV	N	N	N	N	N	N	N	N PLHIV	N	N PLHIV	N	N PLHIV
		pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV	pop.	PLHIV
Gender and sexual orientation	All	2	1 345	4	1 444	5	562	5	898	3	7 487	1	100	2	261
	Women	0	-	0	-	2	149	0	-	0	-	0	-	0	-
	MSM	1	612	3	1 140	1	132	5	898	2	7 367	1	100	1	152
	MSW	0	-	1	304	1	48	0	-	0	-	0	-	0	-
	Combination men	1	733	0	-	0	-	0	-	0	-	0	-	0	-
Geographic region	Combination women and men	0	-	0	-	1	233	0	-	1	120	0	-	1	109
	Africa	0	-	1	304	0	-	0	-	0	-	0	-	0	-
	Asia	0	-	1	123	0	-	1	123	0	-	0	-	0	-
	Latin America	0	-	0	-	0	-	0	-	0	-	0	-	0	-
	Europe	2	1 345	2	1 017	1	233	1	310	1	156	1	100	0	-
Study design	North America	0	-	0	-	4	329	2	313	2	7 331	0	-	1	109
	Australia	0	-	0	-	0	-	1	152	0	-	0	-	1	152
	Randomised controlled trial ²	0	-	0	-	0	-	0	-	2	276	0	-	0	-
	Prospective cohort	2	1 345	4	1444	5	562	4	746	0	-	1	100	1	109
	Cross-sectional ³	0	-	0	-	0	-	0	-	0	-	0	-	0	-
	Record linkage	0	-	0	-	0	-	0	-	0	-	0	-	0	-
Retrospective cohort or chart review	0	-	0	-	0	-	1	152	1	7211	0	-	1	152	
Case-control or convenience	0	-	0	-	0	-	0	-	0	-	0	-	0	-	

¹all study populations combined – of a total of 122 studies included, there were 130 discrete populations; ²three randomised controlled trials designed to evaluate the efficacy of: the quadrivalent HPV vaccine (baseline HSIL status in total cohort in the study) in⁽²⁾; efficacy of imiquimod, topical fluorouracil, and electrocautery for the treatment of AIN (estimate used in this meta-analysis is among total cohort and adjusted for treatment type in⁽³⁾) and efficacy of ablation with infrared coagulation (treatment) or no treatment (active monitoring)⁽⁴⁾; ³can include point prevalence estimate from prospective cohort studies; Studies in the category “combination men” included men only but did not provide effect estimates stratified by sexual orientation; studies in the category “combination women and men” included a combination of women and men but did not provide effect estimates stratified by gender or sexual orientation; N. pop=Number of populations studied; HR=high-risk; ASCUS-AIN1+=atypical squamous cells of undetermined significance or anal intraepithelial neoplasia, grade 1 or greater; HSIL-AIN2+=high-grade squamous intraepithelial lesions or anal intraepithelial neoplasia, grade 2 or greater; MSM=men who have sex with men; MSW=men who have sex with women, PLHIV=people living with HIV

Supplementary Table 2. Pooled prevalence of ART, undetectable HIV PVL, HR-HPV and anal lesion outcomes, by gender and sexual orientation¹

	All		Africa		Asia		Latin America		Europe		North America		Australia	
	N ²	Pooled estimate (%; 95%CI)	N ²	Pooled estimate (%; 95%CI)	N ²	Pooled estimate (%; 95%CI)	N ²	Pooled estimate (%; 95%CI)	N ²	Pooled estimate (%; 95%CI)	N ²	Pooled estimate (%; 95%CI)	N ²	Pooled estimate (%; 95%CI)
Women														
Taking ART	19	77.9 (72.6-83.2)	1	96.5 (92.9-98.6)	4	74.7 (57.7-91.7)	3	69.7 (43.9-95.4)	5	88.8 (82.1-95.5)	6	70.3 (60.3-80.3)	0	-
Undetectable HIV PVL ³	13	71.2 (63.0-79.4)	1	83.0 (77.1-87.9)	0	-	2	54.4 (51.3-57.5)	4	73.7 (59.8-87.6)	6	72.0 (63.9-80.1)	0	-
Ever practiced RAI	17	34.6 (21.9-47.3)	0	-	3	2.8 (-0.4-6.0)	3	56.9 (38.2-75.7)	3	28.0 (16.5-39.6)	8	40.5 (30.7-50.4)	0	-
HR-HPV prevalence	7	43.8 (38.2-49.4)	1	41.2 (34.2-48.4)	3	37.4 (21.3-53.6)	1	49.0 (40.5-57.4)	2	48.0 (43.1-52.9)	0	-	0	-
ASCUS-AIN1+ prevalence	13	18.3 (11.4-25.2)	0	-	2	2.7 (1.6-3.7)	2	26.4 (23.8-29.1)	3	15.2 (4.4-26.1)	6	25.5 (18.1-33.0)	0	-
HSIL-AIN2+ prevalence	5	13.7 (9.1-18.4)	1	15.6 (10.8-21.4)	0	-	0	-	1	12.9 (8.2-19.0)	3	13.6 (6.6-20.6)	0	-
Men who have sex with men														
Taking ART	45	74.7 (70.4-78.9)	0	-	10	53.3 (30.3-76.2)	3	88.1 (74.9-1.01)	21	78.4 (69.1-87.7)	10	81.6 (70.3-92.8)	1	93.6 (89.6-96.5)
Undetectable HIV PVL ³	38	67.0 (60.1-73.9)	0	-	8	46.1 (15.4-76.8)	2	73.0 (69.9-76.0)	16	76.0 (70.9-81.0)	10	65.5 (52.6-78.3)	2	84.8 (82.0-87.6)
Reported recent RAI (≤12 months)	18	60.4 (51.5-69.0)	0	-	6	64.4 (55.6-73.1)	1	49.3 (44.6-54.1)	6	72.2 (67.6-76.9)	5	43.8 (35.8-51.8)	0	-
HR-HPV prevalence	23	69.0 (63.7-74.4)	0	-	7	63.5 (47.9-79.1)	4	69.3 (54.5-84.1)	6	74.9 (68.9-80.9)	6	68.9 (60.3-77.6)	0	-
ASCUS-AIN1+ prevalence	14	38.0 (29.4-46.6)	0	-	3	32.7 (27.9-37.5)	0	-	9	37.0 (24.7-49.2)	2	47.3 (44.3-50.4)	0	-
HSIL-AIN2+ prevalence	12	30.5 (22.8-38.2)	0	-	1	57.3 (48.3-65.9)	0	-	6	21.7 (13.6-29.8)	4	33.5 (13.0-54.0)	1	47.3 (40.5-54.1)
Men who have sex with women														
Taking ART	6	79.7 (71.8-87.5)	1	64.8 (59.1-70.2)	0	-	0	-	1	80.1 (74.1-86.0)	3	84.2 (79.6-88.8)	0	-
Undetectable HIV PVL ³	6	62.5 (47.0-77.9)	1	54.3 (47.1-61.4)	0	-	0	-	2	48.2 (41.2-55.1)	3	78.1 (66.6-89.7)	0	-
Ever practiced RAI	5	6.8 (2.2-11.4)	1	4.9 (2.8-8.0)	0	-	0	-	1	0.0 (-)	3	11.0 (7.0-15.0)	0	-
HR-HPV prevalence	8	28.6 (19.6-37.7)	0	-	3	27.9 (18.3-37.5)	2	13.0 (7.0-19.0)	1	33.3 (26.8-40.4)	2	38.8 (25.1-52.5)	0	-
ASCUS-AIN1+ prevalence	6	23.6 (7.6-39.6)	1	49.0 (43.3-54.8)	1	2.1 (0.1-11.1)	0	-	3	23.5 (5.4-41.6)	1	19.6 (12.0-29.1)	0	-
HSIL-AIN2+ prevalence	1	4.1 (1.9-7.7)	0	-	0	-	0	-	0	-	1	4.1 (1.9-7.7)	0	-

¹Pooled (unadjusted) prevalence calculated using metaprop in Stata version 16; ²number of individual populations studied; ³calculated among all participants irrespective of ART use (few studies calculate among ART users only); AIN=anal intraepithelial neoplasia; ART=antiretroviral therapy; ASCUS=atypical squamous cells of undetermined significance; HSIL=high-grade squamous intraepithelial lesion; PVL=plasma viral load; RAI=receptive anal intercourse

Supplementary Table 3. Summary of studies reporting the association of ART use, HIV viral load and CD4+ count with HR-HPV, anal lesion outcomes and invasive anal cancer incidence

Study, Year	Study no.	Location	Population	Study period	Total sample	Mean or Median age, years [IQR]	ART users (%)	Undetectable PVL ¹ (%)	Median CD4+ (cells/ μ L, IQR) at enrolment	Outcome		
										Definition	Prevalence	Diagnostic method
<i>HPV prevalence</i>												
Goeieman et al, 2017 ⁽⁵⁾	A1	South Africa-Johannesburg	Women	NK	200	38 (33-44)	97.0%	89.0%	430 (311-600)	HR-HPV (13 HR types) ²	43.0%	Hybrid Capture II
Heard et al, 2016 ⁽⁶⁾	A2	France-Paris, Marseille, Colombes	Women	2007-2012	308	45 (40-50)	96.8%	84.1%	612 (450, 802)	HR-HPV (13 HR types)	46.6%	Linear Array
Menezes et al, 2016 ⁽⁷⁾	A3	India-Chennai	Women	2011	50	33 (20-45)	48.0%	NR	425 (range: 106-1229)	HR-HPV (13 HR types)	47.8%	PCR
Sohn et al, 2018 ⁽⁸⁾	A43	Thailand & Vietnam	Perinatally infected females	2013-2015	93	19 (17-20)	94%	62%	593 (392-808)	HR-HPV (13 HR types)	41.9%	Linear Array
Hidalgo-Tenorio et al, 2018 ⁽⁹⁾	A46	Spain-Granada	Women	2012-2016	85	44 (\pm 8)	93.7%	82.4%	646 (\pm 372)	HR-HPV (13 HR types) + HPV26, 53, 66, 73, 82	49.4%	Linear Array
Godbole et al, 2014 ⁽¹⁰⁾	A4	India-Pune	Women	2012-2013	98	35 (30, 38)	64.3%	NR	488 (365, 617) among ART users	Any HPV (37 types)	14.3%	Linear Array
Kojic et al, 2011 ⁽¹¹⁾	A5	USA- 4 cities	Women	2004-2006	120	38 (31-44)	77%	87%	445 (323-598)	Any HPV (37 types)	90.0%	Linear Array
Palefsky et al, 2001 ⁽¹²⁾	A7	USA-San Francisco	Women	1995-1997	223	40 (20-61)	NR (monotherapy only)	42.1%	44% with CD4+ 2001-500	Any HPV (29 types: 6, 11, 16, 18, 26, 31, 32, 33, 35, 39, 40, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 66, 68, 69, 70, 73, AE2, Pap 155, and Pap 291, HPV 2, 13, 34, 42, 57, 62, 64, 67, 72, and W13B).	76.2%	PCR
Volpini et al, 2017 ⁽¹³⁾	A8	Brazil-Vitória	Women	2013-2015	109	41 (\pm 10)	81.6%	64.2%	NR	Any HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59, 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, 89, HPV 2a, 3, 7, 10, 27, 28, 29, 30, 32, 34, 55, 57, 62, 67, 69, 71, 74, 77, 83, 84, 85, 86, 87, 90, 91, 26, 53, 66, 68, 73, 82)	60.3%	PCR (56 types)
Combes et al, 2018 ⁽¹⁴⁾	A10	France-6 cities	MSM	2014-2016	452	51 (IQR:45-56)	95.6%	89.6% ³	685 (507-892)	HR-HPV (13 HR types) + HPV66	70.0%	Cobas4800 and PapilloCheck
Del Amo et al, 2013 ⁽¹⁵⁾	A11	Spain-8 cities	MSM	2007-2013	586	34.9 (30.1-40.8)	25%	NK	532 (IQR, 403-701)	HR-HPV (13 HR types)	83.4%	Linear Array
Gianella et al, 2016 ⁽¹⁶⁾	A12	USA-California	MSM	NK	120	47 (39-52)	100%	84.0%		HR-HPV (13 HR types) + HPV66	45.0%	Aptima HPV Assay (mRNA from E6/E7)
Hidalgo-Tenorio et al, 2017 ⁽¹⁷⁾	A13	Spain Granada	MSM	2010-2016	311	36.7	86.2%	73.7%	699 (\pm 508)	HR-HPV (13 HR types) + HPV26, 53, 66, 73, 82	81.3%	Linear Array
Lee et al, 2016 ⁽¹⁸⁾	A14	Korea_Busan	MSM	2014-2015	133	46 (37-56)	100%	88%	605 (486-851)	HR-HPV (13 HR types) + HPV26, 66, 73, 82	47.4%	HPV Genotyping Chip™ Kit
Li et al, 2015 ⁽¹⁹⁾	A15	China-Xi'an	MSM	2014	193	34 (\pm 9)	86.2%	NR	394 (259-517)	HR-HPV (13 HR types) + HPV26, 34, 53, 55, 66, 69, 82, 83	94.8%	Hybrid HPV DNA test (21 HR types)
Limia et al, 2017 ⁽²⁰⁾	A45	Cuba-Havana	MSM	2012	56	35 (range, 20-61 years)	79%	NR	54% with CD4+ 200-500	6 HR types (16, 18, 31, 33, 45, and 58)	89.3%	PCR (6 HR types)
Wiley et al, 2013 ⁽²¹⁾	A21	USA-Baltimore	MSM	2010-2011	579	55 (\pm 9.4)	NR	NR	609 (\pm 282)	HR-HPV (12 HR types: HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59)	68.4%	Linear array
Nyitray et al, 2018 ⁽²²⁾	A16	USA-Houston	MSM	2014-2016	68	Range: 18-29 yrs	NR	NR	NR	HR-HPV (13 HR types)	79.4%	PCR (36 types)

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										Definition	Prevalence	Diagnostic method
Schwartz et al, 2013 ⁽²³⁾	A17	USA-San Francisco	MSM	2009-2010	305	53 (47-60)	93.8%	91%	81% with CD4+ \geq 350cells/mm ³	HR-HPV (13 HR types) + HPV66	79.1%	Cobas 4800
Somia et al, 2018 ⁽²⁴⁾	A18	Indonesia-Jakarta & Bali; Thailand-Bangkok; Malaysia-Kuala Lumpur	MSM	2013-2015	245	36.9 (\pm 9.2)	79.0%	69.4%	433 (317-595)	HR-HPV (13 HR types)	76.6%	Linear array
Torres-Ibarra et al, 2014 ⁽²⁵⁾	A19	Mexico-Mexico City	MSM	2009-2011	446	33 (18-68)	83.4%	58.7%	65% with CD4+ >350 cells/ μ l	HR-HPV (13 HR types)	72.2%	Linear Array
Van Aar et al, 2013 ⁽²⁶⁾	A20	The Netherlands-Amsterdam	MSM	2010-2011	264	46 (39-53)	86.7%	77.3%	530 (410-700)	HR-HPV (12 HR types: HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59)	64.7%	SPF ₁₀ -PCR DEIA/LiPA ₂₅
Van der Snoek et al, 2012 ⁽²⁷⁾	A22	The Netherlands-Rotterdam	MSM	2007-2009	247	47 (40-53)	80.4%	66.8%	490 (358-640)	HR-HPV (13 HR types) + HPV73, 82	76.3%	INNO-LiPA
Cranston et al, 2015 ⁽²⁸⁾	A44	Thailand-Bangkok	MSM	2006-2010	192	25.8 \pm 5.9	47.9%	30.2%	409.8 \pm 177.1	HPV6,11,16,18,31,33,45, 52, 58	50.0%	GP5+/GP6+ PCR
Hernandez et al, 2016 ⁽²⁹⁾	A24	India- Vellore & Mumbai	MSM	2009-2010	300	42% aged 26-35 years	44.4%	35.3%	NR	Any HPV (37 types + 90/106, 86/87)	95%	PCR
Mendez-Martínez et al, 2014 ⁽³⁰⁾	A25	Mexico-Mexico City	MSM	2008	324	39.1 (\pm 9.4)	92.4%	75%	442	Any HPV (28 types: 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82, 6, 11, 40, 43, 44, 54, 70, 69, 71,74)	86.1%	PCR+INNO-LiPA
Palefsky et al, 1998 ⁽³¹⁾	A26	USA-San Francisco	MSM	1991-1994	346	42 (24-64)	NR	NR	38% with CD4+ between 201-500	Any HPV (29 types: 6, 11, 16, 18, 26, 31, 32, 33, 35, 39, 40, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 66, 68, 69, 70, 73, AE2, Pap 155, and Pap 291, HPV 2, 13, 34, 42, 57, 62, 64, 67, 72, and W13B).	92.8%	PCR
Patel et al, 2018 ⁽³²⁾	A27	USA-4 cities	MSM	2004-2012	403	42 (36-48)	78%	74%	454 (312-655)	Any HPV (37 types)	95%	Linear array
Patel et al, 2018 ⁽³²⁾	A27	USA-4 cities	MSW	2004-2012	96	42 (36-48)	81%	75%	379 (237-555)	Any HPV (37 types)	59%	Linear array
Chikandiwa et al, 2017 ⁽³³⁾	A29	South Africa-Johannesburg	MSW (5% MSM)	2012-2013	304	38 (\pm 8)	65%	54%	445 (328-567)	Any HPV (37 types)	73.7%	Linear Array
Liu et al, 2019 ⁽³⁴⁾	A47	China-Taizhou	Combination men (50% MSM)	2016-2017	160	43 (\pm 13)	NR	NR	43% with CD4+ \geq 500 cells/ μ l	HR-HPV (13 HR types) + HPV53, 66	65.0% (MSM); 27.8% (MSW)	HPV GenoArray
Cranston et al, 2012 ⁽³⁵⁾	A30	USA – Los Angeles	Combination men (80% MSM)	2005-2007	316	50% between 40-49 yrs	NR	52.6%	NR	HR-HPV (13 HR types) + HPV73	64.4%	PCR
Guimaraes et al, 2011 ⁽³⁶⁾	A31	Brazil-Rio de Janeiro & Minas Gerais	Combination men (18% MSM only; 59% MSW&M;23% MSW only)	2007	445	78.2% >35 years	89.6%	59.6%	39% with CD4+ \geq 500 cells/ μ l	HR-HPV (12 HR types: HPV16, 18, 31, 33, 39, 45, 51, 52, 56, 58, 59, 66)	11% (MSW only) 51.0% (MSW&M) 58.7% (MSM only)	PCR
Wilkin et al, 2004 ⁽³⁷⁾	A32	USA-New York City	Men 61% MSM, 39% MSW)	2001-2002	92	NR	82%	50%	NR	HR-HPV (13 HR types)	61%	HC-II & PCR
Yu et al, 2013 ⁽³⁸⁾	A33	Taiwan-Tainan	Combination men (66% MSM)	2010-2011	198	73% \geq 30 yrs	82.8%	21.8%	507.8 \pm 258.3	HR-HPV (11 types: 16, 18, 31, 33, 39, 45, 51, 56, 58, 59, and 66)	39.7%	PCR
Tosato-Boldrini et al, 2018 ⁽³⁹⁾	A36	Brazil-Vitoria	Combination (64% Women, 26% MSM, 9% MSW)	2013-2016	223	Women: 41.0 [\pm 10.2]; Men: 40.0 [\pm 12.6]	81.2%	60.1%	80% with CD4+ >350 cells/ μ l	HR-HPV (13 HR types) + HPV26,53,66,73,82	49% (women); 29% (MSW); 63% (MSM)	PGMY09/11, RFLP, RLB
Nagata et al, 2015 ⁽⁴⁰⁾	A37	Japan-Tokyo	Combination (7% women, 86% MSM, 7% MSW)	2009-2015	421	44 (39, 55)	75.1%	62.5%	369 (179, 582)	HR-HPV (13 HR types) + HPV67	19.2% (women); 20.6% (MSW); 75.9% (MSM)	PCR-Invader assay
Borghetti et al, 2014 ⁽⁴¹⁾	A38	Italy-Rome	Combination (81% men, 56% MSM)	NR	233	44 (39-48)	84%	NR	558 (405-718)	HR-HPV (13 HR types)	61.8%	Hybrid Capture II
Videla et al, 2013 ⁽⁴²⁾	A34	Spain-Badalona	Combination men (73% MSM, 27% MSW)	2005-2009	733	MSM: 40 (35-46) MSW:	79% (MSM); 95% MSW	63% (MSM); 72% (MSW)	MSM:517 (392-683);MSW:457 (241-652)	HR-HPV (13 HR types+ HPV6 and 11)	84% (MSM); 42% MSW	IVD-CE F-HPV typing

Study, Year	Study no.	Location	Population	Study period	Total sample	Mean or Median age, years [IQR]	ART users (%)	Undetectable PVL ¹ (%)	Median CD4+ (cells/ μ L, IQR) at enrolment	Outcome		
										Definition	Prevalence	Diagnostic method
Beachler et al, 2013 ⁽⁴³⁾	A35	USA-Baltimore	Combination (39% women, 18% MSM, 43% MSW)	2006 – 2009	404	44 (40-48) 46 (42-51)	67.8%	34.1%	304 (183-502)	Any HPV (37 types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 6, 11, 26, 40, 42, 53, 54, 55, 61, 62, 64, 66, 67, 69, 70, 71, 72, 81, 82, 83, 84, 89, and IS39)	84.0%	PCR
Chinyowa et al, 2018 ⁽⁴⁴⁾	A41	Zimbabwe-Harare	Combination (60% female, 1% MSM)	2014-2015	122	40 (range: 18-69)	95.1%	NR	375 (235-557)	Any HPV (29 types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 6, 11, 26, 32, 40, 53, 54, 55, 61, 69, 70, 73, 82,83,84)	44.3%	PCR
Gautam et al, 2018 ⁽⁴⁵⁾	A42	India-Varanasi	Combination men (38% reported RAI)	2014-2015	119	35 (\pm 8)	41.3%	NR	253	Any HPV (29 types: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82, 26, 53, 66, 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81)	27.7%	PCR
Geskus et al, 2016 ⁽⁴⁶⁾	A39	Spain-multicentre	MSM	2007-2013	612	33 (28-39)	38.9%	NR	569 (444-741)	HR-HPV (12 types: (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59)	11 per 100 p-y (HPV59) to 19 per p-y (HPV51)	Linear Array
HPV persistence												
Geskus et al, 2016 ⁽⁴⁶⁾	A39	Spain-multicentre	MSM	2007-2013	612	33 (28-39)	38.9%	NR	569 (444-741)	HR-HPV (12 types: (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59)	NR	Linear Array
Phanuphak et al, 2013 ⁽⁴⁷⁾	A40	Thailand-Bangkok	MSM	2009-2012	123	29 (\pm 7)	13.0%	9.8%	353 (\pm 146)	HR-HPV (13 HR types)	49.0% over 12 months	Linear Array
Hidalgo-Tenorio et al, 2019 ⁽⁴⁸⁾	A48	Spain-Granada	MSM	2010-2018	279	36 (\pm 10)	87.7%	85.9%	690 (\pm 475)	HR-HPV (13 HR types) + HPV26, 53, 66, 73, 82	65.1% over 49 months	Linear Array
Chikandiwa et al, 2019 ⁽⁴⁹⁾	A49	South Africa-Johannesburg	MSW	2012-2013	304	38 (\pm 8)	65%	54%	445 (328-567)	Any HPV (37 types)	26% over 18 months	Linear array
SIL-AIN prevalence												
Baranoski et al, 2012 ⁽⁵⁰⁾	B1	USA-Boston	Women	2006-2010	99	40 (range: 22-57)	79%	62%	NR	ASCUS-AIN1+	33.3% (cumulative prevalence over 3 years)	Cytology+, HRA+directed Bx (Bx =36%)
Cambou et al, 2015 ⁽⁵¹⁾	B2	Brazil-Rio de Janeiro	Women	2011-2013	863	42 (35-49)	86% ⁶	53.1%	NR	ASCUS+	31%	Cytology
Chaves et al, 2012 ⁽⁵²⁾	B3	Brazil-Porto Alegre	Women	2006-2008	184	36 (\pm 9)	41.0%	NR	NR	ASCUS+	14.1%	Cytology
Conley et al, 2010 ⁽⁵³⁾	B4	US-4 cities	Women	2004-2006	150	39 (32-45)	73.3%	67.3%	36% \geq 500 cells/mm ³	ASCUS+	35.3%	Cytology
Gingelmaier et al, 2010 ⁽⁵⁴⁾	B5	Germany-Munich	Women	2007-2008	104	36 (\pm 12)	99.0%	64.4%	421 (58-1020)	ASCUS-AIN1+	13.5%	Cytology+, HRA+directed Bx (Bx =13%)
Holly et al, 2001 ⁽⁵⁵⁾	B6	USA-San Francisco	Women	1995-1997	196	40 (20-61)	NR (pre cART era)	42.9%	NR	ASCUS-AIN1+	26.0%	Cytology+, HRA+directed Bx (Bx =20%)
Pittyanont et al, 2014 ⁽⁵⁶⁾	B7	Thailand -Chanthaburi	Women	2013-2014	574	55% aged 30-49 yrs	94.2%	NR	NR	ASCUS+	2.2%	Cytology
Sananpanichkul et al, 2015 ⁽⁵⁷⁾	B8	Thailand -Chanthaburi	Women	2013-2014	393	41 \pm 9	NR	NR	40% \geq 500 cells/mm ³	ASCUS+	3.6%	Cytology
Tandon et al, 2010 ⁽⁵⁸⁾	B9	USA-Boston	Women	2006-2007	100	41 (\pm 8)	78.8%	62.0%	NR	ASCUS-AIN1+	17.2%	Cytology+, HRA+directed Bx (Bx =14%)
Abramowitz et al, 2007 ⁽⁵⁹⁾	B10	France-Paris	Women	2003-2004	150	37 (33-42)	67%	55%	410 (288-584)	AIN1+	6.7%	HRA-directed Bx (Bx =11%)

