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Supplementary appendix 3

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Bruni L, Albero G, Rowley J, et al. Global and regional estimates of genital human papillomavirus prevalence among men: a systematic review and meta-analysis. *Lancet Glob Health* 2023; **11:** e1345–62.

SUPPLEMENTARY MATERIAL

HPV in men

Supplementary introduction. 2

Appendix Table A1. Data Sources and Search Criteria. 2

Supplementary methods 3

Appendix Table A2. Overview of study methods. 3

Appendix Table A3. Quality assessment checklist for prevalence studies (adapted from Hoy et al, and Agbor et al). 5

Appendix Table A4. Countries, number of studies and men included per sub-analysis 6

Appendix Table A5. Meta-analyses of studies reporting prevalence of 2-valent, 4-valent and 9-valent HPV vaccines by United Nations Sustainable Development Goals regional or sub-regional grouping and World Bank income classification. 7

Appendix Table A6. Meta-analyses of studies, median and interquartile range (Q3-Q1) of HR-HPV prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping. 8

Appendix Table A7. Prevalence of genital HPV infection in men: any HPV, HR-HPV, HPV-16 and HPV-6 by selected variables. 9

Appendix Figure A1. Meta-analysis of male genital HR-HPV prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping. 11

Appendix Figure A2. Meta-analysis of male genital HPV prevalence (any HPV) by United Nations Sustainable Development Goals regional or sub-regional grouping. 12

Appendix Figure A3. Meta-analysis of male genital HPV-16 prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping. 13

Appendix Figure A4. Meta-analysis of male genital HPV-6 prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping. 14

Appendix Figure A5. Age-specific prevalence of HR-HPV infection in men for the studies with data by age. 15

Appendix Figure A6. Funnel plot for HR-HPV prevalence by study. 16

Supplementary introduction.

The first global review of genital HPV prevalence in men was published in 2006 and identified 40 publications published between 1990 and 2006 in adult men at any risk of infection who were not immunocompromised[1]. The review included studies that had data on population characteristics and that evaluated male genital anatomic sites or specimens for HPV DNA or included assessments of seropositivity to HPV type 6, 11, 16, or 18 in men. The paper provided a summary of studies but did not make any regional or global estimates.

A second review in 2011 focused on age-specific prevalence of genital HPV-DNA prevalence in men and identified 64 studies published between 1989 and 2009[2]. 38 of these studies were from populations at higher risk of HPV infections, such as human immunodeficiency virus-positive males, male partners of women with HPV infection or abnormal cytology, men who have sex with men, and sexually transmitted infection clinic attendees. There was considerable variation in HPV prevalence - from 1% to 84% among low-risk men and from 2% to 93% among higher risk men. The largest proportions of studies were from Europe (38%) and North America (25%), with smaller proportions from Central and South America (19%), Asia (11%), and Africa (5%).

Appendix Table A1. Data Sources and Search Criteria.

Embase Classic + Embase + Ovid MEDLINE (last searched 01 June 2022) *Included EPub ahead of print, in process, in data review and other non-indexed citations*
((hpv OR papilloma*) AND (male* OR men OR man) AND (prevalence)).mp. Restricted to papers published post 01/01/1995
Global Index Medicus (last searched 01 June 2022)
(tw: (hpv) OR tw:(papilloma*)) AND (tw:(male*) OR tw:(men) OR tw:(man)) AND tw:(prevalence)) Restricted to papers published post 01/01/1995
PubMed (last searched 01 June, 2022)
(HPV [MeSH] OR papillomaviridae [MeSH] OR papillomavirus [MeSH]) AND (Male [MeSH] OR Men [MeSH] OR Males [MeSH] OR Man [MeSH] AND (name of country [Text]) • Name of country: eg.: Burkina Faso, Canada Restricted to papers published post 01/01/1995

[1] Dunne EF, Nielson CM, Stone KM, Markowitz LE, Giuliano AR. Prevalence of HPV infection among men: A systematic review of the literature. J Infect Dis 2006; 194: 1044–57.

[2] Smith JS, Gilbert PA, Melendy A, Rana RK, Pimenta JM. Age-specific prevalence of human papillomavirus infection in males: a global review. J Adolesc Health 2011; 48: 540–52.

Supplementary methods

Articles were included if they met the following eligibility criteria: reported HPV prevalence among men 15 years of age or older with no HPV-related pathology (e.g., studies in men with anogenital warts or penile cancer were excluded); used polymerase chain reaction (PCR) or Hybrid Capture 2 (HC2) techniques for HPV DNA detection; provided detailed methodological description of sampling techniques, transport medium, PCR HPV DNA assays and HPV genotyping techniques used; collected samples from penile and/or anal sites (e.g., glans, shaft, scrotum, urethra, anus, foreskin); had a sample size of at least 50 men; and the majority of samples were collected in 1995 or later. Studies conducted exclusively in men vaccinated against HPV, men who have sex with men (MSM), HIV positive men, partners of women with HPV-related pathology (e.g., anogenital pre-cancer or cancer), drug users, and sex workers were excluded, as well as studies that only included men who have been circumcised. We did include studies which sampled men presenting to sexually transmitted disease clinics who were asymptomatic.