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										Definition	Prevalence	Diagnostic method
Goeieman et al, 2017 ⁽⁵⁾	A1	South Africa-Johannesburg	Women	NK	200	38 (33-44)	97.0%	89.0%	NR	HSIL-AIN2+	17.5%	Cytology+, HRA+directed Bx (Bx =75%)
Gaisa et al, 2017 ⁽⁶⁰⁾	B12	USA-New York	Women	2009-2014	208	47 (41-52)	NR	71.6%	522 (335-773)	HSIL-AIN2+	6.6%	Cytology+, HRA+directed Bx (Bx =80%)
Heard et al, 2015 ⁽⁶¹⁾	B13	France-Paris, Marseille, Colombes	Women	2012	171	47 (37-51)	98.0%	89.0%	655 (476-844)	HSIL-AIN2+	12.9%	HRA+directed Bx (Bx =41%); composite cyto-histology
Hessol et al, 2009 ⁽⁶²⁾	B14	USA-San Francisco, Chicago, and Brooklyn	Women	2001-2003	342	NR (38% between 31-40 years)	NR	NR	NR	HSIL-AIN2+	10.8%	Cytology+, HRA+directed Bx (Bx =9%)
Stier et al, 2019 ⁽⁶³⁾	B49	USA-12 sites	Women	2014-2016	256	49.4 (\pm 8.5)	94.5%	85.2%	664 (444– 881)	HSIL-AIN2+	27.0%	HRA, directed + random biopsy (Bx =100%)
Chikandiwa et al, 2017 ⁽³³⁾	A29	South Africa-Johannesburg	MSW (5% MSM)	2012-2013	304	38 (\pm 8)	65%	54%	445 (328-567)	ASCUS+	49.0%	Cytology
Conley et al, 2010 ⁽⁵³⁾	B4	US-4 cities	MSW	2004-2006	92	42 (38-48)	84.8%	70.7%	34% \geq 500 cells/mm ³	ASCUS+	19.6%	Cytology
Conley et al, 2010 ⁽⁵³⁾	B4	US-4 cities	MSM	2004-2006	379	42 (36-48)	78.9%	71.5%	45% \geq 500 cells/mm ³	ASCUS+	56.5%	Cytology
D'Souza et al, 2016 ⁽⁶⁴⁾	B15	USA-4 cities	MSM	2010-2011	622	55 (49-61)	91%	78%	595 (431-796)	ASCUS+	42.2%	Cytology
Dona et al, 2015 ⁽⁶⁵⁾	B16	Italy-Rome	MSM	2009-2017	388	41 (33-49)	90%	87%	607 (433-800)	ASCUS+	53.2%	Cytology
Goodall et al, 2012 ⁽⁶⁶⁾	B17	UK-Edinburgh	MSM	2006-2007	130	39 (17-68)	80%	NR	503 (87-1201)	Mild dyskaryosis or greater	21.5%	Cytology
Gonzalez et al, 2013 ⁽⁶⁷⁾	B23	Spain – 7 Autonomous Communities	MSM	2007-2011	450	33 (28-39)	16% at study entry	NR	51% $>$ 500 cells/ μ L	LSIL+	54.7%	Cytology
Lacey, 1999 ⁽⁶⁸⁾	B18	UK-Manchester	MSM	1994-1996	57	35 (range 19–62)	0%	NR	273 (range 10–588)	ASCUS+	10.5%	Cytology
Li et al, 2009 ⁽⁶⁹⁾	B19	Thailand-Bangkok	MSM	2007-2008	118	33 (\pm 8)	34.2%	27.8%	342 (216-437)	ASCUS+	33.9%	Cytology
Yang et al, 2012 ⁽⁷⁰⁾	B21	China-Beijing	MSM	2011	93	40% aged 30-39 years	30.5%	NR	73% $<$ 500 cells/ μ l	ASCUS+	37.9%	Cytology
Yaegashi et al, 2017 ⁽⁷¹⁾	A23	Japan-Kanazawa	MSM	2013-2014	148	39 (\pm 8)	100%	98.6%	593 \pm 185	ASC-H+	34.4%	Cytology
Abramowitz et al, 2007 ⁽⁵⁹⁾	B10	France-Paris	MSM	2003-2004	200	41 (36-46)	83%	63%	533 (365-707)	AIN1+	21.0%	HRA-directed Bx (Bx =11%)
Richel et al, 2013 ⁽⁷²⁾	B22	The Netherlands-Amsterdam	MSM	2008-2010	311	47 (41-55)	89%	86%	550 (430-718)	AIN1+	56.3%	HRA-directed Bx (Bx=56%)
Van der Snoek et al, 2012 ⁽²⁷⁾	A22	The Netherlands-Rotterdam	MSM	2007-2009	247	47 (40-53)	80.4%	66.8%	490 (358-640)	AIN1+	16.0%	HRA+directed Bx (Bx=49%)
Clifford et al, 2019 ⁽⁷³⁾	B46	France-6 cities	MSM	2014-2016	502	51 (45-56)	95.8%	92.1%	682 (506-881)	HSIL-AIN2+	10.4%	HRA directed Bx (Bx =45%)
Dalla-Pria et al, 2014 ⁽⁷⁴⁾	B25	UK- London	MSM	NR	368	42 (range: 22-77)	84%	85%	441 (range: 10-1476)	AIN2+	32.0%	HRA-directed Bx (Bx=64%)
Hidalgo-Tenorio et al, 2014 ⁽⁷⁵⁾	B26	Spain-Granada	MSM	2010-2013	140	37 (\pm 9)	77.1%	95.0%	653 (\pm 262)	HSIL-AIN2+	20.0%	Cytology+, HRA+directed & random Bx (Bx =100%)
Hidalgo-Tenorio et al, 2014 ⁽⁷⁶⁾	B27	Spain-Granada	MSM	2010-2014	201	37 (\pm 9)	86.6%	71.1%	725 (\pm 604)	HSIL-AIN2+	18.4%	Cytology+, HRA+directed & random Bx (Bx =100%)
Libois et al, 2017 ⁽⁷⁷⁾	B28	Belgium-Brussels	MSM	2011-2013	320	44 (36-51)	87%	74% $<$ 50c/ml; 54% sustained PVL $<$ 50 c/ml over 2 yrs)	638 (480-800)	HSIL-AIN2+	19.7%	Cytology+, HRA+directed (Bx=38%)
Machalek et al, 2016 ⁽⁷⁸⁾	B29	Australia-Sydney	MSM	2010-2015	152	49 (43-56)	93.6%	89.5%	65% $>$ 500 cells/ μ l	HSIL-AIN2+	47.3%	Cytology+, HRA+directed (Bx=67%); Composite cyto-histology

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										Definition	Prevalence	Diagnostic method
Masia et al, 2019 ⁽⁷⁹⁾	B47	Spain-Alicante	MSM	2013-2017	145	45 (36-53)	100%	86.2% ⁴	557-638	HGAIN	24.1%	HRA + directed biopsy
Marra et al, 2019 ⁽⁸⁰⁾	B48	The Netherlands-Amsterdam	MSM	2010-2011	193	50 (\pm 10)	97.4%	94.3%	681 (\pm 250)	HSIL-AIN2+	25.9%	HRA + directed biopsy (Bx =78%)
Palefsky et al, 2005 ⁽⁸¹⁾	B30	USA-San Francisco	MSM	1998-2000	357	42 (\pm 7)	74.8%	34.3%	47% between 200-500 cells/ μ l	HSIL-AIN2+	51.9%	HRA-directed Bx (Bx=81%); Composite cyto-histology
Salit et al, 2009 ⁽⁸²⁾	B31	Canada-Toronto	MSM	2001-2005	224	44 (38-50)	63.4%	53.1%	381 (231-590)	AIN2-3	33.0%	HRA-directed Bx (Bx =95%)
Schwartz et al, 2013 ⁽²³⁾	A17	USA-San Francisco	MSM	2009-2010	305	53 (47-60)	93.8%	91%	81% with CD4+ \geq 350cells/mm3	AIN2+	29.2%	HRA-directed Bx and composite cyto-histology
Siegenbeek van Heukelom et al, 2017 ⁽⁸³⁾	B32	The Netherlands-Amsterdam	MSM	2008-2015	1678	49 (\pm 10)	96%	89.3%	620 (480-790)	HSIL-AIN2+	29.6%	HRA-directed Bx (Bx =>53%)
Abramowitz et al, 2007 ⁽⁵⁹⁾	B10	France-Paris	MSW	2003-2004	123	42 (37-48)	78%	61%	380 (220-553)	AIN1+	7.3%	HRA-directed Bx (Bx =11%)
Borghetti et al, 2014 ⁽⁴¹⁾	A38	Italy-Rome	Combination (81% men, 56% MSM)	NR	233	44 (39-48)	84%	NR	558 (405-718)	ASCUS+	11.1%	Cytology
Cheng et al, 2014 ⁽⁸⁴⁾	B33	Taiwan -Taoyuan	Combination men (79% MSM, 21% MSW)	2011	230	33 \pm 8	NR	36.9%	NR	ASCUS+	23%	Cytology
Gautam et al, 2018 ⁽⁴⁵⁾	A42	India-Varanasi	Combination men (38% reported RAI)	2014-2015	95	35 (\pm 8)	41.3%	NR	253	ASCUS+	63.2%	Cytology
Piketty et al, 2003 ⁽⁸⁵⁾	B20	France-Paris	Combination men (51% MSM, 49% IDU)	1999-2000	117	MSM: 39 (27-73) IDU: 38 (28-45)	MSM: 91.0% IDU: 84.0%	MSM: 25.4% IDU: 24.0%	MSM: 324 (8-621) IDU: 263 (4-633)	ASCUS-AIN1+	MSM: 71.6% IDU: 36.0%	Cytology+, HRA-directed Bx (Bx =39%); Composite cyto-histology
Rosa-Cunha et al, 2011 ⁽⁸⁶⁾	B34	USA-Florida	Combination men (40% reporting anal sex)	2006	98	51 (\pm 9)	75.6%	46.6%	404 (241-673)	ASCUS+	53.1%	Cytology
Pereira et al, 2008 ⁽⁸⁷⁾	B35	Brazil -Pernambuco	Combination men (58% MSM, 42% MSW)	2006	60	42	88.3%	75.0%	43% with CD4+ >500 cells/ μ L	SIL-AIN1+	MSM: 34.3% MSW: 8.0%	HRA-directed Bx (Bx =28%)
Rovelli et al, 2017 ⁽⁸⁸⁾	B36	Italy-Milan	Combination men (80% MSM)	NR	875	43 (36-50)	98.3%	81.2%	675 (522-874)	ASCUS+	29.0%	Cytology
Chuang et al, 2016 ⁽⁸⁹⁾	B38	USA-Hawaii	Combination (82% male; no stratification by sexual orientation)	NR	61	50 (\pm 8)	100%	82%	NR	ASCUS+	Women : 9.1% Men : 58.0%	Cytology
Payam et al, 2011 ⁽⁹⁰⁾	B39	USA-Hawaii	Combination (94% men)	NR	68	49 (43-56)	91.2%	88.2%	465 (314-665)	ASCUS-AIN1+	54.4%	Cytology+, HRA-directed Bx (Bx =44%)
Gimenez et al, 2011 ⁽⁹¹⁾	B41	Brazil-Manaus	Combination (no stratification given)	NR	128	NR	44.5%	NR	NR	AIN1+	39.1%	HRA directed biopsy + IQ if no visible lesions
Frank et al, 2018 ⁽⁹²⁾	B37	USA-Atlanta	Combination men (77% MSM)	2013-2015	147	39 (32-48)	96.6%	NR	325 (203-473)	HSIL-AIN2+	61.2%	HRA-directed Bx; (Bx=97%)
Scott et al, 2008 ⁽⁹³⁾	B40	USA-Connecticut	Combination (27% MSM, 28% IDU, 18&MSW, 21% women, 6% unkown)	2002-2004	265	44 (26-77)	75.0%	57.0%	458 (\pm 323)	ASCUS-AIN1+	27.9%	Cytology+, HRA-directed Bx (Bx =2%; composite cyto-histology)
Cranston et al, 2018 ⁽²⁾	B42	USA & Brazil	Combination (18% female, 82% male)	2012-2013	575	Women: 48 (42, 55) Men: 47 (40, 52)	98%	Women:76% Men:85%	Women: 623 (432, 801) Men: 599 (437, 767)	HSIL-AIN2+	32.5%	HRA-directed; Composite cytology-histology
Gaisa et al, 2014 ⁽⁹⁴⁾	B43	USA-New York	Combination: Women (23%), MSM (71%), MSW (6%)	2009-2012	728	Women: 48 (43-52) MSM: 42 (33-49) MSW: 50 (43-54)	97% (Women); 92% (MSM); 98% MSW	81% (Women); 78% (MSM); 78% MSW	Women: 514 MSM: 521 MSW: 449	HSIL-AIN2+	8.1% (Women) 12.5% (MSM); 4.1% MSW	Cytology+, HRA-directed Bx (Bx =82%)
Wilkin et al, 2004 ⁽³⁷⁾	A32	USA-New York City	Men (61% MSM, 39% MSW)	2001-2002	92	NR	82%	50%	NR	LGAIN +HGAIN HSIL+	40.2%	HRA+directed Bx (Bx=40%)
Willeford et al, 2016 ⁽⁹⁵⁾	B44	USA-North Carolina	Combination men (91% MSM, 9% MSW)	2008-2013	348	42 (18-75)	NR	NR	NR	HSIL+	30.1%	Cytology+, HRA+directed Bx
Weis et al, 2011 ⁽⁹⁶⁾	B50	USA-Texas	Combination (30% women, 47% MSM, 23% MSW)	2006-2008	692	41 (14-79)	NR	NR	48% \geq 400 cells/ μ L	HSIL-AIN2+	27.8%	Cytology+, HRA directed biopsy (Bx =35%)

Study, Year	Study no.	Location	Population	Study period	Total sample	Mean or Median age, years [IQR]	ART users (%)	Undetectable PVL ¹ (%)	Median CD4+ (cells/ μ L, IQR) at enrolment	Outcome		
										Definition	Prevalence	Diagnostic method
SIL-AIN incidence												
Conley et al, 2016 ⁽⁹⁷⁾	C1	USA- 4 cities	Women	2004-2012	63	40 (32-48)	74%	79%	545 (377-707)	Normal to ASCUS+	9.4 per 100 PY	Cytology
Durante et al, 2003 ⁽⁹⁸⁾	C2	USA- Connecticut and Massachusetts	Women	1995-1998	86	47% aged 30-39 years	40.7%	NR	26% with CD4+ <200	Normal to ASCUS+	22 per 100 PY	Cytology
Conley et al, 2016 ⁽⁹⁷⁾	C1	USA- 4 cities	MSM	2004-2012	132	44 (38-50)	85%	85%	553 (396-729)	Normal to ASCUS+	17.9 per 100 PY	Cytology
Borghetti et al, 2014 ⁽⁴¹⁾	A38	Italy-Rome	Combination (81% men, 56% MSM)	NR	233	44 (39-48)	84%	NR	558 (405-718)	Normal to ASCUS+	15.4 per 100 PY	Cytology
Conley et al, 2016 ⁽⁹⁷⁾	C1	USA- 4 cities	MSW	2004-2012	48	44 (39-49)	89%	90%	482 (353-608)	Normal to ASCUS+	8.9 per 10 PY	Cytology
Burgos et al, 2015 ⁽⁹⁹⁾	C4	Spain-Barcelona	MSM	2009-2014	310	41 (34-47)	85.0%	73.0%	550 (434-754)	<HGAIN to HGAIN	10.5 per 100 PY	HRA directed, random if ASCUS+ on cytology (Bx =26%)
De Pokomandy et al, 2011 ⁽¹⁰⁰⁾	C5	Canada-Montreal	MSM	2002-2005	147	43 (range: 21-66)	90.0%	56.0%	380 (range: 0-1440)	\leq AIN1 to AIN2-3	12.8 per 1000 person months	HRA directed Bx (Bx =89%)
Palefsky et al, 1998 ⁽¹⁰¹⁾	C3	USA-California	MSM	NR	166	NR	NR	NR	47% with CD4+ <200 cells/ μ l	\leq ASCUS to HSIL+	20% over 2 years	HRA directed Bx; Composite cytology-histology
Phanuphak et al, 2013 ⁽¹⁰²⁾	C6	Thailand-Bangkok	MSM	2009-2010	123	28 (24-33)	13.0%	9.8% (69% of ART users)	343 (248-455)	<HSIL-AIN2/3 to \geq HSIL-AIN2/3	2.61 per 100 PY	HRA directed Bx (Bx =67%)
Tong et al, 2013 ⁽¹⁰³⁾	C7	Australia-Sydney	MSM	2004-2011	152	47 (42-53)	NR but considered 100%	83.5%	500 (357-662)	<HSIL-AIN2/3 (HGAIN) to HSIL-AIN2/3 (HGAIN)	7.4 per 100 PY	HRA directed Bx (Bx =44%)
Anal cancer												
D'Souza et al, 2008 ⁽¹⁰⁴⁾	D1	USA - Baltimore, Chicago, Los Angeles and Pittsburgh (MACS)	MSM	1984-2007	6,972	47.4	NR	NR	NR	Anal & rectal cancers ⁵	69.0 per 100,000 P-Y	Histology report or cancer registry
Duncan et al, 2015 ⁽¹⁰⁵⁾	D2	Canada-British Columbia	MSM	1988-2008	1,691	47 (41-54)	100%	NR	NR	Anal cancer	196 per 100,000 P-Y	British Columbia Cancer and HIV/AIDS Drug Treatment Program registries and Anal Dysplasia Clinic database
Aldersley et al, 2019 ⁽¹⁰⁶⁾	D16	USA-multicentre (MACS)	MSM	1984-2014	2,725	34 (30-40)	51.6%	47.3%	NR	Anal cancer	38 (HBV-); 186 (HBV+) per 100,000 P-Y	MACS public dataset (ICD-0-3), includes histological verification
Barnell et al, 2019	D18	USA-California (KPNC)	Combination (10% women, 20% MW and 70% MSM)	1998-2012	13,552	66% \leq 44 years	49.7%	39.1%	55% with CD4+ \geq 350	Anal cancer	101 per 100,000 P-Y	KPNC cancer registry histologically confirmed
Chiao et al, 2013 ⁽¹⁰⁷⁾	D3	USA - nationwide registry of military veterans (VA-CCR)	Combination men (no stratification by sexual orientation)	1985-2009	45,231	37% aged 40-50 years	63.7%	NR	NR	Squamous cell cancer of the anus	134.4 per 100,000 P-Y	Veterans Affairs Clinica Case registry; ICD-9 codes 154.2 and 154.3.
Crum-Cianflone et al, 2010 ⁽¹⁰⁸⁾	D4	USA - nationwide military veterans (US HIV Natural History study)	Combination men (no stratification by sexual orientation)	1985-2008	4,506	42 (33-47)	45.5%	Median log ₁₀ copies/ml: 3.0 (1.4-4.4)	432 (282-509)	Anal cancer	61.9 per 100,000 P-Y	Histology confirmed
Mbang et al, 2015 ⁽¹⁰⁹⁾	D5	USA - nationwide registry of military veterans (VA-CCR)	Men (no stratification by sexual orientation)	1985-2010	28,886	44 (37-51)	100%	58% with PVL<500 c/ml more than 40% of the time	56% with CD4+ >350 cells/ μ l	Squamous cell carcinoma of the anus	138.0 per 100,000 P-Y	Veterans Affairs HIV registry; ICD-9 codes 154.2 and 154.3
Bertisch et al, 2013 ⁽¹¹⁰⁾	D6	Switzerland (Swiss HIV cohort study)	Women (15%), MSM (73%), MSW (12%)	1988-2011	354	NR	88.1%	NR	NR	Anal cancer	59 anal cancer cases	Swiss HIV Cohort Study/Swiss cantonal cancer registries
Bruyand et al, 2015 ⁽¹¹¹⁾	D7	Europe, Australia & USA -11 cohorts (D:A:D study)	Women (27%), MSM (44%), Other, including MSW&IDU (29%)	2004-2012	41,762	39 (33-46)	89.7%	Median log ₁₀ copies/ml: 2.3 (1.7-4.3)	433 (281-620)	Anal cancer	50.0 per 100,000 P-Y	D:A:D study records
Cachay et al, 2014 ⁽¹¹²⁾	D8	USA-San Diego	Women (11%), MSM (78%), MSW (11%)	2001-2012	2,804	40 (34-46)	74.2%	47.3%	384 (217-572)	Anal cancer	23 anal cancer cases (1.7% over 5 years)	Linkage of cytology database and UCSD Cancer registry, verified by histopathology

Study, Year	Study no.	Location	Population	Study period	Total sample	Mean or Median age, years [IQR]	ART users (%)	Undetectable PVL ¹ (%)	Median CD4+ (cells/ μ L, IQR) at enrolment	Outcome		
										Definition	Prevalence	Diagnostic method
Chao et al, 2012 ⁽¹¹³⁾	D9	USA-California (KPSC & KPNC)	Combination (90% male, 62% MSM)	1996-2008	12,872	40 (\pm 9.8)	21.1%	Median: 50,927 (\pm 103,656)	364 (\pm 279)	Anal cancer	90.3 per 100,000 P-Y	KPNC and KPSC HIV and cancerregistries; ICD-9
Guiguet et al, 2009 ⁽¹¹⁴⁾	D10	France-62 University Hospitals (FHDH-ANRS CO4)	Combination (32% MSM, 14% IDU, 27% other men, 28% women)	1998-2006	52,278	45% aged 30-39 years	16.8% at study entry, 73% during whole study period	16.9% at study entry, 50% during whole study period	325 (177-491)	Anal cancer	30.0 per 100,000 P-Y	ICD10 clinic records
Hessol et al, 2007 ⁽¹¹⁵⁾	D11	USA -California	Combination -persons with AIDS (95% male, 88% MSM, 9% IDU)	1990-2000	14,210	44% aged 35-45 years	2.8% taking HAART prior to AIDS diagnosis	NR	65% <200 cells/ μ L at AIDS diagnosis	Anal cancer	134 per 100,000 P-Y	San Francisco AIDS surveillance registry matched with California Cancer Registry; ICD10 clinic records
Piketty et al, 2008 ⁽¹¹⁶⁾	D12	France-62 University Hospitals (FHDH-ANRS CO4)	Combination (28% women, 35% MSM, 37% other men)	1992-2004	86,322	34.2 (29.3-41.0)	60.6%	NR	NR	Anal cancer	28.3 per 100,000 P-Y	ICD10 clinic records validated with histology
Powles et al, 2008 ⁽¹¹⁷⁾	D13	UK-London (Chelsea and Westminster HIV cohort)	Combination (90% male)	1983-2007	11,112	33 (\pm 9)	45.7%	NR	Nadir: 157 (IQR: 33-315)	Anal cancer	122 per 100,000 P-Y	Cancer registries (checked by HIV oncologist)
Richel et al, 2015	D17	The Netherlands (AIDS Therapy Evaluation in the Netherlands cohort)	Combination (80% male)	1995-2012	20,765	NR	85%	NR	Nadir: 200 (80-314)	Anal cancer	116 (MSM), 44 (MSW), 12 (Women) per 100,000 PY	national observational HIV cohort + verified histopathology
Silverberg et al, 2012 ⁽¹¹⁸⁾	D15	USA and Canada (NA-ACCORD)	Combination (26% women, 55% MSM, 19% other men)	1996-2007	34,189	Women: 36 (30-43) MSM: 38 (33-44) MSW: 40 (35-46)	NR	NR	Women: 336 (155-538) MSM: 320 (140-505) MSW: 225 (65-418)	Anal cancer	Women: 30 per 100,000 P-Y MSM: 131 per 100,000 P-Y MSW: 46 per 100,000 P-Y	Medical records, patient interviews, cancer linkage
Response to treatment												
Burgos et al, 2017 ⁽¹¹⁹⁾	C9	Spain-Barcelona	MSM	2009-2016	100	43 (36-49)	84.0%	69.8%	629 (418-801)	HGAIN recurrence following electrocautery	23.5% per year	HRA directed, random if ASCUS+ on cytology
Cranston et al, 2014 ⁽¹²⁰⁾	C10	USA-Pittsburgh	MSM	2009-2013	7211	48 (25-70)	NR	79.2%	573 (\pm 264)	Clearance: AIN2+ to <AIN2 following trichloroacetic acid ⁷	78.6%	HRA + directed Bx
Richel et al, 2013 ⁽³⁾	C11	The Netherlands-Amsterdam	MSM	2008-2010	156	47	85.1%	80.3%	Median range: 560-590 (according to group)	Clearance following treatment: HGAIN to \leq LGAIN ⁸	38.5%	HRA (Bx=100%)
Goldstone et al, 2019 ⁽⁴⁾	C13	USA-7 sites	Combination (93% male)	2011-2014	120	49 (25-78) IRC arm; 51 (27-67) AM arm	90.0%	64.2%	IRC: 669 (501-816; AM: 620 (514-736)	Clearance: complete index lesion clearance following treatment (IRC) or regression of all index HSILs to \leq LSILs to month 12 (AM)	45.8% (62% in IRC arm and 30% in AM arm)	HRA (Bx=100%)
Spontaneous regression												
Liu et al 2018 ⁽¹²¹⁾	C12	USA-New York	Combination (92% men)	2009-2016	109	47 (24-73)	NR	NR	NR	Regression from LSIL to <LSIL	22.0%	HRA + directed Bx
Tong et al, 2013 ⁽¹⁰³⁾	C7	Australia-Sydney	MSM	2004-2011	101	47 (42-53)	NR but considered 100%	83.5%	500 (357-662)	AIN3 to <AIN3	69.9 per 100 person years	HRA directed Bx

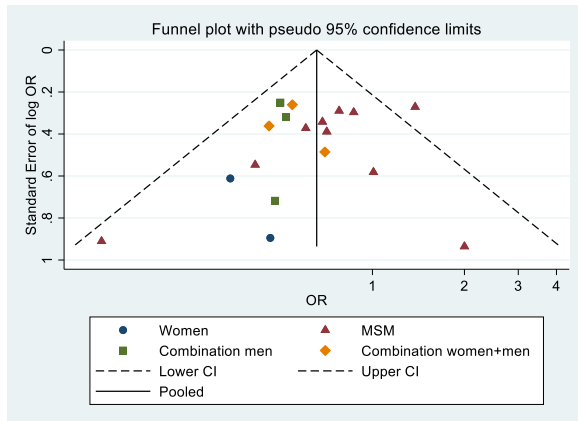
¹Undetectable PVL, irrespective of ART use (<50 copies/ml where available, some studies report undetectable PVL as <400 copies/ml); ²HR-HPV defined according to the 2009 International Agency Research on Cancer classification⁽¹⁰⁾, as those at least "probably carcinogenic to humans" and include HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 (carcinogenic) and 68 (probable carcinogenic); "any HPV" includes combination of high-risk and low-risk types; Linear Array targets 37 different HPV types (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 69, 70, 73, 82, 1539, 6, 11, 40, 42, 54, 55, 61, 62, 64, 71, 72, 81, 83, 84, 89); ³In the meta-analysis, ART defined as effective ART (ART user with undetectable HIV PVL vs. ART users with detectable PVL/ART naïve combined); ⁴Maisa et al presents suppressed HIV PVL (<1000 copies/ml) ⁵14% of all cancers were rectal cancer; ⁶thymidine analogue exposure (no data given for combination ART exposure); ⁷Among 72 men, there were 98 HSIL lesions; the number of lesions was used as denominator in the analyses; ⁸primary outcome was histological resolution of AIN at 4 weeks after end of treatment with either imiquimod, fluorouracil or electrocautery. Complete response was defined as resolution of AIN and partial response defined as regression from HG to LG AIN. Where authors present median values stratified by diseased and non-diseased groups, median value from non-diseased groups is given. MSM=men who have sex with men; MSW=men who have sex with women; NK=not known; PCR=polymerase chain reaction; ASCUS-AIN1=atypical squamous cells of undetermined significance or anal intraepithelial neoplasia, grade 1 or greater; LSIL=low-grade squamous intraepithelial lesion; HSIL-AIN2+=high-grade squamous intraepithelial lesions or anal intraepithelial neoplasia, grade 2 or greater; HGAIN=high-grade anal intraepithelial lesion; ASC-H=atypical squamous cells-cannot exclude high grade squamous intraepithelial lesion; HRA=high resolution anoscopy; HBV=Hepatitis B virus; LBC=liquid based cytology; Bx=biopsy indicates proportion of participants with a biopsy taken; Q=quadrant; IDU=injecting drug users; FHDH-ANRS CO4= French Hospital Database on HIV; p-m=person months; PY=person years; MACS=Multicenter AIDS Cohort Study; KPNC=Kaiser Permanente Northern California; KPSC=Kaiser Permanente Southern California; UCSD=University of San Diego, California; D:A:D study=the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) - a prospective multi-cohort study that focused on the association between antiretroviral drugs and cardiovascular disease, liver and renal disease, and non-AIDS-defining malignancies; VA-CCR=Veterans Administration Clinical Case Registry; ATHENA=AIDS Therapy Evaluation in the Netherlands national observational HIV cohort; NA-ACCORD=North American AIDS Cohort Collaboration on Research and Design; IR=infrared coagulation; AM=active monitoring

Supplementary Table 4. Meta-analysis of association of HIV-related factors and anal HR-HPV prevalence, stratified by gender and sexual orientation and geographic region

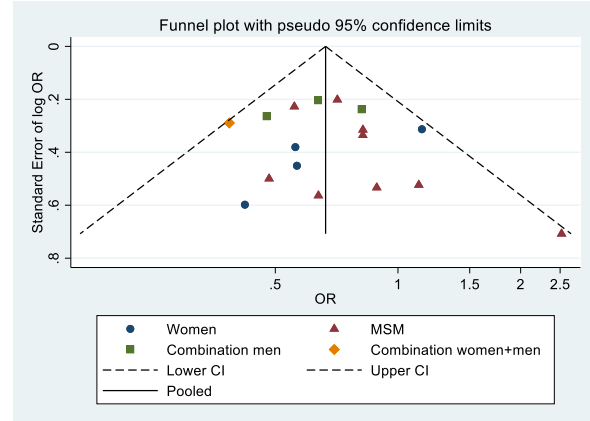
		ART vs. ART-naïve	Undetectable vs detectable HIV PVL	Nadir CD4+ ≥200 vs. <200 cells/μl	Current CD4+ ≥500 vs. <500 cells/μl
All	N studies	18	17	6	8
	Effect estimate (95% CI)	0.65 (0.54-0.79)	0.67 (0.57-0.78)	0.68 (0.40-1.14)	0.72 (0.607-0.87)
	I ²	12.1%	4.0%	58.9%	5.1%
	p for heterogeneity	0.31	0.407	0.033	0.391
By gender and sexual orientation					
Women	N studies	2	4	4	1
	Effect estimate (95% CI)	0.38 (0.14-1.02)	0.71 (0.45-1.11)	0.62 (0.43-0.90)	0.61 (0.38-0.99)
	I ²	0.0%	19.40%	0.0%	-
	p for heterogeneity	0.781	0.293	0.738	-
Men who have sex with men	N studies	10	9	2	3
	Effect estimate (95% CI)	0.79 (0.60-1.05)	0.72 (0.58-0.90)	0.71 (0.13-3.77)	0.79 (0.58-1.06)
	I ²	21.9%	0.0%	84.0%	0.00%
	p for heterogeneity	0.242	0.613	0.013	0.749
Men who have sex with women	N studies	0	0	0	0
	Effect estimate (95% CI)	-	-	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Combination men	N studies	3	3	0	3
	Effect estimate (95% CI)	0.51 (0.35-0.74)	0.64 (0.48-0.84)	-	0.82 (0.54-1.26)
	I ²	0.0%	12.50%	-	0.00%
	p for heterogeneity	0.991	0.319	-	0.899
Combination women and men	N studies	3	1	0	1
	Effect estimate (95% CI)	0.54 (0.37-0.79)	0.39 (0.22-0.68)	-	0.50 (0.29-0.86)
	I ²	0.0%	-	-	-
	p for heterogeneity	0.784	-	-	-
By geographic region					
Africa	N studies	0	1	0	0
	Effect estimate (95% CI)	-	0.56 (0.27-1.18)	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Asia	N studies	5	4	2	3
	Effect estimate (95% CI)	0.58 (0.40-0.84)	0.78 0.53-1.13)	0.40 (0.16-0.99)	0.86 (0.53-1.38)
	I ²	16.1%	0.00%	0.0%	41.4%
	p for heterogeneity	0.312	0.893	0.939	0.181
Latin America	N studies	4	3	0	2
	Effect estimate (95% CI)	0.65 (0.43-0.98)	0.55 (0.42-0.71)	-	0.61 (0.44-0.85)
	I ²	20.9%	1.10%	-	0.00%
	p for heterogeneity	0.285	0.364	-	0.352
Europe	N studies	7	5	4	3
	Effect estimate (95% CI)	0.69 (0.48-0.98)	0.71 (0.50-1.02)	0.78 (0.422-1.43)	0.74 (0.56-0.97)
	I ²	35.9%	35.00%	69.0%	0.00%
	p for heterogeneity	0.154	0.188	0.022	0.52
North America	N studies	2	4	0	0
	Effect estimate (95% CI)	0.75 (0.31-1.82)	0.80 (0.49-1.29)	-	-
	I ²	0.0%	21.40%	-	-
	p for heterogeneity	0.422	0.282	-	-
Australia	N studies	0	0	0	0
	Effect estimate (95% CI)	-	-	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
By Study Design					
Cross-sectional	N studies	16	17	5	8
	Effect estimate (95% CI)	0.68 (0.55-0.84)	0.67 (0.57-0.78)	0.71 (0.41-1.24)	0.72 (0.60-0.87)
	I ²	14.4%	4.0%	64.4%	5.1%
	p for heterogeneity	0.288	0.407	0.024	0.391
Convenience	N studies	2	0	1	0
	Effect estimate (95% CI)	0.51 (0.32-0.82)	-	0.38 (0.08-1.76)	-
	I ²	0.0%	-	-	-
	p for heterogeneity	0.482	-	-	-

Supplementary Figure 1. Funnel plot of publication bias using data from studies on the association of HIV related factors and HR-HPV prevalence

(A) ART vs. ART-naive



(B) Undetectable vs. detectable HIV PVL



Publication bias was not assessed when number of studies was lower than 10.

Supplementary Table 5. Risk of bias assessment of studies evaluating the association of HIV-related factors and anal HR-HPV prevalence

Study	Study ID	Population	Selection			Comparability Adjustment for confounders	Outcome Ascertainment	Total (max=6)	Quality
			Representativeness of the exposed	Selection of the non-exposed	Ascertainment of exposure				
ART vs. ART-naïve									
Menezes, 2016	A3	Women	-	-	*	-	**	3	Low
Hidalgo-Tenorio, 2018	A46	Women	*	*	*	-	*	4	Mid-high
Combes, 2018	A10	MSM	*	*	*	-	**	5	High
Del Amo, 2013	A11	MSM	-	*	-	-	**	3	Low
Cranston, 2015	A44	MSM	-	-	-	-	*	1	Low
Hidalgo-Tenorio, 2017	A13	MSM	*	*	*	-	*	4	Mid-high
Li, 2015	A15	MSM	-	-	-	**	*	3	Low
Schwartz, 2013	A17	MSM	*	-	*	-	**	4	Mid-high
Somia, 2018	A18	MSM	*	*	-	-	**	4	Mid-high
Limia, 2016	A45	MSM	-	-	-	-	*	1	Low
Torres-Ibarra, 2014	A19	MSM	*	-	*	-	**	4	Mid-high
van der Snoek, 2012	A22	MSM	*	*	*	-	*	4	Mid-high
Guimares, 2011	A31	cMen	*	*	*	-	**	5	High
Wilkin, 2004	A32	cMen	-	-	*	**	**	5	High
Videla, 2013	A34	cMen	*	*	*	-	*	4	Mid-high
Boldrini, 2018	A36	Combination	*	*	-	-	*	3	Low
Nagata, 2015	A37	Combination	*	-	-	-	*	2	Low
Borghetti, 2014	A38	Combination	-	*	*	**	*	5	High
Undetectable vs. detectable HIV PVL									
Boldrini, 2018	A36	Combination	*	*	-	-	*	3	Low
Cranston, 2012	A30	cMen	-	*	*	-	*	3	Low
Gianella, 2016	A12	MSM	*	*	*	-	**	5	High
Goeieman, 2017	A1	Women	*	*	-	-	**	4	Mid-high
Guimares, 2011	A31	cMen	*	*	-	-	**	4	Mid-high
Heard, 2016	A2	Women	*	*	*	-	**	5	High
HidalgoTenorio, 2018	A46	Women	*	*	*	-	*	4	Mid-high
Cranston, 2015	A44	MSM	0	*	-	-	*	2	Low
Hidalgo-Tenorio, 2017	A13	MSM	*	*	*	**	*	6	High
Lee, 2011	A14	MSM	*	*	-	-	*	3	Low
Nyitray, 2018	A16	MSM	0	*	*	-	**	4	Mid-high
Schwartz, 2013	A17	MSM	*	*	-	-	**	4	Mid-high
Sohn, 2018	A43	Women	*	*	*	-	*	4	Mid-high
Somia, 2018	A18	MSM	*	*	*	-	**	5	High
Torres-Ibarra, 2014	A19	MSM	*	*	*	-	**	5	High
van Aar, 2013	A20	MSM	*	*	*	**	**	7	High
Videla, 2013	A34	cMen	*	*	*	-	*	4	Mid-high
Nadir CD4+ count ≥200 vs. <200 cells/μl									
Heard, 2016	A2	Women	*	*	*	-	**	5	High
Menezes, 2016	A3	Women	*	*	*	-	**	5	High
Sohn, 2018	A43	Women	*	*	*	-	*	4	Mid-high
Hidalgo-Tenorio, 2018	A46	Women	*	*	*	-	*	4	Mid-high
Hidalgo-Tenorio, 2017	A13	MSM	*	*	*	**	*	6	High
van Aar, 2013	A20	MSM	*	*	*	-	**	5	High
Current CD4+ count ≥500 vs. <500 cells/μl									
Heard, 2016	A2	Women	*	*	*	-	**	5	High

Study	Study ID	Population	Selection			Comparability Adjustment for confounders	Outcome Ascertainment	Total (max=6)	Quality
			Representativeness of the exposed	Selection of the non-exposed	Ascertainment of exposure				
Combes, 2018	A10	MSM	*	*	-	-	**	4	Mid-high
Del Amo, 2013	A11	MSM	-	*	*	-	**	4	Mid-high
Lee, 2011	A14	MSM	*	*	-	-	*	3	Low
Guimaraes, 2011	A31	cMen	*	*	-	-	**	4	Mid-high
Yu, 2013	A33	cMen	-	*	-	-	*	2	Low
Liu, 2019	A47	cMen	-	*	*	-	*	3	Low
Boldrini, 2018	A36	Combination	*	*	-	-	*	3	Low

Refer to page 5 for description of grading system

Supplementary Table 6. Meta-analysis of HIV-related factors and HR-HPV prevalence, ASCUS-AIN1+ and HSIL-AIN2+ prevalence and anal cancer incidence, stratified according to Newcastle-Ottawa quality scoring

	<i>All studies</i>				<i>Studies of mid-high quality</i>				<i>Studies of high quality</i>			
	N studies	Effect estimate ^c (95%CI)	I ²	P	N studies	Effect estimate ^c (95%CI)	I ²	P	N studies	Effect estimate ^c (95%CI)	I ²	P
<i>HR-HPV prevalence</i>												
ART vs. ART naïve	18	0.65 (0.54-0.79)	12.1%	0.310	11	0.62 (0.49-0.78)	0.0%	0.944	4	0.57 (0.38-0.86)	0.0%	0.953
Undetectable vs. detectable HIV PVL	17	0.67 (0.57-0.78)	4.0%	0.407	13	0.66 (0.56-0.79)	0.0%	0.473	6	0.73 (0.58-0.92)	0.0%	0.417
Nadir CD4+ ≥200 vs. <200 cells/μl	6	0.68 (0.40-1.14)	58.9%	0.033	6	0.68 (0.40-1.14)	58.9%	0.033	4	0.68 (0.33-1.40)	71.9%	0.014
Current CD4+ ≥500 vs. <500 cells/μl	8	0.72 (0.60-0.87)	5.1%	0.391	4	0.72 (0.58-0.91)	0.0%	0.707	1	0.61 (0.38-0.99)	-	-
<i>ASCUS-AIN1+ prevalence</i>												
ART vs. ART naïve	28	0.96 (0.74-1.26)	55.4%	<0.001	8	0.92 (0.50-1.71)	73.7%	<0.001	2	0.35 (0.16-0.75)	9.4%	0.293
Undetectable vs. detectable HIV PVL	20	0.73 (0.64-0.83)	0.0%	0.50	9	0.72 (0.53-0.98)	34.2%	0.144	0	-	-	-
Nadir CD4+ ≥200 vs. <200 cells/μl	10	0.52 (0.40-0.67)	0.0%	0.534	1	0.43 (0.18-1.01)	-	-	0	-	-	-
Current CD4+ ≥500 vs. <500 cells/μl ^(7, 15, 16, 19, 37, 39, 40)	11	0.67 (0.48-0.91)	43.4%	0.061	2	0.97 (0.29-3.26)	72.8%	0.055	1	0.59 (0.37-0.92)	-	-
<i>HSIL-AIN2+ prevalence</i>												
ART vs. ART naïve	15	1.18 (0.81-1.73)	48.0%	0.020	12	1.06 (0.70 (1.61)	38.3%	0.085	8	0.83 (0.53-1.28)	30.6%	0.184
Undetectable vs. detectable HIV PVL	16	0.84 (0.72-0.98)	0.0%	0.801	11	0.79 (0.65-0.95)	38.3%	0.085	8	0.78 (0.61-1.00)	30.6%	0.184
^(7-9, 27, 123) Sustained undetectable HIV PVL	4	0.62 (0.41-0.81)	0.0%	0.506	4	0.62 (0.41-0.81)	0.0%	0.506	4	0.62 (0.41-0.81)	0.0%	0.506
Nadir CD4+ ≥200 vs. <200 cells/μl ^(7, 15, 16, 19, 37, 39, 40)	6	0.60 (0.41-0.89)	67.6%	0.009	6	0.60 (0.41-0.89)	67.6%	0.009	3	0.69 (0.42-1.15)	74.2%	0.021
Current CD4+ ≥500 vs. <500 cells/μl	5	0.72 (0.46-1.13)	79.2%	0.001	3	0.71 (0.33-1.52)	75.5%	0.017	2	1.00 (0.57-1.76)	43.4%	0.184
<i>Anal cancer incidence</i>												
ART vs. ART naïve	9	1.34 (0.99-1.81)	0.0%	0.876	8	1.30 (0.96-1.77)	0.0%	0.941	5	1.42 (0.98-2.06)	0.0%	0.895
Per year on ART	2	1.06 (1.01-1.11)	0.0%	0.798	2	1.06 (1.01-1.11)	0.0%	0.798	2	1.06 (1.01-1.11)	0.0%	0.798
Undetectable vs. detectable HIV PVL	3	0.84 (0.56-1.27)	0.0%	0.587	3	0.84 (0.56-1.27)	0.0%	0.587	2	0.90 (0.57-1.42)	0.0%	0.442
Sustained undetectable HIV PVL	2	0.56 (0.44-0.70)	0.0%	0.938	2	0.56 (0.44-0.70)	0.0%	0.938	2	0.56 (0.44-0.70)	0.0%	0.938
Nadir CD4+ ≥200 vs. <200 cells/μl	3	0.33 (0.18-0.60)	0.0%	0.794	2	0.34 (0.16-0.71)	0.0%	0.507	1	0.44 (0.15-1.26)	-	-
Nadir CD4+ per 100 cells/μl increase	2	0.60 (0.46-0.78)	21.7%	0.259								

P for heterogeneity

Supplementary Table 7. Meta-analysis of anal HPV and related-disease outcomes according to HIV-related factors, where number of studies are low

	Crude analysis ¹				Adjusted analysis ²			
	N studies	Effect estimate ³ (95%CI)	I ²	P for heterogeneity	N studies	Effect estimate ³ (95%CI)	I ²	P for heterogeneity
HPV (any) prevalence								
ART vs. ART-naïve ^(10, 29, 33, 44, 45)	5	0.80 (0.54-1.91)	0.0%	0.705	1	1.10 (0.20-5.90)	-	-
HIV-1 PVL undetectable vs. detectable ^(13, 29, 30, 32)	5	0.52 (0.30-0.90)	31.1%	0.214	-	-	-	-
Current CD4+ ≥500 vs. <500 cells/μl ^(11-13, 29, 31)	5	0.39 (0.18-0.84)	65.5%	0.021	-	-	-	-
Current CD4+ ≥500 vs. <200 cells/μl ⁽⁴³⁾	-	-	-	-	1	0.63 (0.48-0.77)	-	-
HR-HPV prevalence								
Adherence 100% vs. <100% ⁽²¹⁾	1	0.86 (0.76-0.97)	-	-	-	-	-	-
HPV16 prevalence								
ART vs. ART-naïve ^(7, 14, 25, 27, 29, 122)	6	0.90 (0.64-1.26)	0.0%	0.96	-	-	-	-
Undetectable vs. detectable HIV PVL ^(6, 29, 30, 122)	4	0.64 (0.43-0.97)	17.9%	0.301	-	-	-	-
Nadir CD4+ ≥200 vs. <200 cells/μl ^(6, 7, 63)	2	0.56 (0.17-1.83)	53.0%	0.145	-	-	-	-
Current CD4+ ≥500 vs. <500 cells/μl ^(6, 14, 29, 122)	4	0.93 (0.68-1.27)	0.0%	0.538	-	-	-	-
HR-HPV incidence								
ART vs. ART-naïve ^(42, 46)	2	0.59 (0.19-1.88)	84.2%	0.012	-	-	-	-
HR-HPV persistence⁵								
ART vs. ART-naïve ^(46, 47)	2	0.82 (0.65-1.02)	0.0%	0.900	-	-	-	-
ART >5 years vs. ≤5 years ⁽⁴⁸⁾	-	-	-	-	1	0.98 (0.97-0.997)	-	-
Per log10 increase HIV PVL ⁽⁴⁷⁾	1	1.05 (0.75-1.47)	-	-	-	-	-	-
Nadir CD4 per 50 cells/μl increase ⁽⁴⁷⁾	-	-	-	-	1	0.85 (0.71-1.03)	-	-
Any HPV persistence⁴								
ART >12 months vs. <6 months ⁽⁴⁹⁾	-	-	-	-	1	0.49 (0.13-1.75)	-	-
Sustained viral suppression ⁽⁴⁹⁾	-	-	-	-	1	0.73 (0.30-1.75)	-	-
ASCUS-AIN1+ prevalence								
Per year on ART ⁽⁷²⁾	-	-	-	-	1	0.92 (0.87-0.97)	-	-
ASCUS-AIN1+ incidence								
ART vs. ART-naïve ^(41, 97, 98)	4	1.15 (0.69-1.92)	0.0%	0.787	1	1.07 (0.40-2.85)	-	-
HIV PVL undetectable vs. detectable ⁽⁹⁷⁾	3	0.69 (0.40-1.17)	0.0%	0.485	-	-	-	-
Nadir CD4+ ≥200 vs. <200 cells/μl ⁽⁹⁷⁾	3	0.73 (0.48-1.10)	0.0%	0.406	-	-	-	-
Current CD4+ ≥500 vs. <500 cells/μl ^(97, 98)	4	0.42 (0.14-1.27)	78.1%	0.003	1	0.24 (0.07-0.85)	-	-
HSIL-AIN2+ prevalence								
≥2 years vs. <2 years/ART-naïve ⁽⁷⁷⁾	1	0.32 (0.16-0.63)	-	-	-	-	-	-
≥5 years vs. <5 years ⁽⁷³⁾	1	0.73 (0.39-1.38)	-	-	-	-	-	-
HSIL-AIN2+ incidence								
ART vs. ART-naïve ⁽⁹⁹⁾	-	-	-	-	1	0.39 (0.21-0.73)	-	-
≥4 years vs. <4 years ART ⁽¹⁰⁰⁾	-	-	-	-	1	0.30 (0.10-0.89)	-	-
HIV PVL undetectable vs. detectable ^(100, 103)	2	0.99 (0.48-2.03)	0.0%	0.745	-	-	-	-
Nadir CD4+ ≥50 vs. <50 cells/μl ⁽¹⁰⁰⁾	-	-	-	-	1	0.09 (0.01-0.84)	-	-
Nadir CD4+ ≥350 vs. <200 cells/μl ⁽¹⁰²⁾	1	0.14 (0.05-0.40)	-	-	0	-	-	-
Current CD4+ ≥500 vs. <500 cells/μl ^(31, 99, 100)	3	0.69 (0.34-1.43)	80.8%	0.006	-	-	-	-
HSIL-AIN2+ clearance following management								
ART vs. ART-naïve ^{5 (4)}	-	-	-	-	1	4.95 (0.77-31.60)	-	-

	Crude analysis ¹				Adjusted analysis ²			
	N studies	Effect estimate ³ (95% CI)	I ²	P for heterogeneity	N studies	Effect estimate ³ (95% CI)	I ²	P for heterogeneity
Per year on ART ⁶ (3)	-	-	-	-	1	1.07 (1.01-1.13)	-	-
HIV viral undetectable vs. detectable ⁽¹²⁰⁾	2	1.17 (0.62-2.21)	0.0%	0.842	-	-	-	-
Current CD4+ ≥500 vs. <500 cells/μl ^(3, 4, 120)	3	1.13 (0.63-2.02)	58.9%	0.088	1	1.58 (0.998-1.13)	-	-
HSIL-AIN2+ recurrence following management								
ART vs. naive ⁽¹¹⁹⁾	1	1.02 (0.96-1.08)	-	-	-	-	-	-
HIV viral undetectable vs. detectable ⁽¹¹⁹⁾	1	0.84 (0.35-2.05)	-	-	-	-	-	-
Nadir CD4+ ≥200 vs. <200 cells/μl ⁽¹¹⁹⁾	-	-	-	-	1	0.38 (0.16-0.94)	-	-
Current CD4+ ≥500 vs. <500 cells/μl ⁽¹¹⁹⁾	1	1.41 (0.74-2.70)	-	-	-	-	-	-
HSIL-AIN2+ spontaneous regression among those not treated								
HIV viral undetectable vs. detectable ^(103, 121)	2	2.17 (0.84-5.57)	0.0%	0.543	-	-	-	-
Anal cancer incidence								
Per year with HIV RNA <100,000 c/ml ⁽¹¹⁴⁾	-	-	-	-	1	0.83 (0.71-0.91)	-	-
Nadir CD4+ ≥110 vs. <100 cells/μl ⁽¹²³⁾	-	-	-	-	1	0.41 (0.26-0.67)	-	-
Per year with current CD4+ >200 cells/μl ⁽¹¹⁴⁾	-	-	-	-	1	0.77 (0.67-0.83)	-	-
Baseline CD4+ ≥350 vs. <350 cells/μl ⁽¹²⁴⁾	-	-	-	-	1	0.46 (0.27-0.79)	-	-
ART started post-1996 vs. pre-1996 ⁽¹⁰⁵⁾	-	-	-	-	1	0.33 (0.16-0.68)	-	-

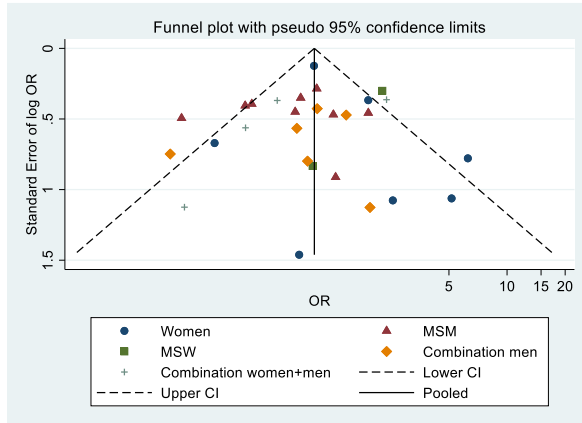
¹includes studies with either 1.) no adjustment and 2.) studies that adjust for sociodemographic factors only but no adjustment for HIV related factors; ²adjusted for at least one of the following: ART status or duration, HIV PVL, current CD4+ cell count; nadir CD4+ cell count, years living with HIV, receptive anal intercourse (RAI); ³Odds Ratio (OR) used for prevalent outcomes, Hazard Ratio (HR) or Rate Ratio (RR) used for prospective outcomes (incidence, progression and regression/recurrence); ⁴ HR-HPV persistence defined as as having the same specific HPV (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) type at 2 consecutive visits (baseline, month 6 (for the first 120 participants), and month 12 visits) in⁽⁴⁷⁾; HR-HPV clearance estimated as time-dependent variable in⁽⁴⁶⁾; i.e. the definition of HR-HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59) clearance includes clearance after an HPV positive visit at study entry (prevalent positive cases) and clearance after an observed new infection (incident positive cases). The authors report that “not using ART was associated with increased clearance rates (AOR=1.23, 95%CI: 0.98-1.55). We thus interpreted the estimate as similar to an increase in HR-HPV persistence among ART users; In⁽⁴⁸⁾, HR-HPV (16, 18, 26, 31, 33, 35, 39, 45, 51–53, 56, 58, 59, 66, 68, 73, and 82) clearance defined as the disappearance of all HR-HPV genotypes from anal canal mucosa in the latest examination, with negative HPV PCR. We inverted the estimate reported (“In the multivariate analysis, ART duration of >5 years was the sole factor favoring oncogenic HPV genotype clearance (OR: 1.016, 95% CI 1.003–1.030)”); i.e ART duration of >5 years was associated with a reduction in HR-HPV persistence (OR=0.98, 95%CI: 0.97-0.997); In⁽⁴⁹⁾, any HPV persistence defined as detection of the same HPV DNA type (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 66, 68, 69, 70, 71, 72, 73, 81, 83, 84) that was detected at enrolment; ⁵adjusted for treatment arm (infrared coagulation vs. no treatment but active monitoring), clinic site of recruitment and number of index; ⁶ including ART-naïve participants as 0 years

Supplementary Table 8. Meta-analysis of association of HIV-related factors and ASCUS-AIN1+ prevalence, stratified by gender and sexual orientation and geographic region

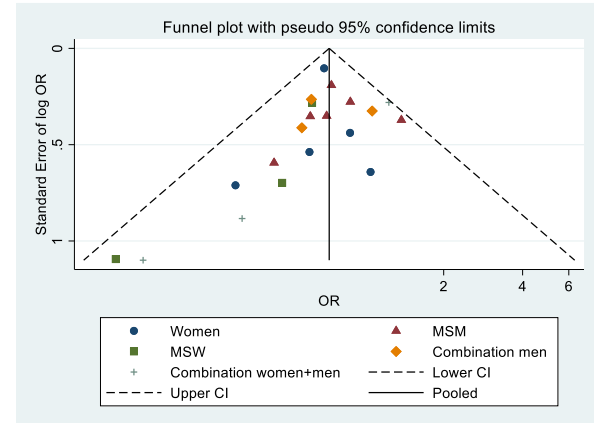
		ART vs. ART-naïve	Undetectable vs detectable HIV PVL	Nadir CD4+ ≥200 vs. <200 cells/μl	Current CD4+ ≥500 vs. <500 cells/μl
All	N studies	28	20	10	11
	Effect estimate (95%CI)	0.96 (0.74-1.26)	0.73 (0.64-0.83)	0.52 (0.40-0.67)	0.67 (0.48-0.91)
	I ²	55.40%	0.00%	0.00%	43.4%
	p for heterogeneity	<0.001	0.495	0.534	0.061
By gender and sexual orientation					
Women	N studies	7	5	4	3
	Effect estimate (95%CI)	1.47 (0.76-2.84)	0.70 (0.58-0.85)	0.46 (0.27-0.79)	0.47 (0.28-0.77)
	I ²	57.90%	0.00%	0.00%	6.50%
	p for heterogeneity	0.027	0.75	0.937	0.343
Men who have sex with men	N studies	9	6	2	4
	Effect estimate (95%CI)	0.75 (0.50-1.14)	0.79 (0.62-0.998)	0.80 (0.47-1.38)	0.73 (0.47-1.14)
	I ²	53.10%	0.00%	34.80%	41.0%
	p for heterogeneity	0.029	0.56	0.216	0.165
Men who have sex with women	N studies	2	3	1	1
	Effect estimate (95%CI)	2.05 (1.18-3.57)	0.52 (0.27-0.99)	0.50 (0.10-2.53)	0.69 (0.22-2.22)
	I ²	0.00%	15.70%	-	-
	p for heterogeneity	0.347	0.306	-	-
Combination men	N studies	6	3	1	3
	Effect estimate (95%CI)	0.90 (0.52-1.56)	0.73 (0.51-1.05)	0.40 (0.21-0.75)	0.82 (0.31-2.17)
	I ²	20.80%	1.70%	-	71.70%
	p for heterogeneity	0.277	0.36	-	0.029
Combination women and men	N studies	4	3	2	0
	Effect estimate (95%CI)	0.77 (0.29-2.01)	0.53 (0.14-2.00)	0.37 (0.22-0.63)	-
	I ²	72.90%	61.40%	0.00%	-
	p for heterogeneity	0.011	0.08	0.739	-
By geographic region					
Africa	N studies	1	1	0	0
	Effect estimate (95%CI)	2.26 (1.25-4.07)	0.63 (0.36-1.10)	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Asia	N studies	4	1	1	3
	Effect estimate (95%CI)	1.32 (0.80-2.18)	1.07 (0.56-2.02)	0.40 (0.21-0.75)	0.79 (0.45-1.39)
	I ²	0.00%	-	-	10.60%
	p for heterogeneity	0.783	-	-	0.327
Latin America	N studies	4	1	0	1
	Effect estimate (95%CI)	1.07 (0.71-1.62)	0.70 (0.57-0.86)	-	2.07 (0.62-6.98)
	I ²	37.70%	-	-	-
	p for heterogeneity	0.186	-	-	-
Europe	N studies	11	10	5	2
	Effect estimate (95%CI)	0.60 (0.42-0.84)	0.71 (0.55-0.93)	0.72 (0.50-1.05)	0.95 (0.66-1.38)
	I ²	13.00%	5.30%	0.00%	0.0%
	p for heterogeneity	0.32	0.392	0.682	0.390
North America	N studies	8	7	4	5
	Effect estimate (95%CI)	1.13 (0.56-2.72)	0.77 (0.57-1.04)	0.39 (0.26-0.58)	0.49 (0.36-0.66)
	I ²	68.70%	11.90%	0.00%	0.00%
	p for heterogeneity	0.002	0.339	0.98	0.507
Australia	N studies	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
By study design					
Cross-sectional	N studies	25	18	10	11
	Effect estimate (95%CI)	1.06 (0.82-1.37)	0.74 (0.65-0.85)	0.52 (0.40-0.67)	0.67 (0.48-0.91)
	I ²	49.8%	0.0%	0.00%	43.4%
	p for heterogeneity	0.003	0.538	0.534	0.061
Retrospective cohort or chart review	N studies	3	2	0	0
	Effect estimate (95%CI)	0.36 (0.13-0.96)	0.44 (0.13-1.51)	-	-
	I ²	44.0%	41.4%	-	-
	p for heterogeneity	0.168	0.191	-	-

Supplementary Figure 2. Funnel plot of publication bias using data from studies on the association of HIV related factors and ASCUS-AIN1+ prevalence

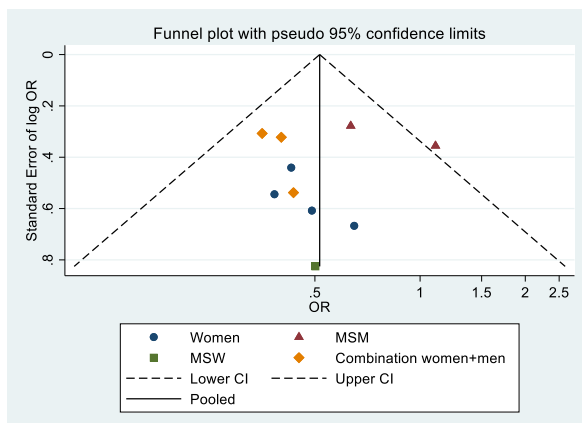
(A) ART vs. ART-naive



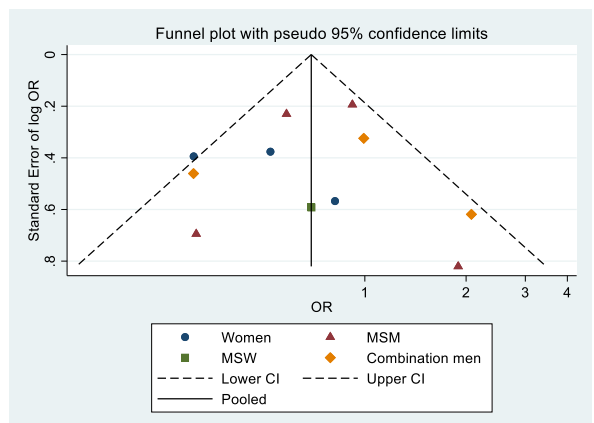
(B) Undetectable vs. detectable HIV PVL



(C) Nadir CD4+ count ≥ 200 vs. < 200 cells/ μ l



(D) Current CD4+ count ≥ 500 vs. < 500 cells/ μ l



There was some evidence to suggest publication bias among studies evaluating the association of undetectable PVL and ASCUS-AIN1+ prevalence (Begg's rank correlation test $p=0.01$ for the crude analysis). There was variation in the study size [range: 50-875] and when excluding one study among 50 male IDU,⁽⁸⁵⁾ the pooled OR among 19 studies was similar (cOR=0.74, 95% CI: 0.65-0.84) with no evidence of publication bias ($p=0.14$).