Appendix Table A2. Overview of study methods.

Methods	Description

Study selection & Eligibility criteria	**Inclusion criteria**
	• Reported HPV prevalence among men 15 years of age or older with no HPV-related pathology.
	• Used either PCR or Hybrid Capture 2 techniques for HPV DNA detection.
	• Collected samples from penile and/or anal sites (e.g., glans, shaft, scrotum, urethra, anus, foreskin).
	• Provided detailed methodological description of sampling techniques, transport medium, PCR HPV DNA assays and HPV genotyping techniques used.
	• Sample size of at least 50 men.
	• Majority of samples were collected in 1995 or later.
	• Population-based surveys.
	• In non-population-based surveys: sample selection criteria not related to known risk factors of HPV infection or HPV related-diseases.
	
	Exclusion criteria
	• Studies conducted **exclusively** in the following populations to avoid either over or under estimation:
	  ◦ Men with HPV related pathology (e.g., anogenital warts or penile cancer).
	  ◦ Men who have sex with men.
	  ◦ HIV positive men.
	  ◦ Partners of women with HPV-related pathology (e.g., anogenital pre-cancer or cancer).
	  ◦ Drug users.
	  ◦ Sex workers.
	  ◦ Men vaccinated against HPV.
	  ◦ Circumcised men.
	• Studies with eligibility uncertainties and no clarification from the correspondent author was received after three attempts.

Data extraction & synthesis	**Data Extracted** • First author, journal, year of publication, country, city, study period (first and last year), description of study population, prevalence of HIV • Type of study and enrolment methods, age (mean/ median/ range) • Anatomic site, sample collection methods, • HPV detection and genotyping methods (tests, probes, targeted HPV types) • Prevalence for any HPV and/or HR-HPV or low-risk HPV disaggregated by age. Only mucosal alpha-type HPV were included. • Type specific prevalence of HPV disaggregated by age • Multi-country studies were broken down by country when possible. • If a study population was described in two or more publications we used the publication with the larger sample size and most detailed information and supplemented it with data from the other publications. • If the data from a study covered multiple years we used the start year of data collection in the analysis
Meta analyses	Random-effects models • Variables included in the univariable analysis: o Geography (Eastern and South-Eastern Asia, all other regions) o Sample size (>500, <=500), o Risk of bias (low, high), o Studies conducted in STI clinics or equivalent o Start year of data collection (before 2006, 2006-2013, 2014 or later), o Method of sampling (self-collected, clinician collected), o Anatomic sites sampled (at least the penile shaft and the glans penis/coronal sulcus sampled, did not collect data from both shaft and glans penis/ coronal sulcus), o Number of HPV types tested in the HPV detection assay (8-15 types, 16-26 types, 27-50 types), o Age (<30 years, >=30 years). • If the year of data collection was missing we used the year of publication
Metaregression	Random-effects meta-regression analyses. Factors associated with prevalence at p≤0·20 in univariable analysis were eligible for inclusion in the multivariable analysis to estimate the magnitude of their effect.

HR: high-risk; HPV: human papillomavirus; PCR: polymerase chain reaction; STI: sexually transmitted infection

Appendix Table A3. Quality assessment checklist for prevalence studies (adapted from Hoy et al[3], and Agbor et al[4]).

Risk of bias items	Risk of bias levels	Points scored
1. Was the study's target population a close representation of the national population in relation to relevant variables, e.g., age, sex, occupation?		
	Yes (LOW RISK): The study's target population was a close representation of the national population	0
	No (HIGH RISK): The study's target population was clearly NOT representative of the national population.	1
2. Was the sampling frame a true or close representation of the target population?		
	Yes (LOW RISK): The sampling frame was a true or close representation of the target population.	0
	No (HIGH RISK): The sampling frame was NOT a true or close representation of the target population.	1
3. Was some form of random selection used to select the sample, OR, was a census undertaken?		
	Yes (LOW RISK): A census was undertaken, OR, some form of random selection was used to select the sample (e.g. simple random sampling, stratified random sampling, cluster sampling, systematic sampling)	0
	No (HIGH RISK): A census was NOT undertaken, AND some form of random selection was NOT used to select the sample	1
4. Was the likelihood of non-response bias minimal?		
	Yes (LOW RISK): The response rate for the study was ≥75%, OR, an analysis was performed that showed no significant difference in relevant demographic characteristics between responders and non- responders	0
	No (HIGH RISK): The response rate was <75%, and if any analysis comparing responders and non-responders was done, it showed a significant difference in relevant demographic characteristics between responders and non-responders	1

[3] Hoy D, Brooks P, Woolf A, Blyth F, March L, Bain C, et al. Assessing risk of bias in prevalence studies: modification of an existing tool and evidence of interrater agreement. J Clin Epidemiol 2012;65:934–9. https://doi.org/10.1016/j.jclinepi.2011.11.014.