Supplementary Table 9. Risk of bias assessment of studies evaluating the association of HIV related factors and ASCUS-AIN1+ prevalence

Study	Study ID	Population	Selection			Comparability Adjustment for confounders	Outcome		Total (max=8)	Quality score
			Representativeness of exposed	Selection of non-exposed	Ascertainment of exposure		Ascertainment	Independent verification		
<i>ART vs. ART-naïve</i>										
Abramowitz, 2007	B10	Women	*	-	*	-	-	*	3	Low
Baronoski, 2012	B1	Women	*	-	*	-	*	-	3	Low
Cambou, 2015	B2	Women	-	-	-	-	-	-	0	Low
Chaves, 2012	B3	Women	-	-	-	-	-	-	0	Low
Gingelmaier, 2011	B5	Women	-	*	-	-	*	-	2	Low
Pittyanont, 2014	B7	Women	-	-	-	-	-	-	0	Low
Tandon, 2010	B9	Women	*	-	*	-	*	-	3	Low
Abramowitz, 2007	B10	MSM	*	*	*	-	-	*	4	Mid-high
D'Souza, 2016	B15	MSM	*	*	*	-	-	-	3	Low
Dona, 2018	B16	MSM	*	*	*	-	-	-	3	Low
Goodall, 2012	B17	MSM	*	*	*	-	-	-	3	Low
Li, 2009	B19	MSM	*	-	*	**	-	-	4	Mid-high
Piketty, 2003	B20	MSM	-	-	*	-	*	*	3	Low
Richel, 2013	B22	MSM	*	*	*	-	*	-	4	Mid-high
van der Snoek, 2012	A22	MSM	*	*	*	**	*	-	6	High
Yang, 2012	B21	MSM	-	-	-	-	-	-	0	Low
iAbramowitz, 2007	B10	MSW	*	-	*	-	-	*	3	Low
Chikandiwa, 2018	A29	MSW	*	*	*	*	-	-	4	Mid-high
Pereira, 2008	B35	cMen	*	*	*	-	*	-	4	Mid-high
Piketty, 2003	B20	cMen	-	-	*	-	*	*	3	Low
Rosa-Cunha, 2011	B34	cMen	-	*	-	-	-	-	1	Low
Rovelli, 2017	B36	cMen	*	*	*	-	-	-	3	Low
Wilkin, 2004	A32	cMen	*	-	*	**	*	*	6	High
Gautam, 2018	A42	cMen	*	-	*	-	-	-	2	Low
Gimenez, 2011	B41	Combination	-	-	-	-	**	-	2	Low
Payam, 2011	B39	Combination	*	*	-	-	*	-	3	Low
Scott, 2008	B40	Combination	*	*	*	-	*	-	4	Mid-high
Borghetti, 2014	A38	Combination	*	*	*	-	-	-	3	Low
<i>Undetectable vs. detectable HIV PVL</i>										
Abramowitz, 2007	B10	Women	*	*	*	-	-	*	4	Mid-high
Baronoski, 2012	B1	Women	-	*	*	-	*	-	3	Low
Cambou, 2015	B2	Women	-	*	-	**	-	-	3	Low
Gingelmaier, 2011	B5	Women	-	*	-	-	*	-	2	Low
Tandon, 2010	B9	Women	-	*	*	-	*	-	3	Low
Abramowitz, 2007	B10	MSM	*	*	*	-	-	*	4	Mid-high
D'Souza, 2016	B15	MSM	*	*	*	-	-	-	3	Low
Dona, 2018	B16	MSM	*	*	-	-	-	-	2	Low
Piketty, 2003	B20	MSM	-	*	*	-	*	*	4	Mid-high
Richel, 2013	B22	MSM	*	*	*	-	*	-	4	Mid-high
van der Snoek, 2012	A22	MSM	*	*	*	-	*	-	4	Mid-high
Abramowitz, 2007	B10	MSW	-	*	*	-	-	*	3	Low
Chikandiwa, 2018	A29	MSW	*	*	*	*	-	-	4	Mid-high
Piketty, 2003	B20	IDU	-	*	*	-	*	*	4	Mid-high

Study	Study ID	Population	Selection			Comparability Adjustment for confounders	Outcome		Total (max=8)	Quality score
			Representativeness of exposed	Selection of non-exposed	Ascertainment of exposure		Ascertainment	Independent verification		
Cheng, 2014	B33	cMen	-	*	*	-	-	-	2	Low
Rosa-Cunha, 2011	B34	cMen	-	*	-	-	-	-	1	Low
Rovelli, 2017	B36	cMen	*	*	-	**	-	-	4	Mid-high
Chuang, 2016	B38	Combination	*	*	-	-	-	-	2	Low
Payam, 2011	B39	Combination	*	*	-	-	*	-	3	Low
Scott, 2008	B40	Combination	*	*	*	-	*	-	4	Mid-high
<i>Nadir CD4+ count ≥200 vs. <200 cells/μl</i>										
Abramowitz, 2007	B10	Women	-	*	*	-	-	*	3	Low
Baronoski, 2012	B1	Women	*	*	*	-	*	-	4	Mid-high
Gingelmaier, 2011	B5	Women	-	*	-	-	*	-	2	Low
Tandon, 2010	B9	Women	-	*	*	-	*	-	3	Low
Abramowitz, 2007	B10	MSM	-	*	*	-	-	*	3	Low
Dona, 2018	B16	MSM	*	*	*	-	-	-	3	Low
Abramowitz, 2007	B10	MSW	-	*	*	-	-	*	3	Low
Cheng, 2014	B33	cMen	*	*	*	-	-	-	3	Low
Chuang, 2016	B38	Combination	-	*	-	-	-	-	1	Low
Scott, 2008	B40	Combination	-	*	*	-	*	-	3	Low
<i>Current CD4+ count ≥500 vs. <500 cells/μl</i>										
Conley, 2010	B4	Women	-	*	*	-	-	-	2	Low
Holly, 2001	B6	Women	-	*	*	-	*	-	3	Low
Sananpanichkul, 2015	B8	Women	-	*	-	-	-	-	1	Low
Conley, 2010	B4	MSM	*	*	*	**	-	-	5	High
Lacey, 1999	B18	MSM	-	*	*	-	-	-	2	Low
Yang, 2012	B21	MSM	-	*	-	-	-	-	1	Low
Gonzalez, 2013	B23	MSM	*	*	*	-	-	-	3	Low
Conley, 2010	B4	MSW	-	*	*	-	-	-	2	Low
Cheng, 2014	B33	cMen	-	*	*	-	-	-	2	Low
Pereira, 2008	B35	cMen	*	*	*	-	*	-	4	Mid-high
Rosa-Cunha, 2011	B34	cMen	*	*	-	-	-	-	2	Low

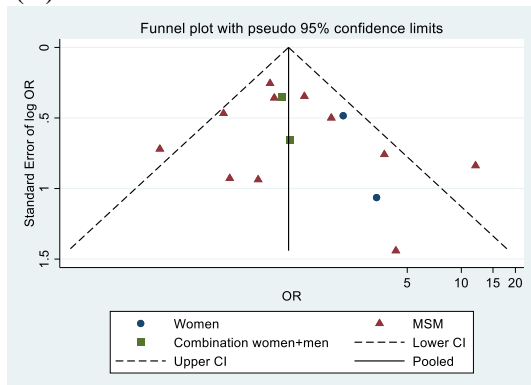
Refer to page 5 for description of grading system

Supplementary Table 10. Meta-analysis of association of HIV-related factors and HSIL-AIN2+ prevalence, stratified by gender and sexual orientation and geographic region

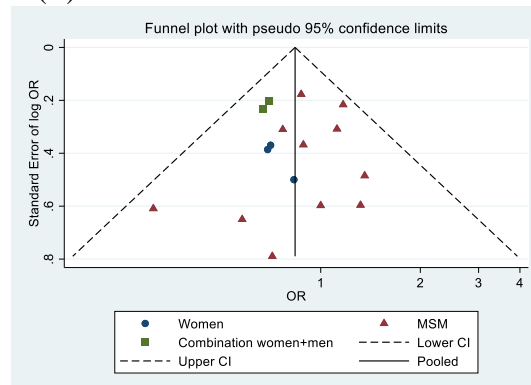
		ART vs. ART-naïve	Undetectable vs detectable HIV PVL	Nadir CD4+ ≥200 vs. <200 cells/μl	Current CD4+ ≥500 vs. <500 cells/μl
All	N studies	15	16	6	5
	Effect estimate (95%CI)	1.18 (0.81-1.73)	0.84 (0.72-0.98)	0.60 (0.41-0.89)	0.72 (0.46-1.13)
	I ²	48.0%	0.00%	67.6%	79.2%
	p for heterogeneity	0.020	0.801	0.009	0.001
By gender and sexual orientation					
Women	N studies	2	3	1	1
	Effect estimate (95%CI)	2.37 (1.00-5.61)	0.73 (0.46-1.15)	0.44 (0.25-0.78)	0.61 (0.23-1.56)
	I ²	0.0%	0.00%	-	-
	p for heterogeneity	0.714	0.954	-	-
Men who have sex with men	N studies	11	11	5	3
	Effect estimate (95%CI)	1.11 (0.68-1.83)	0.94 (0.77-1.14)	0.65 (0.43-0.97)	0.87 (0.53-1.41)
	I ²	57.3%	0.00%	63.6%	71.7%
	p for heterogeneity	0.009	0.741	0.027	0.029
Men who have sex with women	N studies	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Combination men	N studies	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Combination women and men	N studies	2	2	0	1
	Effect estimate (95%CI)	1.02 (0.56-1.88)	0.69 (0.51-0.92)	-	0.51 (0.35-0.74)
	I ²	0.00%	0.00%	-	-
	p for heterogeneity	0.889	0.877	-	-
By geographic region					
Africa	N studies	0	1	0	0
	Effect estimate (95%CI)	-	0.83 (0.31-2.21)	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Asia	N studies	0	0	1	0
	Effect estimate (95%CI)	-	-	0.29 (0.12-0.67)	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Latin America	N studies	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Europe	N studies	8	7	3	2
	Effect estimate (95%CI)	0.88 (0.58-1.33)	0.83 (0.64-1.06)	0.87 (0.67-1.13)	1.00 (0.57-1.76)
	I ²	36.7%	0.00%	20.70%	43.3%
	p for heterogeneity	0.136	0.709	0.283	0.184
North America	N studies	6	7	1	2
	Effect estimate (95%CI)	2.19 (1.08-4.43)	0.85 (0.69-1.05)	0.44 (0.25-0.78)	0.69 (0.37-1.28)
	I ²	49.3%	7.3%	-	78.6%
	p for heterogeneity	0.079	0.373	-	-0.031
Australia	N studies	1	1	1	1
	Effect estimate (95%CI)	0.74 (0.12-4.64)	0.71 (0.15-3.35)	0.54 (0.27-1.09)	0.39 (0.17-0.86)
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
By study design					
Randomised controlled trials	N studies	0	1	0	0
	Effect estimate (95%CI)	-	0.67 (0.42-1.05)	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-
Cross-sectional	N studies	14	14	6	5
	Effect estimate (95%CI)	1.12 (0.80-1.79)	0.87 (0.74-1.03)	0.60 (0.41-0.89)	0.72 (0.46-1.13)
	I ²	51.7%	0.0%	67.6%	79.2%
	p for heterogeneity	0.013	0.780	0.009	0.001
Retrospective cohort or chart review	N studies	1	1	0	0
	Effect estimate (95%CI)	1.11 (0.31-4.01)	0.71 (0.34-1.46)	-	-
	I ²	-	-	-	-
	p for heterogeneity	-	-	-	-

Supplementary Figure 3. Funnel plot of publication bias using data from studies on the association of HIV related factors and HSIL-AIN2+ prevalence

(A) ART vs. ART-naive



(B) Undetectable vs. detectable HIV PVL



Publication bias was not assessed when number of studies was lower than 10.

There was some evidence to suggest publication bias among studies evaluating the association of nadir CD4+ count (≥ 200 cells/ μ l) and HSIL-AIN2+ prevalence (Begg's rank correlation test $p=0.09$ for the crude analysis). One study⁽⁷¹⁾ found a significantly decreased risk of atypical squamous cells cannot exclude HSIL (ASC-H) prevalence with high nadir CD4+ cell count. Removing this study from the analysis resulted in a non-significant association of high nadir CD4+ cell count and HSIL-AIN2+ prevalence (cOR=0.80, 95% CI: 0.60-1.07, I²=31%, $p=0.22$) with no evidence of publication bias ($p=0.174$).

Supplementary Table 11. Risk of bias assessment of studies evaluating the association of HIV related factors and HSIL-AIN1+ prevalence

Study	Study ID	Selection			Comparability	Outcome		Total (max. =8)	Quality score
		Representativeness of exposed	Selection of non-exposed	Ascertainment of exposure		Adjustment for confounders	Ascertainment		
ART vs. ART-naïve									
Hessol, 2009	B14	-	-	*	**	*	-	4	Mid-high
Dalla Pria, 2014	B25	*	*	-	-	*	-	3	Low
Hidalgo-Tenorio, 2014	B26	*	*	*	*	**	-	6	High
Hidalgo-Tenorio, 2015	B27	*	*	*	-	**	-	5	High
Libois, 2017	B28	*	*	*	-	*	*	5	High
Machalek, 2016	B29	*	*	*	-	*	*	5	High
Palefsky, 2005	B30	-	-	-	**	*	-	3	Low
Salit, 2009	B31	-	-	-	-	**	*	3	Low
Schwartz, 2013	A17	*	*	*	-	*	-	4	Mid-high
Siegenbeek van Heukelom, 2017	B32	*	*	*	-	*	*	5	High
Clifford, 2018	B46	*	*	*	-	-	*	4	Mid-high
Gaisa, 2014	B43	*	*	-	**	**	-	6	High
Willeford, 2016	B44	-	-	-	**	*	*	4	Mid-high
Stier, 2019	B49	*	*	*	0	**	*	6	High
Marra, 2019	B48	*	*	*	-	*	*	5	High
Undetectable vs. detectable HIV PVL									
Clifford, 2018	B46	*	*	*	*	-	*	5	High
Cranston, 2018	B42	*	*	-	-	-	-	2	Low
Goeieman, 2017	A1	*	*	-	-	**	*	5	High
Schwartz, 2013	A17	*	*	-	-	*	-	3	Low
Siegenbeek van Heukelom, 2017	B32	*	*	*	-	*	*	5	High
Gaisa, 2017	B12	*	*	-	-	**	-	4	Mid-high
Dalla Pria, 2014	B25	*	*	-	-	*	-	3	Low
Hidalgo-Tenorio, 2015	B27	*	*	*	*	**	-	6	High
Libois, 2017	B28	*	*	*	-	*	*	5	High
Machalek, 2016	B29	*	*	-	*	*	*	5	High
Palefsky, 2005	B30	-	*	*	-	*	-	3	Low
Salit, 2009	B31	-	*	-	-	**	*	4	Mid-high
Gaisa, 2014	B43	*	*	-	-	**	-	4	Mid-high
Masia, 2019	B47	*	*	-	-	-	-	2	Low
Stier, 2019	B49	*	*	*	0	**	*	6	High
Marra, 2019	B48	*	*	*	-	*	*	5	High
Sustained viral suppression									
Clifford, 2018	B46	*	*	*	*	-	*	5	High
Libois, 2017	B28	*	*	*	-	*	*	5	High
Siegenbeek van Heukelom, 2017	B32	*	*	*	**	*	*	7	High
Marra, 2019	B48	*	*	*	-	*	*	5	High
Nadir CD4+ count ≥200 vs. <200 cells/μl									
Libois, 2017	B28	*	*	*	-	*	*	5	High
Machalek, 2016	B29	*	*	-	-	*	*	4	Mid-high
Siegenbeek van Heukelom, 2017	B32	*	*	*	-	*	*	5	High
Yaegashi, 2017	A23	*	*	*	*	-	-	4	Mid-high
Clifford, 2018	B46	*	*	*	-	-	*	4	Mid-high
Stier, 2019	B49	*	*	*	0	**	*	6	High
Current CD4+ count ≥500 vs. <500 cells/μl									

Study	Study ID	Selection			Comparability	Outcome		Total (max. =8)	Quality score
		Representativeness of exposed	Selection of non-exposed	Ascertainment of exposure	Adjustment for confounders	Ascertainment	Independent verification		
Heard, 2015	B13	*	*	*	-	*	*	5	High
Machalek, 2016	B29	*	*	-	-	*	*	4	Mid-high
Palefsky, 2005	B30	-	*	*	-	*	-	3	Low
Siegenbeek van Heukelom, 2017	B32	*	*	*	-	*	*	5	High
Weis, 2011	B50	*	*	-	*	-	-	3	Low

Refer to page 5 for description of grading system

Supplementary Table 12. Meta-analysis of association of HIV-related factors and anal cancer incidence, stratified by gender and sexual orientation and geographic region

		ART vs. ART-naïve	Undetectable vs detectable HIV PVL	Sustained viral suppression	Nadir CD4+ ≥200 vs. <200 cells/μl	Current CD4+ ≥500 vs. <500 cells/μl
All	N studies	9	3	2	3	0
	Effect estimate (95%CI)	1.40 (1.03-1.89)	0.84 (0.56-1.27)	0.56 (0.44-0.70)	0.33 (0.18-0.60)	-
	I ²	0.00%	0.0%	0.00%	0.00%	-
	p for heterogeneity	0.883	0.587	0.938	0.794	-
By gender and sexual orientation						
Women	N studies	0	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
Men who have sex with men	N studies	2	0	0	2	0
	Effect estimate (95%CI)	1.41 (0.61-3.27)	-	-	0.36 (0.17-0.77)	-
	I ²	0.00%	-	-	0.00%	-
	p for heterogeneity	0.874	-	-	0.648	-
Men who have sex with women	N studies	0	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
Combination men	N studies	1	1	1	0	0
	Effect estimate (95%CI)	2.10 (0.55-8.02)	0.64 (0.24-1.71)	0.56 (0.41-0.77)	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
Combination women and men	N studies	6	2	1	1	0
	Effect estimate (95%CI)	1.36 (0.97-1.90)	0.89 (0.57-1.41)	0.55 (0.40-0.76)	0.26 (0.09-0.75)	-
	I ²	0.00%	0.0%	-	-	-
	p for heterogeneity	0.654	0.401	-	-	-
By geographic region						
Africa	N studies	0	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
Asia	N studies	0	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
Latin America	N studies	0	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
Europe	N studies	3	0	0	1	0
	Effect estimate (95%CI)	1.41 (0.77-2.61)	-	-	0.26 (0.09-0.75)	-
	I ²	35.50%	-	-	-	-
	p for heterogeneity	0.212	-	-	-	-
North America	N studies	6	3	2	2	0
	Effect estimate (95%CI)	1.43 (0.94-2.17)	0.84 (0.56-1.27)	0.56 (0.44-0.70)	0.36 (0.17-0.77)	-
	I ²	0.00%	0.0%	0.00%	0.00%	-
	p for heterogeneity	0.989	0.587	0.938	0.648	-
Australia	N studies	0	0	0	0	0
	Effect estimate (95%CI)	-	-	-	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
By study design						
Prospective cohort	N studies	6	2	0	2	0
	Effect estimate (95%CI)	1.32 (0.93-1.87)	0.90 (0.57-1.42)	-	0.34 (0.16-0.71)	-
	I ²	0.0%	0.0%	-	0.0%	-
	p for heterogeneity	0.810	0.442	-	0.507	-
Record linkage	N studies	1	0	0	1	0
	Effect estimate (95%CI)	1.23 (0.62-2.45)	-	-	0.31 (0.11-0.87)	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-
Retrospective cohort or chart review	N studies	1	1	2	0	0
	Effect estimate (95%CI)	1.39 (0.20-9.81)	0.62 (0.24-1.62)	0.56 (0.44-0.70)	-	-
	I ²	-	-	0.00%	-	-
	p for heterogeneity	-	-	0.938	-	-
Case-control	N studies	1	0	0	0	0
	Effect estimate (95%CI)	4.75 (0.60-37.50)	-	-	-	-
	I ²	-	-	-	-	-
	p for heterogeneity	-	-	-	-	-

Supplementary Table 13. Risk of bias assessment of studies evaluating the association of HIV related factors and anal cancer incidence

Study	Study ID	Population	Selection			Comparability	Outcome			Total (max=9)	Quality score
			Representativeness of exposed	Ascertainment of exposure	Outcome not present at baseline		Adjustment for confounders	Ascertainment	Sufficient FU duration		
ART vs. ART-naïve											
Aldersley, 2019	D16	MSM	-	-	-	*	**	*	*	5	Mid-high
D'Souza, 2008	D1	MSM	*	-	-	*	**	*	*	6	High
Crum-Cianflone, 2010	D4	cMen	-	*	*	**	**	*	-	7	High
Powles, 2008	D13	Combination	-	*	-	**	*	*	-	5	Mid-high
Bertisch, 2013	D6	Combination	-	*	*	*	*	-	-	4	Low
Hessol, 2007	D11	Combination	-	*	*	*	*	*	*	6	High
Chao, 2012	D9	Combination	*	*	*	**	*	*	-	7	High
Piketty, 2008	D12	Combination	*	*	*	*	**	*	-	7	High
Cachey, 2015	D8	Combination	*	-	*	-	**	*	-	5	Mid-high
Per year on ART											
Bruyand	D7	Combination	*	-	*	-	**	*	*	6	High
Chao, 2012	D9	Combination	*	*	*	**	*	*	-	7	High
Undetectable vs. detectable HIV PVL											
Cachey, 2015	D8	Combination	*	-	*	-	**	*	-	5	Mid-high
Crum-Cianflone, 2010	D4	cMen	-	*	*	**	**	*	-	7	High
Barnell, 2019	D18	Combination	*	-	*	**	**	*	-	7	High
Sustained undetectable HIV PVL											
Mbang, 2015	D5	cMen	-	*	*	**	*	*	*	7	High
Chiao, 2013	D3	Combination	-	*	*	**	*	*	*	7	High
Nadir CD4+ count ≥200 vs. <200 cells/μl											
D'Souza, 2008	D1	MSM	*	*	-	*	**	*	*	7	High
Duncan, 2015	D2	MSM	-	*	-	-	*	*	-	3	Low
Powles, 2008	D13	Combination	-	*	-	**	*	*	-	5	Mid-high

Refer to page 5 for description of grading system

Supplementary Table 14. Details of included studies

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
HPV studies				
Beachler et al, 2013	Convenience sample of 404 HIV-infected men and women recruited from a clinic at the Johns Hopkins Hospital (JHH) in Baltimore, Maryland, in 2006. Participants were followed semiannually for up to 2 and a half years. Women had higher risk of anal HPV compared to MSM – bias toward high risk women? Medium risk	A physician collected anal samples. Purified DNA was evaluated for the presence of 37 HPV types by use of PGYM09/11 PCR primer pools and reverse line-blot hybridization (Roche Molecular Systems) Low risk	Adjusted for sex, sexual orientation, smoking, number lifetime anal sex partners, number recent receptive anal sex partners, condom use and current and nadir CD4+ Low risk	Anal HPV prevalence associated with younger age, being female, higher number of lifetime anal sex partners and lower current CD4+; Similar for incident HPV infection.
Boldrini et al, 2018	A cross-sectional study of HIV-positive men and women (18±69 years of age) attending a public STI/HIV screening and treatment center in Vitoria, Brazil, from March 2013 to February 2016. Low risk	PGMY09/11, RFLP, RLB. Low risk	None. High risk (no adjustment for sexual behaviour or HIV related factors)	ART use and undetectable PVL associated with decreased risk of HR-HPV prevalence among men and women combined. No data stratified by gender or sexual orientation
Borghetti et al, 2015	Longitudinal, observational study on a cohort of consecutively enrolled, HIV-seropositive patients followed at a single Italian center including HIV-1 infected patients aged 18 years or older. Recruitment procedure unclear. Medium risk	Hybrid Capture II. Low risk	adjusted for CDC stage, AGW and current CD4+. Low risk	Non nucleoside reverse transcriptase inhibitors (NNRTI) users has lower HR-HPV compared to users of Protease Inhibitors.
Chinyowa et al, 2018	Cross-sectional study performed on 152 consecutive patients (88 females; 64 males) attending OIC at Parirenyatwa Group of Hospitals and Harare Central Hospital between November 2014 and June 2015. Eleven patients opted not to be included in this study with the main reason given for refusal being lack of time. 85% of patients enrolled at the centre are on HAART. Low risk	PCR (29 types) Low risk	No adjustment. High risk	
Chikandiwa et al, 2017	Baseline data from men living with HIV enrolled in a prospective cohort study to evaluate the natural history of HPV infection and disease in HIV-infected men in South Africa between October 2012 and August 2013, men in the community or attending HIV clinics were approached and asked to volunteer for the study. Potential participants were screened for eligibility and enrolled if they were willing to provide informed consent, 18 years or older, reported at least one episode of sexual intercourse in the past 3 months and were HIV positive on rapid testing. Low risk	HPV determined by Linear Array.	Crude estimate only	
Chikandiwa, 2019	As for Chikandiwa, 2017 Low risk	HPV determined by Linear Array. Any HPV persistence defined as detection of the same HPV DNA type (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 66, 68, 69, 70, 71, 72, 73, 81, 83, 84=32 types) that was detected at enrolment. Medium risk (any HPV only)	Adjusted for marital status, smoking, alcohol use, age at sexual debut, number of sexual partners	Persistent anal HPV infection was associated with persistent SILs (aOR=2.95; 95%CI: 1.08-10.89).
Combes et al, 2018	HIV-positive MSM aged ≥35 years attending infectious disease units in 6 University Hospitals across France (Dijon, Lyon, Marseille, Montpellier, Paris and Rennes) from December 2014 to June 2016, as part of APACHES study. Subjects were ineligible if they had any of the following: history of anal cancer or pelvic radiotherapy; anal intraepithelial neoplasia (AIN) grades 2/3 treated during the last 12 months; any anticancer chemotherapy during the last 24 months; nonaffiliation with the French social insurance system. Out of 738 participants screened, 575 were enrolled and randomized between March 2012 and August 2013. Low risk	Cobas4800 and PapilloCheck (genotyping), performed at the HPV National Reference Centre at the Pasteur Institute, Paris, France. Detection of non-HR types by PapilloCheck were ignored. Low risk	No adjustment (re-calculated for review). High risk (no adjustment for sexual behaviour or HIV related factors).	ART use was not associated with a reduction in HR-HPV prevalence.
Cranston et al, 2012	Men participating in one of the two waves of data collection (2005–2007) at the Los Angeles site for National Institute on Drug Abuse's Sexual Acquisition and Transmission of HIV - Cooperative Agreement Program (SATH-CAP). The sample for each wave was recruited using Respondent Driven Sampling (RDS). An initial set of 'seeds' who were MSM or drug users were passively recruited via advertisements posted on walls and online, others recruited to the study were either an MSM and/or drug user or was their sexual partner. Low risk	Clinician or self taken internal anal swab, HPV DNA detected using (AmpliQ Gold (Applied Biosystems, Foster City, CA) PCR was performed on purified HPV DNA using MY09/MY11 consensus HPV L1 primers as well as primers for amplification of the human beta-globin. Low risk	Crude estimate only. High risk	having a sex partner who injected drugs was associated with having HR-HPV
Cranston et al, 2015	The Bangkok MSM Cohort study was established in 2006 as part of the US Centers for Disease Control and Prevention (CDC) collaboration with the Thailand Department of Disease Control of the Ministry of Public Health. For the HPV substudy, convenience sample of frozen anal swab specimens obtained between 2006 and 2010 from 200 HIV-infected and 200 HIV-uninfected participants to the University of Pittsburgh for HPV testing. High risk	PCR. Low risk	Crude estimate only. High risk	
Critchlow et al, 1998	Between October 1989 and February 1997, men attending the AIDS Prevention Project of the Seattle King County Department of Public Health, Washington, DC, USA, were recruited into a longitudinal study of HIV infection and anal HPV infection. Of the 910 men enrolled, 287 HIV-seronegative and 322 HIV-seropositive men were seen for at least two visits at which specimens adequate for the detection of anal HPV DNA were obtained. Medium risk (35% loss to follow up)	Anal specimens for assessment of HPV DNA were collected using a dry Dacron swab (Medical Packaging Corp., Camarillo, California, USA), with sampling of both the anal canal and lower rectal mucosa. Low risk	Crude estimate only. High risk	

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
Del Amo et al, 2013	MSM recruited in to the CoRIS study– an open and multicenter cohort established in January 2004 that consists of adult patients with confirmed HIV infection who were naive to cART at study entry. Patients are followed periodically according to routine clinical practice, usually every 4 months at following sites: Granada, Madrid, Seville, Alicante, La Rioja, San Sebastian, Tenerife and Barcelona). Median time since HIV diagnosis was 5 months (IQR: 1-13) and median CD4+ was 532 (403-701) and HIV PVL (15672, 3020-46697). Men were only recently diagnosed with HIV and those not taking ART still have high CD4+. Medium risk (bias towards well controlled HIV/recently HIV infected)	Linear Array Genotyping test at the Retroviruses and Papillomavirus Unit of the National Center for Microbiology in Madrid Low risk	Crude estimate only. High risk.	No association of ART nor CD4+ with decrease risk of HR-HPV
Gautam et al, 2018	Cross-sectional exploratory study was conducted between 2014 and 2015 in HIV positive men attending the ART Center of Banaras Hindu University (BHU) with approximately 15,000 PLHIV registered in it. All HIV positive men above the age of 18, attending the ART centers were eligible for the study. Low risk	PCR (29 types); Low risk	Crude estimate only. High risk.	
Geskus et al, 2016	MSM recruited in to the CoRIS study (as in Del Amo, 2013). Of 1476 HIV-positive MSM within CoRIS-HPV, 612 had at least two visits; characteristics of these 612 men did not differ substantially from the other 864. Low risk	Anal HR-HPV determined through the Linear Array HPV Genotyping test. HR-HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59=12 types) <u>clearance</u> defined as time-dependent variable; i.e. the definition of HR-HPV clearance includes clearance after an HPV positive visit at study entry (prevalent positive cases) and clearance after an observed new infection (incident positive cases). The authors report that “not using ART was associated with increased clearance rates (AOR=1.23, 95%CI: 0.98-1.55). We thus interpreted the estimate as similar to an increase in HR-HPV persistence among ART users. Incidence and clearance rates estimated using a two-stage Markov model that allowed for interval censored event data. Authors report associations of HIV related factors and HPV clearance; in the review the estimates are inverted for outcome of persistence. Low risk	Age, HIV viral load, university education and asymptomatic CDC stage	Age and HIV-RNA viral load had a statistically significant effect on HR-HPV clearance
Gianella et al, 2016	Participants prospectively enrolled and followed as part of the California Collaborative Treatment Group (CCTG) 592 study, which was an internet-based behavioral intervention study of HIV infected MSM at high-risk for sexually transmitted infections. Selection criteria for inclusion unclear. High risk.	Aptima HPV Assay (mRNA from E6/E7) – may explain the lower prevalence of HR-HPV compared to other studies High risk	Crude estimate only. High risk.	Decreased risk of HR-HPV among those with undetectable vs. detectable PVL but not significant
Godbole et al, 2014	Cross-sectional study conducted between December 2012 and October 2013 with a planned sample size of 100. HIVinfected women older than 18 years, attending the HIV care and research clinics run by National AIDS Research Institute (NARI), Pune, India, were assessed for eligibility. Women were recruited regardless of CD4+ counts and antiretroviral therapy (ART) status. Women who were pregnant, had conditions that could preclude pelvic and/or anal examination, had a hysterectomy or history of screening/treatment for anal neoplasia, and history of HPV vaccination were excluded. Of 178 women attending the NARI clinics during the study period, 124 were found eligible and offered informed consent. Of these, 24 (19.3%) women refused participation. Medium risk (small sample size)	PCR-based amplification of target DNA using the Linear Array HPV genotyping assay. Low risk	Adjusted for sexual abstinence, menopausal, bowel hygiene (front to back wiping), rectal insertion, anal sex, education, cervical HPV and cervical cytology, number of lifetime sex partners. Low risk	Anal sex associated with anal HPV in MVA
Goeieman et al, 2017	HIV-infected women aged 25–65 years recruited from Themba Lethu Clinic (TLC), the HIV unit at Helen Joseph Hospital, Johannesburg, South Africa. The inclusion criteria were documented HIV infection, age 25–65, and ability to give consent and participate in study-related activities. Exclusion criteria were pregnancy, clinically active sexually transmitted infection (participation was allowed after the sexually transmitted infection treatment was completed), previous hysterectomy with removal of the cervix, and significant medical/mental illness that would prevent the participant from completing the study. Low risk	Hybrid Capture II. Low risk	Adjusted for HIV related factors where associations found in MVA. No data or adjustment for receptive anal intercourse. Low/medium risk	Weak evidence that longer duration ART and higher current CD4+ count associated with decreased risk of HR-HPV
Guimaraes et al, 2011	A multicenter cross-sectional study of HIVseropositive male patients attending 6 public AIDS referral clinics in urban Brazil (4 in Rio de Janeiro and 2 in Belo Horizonte, Minas Gerais), from May through November 2007 (PAPBRASIL). All participants were required to have a confirmed HIV diagnosis and be 18 years of age or older at the time of the study. Low risk	PCR (39 HPV types). Unclear methods. High risk	Unadjusted (ART and PVL detection). Published data reports significant association of HR-HPV with low (<200 cells/mm3) current CD4+ count, adjusted for sexual orientation and receptive anal intercourse. Data used in meta-analysis are unadjusted because different CD4+ count thresholds are used (500 cell/mm3 used as cut-off). Associations not stratified by sexual orientation. High risk	Low contemporary CD4+ count
Heard et al, 2016	Cross-sectional and screening study nested within the VIHGY cohort, a multicenter study of HIV-infected women conducted in 5 sites within France. Women were recruited during their first VIHGY visit in 2012 at 3 of the VIHGY hospital sites: Paris-Pitié-Salpêtrière, Colombes-Louis-Mourier, and Marseille-Sainte Marguerite, 43% of the women originated from Sub Saharan Africa. Women were eligible if they had no history of anal cancer, and were invited to participate	Linear Array. Low risk	Crude estimate only. High risk.	HR-HPV prevalence lower among women current CD4+ >500, and nadir CD4+ <200. No association with HIV PVL.

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
	in a 2-step study: (1) anal HPV specimen collection during the gynecological visit and (2) to undergo an HRA at specialized anal dysplasia clinics. Low risk			
Hernandez et al, 2016	HIV-positive MSM recruited from 2 study sites, Christian Medical College (CMC), Vellore (a large research and teaching institution) and Humsafar Trust (HT), Mumbai [a male sexual health nongovernmental organization]. Men were recruited through outreach workers and local HIV/AIDS support groups and were also referred from other NGOs. Enrollment occurred from September 2009 to August 2010. Men were eligible for the study if they had had sexual contact with another man in the preceding 6 months and were HIV-positive. Low risk	PCR (39 HPV types); the outcome was any HPV (39 types), so few HPV negative participants and low power to observe a difference between exposure groups. Medium risk	Crude estimate only. High risk.	Higher HPV prevalence among men reporting RAI and among men with low/no vaginal sex partners. No associations observed with any of ART use, undetectable VL or CD4+ count.
Hidalgo-Tenorio et al, 2017	A screening, diagnosis and treatment and follow-up program for dysplastic anal mucosa lesions in the Infectious Diseases Department of 3 rd level hospital in Southern Spain. Inclusion criteria were: age ≥18 years, self-reported MSM, HIV positivity, and signing of informed consent to study participation. Exclusion criteria were: female sex, self-reported heterosexuality, and history of anal canal neoplasm. Low risk	Linear Array. Low risk	Unadjusted for associations with ART and PVL; associations with nadir CD4+ adjusted for age, employment, number sex partners in last 12 months, condom use, AGW, syphilis/other STI, smoking, current and nadir CD4+, VL, time since HIV diagnosis. Medium risk	Nadir CD4= <200 cells/ul associated with increased HR-HPV
Hidalgo-Tenorio et al, 2018	A single-centre, longitudinal, prospective study among WLHIV who were consecutively enrolled in a programme for screening, diagnosis, treatment and follow-up of dysplastic lesions of the anal mucosa (May 2012–December 2016). The patients were recruited from the infectious disease unit at a Spanish tertiary hospital. Small sample. Medium risk	Linear Array genotyping. Low risk	Crude estimate only. High risk	
Hidalgo-Tenorio, 2019	A longitudinal, prospective, single-center study of 405 HIV+ MSM patients consecutively enrolled between May 2010 and December 2018 in a program for the screening, diagnosis, treatment, and follow-up of dysplastic anal mucosa lesions conducted by the Infectious Disease Department at “Virgen de las Nieves” University Hospital, Granada, Spain. The inclusion criterion was being an HIV+ MSM aged >18 years with no history of ASCC. Unclear recruitment method and numbers of men lost to follow-up.	At V0 and all subsequent visits, genotyping by qualitative PCR (Linear Array HPV Genotyping Test). HR-HPV (16, 18, 26, 31, 33, 35, 39, 45, 51–53, 56, 58, 59, 66, 68, 73, and 82=18 types) <u>clearance</u> defined as the disappearance of all HR-HPV genotypes from anal canal mucosa in the latest examination, with negative HPV PCR. We reversed the estimate reported (“In the multivariate analysis, ART duration of >5 years was the sole factor favoring oncogenic HPV genotype clearance (OR: 1.016, 95% CI 1.003–1.030)”; i.e ART duration of >5 years was associated with a reduction in HR-HPV persistence (OR=0.98, 95%CI: 0.97–0.997). Follow-up visits: The timing of the next follow-up visit depended on the results of HRA and cytology conducted at baseline. Patients with normal anoscopy and LSIL (AIN1) were evaluated one year later with cytology, HPV PCR, and anoscopy studies. Once their treatment was completed, these patients underwent another anoscopy, and those with normal histology or LSIL were given an appointment one year later, while those with HSIL were re-treated. When ASCC was detected, patients were referred to the oncology department for treatment. (Unclear if anal swabs for HPV were taken during these visits).	Adjusted for age, Charlson co-morbidity index, number sex partners in the last month or since last visit, condom use, infection with LR-HPV	HR-HPV persistence associated with shorter time on ART, and multiple sex partners
Kojic, 2011	Women enrolled in Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy (the SUN Study), a prospective observational cohort study, from March 2004 to June 2006 from 7 clinics in 4 US cities. A total of 167 women were enrolled of total cohort of 700 women; of these, 120 women had data on HPV and cytology. Participants were generally healthy patients with HIV receiving routine outpatient care. Patient data was extracted from medical records. Unclear how the 167 women were chosen (given the especially high prevalence of anal HPV at 90%). High risk	Clinician collected swabs, Linear Array. Low risk	Crude estimate only. High risk	Current low CD4 (<500) associated with higher risk of anal HPV
Lee et al, 2016	Cross sectional study conducted at the Pusan National University Hospital, a university-affiliated teaching hospital providing HIV care for HIV-infected patients in southeastern region of Korea. HIV-infected men who attended the HIV outpatient clinic of the study hospital were enrolled between July 2014 and January 2015, who were aged >18 years, and who had not received a diagnosis of anal cancer prior to enrollment. Relatively small sample, may not be representative of wider MSM HIV+ community. Medium-high risk	HPV Genotyping Chip™ Kit. Low risk	Crude estimate only. High risk. No associations found with sexual preference (vaginal, anal sex), no of female or male sex partners or history of STI. RAI and anal sex history not measured.	Younger age only significant factor associated with HR-HPV
Li et al, 2015	The study was conducted in the Eighth People’s Hospital in Xi’an from April to July 2014. Study participants were recruited through a local nongovernment organization (Xi’an Tongkang Volunteers Workstation). Multiple methods were used for recruitment including website advertisements, distributing flyers with study-related information at MSM frequented venues (e.g., MSM clubs, bars, parks and bathhouses), and eligible study participants were also encouraged to refer their peers to attend the study. Those eligible participants were HIV-seropositive males, at	Hybridio HPV DNA test (21 HR types). Low risk	A priori adjustment for age, ART status and CD4+ count. Adjusted for RAI in MVA. No data on HIV-1 PVL or nadir CD4+ to assess how well the men were controlled HIV disease (86% were taking ART yet median CD4+ count was 394 cells/ul). No data on STI. Low risk	ART use associated with decrease in HR-HPV prevalence. RAI associated with increase HR-HPV prevalence. Higher HR-HPV among men with higher current CD4 count (but unadjusted for RAI or nadir CD4+)

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
	least 18 years old, ever had homosexual behaviors, willing to provide anal swabs and blood for the test, and physically able and willing to provide written informed consent. Low risk			
Liu et al, 2019	A cross-sectional study conducted in Taizhou City, Zhejiang Province from August 2016 to October 2017. Participants were recruited by Taizhou City Center for Disease Control and Prevention (CDC) and three county-level CDCs. Convenient sampling was used to enrol HIV-positive men who were routinely followed-up by the four CDCs and HIV-negative men attending HIV Voluntary Counselling and Testing (VCT) clinics in the same CDCs. A total of 1286 HIV infected men had been routinely followed-up and 473 men had visited the VCT clinics during the study period.	HPV genotyping using the HPV GenoArray Test Kit (HybriBio Ltd., Guangdong, China) detecting 21 HPV genotypes, 15 are HR-HPV including 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66 and 68.	Crude estimate only	“Ever had homo-sexual behaviour “ associated with increased risk of HR-HPV
Mendez-Martinez, 2014	Anal samples from HIV+ MSM patients attending the HIV Clinic at the Instituto Nacional de Ciencias Médicas y Nutrición “Salvador Zubirán” (INCMNSZ) in Mexico City were used for this study. Patients over 18 years old, who presented to care between August and December 2008, were invited to participate. Medium-high risk . Unclear selection method.	INNO-LiPA. Low risk	Crude estimate only. High risk	No MVA conducted
Menezes et al, 2016	Consecutive women receiving care at Y.R. Gaitonde Center for AIDS Education and Research in Chennai, India. Low sample number (n=50). Medium risk	PCR based (TS-E7-MPG). Low risk	Unadjusted analysis due to small numbers. High risk	
Moscicki, 2003	Adolescent girls (13 to 18 yrs) recruited in the REACH project (Reaching for Excellence in Adolescent Care and Health) of the Adolescent Medicine HIV/AIDS Research Network across 15 different clinical sites in 13 cities in US, The study enrolled participants who were in care and acquired HIV through sexual activity of injecting drug use. Low risk	Anal samples taken by clinician for cytology and HPV DNA testing using single dacron swab. Low risk	Adjusted for AGW. High risk	Low CD4 count associated with higher prevalence of any HPV
Nagata, 2015	Convenience sample of HIV+ participants attending the Department of Gastroenterology and Hepatology at the National Center for Global Health and Medicine (NCGM), Tokyo, Japan between September 2009 and March 2015. Eligible patients were HIV-positive patients, at least 18 years old, who were willing to receive gastrointestinal (GI) tract cancer screening, provide anal swabs and blood for tests, and physically able and willing to provide written informed consent. Convenience sampling of participants may not be generalizable to wider HIV+ population despite high sample size. Medium risk	PCR-Invader assay. Low risk	A priori adjusted for age, sexual orientation, CD4+ count, HIV PVL, presence of other STIs. No data on RAI, number sexual partners, condom use. Analysis not stratified by gender or sexual orientation (although the majority of participants identified as MSM and associations of HR-HPV with ART adjusted for sexual orientation). Medium/low risk .	HR-HPV higher among those with younger age, MSM, CD4+ count <100 cells/ul, and having ≥2 STIs
Nyitray et al, 2018	Men were recruited from 2014 to 2016 for the parent study, the Young Men’s Affiliation Project (YMAP), which examined their attendance history at risk and health venues and the HIV infection/sexually transmitted disease risk and prevention among young MSM in Houston and Chicago, Illinois. Participants were recruited using a respondent-driven sampling (RDS) method, where young MSM “seed” participants were identified first from health-promoting and social venues. Each seed and successive waves of respondents were asked to refer up to 4 peers into the study by offering them vouchers. Low risk	PCR genotyping. Low risk	Crude estimate only. High risk	
Palefsky et al, 1998	Homosexual and bisexual men recruited in the San Francisco Men’s Health (SFMHS), in the San Francisco General Hospital Co-hort Study (SFGH), and at the University of California, San Francisco (UCSF), responding to newspaper advertisements. Small sample and early HAART era. High risk	PCR and HC-II. Low risk	Adjusted for anogenital warts	
Palefsky, 2001	Participants in this study were recruited between November 1995 and January 1997 from women who were participating at the San Francisco Bay Area site of the multicenter WIHS, a natural-history cohort study of HIV disease in women. Low risk	Hybrid Capture II. Low risk	Crude estimate only. High risk	Anal HPV associated with detectable PVL and low CD4
Patel, 2018	The SUN study enrolled 700 HIV-infected adults from 7 clinics in 4 US cities into a prospective observational cohort study. Participants were generally healthy HIV-infected patients receiving routine outpatient care and whose entire antiretroviral experience consisted only of highly active combination antiretroviral therapy (cART). Participants were classified as MSM or MSW according to self-report. Study follow up period ended in 2012. Low risk	Linear Array. Low risk	Associations of ART and HPV stratified according to sexual orientation but associations are unadjusted for confounding despite measures of sexual behaviour (including RAI, number of sex partners and rectal STI measured). High risk	Among MSW, smoking was associated with HPV prevalence (unadjusted estimate)
Phanuphak et al, 2013	Thai men aged 18 years or older who reported a history of anal sex with men were recruited in the study at the Thai Red Cross AIDS Research Centre in Bangkok, Thailand. Men were excluded if they had prior treatment for anal cancer, anal cytology, high-resolution anoscopy, or infrared coagulation within 12 months before enrollment; trichloroacetic acid or podophyllin application to the intra-anal area in the month before enrollment; or evidence of active concurrent intra-anal or perianal bacterial or herpes simplex virus infection at the time of enrolment. Low risk	Anal samples were collected from participants at the baseline, month 6 (for the first 120 participants), and month 12 visits by 1 study physician. Linear Array. HR-HPV (HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68=13 types) persistence defined as having the same specific HPV type at 2 consecutive visits. Anal samples were collected from participants at the baseline, month 6 (for the first 120 participants), and month 12 visits. . Low risk	Crude estimates for ART and PVL (no significance on univariate analysis); nadir CD4+ adjusted for sex acts per week, age, smoking. High risk	Smoking was the only factor with significant association with any high-risk HPV persistence in the multivariate model (OR: 2.3, 95% CI: 1.17 to 4.5, P = 0.015).
Schwartz, 2013	Using the Kaiser HIV registry at San Francisco KPNC anal cancer screening clinic, men aged ≥18 years, not diagnosed with anal cancer prior to enrolment were identified and enrolled between 2009-2010. Low risk	Anal swabs collected, HPV DNA testing by Cobas 4800. Low risk	Crude estimate only. High risk	

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
Sohn, 2019	Perinatally infected (PHIV) and HIV uninfected (HU) female adolescents and young adults aged 12–24 years with a history of vaginal intercourse were recruited at 5 study sites as part of The HPV in Adolescents Study: Thailand—HIV-NAT-Thai Red Cross AIDS Research Centre, and Siriraj Hospital Mahidol University both in Bangkok, and Chiang Rai Prachanukroh Hospital in Chiang Rai, and Vietnam—Children’s Hospital 1 and Hung Vuong Hospital, both in Ho Chi Minh City; all Thai sites and Children’s Hospital 1 were providing routine HIV care to the PHIV youth invited to participate in the study. Participants excluded if they were pregnant at the screening visit, if they had an untreated symptomatic STI (except genital warts), or had received prior doses of HPV vaccine and if they were unable to independently complete the study’s audio computer-assisted self-interview. Individuals were excluded if they were behaviourally HIV infected or if they were HIV uninfected with other chronic diseases or were using medications associated with compromised immune function. Low-medium risk (small sample)	LBC fluid from the 3 anogenital compartments and oral rinses were tested using the LINEAR ARRAY test. Low risk	Crude estimate only. High risk	
Somia, 2018	Prospective cohort study to assess anal hr-HPV infection and anal HSIL in MSM and TGW, with clinic sites in Jakarta and Bali (Indonesia), Bangkok (Thailand), and Kuala Lumpur (Malaysia). Between June 2013 and April 2015. MSM visiting 1 of the 4 clinics were invited to participate. Participants were eligible if they were Indonesian, Malaysian, or Thai citizens, at least 18 years of age, male at birth, and had a history of anal intercourse. They were not eligible for enrollment if they had prior treatment of anal cancer; anal cytology, high resolution anoscopy (HRA), or infrared coagulation within the previous 12 months; trichloroacetic acid/podophyllin application of the intraanal area in the previous month; or evidence of active concurrent intra- or peri-anal bacterial or herpes simplex infection. Low risk	Anal swab collected by trained study physician/nurse. Linear Array. Low risk	Crude estimate only. High risk (no associations found in univariate analysis) – limited by high prevalence of HR-HPV	
Torres-Ibarra, 2014	Cross-sectional study based on baseline information from a cohort of HIV-positive MSM recruited at Condesa Clinic, which provides free HIV care in Mexico City. Men were eligible for participation if they were 18 years or older and had any type of sexual intercourse at least once with another male. Participants enrolled from December 2009 through October 2011 were included in the analysis. Medical personnel recruited subjects during their routine clinical visits. A total of 740 HIV+MSM were invited to participate in the study, of whom 82 declined, and 133 did not return for the baseline visit, representing an acceptance rate of 70.9%. Low risk	Linear Array. Low risk	Crude estimate only. High risk	A higher number of recent receptive sex partners, low CD4+ count were associated with prevalent HPV16/18 infection
Van Aar, 2013	HIV negative and HIV-infected MSM were invited to participate in the H2M (HIV & HPV in MSM) study at three sites in Amsterdam, the Netherlands: the Amsterdam Cohort Study (ACS) among MSM (Public Health Service Amsterdam), a sexually transmitted infections clinic (Public Health Service Amsterdam), and an infectious disease outpatient clinic (Jan van Goyen Medical Center). Men were eligible for participation if they were aged 18 years or older and conversant in Dutch or English. Cohort of well controlled HIV and homogenous in terms of sexual behaviour risk (correlated) reducing power to detect any differences between exposure groups. Low-medium risk	Self collected anal samples using regular flocked swab with 1mul Universal Transport Medium (UTM). => interindividual variation in viability of samples. Low-Medium risk SPF10-PCR DEIA/LiPA25. Quality Control for detection and typing performed by retesting 5% of all HPV-positive and HPV-negative DNA extracts in different laboratory using the same technique. Discordance was 10% among HPV-positive and 3% among HPV-negative samples. Low risk	Adjusted for age, smoking, use of poppers, recent anal sex partners, RAI in past 6 months, fisting in last 6 months, number lifetime male sex partners, nadir CD4+ and HIV PVL. Low risk	Anal HR-HPV associated with younger age, RAI in last 6 months, higher nadir CD4+ count and HIV PVL detection at enrolment.
Van der Snoek, 2012	Cross-sectional study; participants were included in a Rotterdam study on the screening of HPV related anal premalignancies in HIV-positive MSM. All patients were recruited from the outpatient clinics of 4 hospitals. No information on recruitment procedures. Medium risk	Swabs collected swabbing perianal and intra-anal area. INNO-LiPA. Low risk	Crude estimate only High risk	ART associated with decreased risk of AIN and HR-HPV. No association with nadir CD4+ (few men with low nadir CD4+)
Videla, 2013	The Can Ruti HIV+ Men cohort was a single-center, prospective cohort study, annually assessing HPV infection at anal, penile, and oral sites of HIV-positive men attending the Outpatient HIV Clinic of the Hospital Germans Trias i Pujol (Badalona, Spain). HIV-positive men were eligible for participation if they were older than 18 years and reported no previous diagnosis of HPV-related pathology at anal, penile, and oral sites. Consecutive patients’ recruitment, based on outpatients who attended their AIDS routine clinic visit. The patients were informed of the study and invited to be seen in the Clinical Proctology HIV UnitY created ad hoc. Low risk	IVD-CE F-HPV typing (13 HR types+ HPV6 and 11). Low risk	Association of HR-HPV with ART and HIV PVL unadjusted for confounders (estimate in MVA not provided). Crude estimate combines MSM and MSW (no stratified analysis). High risk	HR-HPV associated with sexual orientation, history of AGW, increasing duration on ART (per year)
Volpini, 2017	Case series study in HIV-seropositive sexually active women, aged 18 to 65 years old who attended a STI/AIDS Reference Clinic in Vitoria, southeastern Brazil, from August 2013 to December 2015. Unclear recruitment/selection method and sample. Medium-high risk	PCR (PGMY09/11). Low risk	Crude estimate only. High risk	Anal HPV associated with younger age, CD4+ count <500 cells/mm ³ and HIV PVL >50 copies/ml.
Wilkin, 2004	Clinicians referred men from the Columbia-Presbyterian Medical Center Infectious Diseases Clinic, an urban clinic that serves ~1000 HIV-positive patients. Primary care providers from the referring clinic were asked to refer men without regard to the patient’s previous history of genital or perianal condyloma, other sexually transmitted diseases, or sexual behavior. Primary care providers were more likely to refer subjects who reported sex with other men and may have been more likely to refer subjects with a prior history of genital condyloma, which may limit the generalizability. Early ART period (2001-2002), 65% men started ART <200 cells/mm ³ . Mean nadir of men who started ART was 63 cells/mm ³ vs. 290 cells/mm ³ among ART naïve men; Small sample (not clear how many men refused). Medium risk	HC-II and PCR. Low risk	Associations of ART and HR-HPV not stratified by sexual orientation but adjusted for history of RAI. Low risk	HR-HPV associated with history of RAI only in MVA (adjusted for ART use, age and nadir CD4+)
Wiley et al, 2013	Men were invited by research personnel to participate in the AHS at the first MACS visit following the study’s opening in May 2010. anal Pap test and HPV genotyping was obtained and	PCR. Low risk	Crude estimate only. High risk	

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
	study specimens were collected for 1,296 MSM at the first AHS study visit completed between May 2010 and February 2011. Low risk			
Yu et al, 2013	HIV-positive men attending the outpatient clinics of Infectious Diseases at the National Cheng Kung University Hospital for HIV care from August 2010-February 2011. Eligibility criteria included C20 years of age, no history of HPV vaccination, being able to provide informed consent and having no current symptomatic HPV-related anogenital lesions or diseases. Low risk	PCR (34 types). Low risk	Crude estimate for >500 vs. <500; high risk For >500 vs. <350, estimate adjusted for time since HIV diagnosis, age, HIV exposure category, number recent sex partners, presence of STI, history of anal disease, RAI in past 6mths, use of condoms in past 6 mths	RAI in last 6 months and No. of sex partners in the past 6 month associated with anal HR-HPV
Anal lesions/anal cancer studies				
Abramowitz, 2007	Participants recruited during routine follow-up visit at the infectious diseases units of Bichat Claude Bernard University Hospital in Paris, France. The sample was composed of all consecutive patients consulting any of the medical doctors present during three randomly determined half-days per week. The three selected halfdays were modified three times during the study period to allow for the screening of a representative sample of patients. Anal exam proposed to 516 HIV positive patients, of whom 92% accepted. (Authors note potential referral bias of a large tertiary care centre, cannot rule out geographical variation in characteristics of patients). Low risk	Ocular inspection (with and without aceto-white test) of the anal and through anoscopy. An HPV intraepithelial lesion was suspected in the case of either an aceto-white area or a slightly elevated mucosa resembling tumours white to pink in color or of exophytic elevated lesions easily distinguishable from normal mucosa. A biopsy was systematically performed to confirm the diagnosis of HPV-related lesion. Histological analysis: HPV intraepithelial lesions were diagnosed by two independent observers. Low risk	Associations of AIN1+ and ART, PVL and CD4+ unadjusted for confounders. ART and PVL not included in MVA due to lack of association in univariate, CD4+ included in MVA but not stratified by sexual orientation or gender (although adjusted for RAI history). High risk (ART and PVL analysis)	History of RAI and history of anal condyloma associated with AIN1+
Abramowitz, 2016	As above	As above		
Aldersley et al, 2019	Nested prospective cohort study in the MACS, an ongoing study established in 1984 that has enrolled 7343 HIV-positive and HIV-negative MSM. Clinical and laboratory data were collected at semiannual visits as described. Eligible participants were 5298 MSM aged 30–70 years with at least 5 years of follow-up during 1984–2014 and one or more visits with HBV laboratory test data. Baseline was first visit after age 30 years. Low risk	Not reported. High risk	Adjusted for nadir CD4+. Low risk	
Baranoski, 2012	Prospective observational study conducted at Center for Infectious Diseases at Boston Medical Center, an inner city hospital. English speaking HIV positive women between 18–64 years who had not had a cervical or anal cytology test, colpo or HRA in the 6 months prior to enrollment were eligible to participate. Exclusion criteria included: pregnancy, use of chronic anticoagulation medication and life expectancy less than one year. Study participants were recruited by nurse practitioner in CID from HIV positive women scheduled for gynecology care (including cervical cytology). Small sample size may not be representative of wider population of WLHIV: 10% of women had prior history of VIN and 27% had prior treatment for CIN (high risk population). Medium/high risk	All women had HR-HPV (HC-II) and anal cytology performed. Women with any grade of anal cytology abnormality or anal HR-HPV were referred for HRA. Identified lesions were biopsied under direct visualization with biopsy forceps. Medium risk	Crude estimate only. High risk No risk factor analysis conducted using histology outcome- only available for cytology outcome	In MVA, ASCUS+ associated with current CD4+ <200 cells/mm3, anal HPV infection and history of other STI.
Barnell et al, 2019	Using a cohort study design, changes in cancer incidence were evaluated from 1998 to 2012 among 13,552 adult (≥18 years) KPNC members with HIV infection. Study subjects were identified from the KPNC HIV registry, which includes all known cases of HIV infection among KP members since the early 1980s and includes more than 25,000 cumulative patients. The registry maintains up-to-date lists of all HIV patients confirmed by medical chart review, and includes data on HIV transmission risk factors, dates of known HIV infection, clinical AIDS diagnoses, HIV-related lab and pharmacy data, and associated clinical data from the electronic health record (EHR). The study cohort was followed from 1998 through 2012, corresponding with 10 years before and 5 years after the introduction of HRA capability at KPNC in 2008. The start of follow-up for each cohort member was assigned as the latest of: January 1, 1998; first KPNC membership; HIV diagnosis date; or the member's 18th birthdate. Follow-up continued until earliest of: the outcome of interest (ie, anal cancer or advanced anal cancer); death; departure from the KPNC health plan (disenrollment or membership gap of 4 or more months); or December 31, 2012.	HRA was offered at 2 clinic locations—in San Francisco, as part of a screening program based in the HIV primary care clinic, and in Oakland, as a referral site for all other KPNC medical centers. Anal cancer diagnoses were identified from the KPNC cancer registry, a contributing site to the Surveillance, Epidemiology, and End Results Program. Participants with evidence of anal cancer diagnosed before January 1, 1998 were excluded. Anal cancer confirmed using tissue biopsy with pathologic diagnosis of invasive or superficially invasive squamous cell carcinoma of the anus	Adjusted for year of HIV diagnosis, age at baseline, race, sexual risk group, ever smoked, baseline CD4+, baseline prior clinic AIDS	Anal cancer decreased in later years (2011-2012) compare to 1998-2007; was higher among those aged ≥45 years, among MSM, smokers, those with baseline CD4+ <350 cells/u1, and baseline prior clinical AIDS
Bertisch et al, 2013	Swiss HIV Cohort Study has enrolled people living with HIV since 1998 from 7 large hospitals in Switzerland representing 103,000 person years of follow-up until Dec 2011. A total of 68 anal cancer cases were identified in SHCS, 54 of these were identified from the SGCS database and 11 through record linkage with 8 Swiss cantonal cancer registries. Six prevalent cancer cases before or within 1 month of enrolment in the SHCS and 3 diagnosed more than 6 months after the last SHCS FU data were excluded leaving 59 eligible incident cancer cases. For each anal cancer case, 5 control subjects were matched at random using incidence density sampling from SHCS participants who were never diagnosed with anal cancer. Low risk	Anal cancer cases identified from the SGCS database and through record linkage with 8 Swiss cantonal cancer registries. Low risk	Odds Ratios conditioned on matching variables (SHCS centre, sex, HIV transmission category, age at enrolment, year at enrolment date). Association with ART adjusted for nadir CD4. Analysis not stratified by sexual orientation	Anal cancer associated with current smoking, antibodies against HPV16 L1, low nadir CD4+ count, current CD4 at cancer diagnosis. Influence of CD4 was strongest 6–7 years prior to anal cancer diagnosis.
Borghetti et al, 2015	Longitudinal, observational study on a cohort of consecutively enrolled, HIV-seropositive patients followed at a single Italian center including HIV-1 infected patients aged 18 years or older. Recruitment procedure unclear. Medium risk	Participants underwent anoscopy by a single specialist surgeon. Traditional pap and thin prep pap test o anal samples. Cytology results read by single reader according to Bethesda 2001, anal lesions classified as ASCUS+.	Crude estimate only	Anal warts and HPV DNA associated with ASCUS+

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
Bruyand et al, 2015	D:A:D study is a prospective study formed by the collaboration of 11 cohorts in Europe, Australia and the USA. Information on AIDS events, including ADC have been provided prospectively on an annual basis since the start of the study in 1999, and on NADC since 2008. Information also collected retrospectively on events occurring between Jan 2004 to Jan 2008. Participants were followed from the latest of Jan 2004 (start of cancer data collection) or D:A:D study entry until the earliest of a first incident cancer diagnosis (any type, excluding precancer stages), Feb 2012, death or 6 months after the last visit. Low risk	Detailed information on events collected on specific case report form. All reported events are validated centrally at the D:A:D coordinating centre with a proportion of events selected for discussion with an external consultant oncologist. All events are monitored for accuracy, and random monitoring is performed at participating centres to ensure complete ascertainment of events. Low risk	adjusted for age, gender, cohort, mode of HIV acquisition, ethnic group, calendar year, body mass index, any previous cancer, previous AIDS diagnosis, smoking status, and HCV and HBV status. Time updated covariates used. Medium risk	Increasing time on PI associated with increase in anal cancer, no association with NNRTI
Burgos et al, 2015	All MSM with HIV attending the HV unit at University Hospital Vall d'Hebron (Barcelona, Spain) and the University Hospital of Mar (Barcelona, Spain) were informed of the screening programme (The Screening and Treatment of Anal Dysplasia Unit), created in May 2009 in the) and participation was advised. Between 2009-2014, 47% of all MSM attending the HIV units of both hospitals agreed to participate. Not clear reasons for refusal or description of men refusing to participate. Medium risk (selection bias)	Anal cytology followed by a digital anorectal examination (DARE) and HRA, including topical application of 3% acetic acid and lugol solution in the anal canal. Anal biopsy was performed from abnormal areas revealed by HRA. In cases with previous HSIL or ASCUS but with no visible lesions on HRA, a random biopsy of the squamocolumnar junction area was performed. Histology specimens were classified according to the Bethesda classification; 26% men had biopsy taken. Random biopsy included but no review of pathology indicated. Low risk	adjusted for stable sexual partner, anal cytology result, abnormal HRA, HPV16/18 infection High risk	ART use, stable sexual partner, anal cytology result, abnormal HRA, HPV16/18 infection
Burgos et al, 2015	MSM with HIV attending the HV unit at University Hospital Vall d'Hebron (Barcelona, Spain) and the University Hospital of Mar (Barcelona, Spain) were informed of the screening programme (The Screening and Treatment of Anal Dysplasia Unit), created in May 2009 in the) and participation was advised. Patients with previous intra-anal HGAIN who received treatment (electrocautery and ablation) and histological documented successes were included in this study. All patients have a biopsy-proven response obtained within 6-8 weeks after last treatment. Of 692 MSM participating in screening programme, 185 (27%) presented with or developed intra-anal HGAIN. Of these, 141 accepted to be treated with electrocautery of which 100 achieved a successful treatment (complete or partial response confirmed based on post treatment biopsy) and were included in this analysis. Small samples (generalizable?). Medium risk	Approx 6-8 weeks after treatment, men underwent another evaluation involving HRA and biopsy. Biopsies were taken from sites where HGAIN was previously reported to assess response to treatment. New anal biopsies were obtained from areas that were suspected for HGAIN recurrence (the same site or a different site from a previously high-grade lesion). If no changes suggestive of high-grade lesions were noted based on HRA, but ASC-H or HSIL cytology suggested presence of a lesion, a new HRA was conducted to perform random biopsies of the squamocolumnar junction. Recurrent HGAIN was defined as biopsy-proven intraanal HGAIN diagnosed at follow-up subsequent to prior successful treatment. Complete response (CR) was defined as the resolution of AIN on the posttreatment biopsy, and partial response (PR) was defined as regression from highgrade to low-grade AIN. Low risk	ART not associated with recurrence in univariate analysis, not included in MVA	HepC antibodies, nadir CD4+ <200 and previous large HGAIN were associated with increased risk of recurrence.
Cachey et al, 2014	Retrospective inception cohort analysis of HIV infected patients attending University of California, San Diego (UCSD) Owen Clinic between 2001 and 2012. Included patients had at least two cytology results without diagnosis of invasive anal cancer (IAC) or at least one cytology result if subsequently diagnosed with IAC. Patients diagnosed with IAC within 180 days of first anal cytology test were excluded to avoid prevalence bias. Overall, 71% patients attending the clinic were screened for anal cytology at least once. Inclusion of patients who underwent IRC ablation. Screening uptake differentially associated with being MSM, non-white and older. Low risk	All participants underwent DRE and anal cytology collection at first clinical evaluation and annually thereafter. Patients with abnormal cytology (ASCUS+) were referred to HRA. Due to limited availability, those with HSIL lesions symptoms or DRE abnormalities were preferentially triaged to HRA. Cytology rather than histopathology used as outcome in order to avoid selection bias introduced by restricting analysis to patients who had undergone HRA procedures. Cytology smears reviewed at UCSD pathology laboratory. Anal cancer diagnosis ascertained by linking the clinic oncology database to UCSD Cancer registry and verified using UCSD histopathology reports. High risk	ART as time dependent variable Low risk	Anal cancer not found to be associated with any of the covariates (IRC ablation, ART, HIV viraemia and current smoking).
Cambou, 2015	Cross-sectional analysis of participants enrolled in Women's HIV cohort of the Evandro Chagas Clinical Research Institute (IPEC) at Fiocruz, Rio de Janeiro. Participants in the IPEC women's HIV cohort ≥18 years were invited by their gynaecologists to participate in the IPEC Women's HIV anal HPV and Lesions Study. Swab specimens were collected by on site gynaecologists between Jan 2011 and Aug 2013. Women in this cohort regularly receive cervical pap smears (cervical lesions found to be associated with ASIL and so may not accurately reflect those of WLHIV in Brazil). Large sample. Low risk	Anal cytology performed in Sao Paulo using Bethesda classification. High risk (no histology)	Unadjusted for ART in MVA (lack of association in univariate). Associations of PVL and nadir CD4+ and ASCUS+ were adjusted age, cervical cytology abnormality, anal HR-HPV. No association with high risk sexual behaviour, including RAI. High risk	ASCUS+ associated with cervical LSIL+, nadir CD4+, HIV PVL detection and anal HPV in MVA.
Chao et al, 2015	Cohort study of adult HIV infected patients within Kaiser Permanente Northern California (KPNC) and Kaiser Permanente Southern California (KPSC) from 1996-2008. HIV infected persons were identified KP maintained HIV registries. Eligible participants included adults ≥18 years HIV infected who were KP health plan members during the ART era, only participants for whom duration on ART was known were included. The baseline date for analysis was assigned as earliest date after 1996 for KPNC and 2000 for KPSC. Low risk	Incident cancers were identified by record linkage with the KPNC and KPSC cancer registries, contributing sites to the Surveillance, Epidemiology and End Results (SEER) program. Cancer case ascertainment considered highly valid since reporting of cancers to the California Cancer Registry and National Cancer Institute SEER program mandated under state law. Low risk	Adjusted for time updated CD4 and HIV PVL Adjusted for sexual orientation but no data on sexual behaviour and history of unprotected anal sex. Low risk	
Chaves et al, 2012	Anal smear screening was offered to all women infected with HIV seen at the outpatient sexually transmitted infections clinic of Hospital de Clinicas de Porto Alegre, Brazil, from March 2006 to March 2008. The test was performed only on patients who provided written consent. Low risk	Anal cytology. No independent verification noted. High risk	Crude estimate only. High risk	
Chiao et al, 2013	Veterans Administration (VA) Clinical Case Registry (CCR) is a nationwide registry for all known HIV infected persons utilising VA services established in 1992. Study population comprised of HIV infected male veterans entered into the registry between Jan 1985 and Jan 2009.	Squamous cell cancer of the anus (SCCA) was defined as ICD-9 codes 154.2 and 154.3. These codes were previously validated in the VA, with PPV of 88%. Low risk	Age adjusted. CD4 and HIV PVL time dependent variables. Crude estimate given for ART. HIV VL estimate among ART users only	History of drug use, race, Nadir CD4 and time with HIV VL

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
	Inclusion criteria included well documented HIV diagnosis dates, patients over 18 years, confirmed HIV diagnosis, or at least one prescription for ART. Female veterans were excluded because they represented a small percentage of the population (2%). Patients with anal cancer diagnosis up to 90 days after HIV diagnosis were excluded, as were persons without CD4 count data over follow up. Only those patients with at least one HIV viral load were included. Low risk , generalizable to male veterans only.		and adjusted for age at time of ART initiation, race, time from HIV diagnosis to ART initiation, illegal drug use, current CD4+ and duration of HIV viral undetection. No stratification by sexual orientation. Low risk	undetection associated with anal cancer.
Cheng, 2014	Cross sectional study among HIV positive men attending outpatient clinics of Taoyuan General Hospital, a regional hospital in northern Taiwan where 500 HIV infected patients receive regular follow up were invited to participate in the study. Participation rate was 52% and high proportion of injection drug users in the non-participants compared to final sample. Medium risk	Anal swabs were self-collected after receiving instructions. Anal cytology using liquid based thin preparation Pap smears sent to certified laboratory where two cytopathology technicians and two blinded pathologists evaluated pap smears. Results classified according to Bethesda 2001 System. High risk	Authors do not report proportion of ART users, although nadir CD4+ and HIV PVL given	ASCUS+ associated with MSM, number HR-HPV types, after adjustment for age, experience of web sex, nadir CD4 and HIV PVL.
Chikandiwa et al, 2017	Baseline data from men living with HIV enrolled in a prospective cohort study to evaluate the natural history of HPV infection and disease in HIV-infected men in South Africa between October 2012 and August 2013, men in the community or attending HIV clinics were approached and asked to volunteer for the study. Potential participants were screened for eligibility and enrolled if they were willing to provide informed consent, 18 years or older, reported at least one episode of sexual intercourse in the past 3 months and were HIV positive on rapid testing. Low risk	Anal smears were stained by the Papanicolaou stain before being analysed and classified according to the Bethesda System. Smears were read independently by a cytotechnologist and one cytopathologist at the NHLS in Johannesburg. If there was a discrepancy between these two readings, the smear was given to a second cytopathologist. Grade ASCUS or higher was considered abnormal. High risk	Adjusted for age. Although duration ART, CD4+ count and virological control status not associated with ASCUS+. High risk	Current ART use associated with increased risk of ASCUS+
Chuang et al,	During a 12-month period, men and women, 18–65 years of age, were either self-referred or referred by community physicians for anal dysplasia/cancer screening in collaboration with the Hawaii Center for AIDS, University of Hawaii (UH), and UH Cancer Center. Subjects were included if HIV-positive regardless of previous history of HPV infection, anal dysplasia/cancer, or related treatment Small sample size and not stratified by gender or sexual orientation. Medium-high risk	Two anal cytology specimens were collected with a Dacron swab and stored in ThinPrep. One anal specimen was processed by a CLIA-certified clinical laboratory with cytopathology reviewed and reported by the same experienced cytopathologist according to the Bethesda system: anal cytology was evaluated, using criteria and terminology adapted from standardized cervical cytology screening. High risk	Crude estimate only. Not possible to stratify by gender given small sample size. No data on sexual orientation or sexual behaviour. High risk	ASCUS+ more likely among males compared to females but sample of women
Clifford et al, 2018	As for Combes et. 2018 (HPV study). Study participants were HIV-positive MSM aged 35 years and older attending infectious disease units in six hospitals across France (Dijon, Lyon, Marseille, Montpellier, Paris, Rennes), recruited from December 2014 to June 2016. Ineligibility criteria included: history of anal cancer or of hHSIL treated during the last 12 months. Low risk	Anal swabs taken for cytology and HR-HPV DNA. Participants received a proctologic examination including inspection, naked eye anoscopy, DARE, and HRA. Lesions identified by HRA were biopsied and processed for histological examination. Final histology diagnosis was established by a histopathology review panel: all slides concurrently read by pathologists from five of the six APACHES centres using a multihead microscope, blinded to HPV and cytology results. Low risk	No adjustment for ART or CD4+ analysis. For PVL : adjusted for city, tobacco smoking and worst previous anal cytology/histology. High risk No adjustment for sexual behaviour (but have adjusted for history of anal cyto/histo abnormalities). Medium risk	HSIL-AIN2+ associated with city, smoking and history of anal lesions
Conley et al, 2010	Prospective observational cohort (Study to Understand the Natural History of HIV/AIDS in the Era of Effective Therapy [SUN] study) of 700 HIV infected persons enrolled from 7 clinics in Denver, Colorado; Minneapolis, Minnesota; Providence, Rhode Island; St Louis, Missouri enrolled between 2004-2006. Approx 20% LTFU and 42% were ineligible for study on progression. Low risk	Anal cytology (thinPrep) read by single cytopathologist, reported according to Bethesda. High risk	Separate analyses for women, MSM and MSW. Associations of current and nadir CD4 with ASCUS+ unadjusted among women and MSW, and adjusted for HPV genotypes among MSM. Adjustment for history of RAI and rectal STI for all groups, not included in MVA as no association, perhaps due to small numbers for individual groups. When women, MSM and MSW combined, history of RAI significantly associated with ASCUS+, as was nadir and current CD4+ and HPV genotypes. Low risk .	Low nadir and current CD4 associated with increased prevalence of ASCUS+
Conley et al, 2016	As for Conley, 2010. Of 700 participants enrolled in the SUN study, 297 (42%) had abnormal cytology at baseline, 50(7%) had unsatisfactory cytology or HPV specimen and 101 (14%) had no follow-up specimen. Small sample. Medium risk	As for Conley, 2010. High risk	Separate estimates for women, MSM and MSW. Small numbers among individual population mean low power to detect different in associations. Low- Medium risk	Among MSM, greater number of persistent HR types associated with progression. Among women and MSW, low CD4 count at follow-up visit and persistent HR types other than HPV16/18 were associated with progression.
Cranston et al, 2014	Retrospective chart review of patients attending University of Pittsburgh Anal Dysplasia Clinic (UPADC) with biopsy proven internal anal HSIL in a study to assess efficacy of topical 80% trichloroacetic acid (TCA) for treatment of biopsy proven internal anal HSIL, between July 2009 and June 2012. The UPADC received referrals of HIV positive men and women with abnormal anal cytology. The UPADC database was searched using following criteria: male or female HIV positive patients with biopsy proven ain2+ who had TCA treatment only and had at least one follow up HRA visit at least 3 months after initial ablation procedure between July 2009 and June 2012. Low risk	Initial assessment of participants included HRA (by two certified HRA providers) and biopsy of any suspicious lesion consistent with AIN2+. Images of lesions were captured using Second Opinion image capture software which allowed reidentification of index lesion during follow-up. Low-Medium risk	Analysis conducted on lesion-level data (98 lesions among 72 men). Crude estimates calculated only. High risk	

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
Cranston et al, 2018	A multicenter, randomized, double-blinded, placebo controlled, phase III study was opened at selected ACTG sites (N = 24, 23 domestic US sites with 540 participants and one site in Brazil with 35 participants) with anal cancer screening programs that included capacity for anal cytology, HRA, and ready access to minimally invasive treatments for HSIL, such as topical application of trichloroacetic acid or infrared coagulation. At least 30% or 140 men were required to have bHSIL as were 50% or 50 of the women to ensure adequate power for the secondary objective of the study assessing the effect of qHPV following treatment of bHSIL. Individuals with current invasive or microinvasive cancer were not eligible. Potential bias toward individuals with disease? Medium risk	Participants had anal swabs taken for cytology. A certified HRA provider performed the screening HRA with biopsies of lesions suspicious for either HSIL, low-grade SIL (LSIL), or condyloma. All cytologies and anal pathologies were evaluated locally in College of American Pathologists accredited cytology/pathology laboratories in the United States, by local standard of care in Brazil. Low-medium risk	Crude estimate only. High risk	
Crum-Cianflone et al, 2010	Data from US Military Natural History Study (NHS), a multicentre observational study which enrolled 5,042 HIV infected participants at 7 geographic locations in US between 1985-2008. Participants were military beneficiaries (active duty, retirees and dependents) evaluated on a biannual basis with medical histories and blood collection. Participants excluded from analysis were those without documented HIV positive test date, HIV infection diagnosed prior to 1985, age <18 years, with anal cancer prior to HIV seroconversion and females as they only accounted for 8% of the study population. Low risk	Anal cancer was histopathologically confirmed: types of cancer located in the anal area that were not confirmed to be squamous cell (e.g adenocarcinoma, carcinoid tumour, pre-invasive disease) were not included as anal cancer events but contributed to follow-up time in the models (n=4). Histopathologic specimens were not available for re-confirmation or HPV testing. No data on staging and treatment information related to anal cancer. Low risk	MVA adjusted for year of HIV diagnosis, time updated calendar year of event, age, variables that may change during follow-up (CD4+, HIV RNA, hep B infections, STI, AIDS events, and use of ART) were considered as time updated covariates. HIV RNA level (time updated) not associated with anal cancer). Low risk	Nadir CD4 and AIDS event associated with anal cancer
Dalla-Pria, 2014	Data collected from prospectively from HRA service available to PLHIV since 2000. Patients with anal symptoms routinely referred for HRA. Asymptomatic HIV positive MSM offered HRA on a voluntary basis. Authors suggest possibility of selection bias as high proportion of high risk men (32% with HSIL-AIN2+) who for reasons of lifestyle or past medical history were at higher risk of anal cancer. Patients attended on voluntary basis- potential for self/clinician selected bias. Medium risk	Anal cytology and HRA exam with biopsies of viable anal lesions. Initial screening by HRA (and not cytology). Medium risk	Crude estimates only. High risk	Higher grade histology associated with lower current CD4+ count (no estimate given). Progression from first HRA to anal cancer was associated with older age, and histopathological findings of AIN3 (but not any HIV associated factors, although no estimates given).
De Pokomandy et al, 2011	Participants in the Human Immunodeficiency and Papilloma Virus Research Group (HIPVIRG) cohort were enrolled from January 2002 through January 2005. Men 18 to 65 years of age with a history of sexual intercourse with men who were receiving HAART (n= 221) or expected to be treated with HAART within the next 6 months (n = 26) were recruited. Of 172 participants without AIN2-3 at baseline, 25 (15%) men were LTFU. Relatively small sample. Medium risk	Anal cytology was conducted. High-resolution anoscopy (HRA) was performed at baseline and repeated yearly thereafter for those without AIN or with AIN-1 and was repeated every 6 months for individuals with AIN-2,3, if not treated. Aceto-white areas were biopsied and processed for routine histopathological examination. Histological slides were reviewed by 2 pathologists. Four participants with classical exophytic condylomas at the accrual HRA never had a biopsy of these condylomas during the study period and were considered to have AIN-1. The outcome of interest was histological diagnosis of AIN2-3 on biopsy specimens obtained during HRA. Some cases of AIN2-3 may not have been detected on first HRA resulting in underestimation of the baseline prevalence and overestimation of incidence of AIN2-3. Low-Medium risk of disease misclassification.	adjusted for number visits, age, CD4+ at time of ART initiation, have removed HPV type (on causal pathway); finding is significant when remove HPV from model. Low risk	Age, CD4+ at time of ART initiation and duration of ART use
Dona et al, 2015	Male attendees of the STI/HIV unit of the San Gallicano Dermatological Institute (Rome, Italy) between August 2009 and June 2017 who were 18 years old or older and had reported at least 1 instance of sexual intercourse with a man in the preceding 6 months were offered an anal Pap test and an HPV-DNA test, included HIV-infected MSM attending the center for the management of HIV-1 infection or for the anal Pap test only. Low risk	Cytological slides, obtained with a ThinPrep 2000 processor (Hologic), were read by 2 expert cytopathologists. Findings were classified according to the Bethesda guidelines. Medium-high risk	Crude estimate only, although data on sexual behaviour including RAI was presented. High risk	No associations observed between HIV related factors and ASCUS+, marginally associated with lower nadir CD4+
D'Souza et al, 2016	Men enrolled in the Multicenter AIDS Cohort Study (MACS), a prospective study of HIV-infected and uninfected MSM, across four sites (Baltimore, Chicago, Pittsburgh, Los Angeles) over four enrollment periods (1984-85, 1987-1991, 2001-03, and 2010-12). All MACS participants who attended any MACS study visits between June 2010 and July 2011 were eligible to participate in the Anal Health Study (AHS) and were offered a free ACyt test by study staff. Men with an inadequate ACyt were offered another ACyt at their next study visit six months later. Low risk	Liquid based cytology using Hologic T-2000 instrument. Specimens were initially screened for abnormalities by certified cytotechnologists and each was examined by a board certified cytopathologist. Frequency of technically inadequate ACyt results was greater than expected from previous studies. High risk	Crude estimate only (no MVA for prevalent ASCUS+). High risk	ASCUS+ associated with decreasing CD4+ count
D,Souza et al, 2008	Men enrolled in the Multicenter AIDS Cohort Study (MACS), a prospective study of HIV-infected and uninfected MSM, across four sites (Baltimore, Chicago, Pittsburgh, Los Angeles) over four enrollment periods (1984-85, 1987-1991, 2001-03, and 2010-12). Large proportion of men in the original MAC cohort died before HAART became available, many of these died before having the "opportunity" to develop cancer but still contributed to the longitudinal analysis competing risk could affect interpretation of longitudinal analysis. Medium-high risk	Anal cancer cases included only men with T1 invasive cancer or rectal disease. Subjects self report of cancer was verified by histology report or cancer registry. When no medical documentation was available, self report of anal cancer by study subject was accepted (n=4). Histology reports and medical reports were collected, reviewed and summarised by trained abstractors and centrally re-reviewed for this paper. Tumor specimens were not available for histological review, testing or adjudication for these analyses. Incident anal, perianal and rectal ICD codes were classified together as anal cancer for these analyses. Low risk	adjusted for number of unprotected anal receptive partners reported, smoking, nadir CD4+. Low risk	

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
Duncan et al, 2015	A retrospective population-based cohort was created for this study from a linkage of health administrative data from two province-wide health databases: the British Columbia Cancer Registry (BCCR) and the HIV/ AIDS Drug Treatment Program (DTP) Registry. Data were obtained from the Anal Dysplasia Clinic database at St Paul's Hospital. The linked cohort was further linked with the Anal Dysplasia Clinic database, established in 2003, to collect demographic, diagnostic, treatment and outcome data on individuals receiving screening or treatment for AIN at the Anal Dysplasia Clinic at St Paul's Hospital. The population study cohort was created by the BCCR and then populated by the DTP with ART-related information. The BCCR uses a probabilistic-match procedure on the basis of Personal Health Numbers, names and birth dates contained in the two registries to generate a province-wide listing of HIV-positive individuals in the DTP who were diagnosed with cancer or a precancerous malignancy. This cancer information was then augmented by the DTP with antiretroviral-related treatment information. Low risk	The diagnosis of anal cancer was histopathologically confirmed and cancers located in the anus that were not confirmed to be invasive squamous cell carcinoma were excluded. Low risk	Adjusted for nadir CD4+, ART starting prior to 1995, percentage time CD4+ less than 100 cells/ μ l. Low risk	
Durante et al, 2003	Women enrolled as part of the GRACE prospective cohort study, focussed on prevention of vaginal candidiasis infection and the natural history of anogenital HPV infection in HIV infected women. Study was conducted in Connecticut and Massachusetts, USA from 1995-1998, women were recruited through a program of community outreach. Women were eligible if they were HIV infected, at least 18 years, English or Spanish speaking, not pregnant and not on long term antifungal medications. Women were seen for study procedures every 6 months. Of 225 enrolled in GRACE study, 73% returned for at least one follow-up visit., 100 of these women (61%) had satisfactory anal cytology. Small sample. Medium risk	Anal cytology smear taken, slides read by a pathologist using the Bethesda System (1996). Cytology specimens considered abnormal of result was ASCUS+. No review of cytology slides: 39% with unsatisfactory cytology smear at baseline and over follow-up. High risk	HAART was examined as time dependent variable. -associated with reduction in incidence in univariate but not MVA following adjustment for CD4+, smoking and HPV type. No data on HIV PVL (HAART was introduced during course of study); Not adjusted for sexual behaviour (although no association found with anal HPV infection). Low-medium risk	Incidence of ASCUS+ associated with low baseline CD4+ and smoking
Frank et al, 2018	Retrospective chart review between December 1, 2013, and September 30, 2015 of patients at the Grady Ponce de Leon Center (Atlanta, GA). The Ryan White funded clinic provides comprehensive care for over 6,000 HIV infected patients annually, predominantly with advanced stages of HIV. Females were excluded from the chart review. Medium risk	During the HRA visit, all patients underwent anal cytology collected in liquid media; HRA was performed by a single gynecologist. Abnormal lesions within the perianus and intraanal canal identified using 3% acetic acid or Lugol's solution were biopsied. The majority of HRA patients, 143 (97%), had at least one biopsy; 2 were unable to tolerate the procedure, 1 had no visible lesions, and in 1 the practitioner was unable to adequately visualize the SCJ. Low risk	Adjusted for number of biopsies taken, history of high-grade anal cytology, age and STI. High risk	HSIL-AIN2+ associated with number of biopsies and history of high grade cytology
Gaisa et al, 2014	Cohort study using data from treatment database of HIV infected outpatients engaged in care at three clinical sites. All HIV positive patients, irrespective of gender and sexual behaviour were offered anal cytology screening and referred for HRA if cytology was abnormal. Patients with benign or inadequate anal cytology were not referred for HRA and not included in final analysis. Analysis includes only patients with abnormal anal cytology and HRA; bias towards individuals with disease (less likely to see difference in ART if fewer non diseased individuals?). 65% participants referred for HRA attended the HRA visit (similar among MSM, MSW and women). High risk	Biopsy indicated if cytology ASCUS+ and HRA abnormal. HRA was performed among participants with ASCUS+ on cytology only after treatment with 3% acetic acid and Lugol's iodine. Areas suspicious for HSIL or cancer were biopsied. If no lesion was seen, then no biopsy was taken and the patient was scored as having a 'benign' examination. Random biopsies of normal appearing tissue were not performed in this study. No review of pathology. Medium risk	Estimate adjusted for age, sexual risk group, receptive anal intercourse (RAI), smoking, AGW and recent CD4+. Low risk	HSIL-AIN2+ associated with RAI and lower CD4+ count
Gaisa et al, 2017	Retrospective cohort study abstracted data from a longitudinal clinical database of HIV-infected women. Women were engaged in care at 1 of 3 clinical sites where they were offered anal cytology screening, and subsequently referred for HRA if anal cytology was abnormal. Women with benign or inadequate anal cytology were not routinely referred for HRA and were not included in the analysis of HRA results. The primary analytic sample included 208 individual women with abnormal anal cytology who underwent HRA between April 2009 and July 2014. Analysis includes only patients with abnormal anal cytology and HRA; bias towards individuals with disease; 50% women referred for HRA attended the HRA visit. High risk	As for Gaisa, 2014	Crude estimate only. High risk	Smoking status associated with HSIL-AIN2+ (adjusted for RAI and current CD4+, age and years since HIV diagnosis)
Gautam et al, 2018	Cross-sectional exploratory study was conducted between 2014 and 2015 in HIV positive men attending the ART Center of Banaras Hindu University (BHU) with approximately 15,000 PLHIV registered in it. All HIV positive men above the age of 18, attending the ART centers were eligible for the study. Low risk	Cytology smears were evaluated by a pathologist under light microscope and cytological changes were classified according to Bethesda system normal i.e. no cell changes; NILM (negative for intraepithelial lesions and malignancy) which includes inflammatory changes, organisms, atrophic changes and reactive changes; ASCUS (atypical squamous cells of undetermined significance); ASCH (atypical squamous cells cannot exclude a high grade squamous intraepithelial lesion); LSIL (low-grade squamous intraepithelial lesions) and HSIL (high-grade squamous intraepithelial lesions). Out of 126 cases, 31 (25%) slides were broken, lost or found to be inadequate for result.	Crude estimate only. High risk.	history of anal intercourse (OR, 6.1; 95% CI, 2.0– 18.7) p-value 0.00 and WHO clinical stage (III+IV) (OR, 2.7; 95% CI, 1.1–7.5), p-value 0.04) in univariate analysis
Gimenez et al, 2011	Cross sectional study conducted among 128 HIV-positive patients of both genders seen in the coloproctology outpatient clinic of the Tropical Medicine Foundation of Amazonas. Unclear on recruitment method. Participant demographics unclear, proportion female, sexual orientation and median age not given. High risk.	Following anal canal cytological sampling, patients were submitted to HRA, by three colorectal surgeons after topical application of 3% acetic acid, in the anal canal, for 2 minutes. Biopsies of acetowhite lesions were performed. When no acetowhite lesion was observed, biopsies were performed in a standardized location (just above the pectinate line	Crude estimate only. High risk	None reported

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		at the 7 o'clock position, considering 12 o'clock the anterior commissure). Results (Table 2) do not clearly define outcome grade – understood to be AIN1+ . Medium-high risk		
Gingelmaier et al, 2010	Prospective study performed at a specialized gynaecological outpatient clinic for HIV-infected women at the University of Munich. Consecutive women with a known HIV infection who came for a gynaecological examination for different reasons between September 2007 and September 2008 were included in the analysis. Small sample. Medium risk.	Perianal cytology samples taken. Author do not specify how “abnormal” cytology is defined, but assumed to be ≥ASCUS (according to Bethesda). If the cytology was suspicious of a low-grade or high-grade lesion, high resolution anoscopy (HRA) and anal biopsy of visible lesions were undertaken. Medium-high risk	Crude estimate only. High risk	None
Goeieman et al, 2017	As per previous. Low risk	Participants with an abnormal anal cytology defined as atypical squamous cells (ASC) or greater, and 20% of those with a negative cytology were asked to return for HRA with biopsy of visible lesions. Authors suggest potential underestimation of the HSIL-AIN prevalence (60% of NILM on cyto were LSIL on HRA). Quality assurance activities included quarterly reviews of digital HRA photographs and periodic in-person observation and mentoring of HRA procedures. The pathologists were not masked to the cytology results but were masked to the HRHPV results. Histology specimens were interpreted by multiple pathologists from the South African National Health Laboratory Service in Johannesburg. Low risk	Adjusted for HIV related factors where associations found in MVA. No data or adjustment for receptive anal intercourse. Medium risk	No relationship between CD4+ and anal HSIL –possible ascertainment bias of HSIL.
Goldstone et al, 2019	a randomized, open-label trial in HIV-infected participants comparing the 1-year clearance of biopsy-proven intra-anal HSILs treated with IRC with regression of HSILs absent treatment at 7 US AIDS Malignancy Consortium (AMC) trial sites (ClinicalTrials.gov No. NCT01164722). Participants were recruited between 2011 and 2014. All clinicians performing HRA and IRC were certified according to standards developed by the AMC HPV Working Group. Study participants were HIV-infected adults aged ≥27 years with 1–3 anal canal HSILs (index lesions). At enrollment HRA determined the presence of ≥1 previously identified, biopsy-proven index HSILs. Study participants were randomized 1:1 to HSIL ablation with IRC or active monitoring (AM)	Treatment arm (TA) participants were seen every 3 months for digital anorectal examination, anal cytology, and HRA with biopsy of areas with suspected HSILs. After ablation, HSILs were characterized in 2 ways: at the site of the original index lesion (recurrence) or at a new site (metachronous). Biopsy-proven recurrent or metachronous HSILs were treated with IRC within 4 weeks of diagnosis. Participants were followed up for 24 months after baseline treatment. At 12 and 24 months, TA participants underwent biopsy at index lesion sites (even if no lesion was seen) and sites with lesions suspected of being new HSILs. Study participants in the AM arm were examined by means of digital anorectal examination, anal cytology, and HRA every 3 months. Anal biopsy specimens were obtained only for lesions suspected of possible progression to invasive cancer. At 12 months after enrollment, AM arm participants underwent biopsy at index lesion sites (even if no lesion was seen) and sites with lesions suspected of being new HSILs. Anal biopsy specimens were interpreted at local site laboratories. A single pathologist reviewed biopsy specimens centrally. Discordant interpretations were reviewed and adjudicated with a second central pathologist. The central pathology interpretation was used for analysis. If a biopsy specimen was not available for central review (for 4 follow-up biopsy specimens through 12 months), the local histology result was used. The primary end point was complete index lesion clearance (CILC) at month 12. In the TA, CILC was defined as no biopsy-proven HSIL at the site of all index lesions from the time of the initial treatment through month 12. In the AM arm, CILC was defined as regression of all index HSILs to LSILs or normal findings at month 12.	Association of ART and lesion clearance adjusted for treatment arm (infrared coagulation vs. no treatment but active monitoring), clinic site of recruitment and number of index lesions	Complete lesion clearance associated with IRC treatment, clinical trial site and smaller number of index lesions
Gonzalez et al, 2013	CoRIS-HPV is a cohort study within CoRIS, an open, prospective and multicenter cohort of adult patients with confirmed HIV infection and naive to antiretroviral treatment at study entry, established in January 2004 in 30 sites from 13 of Spain's 17 Autonomous Communities. CoRIS-HPV was set up in 2007 with the objective to study the epidemiology of HR-HPV infection in MSM. Low risk	Anal cytology samples were obtained in Thinprep, most of them (83.0%) were read by two independent cytologists, and those with discordant results were re-evaluated to achieve a consensus diagnosis. High risk (cytology only)	Crude estimate only. High risk	
Goodall et al, 2012	Case-notes of all (n= 287) HIV-positive MSM attending HIV clinic at Chalmers Sexual Health Centre over a 12-month period after implementation of protocol for anal cytology screening for HIV positive MSM on a yearly basis were reviewed. Of 285 HIV positive MSM seen during this period, 25% were not offered anal cytology screening. Of those that were offered, 38% declined (of 285 MSM, 47% men had a cytology result included in the final analysis). Patients not offered anal cytology screening were more recently diagnosed with HIV, were less likely to be on ART and have a higher nadir CD4+. High-medium risk	LBC material was examined by a pathologist and graded as normal, insufficient sample, and abnormal (mild dyskaryosis, moderate dyskaryosis or high-grade dyskaryosis.) High risk (cytology only)	Crude estimate only. High risk	ART status, previous AGW and CT infection (not evaluated in MVA)
Guiguet et al, 2009	Large prospective hospital cohort – French Hospital Database on HIV (FHDH-ANRS CO4). Patients infected with HIV-1 were eligible if they had never received ART before enrolment in the	Clinical events were recorded with International Classification of Diseases (ICD) definitions (version 10). Disease misclassification could	Adjustment for age, sex and HIV transmission group, and sub-Saharan origin. ART not	Anal cancer associated with duration of time with high

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	FHDH cohort, had never been included in a double-blind clinical trial, and had not been diagnosed with cancer before 1998 (which could act as competing risk). Patients were excluded if information about AIDS defining events was incomplete. Patients were followed up until diagnosis of cancer, death, the end of follow-up, or Dec 31, 2006, whichever occurred first. Low risk	have occurred; however, because of the magnitude of person-time in the cohort, the probability of being wrongly classified as having a malignancy will be negligible, limiting bias for the rate ratios. No histopathological diagnosis but ICD10 codes selected because they were validated and found to be highly sensitive to a diagnosis of invasive anal cancer. Low risk	included in the model. Almost all anal cancer cases were receiving ART. Low risk	(>100,000 c/ml) HIV VL duration with low CD4+, HIV transmission group (ID1 and women at lower risk).
Heard et al, 2015	A cross-sectional and screening study nested within the VIHGY cohort, a multicenter study of HIV-infected women conducted in 5 sites within France. Women were recruited for this substudy during their first VIHGY visit in 2012 at 3 of the VIHGY hospital sites: Paris-Pitié-Salpêtrière, Colombes-Louis-Mourier, and Marseille-Sainte Marguerite. Women were eligible if they had no history of anal cancer, and were invited to participate in a 2-step study: (1) anal HPV specimen collection during the gynecological visit and (2) to undergo an HRA at specialized anal dysplasia clinics. Of 171 women enrolled, 36% were from SSA. Contemporary cohort of WLHIV receiving effective ART and regular gynaecological follow-up. Of 352 women invited to participate, 91% accepted. Of these, 54% attended the HRA exam. These women were older with higher median CD4+, more received ART with undetectable PVL. Bias towards women with well controlled HIV (less likely to see impact of ART, PVL). Significant loss to follow-up (to HRA). Low/medium risk	Anal swab specimens were collected for cytology before the physical examination, which included a DARE. HRA was performed by trained anoscopists without knowledge of the cytology and HPV results. Acetowhite areas were biopsied and processed for histological examination. Anal cytology and biopsies were read in local laboratories, blinded to the HPV result, and then reviewed centrally. If no biopsy was taken, histology was considered to be benign, provided that the HRA was normal. Composite endpoint of the most severe diagnosis on cytology or histology. In absence of histology, the grade was based on cytology alone. If the anal cytology was unsatisfactory, and the HRA was normal, those who were HPV negative were categorized as benign. Women with unsatisfactory cytology and no biopsy were excluded from the analyses if HR-HPV was positive. HG-AIN+ was defined as histological HG-AIN+ or HSIL on cytology, in the absence of biopsy. Low risk	Unadjusted estimate (HIV related factors not significant in MVA; no data on sexual behaviour). High risk	Strongest predictor was history of cervical lesions and concurrent HPV16 anal infection
Hessol et al, 2009	Study nested within the Women's Interagency HIV Study (WIHS), a prospective study of HIV-1 infection in women, conducted in five locations within the United States. Briefly, between October 1994 and November 1995, 2056 HIV-1 infected and 569 uninfected women were enrolled. A second enrollment, between October 2001 and September 2002, added 737 HIV-infected and 406 HIV-uninfected women. Women were recruited in years 2001–2003 from the Brooklyn, Chicago, and San Francisco Bay Area WIHS sites. Women were eligible if they had no history of HGAIN or anal cancer. Low risk.	Women with abnormal anal cytology were referred for HRA and biopsy of visible disease. Among the 148 women with abnormal anal cytology results, 50% had anoscopy and 41% had a biopsy for histological evaluation. Grade of the lesion defined as the more advanced diagnosis on cytology or histology when both were available. In the absence of histological data, grade was based on cytology alone. Medium risk	Estimate adjusted for age, smoking, CD4+, PVL, anal HPV, cervical HPV, but not nadir CD4+ or duration on ART. Medium risk	Anal HPV only significant factor associated with HSIL-AIN2+
Hessol et al, 2007	All adult AIDS cases aged 16-86 years whose AIDS was initially diagnosed between 1990-2000 were identified from the San Francisco, California AIDS surveillance registry. AIDS cancer patients were matched cancer cases diagnosed between 1985-2002 in the California Cancer Registry, a statewide population based registry. Of 17,709 adult AIDS cases initially identified, 12% were excluded as they were non-San Francisco residents at the time of AIDS diagnosis, 8% were excluded as they had no information on HAART use or were lost to follow up. Low risk	Each cancer was classified by using the SEER program site recoding which is based on ICD10 FOR Oncology. Low risk	Adjusted models considered year and ART era (Jan 1996 or later) as time varying covariate, age at AIDS diagnosis, race, HIV transmission group and gender. Medium risk (no adjustment for nadir CD4+)	
Hidalgo-Tenorio et al, 2014	Cross-sectional study conducted between May 2010 and Sept.2013 in a cohort of 140 patients with HIV-MSM recruited consecutively into a program of screening, diagnosis, treatment and follow-up of dysplastic lesions of the anal mucosa. The HIVpositive patients were from among those receiving care in the Infectious Disease Unit of the Hospital Universitario Virgen de las Nieves (Granada, Spain) The inclusion criteria were: adult (≥18 years of age) MSM infected with HIV. The exclusion criteria were: females, heterosexual HIV-positive males, and history of anal canal neoplasia at the time of recruitment into the study. Low risk	Cytology using the ThinPrep Pap Test; the same senior pathologist carried out the cytology evaluation, validation of the PCR, and histology analyses. Anoscopy was performed; samples were taken for histology examination not only from the lesions (color change with irrigation with 5% acetic acid), but also from other parts of the quadrant with ostensibly-normal mucosa. No pathology review. Medium risk.	Estimate adjusted for perianal condylomas, HPV68, previous syphilis diagnosis No data on RAI. High risk	AIN2+ associated with ART status, perianal condylomas, HPV68, previous syphilis diagnosis
Hidalgo-Tenorio et al, 2015	As for Hidalgo-Tenorio et al, 2014 (cannot rule out the possibility this cohort may be the same as Hidalgo-Tenorio et al, 2014, or different individuals). Medium risk	As for Hidalgo-Tenorio et al, 2014, Medium risk.	Unadjusted estimate for ART. PVL estimate adjusted for HPV68, previous syphilis diagnosis. No data on RAI. High risk	AIN2+ associated with HIV PVL detection, HPV68, previous syphilis diagnosis
Holly et al, 2001	Participants recruited from November 1995 to January 1997 from women who were participating at the San Francisco Bay Area site of the multicenter Women's Interagency HIV Study (WIHS); baseline visits (study entry) occurred from October 1993 through November 1994, with follow-up evaluations at 6-month intervals. A total of 251 HIV-positive and 68 HIV-negative women were enrolled. May include some women in the pre-HAART era. Medium risk	Anal cytology was evaluated by an experienced pathologist who had no knowledge of the clinical status of the participants, their questionnaire responses, or other test results. HRA conducted if they had abnormal anal cytologic results. Women who consented underwent an anal biopsy if a lesion was present. If more than one lesion was seen, biopsy specimens were obtained from areas with different colposcopic appearances. Low-medium risk	Estimates for PVL and CD4+ adjusted for anal HPV, history of anal intercourse and concurrent cervical cytology abnormalities. Low risk	ASCUS+ associated with HIV PVL detection, anal HR-HPV detection, history of anal sex and concurrent cervical cytology abnormalities
Lacey et al, 1999	In January 1994 HIV positive homosexual men were recruited for this study. Subjects were recruited from a larger cohort (300 patients, 33% CDC group C) attending North Manchester General Hospital for their HIV care. Medium risk (low number)	Anal cytology and anoscopy conducted on all. All cytology smears were examined by one observer who had knowledge of the previous results but not of the clinical findings at the time when the smear was taken. High risk	Crude estimate only. High risk	
Libois et al, 2017	Since June 2011, a systematic anal cancer screening programme is offered to all HIV-positive MSM followed at the AIDS reference centre of Saint-Pierre University Hospital in Brussels, where 2950 patients who are HIV positive (33% MSM) are currently in care and included in the	Anal swab for cytology was followed by HRA in case of any significant abnormalities at cytology. In case of abnormal cytology (including ASC-US), HRA with biopsies was performed by a single	Adjusted estimate for ART status, adjusted for age only (though other HIV related factors not found to persist in MVA) Low risk.	HSIL-AIN2+ associated with long duration ART

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	Saint-Pierre HIV Cohort. Between June 2011 and February 2013, patients who performed this screening and had appropriate follow-up (normal swab or HRA with biopsies in case of abnormal cytology) were included in this cross-sectional study. Low risk	gastroenterologist, specifically trained in HRA. Immunostaining for Ki67 and P16 was routinely carried out on all biopsies as help for histological grading of lesions. The same expert pathologist assessed all the samples. The first 250 anal cytology samples were blindly reviewed by another pathologist with international experience in quality control. Medium risk		
Li et al, 2009	Cross-sectional study of anal Pap smear results and linked clinical, sociodemographic and behavioural information collected at the TRC-ARC in Bangkok. The Thai Red Cross AIDS Research Centre (TRC-ARC) began offering anal Pap smear as part of an annual health examination programme to HIV positive and HIV negative MSM in January 2007. Participants were those receiving anal Pap smears between January 2007 and April 2008. Participants were part of a self-pay service cohort and may not be representative of all Thai MSM due to the cost of Pap smear screening. Our clients receiving anal Pap smears had on average twice the median household monthly income of all Thais surveyed at the TRC-ARC. This difference in socioeconomic status may result in lower ASIL prevalence due to better access to health care. Small sample size – unclear how the men were selected for inclusion. High risk	Anal Pap smears were performed; a cytotechnician screened all slides and positive slides were re-screened by the head cytotechnician. High risk	Adjusted for age, CD4+ count, anal condyloma symptoms. Sexual behaviour not included in MVA model. Low risk	ASCUS+ associated with anal conylooma only
Limia et al, 2017	Cross-sectional study to detect ASIL and HPV infection. Study participants were outpatients of the sexually transmitted diseases (STD) clinic at the Institute of Tropical Medicine “Pedro Kourí” recruited between April and August 2012. Those eligible to participate were HIV-positive males with a history of a previous or current STD, willing to give informed consent to an interview and tests for anal HPV infection and anal cytology. Small sample. High risk	Outcome is 6 high risk types only (16, 18, 31, 33, 45, 58). High risk	Crude estimate only. High risk	
Liu et al, 2018	The Mount Sinai high-resolution anoscopy (HRA) database was searched from 2009 to 2016 for patients diagnosed with anal LSIL by HRA-guided biopsy. Patients meeting the following criteria were included in the study: no prior history of HSIL, initial HRA and biopsy revealing LSIL without any concomitant HSIL, and surveillance HRA and biopsy of the index LSIL site having been performed within 2 years of initial diagnosis. Individuals with risk factors for anal cancer were screened by either primary care physicians or infectious disease/HIV specialists using anorectal cytology (ARC). Patients were offered referral for HRA and biopsy of lesions suspicious for HSIL or cancer if ARC was abnormal (ASCUS+). Medium risk	All patients underwent HRA examination and biopsy twice within 2 years. On the basis of surveillance biopsy results, lesion outcomes were categorized as progression (if HSIL was detected at the prior LSIL site), persistence (if LSIL was detected) or regression (if benign mucosa was detected). Low risk	Crude estimate only. High risk	
Machalek et al, 2016	The Study of Prevention of Anal Cancer (SPANC) is a prospective study of HIV-positive and HIV-negative MSM, based in Sydney, Australia. Participants were recruited mainly from community based settings; about 35% of HIV positive and 5% HIV negative men were recruited through medical clinics. Eligible participants were men aged 35 years or older who reported sex with another man in their lifetime. Participants were excluded if they were unable to understand English, unable to attend scheduled visits, or were unwilling to undergo HRA, had bleeding disorder or were on anti-coagulation medication. Men who previously received HRA or with a history of anal cancer were also excluded from the study. Low risk	Anal swab collected for cytology analysis, followed by HRA with acetic acid and lugol’s iodine. Abnormalities suggestive of ASIL were biopsied for histological assessment. Men without visual abnormalities did not undergo biopsy. When a diagnosis of HSIL-AIN 2 was proposed based on histo-morphologic features on H&E stained slides, immunostaining for p16-INK4A was performed. Positivity of p16 coupled with H&E features of AIN2 were both required for diagnosis of HSIL-AIN2. If p16 was negative, lesion was downgraded to LSIL or negative for SIL depending on other criteria. When multiple biopsies were taken, the result with the highest grade was used. ASIL disease classification based on composite endpoints of the most severe cytology or histology. Low risk	Adjusted for number HR-HPV types, and HPV16 positivity, age and smoking status. No associations observed with HIV related factors. Men with well controlled HIV may prevent observing any associations by HIV related factors (small number of men not on ART, with HIV PVL detection, low CD4+). Low-medium risk	None observed for men with HIV
Masia et al, 2019	A prospective study conducted in the HIV cohort from the Hospital General Universitario de Elche (Spain) between November 2013 and February 2017. Eligible participants were MSM ≥18 years old, who were invited to be explored through high-resolution anoscopy (HRA) for screening of anal dysplasia and for anorectal secretion sampling for STIs investigation. Recent anorectal surgery was an exclusion criterion. Unclear recruitment method or number of refusals.	Study participants underwent HRA, performed by a single, trained, infectious diseases specialist. The anal transformation zone and distal canal were afterwards explored using lugol solution. All suspicious areas were biopsied for a histopathological assessment. Lesions were classified by the Bethesda system into 3 categories: without dysplasia, low-grade dysplasia (AIN-I), and high-grade dysplasia (AIN-II/III). If multiple biopsy samples were taken at once, the sample with the highest AIN grade was considered.	Crude estimate only	
Marra et al, 2019	HIV-positive MSM aged ≥18 years were recruited for a prospective cohort study in 2010–2011 at 3 sites in Amsterdam, the Netherlands [19]. Participants were followed up approximately every 6 months, up to 24 months. Independent of the H2M study, HIV-positive patients in regular care were offered HRA at 3 clinics in Amsterdam. Data of all HRAs of these clinics up to December 2015 were extracted from patient records for research purposes and merged with the H2M data set. Only HIV-positive H2M participants who underwent a first HRA after their last H2M visit in 1 of these 3 clinics were included in the present study. Only results of the first HRA of each participant were included. HIV-related data were obtained from the Dutch HIV Monitoring Foundation. Clinical information related to the HRA was obtained from the infectious diseases	HRA consisted of a digital rectal examination, followed by intra- and perianal inspection with a high-resolution colposcope after repeatedly applying acetic acid (3–5% solution) and staining with Lugol’s iodine when indicated. Areas suspicious for squamous intraepithelial lesions were biopsied (151 or 78% men had at least one biopsy) The biopsied lesions were graded by specialized pathologists. In 2 out of 3 clinics, the pathologists used p16 staining for AIN2 grading of biopsies. The majority of AIN2 diagnoses were confirmed by p16 staining. The highest-grade biopsy defined the overall diagnosis.	Crude estimate only	In a multivariable logistic regression, anal HPV16 and HPV35 persistence remained significantly associated with anal HSIL (adjusted OR 2.41, 95% CI 1.09–5.35, and adjusted OR 3.19, 95% CI 1.10–9.23, respectively)

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
	physician or dermatologist. This is possibly the same cohort as that described by Siegenbeek et al (2017).			
Mbang et al, 2015	A retrospective cohort study of male US veterans with HIV who were diagnosed between 1985–2010 using the Veterans Affairs HIV Clinical Case Registry (CCR) HIV-infected individuals were identified from the VA HIV clinical case registry (CCR). Established in 1992, the registry draws upon the electronic medical records of over 60,000 HIV infected patients diagnosed after 1985 who were ever cared for by the VA. The study population was restricted to HIV-infected veterans who were diagnosed between 1985–2010, were over the age of 18 with an identifiable HIV diagnosis date, or the earliest initiation of antiretroviral therapy. Individuals with only a single ICD-9 code for HIV and no lab or confirmatory pharmacy records were not included. Only men were included because of the small number of HIV-infected women veterans (<2%). Individuals excluded if date of death or censor was the same as their initial HIV diagnosis date. Only veterans ever receiving cART were included; cART users with less than 90days of follow-up or without quantifiable CD4 or HIV RNA measurements within 90days of cART initiation were excluded. A total of 28,886 HIV-infected male veterans included in the registry (43% met inclusion criteria. Low risk	The primary endpoint was incident SCCA, identified from inpatient and outpatient ICD-9 codes 154.2 and 154.3. These SCCA ICD-9 codes have been previously validated in the VA and determined to have a positive predictive value of 88%. Prevalent SCCA cases (i.e., individuals diagnosed before or within 90days after the initial HIV diagnosis date) were excluded. The follow-up interval spanned from the index HIV diagnosis date to SCCA diagnosis, death, or December 31, 2010 (the final date of the current CCR iteration), whichever occurred first. Low risk	adjusted for age at HIV diagnosis, race/ethnicity, illicit drug use, era of HIV diagnosis, Deyo comorbidity score, nadir and recent CD4, percent of time with undetectable HIV RNA, and number of HIV RNA measurements per year). No stratification by sexual orientation. Low risk	Protease Inhibitors associated with increased risk of anal cancer Time spent with HIV viral suppression also associated with reduction.
Palefsky et al, 1998 (C3)				
Palefsky et al, 2005	MSM were recruited into this cohort study between February 1998 and January 2000 through newspaper advertisements and other community outreach at University of California, San Francisco (UCSF). Low risk	Anal cytology (conventional, direct smears) was performed and interpreted using the Bethesda criteria. High-resolution anoscopy (HRA) after application of 3% acetic acid was completed with a biopsy of visible anal lesions unless there were medical contraindications. An anal biopsy was performed if one or more lesions were visualized. If more than one lesion was seen, biopsies were obtained from areas within the lesions that had different colposcopic appearances. A composite anal diagnosis based on cytology and histology was used in analysis. If both cytological and histological results were available, the diagnosis used for analyses was the more severe result. Participants were classified as normal if they had normal cytology and no lesions seen by anoscopy, or if both the cytology and histology results were normal. If a lesion was seen by anoscopy but not biopsied, the cytology result was used for diagnosis unless the cytology was normal. In that case, the diagnosis was considered indeterminate and the data were excluded from analysis. Medium risk.	Adjusted for months of HIV positivity and age as a continuous variable; number of HPV types, CD4+ cell count, HIV viral load. No adjustment for sexual behaviour. Low risk	HSIL-AIN2+ associated with higher number HPV types, and HAART use
Payam et al, 2011	Retrospective chart review evaluating the proportion of anal dysplasia among a multiethnic population from an ambulatory university-based HIV clinic in Hawaii. Unclear selection method and small sample. High risk	Anal Pap specimens placed in a CytolyThinPrep medium and sent to a Clinical Laboratory Improvements Amendments (CLIA) certified laboratory for processing and diagnostic work up. If an anal Pap cytology result was abnormal, then the patient received recommendations for HRA. Biopsies obtained from the HRA procedure were sent to the same CLIA-certified laboratory for pathology diagnosis. An abnormal Pap smear was defined as anal dysplasia on routine Pap smear. Unclear outcome definition (ASCUS+?). No cytology review. Medium/high risk	Crude estimate only. No data on sexual behaviour. High risk	None reported in MVA
Pereira et al, 2008	Descriptive study carried out in the Infectious and Parasitic Diseases Outpatient Clinic of the University Hospital of the Federal University of Pernambuco and in the Colposcopy and Lower Genital Tract Sector (SCTGI) of the same hospital from July to November 2006. Out of a total of 118 male patients invited, a group of 60 agreed to take part in the study. Unclear selection criteria (eligibility) and reasons for refusal (49% refusals), small sample size. High risk	Anal cytology performed; anoscopy was performed after cytology with acetic acid and lugol's iodine and findings suggestive of anal lesion were biopsied (biopsy indicated by anoscopy only) Histological evaluation was carried out by a single pathologist. The outcome of interest was the presence of a perianal and an anal lesion characterized by the condyloma acuminata and intraepithelial neoplasia according to anoscopy under colposcopic vision summed to anal oncotic cytology and anal histology. Outcome in analysis assumed to be AIN1+. Medium-high risk	Crude estimate only. No stratified analysis according to sexual behaviour/sexual orientation. High risk	None reported in MVA
Phanuphak et al, 2013	Thai men aged ≥18 yrs with history of anal sex with men, with documented HIV positive status (within previous 30 days) and who visited Men's Health Clinic at the Thai Red Cross AIDS Research Centre in Bangkok, Thailand were consecutively enrolled over a 12 month period into this prospective study. MSM were excluded if they had prior treatment for anal cancer, anal cytology or HRA or infrared coagulation within 12 months prior to enrolment, trichloroacetic acid or podophyllin application to intra-anal area in past month, or evidence of active concurrent intra anal or perianal bacterial or HSV infection. Low risk	Anal swab collected for cytology at baseline, month 6 and month 12 and added to liquid based medium. Anal cytology performed prior to HRA. All participants had HRA at baseline, month 6 and 12, regardless of anal cytology results by the same study physician. Abnormal anal tissue was biopsied. Histological diagnosis was made by three different pathologists; each pathologist was blinded to diagnosis of the other two pathologists. Discrepancies resolved through review and consensus.	Crude estimates only (CD4 did not persist in MVA). High risk	Persistent HPV16/18 associated with increased risk of incident HSIL-AIN2+

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
		A composite anal diagnosis was used based on cytology and histology results. Cytology results were used for men with normal HRA findings and for men with abnormal cytology who refused a biopsy. Low risk		
Piketty et al, 2003	Between June 1999 and October 2000, 120 HIV seropositive men attending the outpatient clinic of Hôpital Européen Georges Pompidou, Paris, France, were recruited in a cross-sectional study of anal HPV infection and anal SIL in HIV-seropositive men. Men were eligible for the study if they had acquired HIV through homosexual or bisexual contact or through injection drug use, were older than 18 years of age, and had absolute CD4+ cell counts less than 500 x 10 ⁶ cells/L. Injection drug users who had sex with men were excluded from the study. The patients were recruited from a cohort of 1198 HIV-infected patients who were followed at the Clinical Immunology unit of Hôpital Européen Georges Pompidou. All patients were consecutively enrolled into the study. No eligible patient declined participation. Low risk	When cytologic abnormalities were found (ThinPrep cytologic screening), consenting patients underwent anoscopic examination and biopsy with the use of a colposcope. If both cytologic and histologic results were available for analysis, a patient's diagnosis was categorized as the more severe result. Definition of outcome is unclear but understood to be SIL-AIN1+ (composite cytology-histology endpoint) Medium-High risk	Crude estimate only. High risk	Among IDU, low CD4+, HIV viral detection, AIDS defining illness and anal HPV. Among MSM, higher number sex partners and anal HPV.
Piketty et al, 2008	Large prospective nationwide hospital cohort – French Hospital Database on HIV (FHDH-ANRS CO4) created in 1989. The only inclusion criteria are HIV-1 or HIV-2 infection and written informed consent. Patients were not eligible for this study of <13 years, not followed between Jan 1992 AND Dec 2004, if they had less than 6 months follow up or if they had a history of anal cancer or ongoing anal cancer at FHDH enrolment, or if they were receiving ART in a double blind trial. Overall, 86,332 were eligible for this study. Low risk	ICD codes used by FHDH (ICD9 prior to 1997 and ICD10 thereafter). Available histological data was used to validate the diagnosis of invasive anal cancer and excluded all cases of carcinoma in situ. Eight cases were classified as presumptive anal cancer as no histological data was available. All cases of anal cancer were validated and 94% were histologically confirmed. Low risk	Adjusted for age, HIV transmission route, nadir CD4+, AIDS diagnosis before event, ART period. No data on HIV viral suppression. Low risk	Anal cancer more likely among older participants, MSM, in patients with prior diagnosis of AIDS and in patients with lower nadir CD4+ Anla cancer more likely in recent ART era compared to pre ART period.
Pittayanont et al, 2014	HIV infected women who came for a routine visit at HIV clinic of Prapokkiao Hospital, Chanthaburi, Thailand, between March 2013 and February 2014. Inclusion criteria were confirmed HIV infected women who visited Prapokkiao Hospital HIV clinic during the study period. Exclusion criteria were if patients had active lower gastrointestinal bleeding, anal inflammation, acute anal fissure and those who declined to participate in the research. Unclear on recruitment method (number screening and enrolled) Medium risk	Anal cytology using pap method and read according to Bethesda 2001 System. Not clear if any review of cytology reading conducted. High risk	Crude estimate only. High risk	In univariate analysis, duration since HIV diagnosis, duration on ART
Powles et al, 2008	The Chelsea and Westminster cohort; people living with HIV seen at regular intervals for clinical assessment, attending since 1983. Low risk	The registration of cancers is checked by a dedicated HIV oncologist and also collected in a separate HIV cancer database. Observed numbers of anal cancer cases compared with expected numbers for the general population, derived from the Thames Cancer Registry. Low risk	adjusted for age, sex, ethnic group, presence/absence of AIDS, nadir CD4 and duration of HIV infection. Low risk	Low nadir CD4 associated with increased risk of anal cancer
Richel et al, 2013	The study was performed at the HIV and dermatology outpatient clinics of the Academic Medical Center in Amsterdam, the Netherlands. All HIV+ MSM in care over 18 years of age were eligible if they did not have a history of anal cancer or current active inflammatory bowel disease. Of 656 MSM invited for screening, 311 were eligible and consented (29% refused, 2% fulfilled exclusion criteria, 9% had significant comorbidity, 11% were excluded as they participate in co-existing study). Low risk	Screening for AIN was performed by HRA by a single HRA experienced physician. Suspect lesions were biopsied for histopathological analysis, including Ki-67 and p16 immunostaining. A single pathologist evaluated all biopsies. If more than one biopsy was taken, the highest AIN grade was considered as outcome. 56% men had histologically confirmed AIN (AIN1+); remaining 44% did not have suspect lesions on HRA or AIN was ruled out in biopsies from suspect lesions. 305 men had HGAIN. Possibility too underestimate prevalence of disease using HRA as screen test. Medium risk .	For ART status, HIV PVL and CD4+ count, crude estimate only (only duration ART, years since HIV diagnosis, anal ecstasy use, use of GHB and history of AGW associated with AIN1+ in univariate analysis). Separate MVA for HGAIN outcome did not find any association with HIV related factors (HIV PVL, nadir and current CD4+). Low risk	Duration on ART (per year on ART) associated with AIN1+, adjusted for GHB use and anal ecstasy use.
Richel et al, 2013 (Lancet Oncology)	An open-labelled randomised trial to compare efficacy and side-effects of imiquimod, topical fluorouracil and electrocautery for the treatment of AIN. MSM with HIV aged ≥18 years visiting the HIV outpatient clinic of the Academic Medical Centre, Amsterdam, Netherlands were offered screening for AIN. Of 650 men screened for participation, 388 (60%) were eligible and consented to participate; of those 246 (63%) had AIN. Men with histologically confirmed AIN were randomly assigned to receive either 16 weeks of imiquimod, 16 weeks of fluorouracil, or monthly electrocautery for 4 months. Participants were assessed by HRA 4 weeks after treatment. The primary endpoint was histological resolution of AIN at 4 weeks after end of treatment. Low risk	At enrolment, all men underwent HRA. Suspect lesions were biopsied for histopathological analysis (assessed by a single histopathologist). Biopsy samples taken 4 weeks after last treatment date; samples were taken areas where AIN had been reported previously and if necessary from suspect lesions. Patients with persisting or progressing lesions were referred for further treatment and excluded from further study assessments. Complete response was defined as resolution of AIN and partial response defined as regression from HG to LG AIN. Low-Medium risk	Associations with duration on ART were conducted, irrespective of treatment used. Estimates were adjusted for type of treatment, years of HIV, current CD4+ and high grade AIN. Low risk	Prolonged duration on ART was associated with complete or partial response to treatment.
Richel et al, 2015	Data were selected from the ongoing AIDS Therapy Evaluation in the Netherlands (ATHENA) national observational HIV cohort, a nationwide data set, which includes anonymized data from all HIV-1-infected patients under care in the 26 HIV treatment centers in the Netherlands. Epidemiological, clinical, virological, and immunological data are collected retrospectively at entry in the cohort and prospectively thereafter	cases of anal cancer were identified for the period 1995–2012 and incidence rates of anal cancer were calculated per 100,000 person-years of follow-up. Follow-up time was from the date of HIV diagnosis till the date of diagnosis of anal cancer, death, last clinical visit, lost to follow-up, or closure of the database (February 1, 2013). Each treatment center was visited to verify the source documents and confirm pathological diagnoses.	Association of nadir CD4 and anal cancer adjusted for alcohol abuse and smoking	Anal cancer associated with a low nadir CD4 cell count, alcohol abuse and smoking (HR, 1.64; 95% CI: 1.10 to 2.45)
Robbins et al, 2018	Data from the MultiCenter AIDS Cohort Study (MACS), a cohort study of HIV positive and HIV negative MSM from 4 sites (Baltimore, Chicago, Pittsburgh and Los Angeles), visits occur every 6 months. For this sub-study, all participants who attended any study visits between June 2010 and	Cytology conducted; High number of inadequate cytology results. Outcome is abnormal cytology on first 3 consecutive abnormal cytology	Adjusted for sexual behaviour. High risk	Consistently abnormal cytology (ASCUS+) associated with current CD4 count decrease, low nadir CD4

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
	July 2011 were offered a free anal cytology test. Men with unsatisfactory cytology result were offered another test at their next visit. HIV positive men were offered annual cytology up to 4 cytologies in total. Men who had treatment of anal dysplasia between first and second cytology (n=38) were excluded from analysis. Of a total 709 HIV positive with baseline cytology test, 502 did not require treatment and had 2 valid cytology results, 328 had at least 3 valid cytology results and no treatment. Low risk	smears compared to men with first 3 consecutive negative cytologies. High risk		count , increased number of condomless receptive anal sex acts, older age and race other than non-Hispanic white.
Rosa-Cunha et al, 2011	From February to July 2006, patients 18 years and older with HIV infection attending routine clinic visits and two having no history of anal cancer or prior anal cytology screening were informed of the study. Of a total 160 HIV infected patients invited to participate, 131 (82%) agreed to participate; of those 98 (75%) had adequate cytology results and were included in final analysis. Small sample. Medium risk	Anal cytology was performed and all samples were read by one pathologist. Patients with abnormal cytology classified as AS-CUS or greater referred for HRA with biopsy of visible lesions seen by addition of 3% acetic acid. HRAs were performed by proctology surgeons trained in HRA. Biopsy results were coded as the most severe category, if multiple biopsies were taken. Associations of ART and histologically confirmed AIN available for only 31 participants; results from cytology (outcome of cytology ASCUS+ presented in place) . High rate of inadequate cytology results High risk	Crude estimate only (no MVA conducted) High risk	None reported in MVA
Rovelli et al, 2017	Retrospective observational study on HIV-infected male patients who were receiving primary inpatient or outpatient care for HIV infection at the Infectious Diseases Department of the San Raffaele Scientific Institute (Milan, Italy). Medium risk	Cytology conducted using liquid based cytology preparation. Anal cytology findings were classified as normal if the finding was reported as negative and abnormal if reported as ASCUS or greater. Outcome in the risk factor analysis is LSIL/HSIL. High risk	For CD4+ and ART, unadjusted estimates only (not found to be significant in univariate analysis). HIV PVL adjusted for age, HIV transmission route, yrs of HIV, HbsAg, previous AIDS diagnosis, previous syphilis diagnosis, CD4+/CD8+ ratio, number of HPV types and HPV16 infection. Medium risk	Previous syphilis infection HIV PVL detection, HPV16+, number HPV types,
Salit et al, 2010	Participants were part of the Toronto Research for Anal Cancer Evaluation (TRACE) anal cancer screening study and were enrolled between December 2001 and November 2005. All were HIV-infected men aged 18 years or more with a history of anal receptive intercourse and who were attending tertiary care hospital HIV clinics or primary care clinics in Toronto, Canada. Participants were excluded if they had a history of anal cancer. At entry, none of the participants had known previous anal cytologic studies or anal biopsies, so no prior results were available. The presence or absence of any symptoms, including anal symptoms, did not affect eligibility. Low risk	Participants had concomitant anal cytology (Pap smears), HPV testing and HRA with directed biopsies. Evaluation of anal cytology was performed on a specimen in liquid-based ThinPrep; HRA was done using a plastic anoscope with visualization of the anal squamocolumnar junction staining with 3% acetic and Lugol's iodine. Biopsies were taken by endoscopic forceps from areas that appeared abnormal . Two anoscopists had received formal training in HRA and they examined all the participants. If anal canal at HRA appeared normal, no biopsy was taken and patient was designated as 'Normal'. Where multiple biopsies were taken, diagnosis of most severe histologic lesion was taken. Cytology and biopsy specimens were independently assessed by two experienced gynecologic pathologists using a multiheaded microscope and reached consensus on any specimen for which there had not been agreement in the independent review. Low risk	Crude estimate only (not significant in univariate, no MVA). Medium risk	AIDS-defining illness, low CD4+ and HPV types -16 and -31
Sananpanichkul et al, 2015	As for Pittyanont et al, 2014	Anal cytology using pap method and read according to Bethesda 2001 System. Inadequacy of the collected specimen for evaluation was 34.4% (206/599). High risk	Crude estimate only. High risk	
Scott et al, 2008	In November 2002, an anal cancer-screening program was implemented, using anal cytology, into HIV clinical care at Hospital of Saint Raphael (HSR) . All HIV infected patients seen at the HIV clinic at the HSR were offered anal cytology as part of routine clinical care. Outpatient charts were reviewed for all patients seen between November 2002 and November 2004 who had an anal cytology examination. Of 560 patients seen at HIV clinic, 276 (49%) had at least 1 pap smear and 265 (96%) had sufficient cytology results and were included in final analysis. Unclear selection criteria (significant proportion did not have anal cytology). High risk	All samples were read by 1 pathologist at the HSR who was trained in interpreting anal cytology. Patients with insufficient cells on cytology slide or missing cytology results were excluded. Patients with abnormal anal cytology findings, classified as ASCUS or greater, were referred for surgical evaluation and anoscopy. Anoscopy was performed using a HRA with biopsy of any obvious lesions seen with addition of 3% acetic acid. Medium risk	Results not stratified by risk group (gender or sexual orientation) nor adjusted for sex behaviour. Crude estimate for ART status and HIV PVL not significant in univariate analysis (HIV transmission route - MSM, IDU, heterosexual route - included in model). Medium risk	ASCUS+ associated with low CD4+ , anal disease on physical exam, history of HSV, history of AGW, adjusted for age, race, sex, HIV risk factor (MSM, IDU, heterosexual route), nadir CD4+
Siegenbeek van Heukelom et al, 2017	HIV-positive MSM visiting one of three outpatient HIV clinics in Amsterdam, the Netherlands, were offered AIN screening by their HIV-treating physician. The only exclusion criterion was a life expectancy of less than 12 months. Unclear selection method – however large sample size recruited from three separate clinics. Low risk	HRA was performed by individually trained anoscopists, did not include anal cytology, or human papillomavirus (HPV) testing and consisted of a DARE followed by intra- and perianal inspection with a colposcope after repeatedly applying acetic acid (3–5% solution) and staining with Lugol's iodine when indicated. Lesions suspicious for SIL were biopsied and graded by pathologists specialized in SIL. In clinics A and C, pathologists used p16 staining for AIN2 graded biopsies. The highest grade biopsy defined the overall diagnosis. Assessed outcome variables HSIL-AIN2+. Low -medium risk	years living with HIV viral suppression adjusted for age, current and nadir CD4+, having an AIDS defining illness, ART, nadir CD4+ and HIV PVL suppression (one point in time) unadjusted as found to be not significant in univariate analysis. Low risk	Only years living with HIV viral suppression associated with HSIL-AIN2+ (considered to be equivalent to effective ART use)

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
Schwartz, 2013	Using the Kaiser HIV registry at San Francisco KPNC anal cancer screening clinic, men aged ≥ 18 years, not diagnose with anal cancer prior to enrolment were identified and enrolled between 2009-2010.	Anal swabs collected, after specimen collection, participants received a DARE followed by HRA. At most, 2 suspicious appearing lesions identified during HRA were biopsied and sent for routine histopathological evaluation. Combined endpoints based on cytology, histology, and HPV testing. Medium risk	Crude estimates for ART and PVL. Associations with CD4 adjusted for age at enrolment, ethnicity, number lifetime male partners, chlamydia infection, smoking history. High risk	
Silverberg, 2012	Data analysed from 13 cohort studies (10 from US and 3 from Canada), included in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) between 1996-2007. Eleven of the cohorts were clinic based and data obtained from medical records. The remaining 2 cohorts (Multicenter AIDS Cohort Study) and Women Interagency HIV Study were interval based and data obtained at 6 monthly study visits. Low risk	Incident anal cancer diagnoses were ascertained separately by each cohort from medical records, patient interviews, or linkage with cancer registry. Cases comprised all anal cancer diagnoses, regardless of histology as histological information was not provided by all cohorts. Individuals with prevalent anal cancer at time of enrolment were excluded. Low risk	Adjusted for gender, HIV transmission route, calendar era of diagnosis, ethnicity, age. Medium risk	Low CD4 at time of enrolment associated with increased risk of anal cancer incidence
Stier, 2019	The AIDS Malignancy Consortium (AMC) 084 study, "Screening HIV-Positive Women for Anal Cancer Precursors," was a multicenter national trial to evaluate the prevalence, risk factors, and incidence of anal HSIL in a cohort of WLHIV in the United States; participants recruited between 2014 and 2016. The clinicians responsible for performing HRA at each AMC clinical site were certified; the certification process included each clinician's assembling a log of 50 HRA procedures with concurrent anal cytology and histology results as well as having a site visit by an expert HRA provider who observed the clinicians' HRA skills. At baseline, all women were evaluated with collection of specimens for cervical/vaginal and anal assessments and by HRA with directed biopsies. If a study participant was diagnosed with anal hHSIL at any visit she was exited from the study. Eligible women were 18 years or older, with HIV infection, having no history of anal HSIL by cytology or histology, and having laboratory test results within the past 120 days showing absolute neutrophil >750 cells/ μL and platelet count $\geq 75,000$ cells/ μL . Women with a history of pelvic radiation, anal or perianal cancer, treatment for anal or perianal condyloma, or low-grade squamous intraepithelial lesion (hLSIL) within 4 months of study entry were ineligible. Women with previous hysterectomy were not excluded	LBC required for local processing at each local institution (PreservCyt or SurePath. Site -specific pathology departments and cytopathologists processed the anal cytology specimens using the Bethesda classification system. Following anal cytology specimen collection, a digital anal/rectal examination was performed followed by HRA. During the HRA, each study participant had at least 2 biopsies. Biopsies were taken of anal lesions most suspicious for anal hHSIL from 2 different quadrants of the anus. If <2 anal lesions were noted, 1-2 random biopsies were performed such that there were at least 2 anal biopsies from at least 2 different quadrants of the anal canal. After evaluation of the anal canal, 5% acetic acid was applied to the perianus, and the perianus was then examined under colposcopic guidance for any abnormalities. Biopsies were performed of any perianal abnormalities. The study outcome of interest was anal hHSIL (vs less than hHSIL) as determined by consensus pathology review. Biopsy specimens were evaluated using terminology and classifications (including recommendations for p16 staining) from the Lower Anogenital Squamous Terminology Project. Central pathology review was submitted to a central pathologist. If there was a disagreement between the local and the central pathologist, then a third pathologist reviewed the slide and consensus for 2 of 3 pathologists was required. When several biopsies were taken from the same patient, the most severe histological grade was used for the analysis. In this study, anal hHSIL diagnosis refers to the consensus histologic diagnosis; a composite anal HSIL diagnosis of anal cytology and histology results was not used for this analysis.	Crude estimate only	Women with current CD4+ ≤ 200 cells/ μL showed 10-fold higher odds of hHSIL (adjusted odds ratio [aOR], 10.34 [95% CI, 3.47-30.87]) compared with the reference CD4 count category of >350 cells/ μL ; and 1 or more lifetime anal sex partners was associated with anal hHSIL (aOR, 2.44 [95% CI, 1.22-4.76]) compared with those who never had an anal sex partner
Tandon et al, 2010	Cross sectional study conducted at the Center for Infectious Diseases, primary site of HIV care at Boston Medical Center, an inner city hospital in Boston. English speaking, HIV infected women aged 18-64 years who had not had cervical or anal pap smear, colposcopy or HRA in previous 6 months were eligible to participate. Exclusion criteria included pregnancy, use of chronic anticoagulation medication, and life expectancy of less than 1 year. Small sample size (based on sample size calculations for pilot study) Medium risk	Anal smear collected with BD SurePath Papanicolaou Test. Follow up exam determined by anal cytology. Subjects with any grade of anal cytology abnormality (understood to be ASCUS+) were referred for HRA. 19 women were referred for HRA : 5 refused and anal histological abnormalities were found in 10/14 (3 HGAIN2+). High risk	Unadjusted estimate (HIV related factors not associated in MVA). History of anal sex included in the model (no association). Low-Medium risk	History of STI other than HIV/HPV, low current CD4+, concurrent cervical cytology abnormality
Tong et al, 2013	Retrospective clinical audit of a cohort of men with untreated high-grade ASILs with at least one visit for anal Papanicolaou smear or HRA. Patients were referred from within the St Vincent's Hospital HIV service and from local general practitioners specializing in HIV care. An anal cancer screening clinic was established at St Vincent's Hospital in Sydney, Australia. High-grade ASILs diagnosed at this clinic were not routinely treated because there is no high-quality evidence to indicate current treatments prevent anal cancer. Maybe selection bias of men more likely to return for follow up (who may have more severe disease). Low risk	Each patient had anal Papanicolaou smear or HRA. Biopsies were taken of abnormal areas. Liquid-based anal cytology and histology were reported by St Vincent's Hospital's diagnostic laboratory (SydPath) using standard laboratory protocols developed for cervical reporting. All anal cytology and intra-anal histology diagnoses (from HRA biopsies and anal surgery) were reviewed by one physician. The most abnormal result was used if histology results were available from more than one biopsy collected at any one HRA. A composite endpoint of histologically confirmed AIN2/3 and/or HSIL on anal cytology was defined as highgrade anal intraepithelial neoplasia (HGAIN). Low-Medium risk	Crude estimate only. No association with effective ART (as measured by detectable HIV PVL) but too few participants with detectable PVL – low power to detect a difference. Medium risk	None observed for HGAIN progression but progression to AIN3 more men with low nadir CD4+ No associations observed for regression
Van der Snoek et al, 2012	Cross-sectional study; participants were included in a Rotterdam study on the screening of HPV-related anal premalignancies in HIV-positive MSM. All patients were recruited from the outpatient clinics of 4 hospitals. No information on recruitment procedures or proportion men refused to participate. Medium risk	Anal exam was performed by HRA; Biopsies were taken from the centre of suspicious lesions detected during examination. All biopsies were examined by the same pathologist. Medium risk	adjusted for age, length of known HIV positivity. Sexual behaviour including RAI included in model. Low risk	ART use associated with AIN1+

First author, year	Participant selection	HPV test method (HPV studies), or Endpoint determination and biopsy decision (lesion/cancer studies)	Adjustment for confounding	Summary findings
Weis et al, 2011	prospective cohort of all patients receiving primary care services at the Preventive Medicine Clinic at Tarrant County Public Health from March 2006 to March 2008. The clinic provides medical and social services for HIV-infected patients living in North Texas who meet the Ryan White financial criteria; ie, uninsured or underinsured with income less than 3 times the federal poverty level.	Cytology using the ThinPrep system (Cytoc Corporation). A conventional cytological assessment of stained cellular material was performed by experienced pathologists using Bethesda criteria. A second cytological assessment was made in patients for whom the results of the initial cytological assessment was normal. High-resolution anoscopy (HRA) was recommended to patients with abnormal anal cytology on consenting patients (19% did not have HRA); the most abnormal acetowhite areas suspicious for AIN were biopsied. biopsies sent for routine histopathologic examination by university-associated pathologists	Crude estimate only	Those reporting history of RAI, MSM and with history of HPV infection had higher risk of HSIL-AIN2+
Wilkin et al, 2004	As for previous Wilkin, 2004	Anal cytology conducted using two methods; pap (fixed on slide) and LBC; anal colposcopy was performed using 3% acetic acid. Any areas of acetowhitening or vascular changes suspicious for AIN were sampled by use of cervical biopsy forceps. If no visible lesions were seen, then no biopsy was done. Cytological specimens were initially screened by a cytotechnologist, with the final interpretation being made by a single pathologist who was blinded to all clinical information and other pathological results. A participant was classified as having normal results in the histology based analysis if no biopsy was performed because of a lack of visible lesions on anal colposcopy with normal cytological results or if there was no evidence of condyloma acuminata, AIN, or cancer on any of the biopsy specimens. Where a participant had abnormal cytology result but did not return for follow-up, he was excluded from analysis. Medium risk	Estimates adjusted for history of RAI, age, nadir CD4. Low risk	History of RAI, ART use, younger age and lower nadir CD4+
Willeford et al, 2016	Retrospective chart review of 348 male HIV positive patients from a North Carolina-based HIV clinic who were 18 years or older and had received at least 1 anal pap smear between January 1, 2008, and August 31, 2013. Unclear selection criteria- mostly MSM (96%). High risk	Yearly anal pap smear introduced for HIV positive MSM as part of routine HIV care. Results of ASCUS+ prompted referral to HRA. If HSIL+ was confirmed on biopsy, treatment was pursued. The HSIL biopsy was defined as any anal intraepithelial neoplasia (AIN2) or higher (regardless of P16 status). Outcome is HSIL on first HRA; 28% men referred to HRA failed to attend visit. High risk	adjusted for race, yrs since HIV, current CD4+, nadir CD4+, smoking, PVL suppression). No adjustment for history of RAI, although number of lifetime partners included in the model. Low risk	Current CD4+ count
Yaegashi et al, 2017	Japanese HIV-infected MSM patients that visited the outpatient clinic of Kanazawa University Hospital, Ishikawa Prefectural Central Hospital, and the Shirakaba clinic recruited between April 2013 and August 2014. There was a total of 148 patients enrolled - all participants were MSM; MSW, and bisexual men were excluded. Unclear recruitment procedures, small sample. High risk	Liquid based cytology; 24/148 (16%) were classified as unsatisfactory. All slides assessed by two cytopathologists. High risk	Adjusted for HR-HPV. High risk	Low nadir CD4+ and anal HR-HPV associated with ASC-H
Yang et al, 2012	Study participants were outpatients of the Capital City Dermatology Hospital recruited through local MSM nongovernment organization (Beijing Rainbow Volunteers Workstation) between January and April 2011. To maximize outreach of study information to HIV-infected MSM community, multiple methods were used for recruitment including MSM website advertisement, distributing flyers with study-related information at MSM-frequented venues (e.g., MSM clubs, bars, parks and bathhouses), and participants were also encouraged to refer friends and acquaintances to attend the study. Those eligible to participate were males, 18 years or older, HIV positive, ever had homosexual behaviors, willing to take tests for anal HPV infection and anal cytology, and provision of written informed consent. The presence or absence of any symptoms, including anal symptoms. Medium risk (small sample)	Anal cytology slides were read by a single cytologist. Smears were classified as unsatisfactory if no epithelial cells were present. 3/98 were unsatisfactory. High risk	Unadjusted estimates only. Data available on sexual behaviour (not included in MVA) No data on HIV PVL. High risk	No MVA conducted

RFLP=restriction fragment length polymorphism, RLB=reverse line blot; cART= combined antiretroviral therapy; PCR=polymerase chain reaction

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