[4] Agbor VN, Takah NF, Aminde LN. Prevalence and factors associated with medication adherence among patients with hypertension in sub-Saharan Africa: protocol for a systematic review and meta-analysis. BMJ Open 2018;8:e020715. https://doi.org/10.1136/bmjopen-2017-020715.

Appendix Table A4. Countries, number of studies and men included per sub-analysis.

Analysis	N studies	N men
HPV-16 prevalence	54	41 482
HPV-18 prevalence	52	40 705
HPV-31 prevalence	52	40 694
HPV-33 prevalence	52	40 696
HPV-35 prevalence	50	40 156
HPV-39 prevalence	48	39 042
HPV-45 prevalence	50	40 223
HPV-51 prevalence	47	38 929
HPV-52 prevalence	48	39 494
HPV-56 prevalence	50	40 275
HPV-58 prevalence	51	40 391
HPV-59 prevalence	46	38 768
HPV-6 prevalence	53	41 045
HPV-11 prevalence	51	39 995
Age-specific prevalence (Any type)	47	39 183
Age-specific prevalence (HR-HPV)	38	36 331
Age-specific prevalence (HPV-16)	33	29 966

Region	Countries
Eastern and South-Eastern Asia	China, Japan, Malaysia, and South Korea
Europe	Croatia, Denmark, Finland, Germany, Netherlands, Norway, Portugal, Russia, Slovenia, Spain, Sweden, and the UK
North America	Canada and the USA
Central and South America	Brazil, Costa Rica, Mexico, and Peru
Sub-Saharan Africa	Botswana, Kenya, Mozambique, Rwanda, South Africa, and Uganda

Appendix Table A5. Meta-analyses of studies reporting prevalence of 2-valent, 4-valent and 9-valent HPV vaccines by United Nations Sustainable Development Goals regional or sub-regional grouping and World Bank income classification.

	2v (16, 18)			4v (6, 11, 16, 18)			9v (6, 11, 16, 18, 31, 33, 45, 52, 58)		
	N Studies	N Men	HPV prevalence % (95% CI)	N Studies	N Men	HPV prevalence % (95% CI)	N Studies	N Men	HPV prevalence % (95% CI)
Global	**53**	**41,317**	**7% (6 - 8)**	**52**	**40,880**	**11% (9 - 13)**	**52**	**41,007**	**16% (14 - 18)**
SDG Region*									
Australia and New Zealand	1	511	4% (3 - 6)	1	511	7% (5 - 10)	1	511	15% (12 - 18)
Eastern and South-Eastern Asia	9	10,110	4% (2 - 6)	9	10,110	7% (3 - 13)	9	10,110	11% (6 - 16)
Eastern Asia	8	9,721	3% (2 - 6)	8	9,721	7% (2 - 13)	8	9,721	10% (6 - 16)
Europe and Northern America	26	13,412	8% (6 - 10)	25	12,975	12% (10 - 15)	25	13,102	16% (13 - 20)
Europe	15	6,566	6% (5 - 8)	14	6,129	10% (7 - 13)	15	6,566	15% (11 - 20)
Northern America	12	6,846	10% (7 - 13)	12	6,846	15% (11 - 19)	11	6,536	18% (14 - 23)
Latin America and the Caribbean	10	8,463	9% (5 - 12)	10	8,463	15% (10 - 20)	10	8,463	20% (14 - 27)
Central America	5	3,923	6% (3 - 11)	5	3,923	9% (4 - 16)	5	3,923	13% (5 - 23)
South America	5	3,239	14% (6 - 23)	5	3,239	24% (15 - 34)	5	3,239	30% (21 - 40)
Sub-Saharan Africa	10	8,558	6% (4 - 8)	10	8,558	11% (9 - 14)	10	8,558	19% (15 - 24)
Eastern Africa	6	5,551	6% (3 - 9)	6	5,551	10% (7 - 14)	6	5,551	18% (12 - 26)
Southern Africa	4	3,007	6% (4 - 9)	4	3,007	13% (10 - 15)	4	3,007	20% (16 - 25)
Income level									
High income	29	14,229	8% (6 - 10)	28	13,792	12% (10 - 15)	28	13,919	17% (14 - 21)
Low and middle income	26	26,825	6% (5 - 7)	26	26,825	10% (8 - 13)	26	26,825	16% (13 - 19)
Upper middle income	20	21,274	6% (4 - 7)	20	21,274	10% (8 - 13)	20	21,274	15% (12 - 19)
Lower middle income	3	4,231	7% (3 - 14)	3	4,231	12% (6 - 18)	3	4,231	20% (11 - 32)
Low income	3	1,320	5% (1 - 11)	3	1,320	9% (3 - 17)	3	1,320	16% (4 - 33)

* Estimates provided only for those regions with over 500 men sampled. SDG: Sustainable Development Goals; CI: confidence intervals; HPV: human papillomavirus; v: valent

Appendix Table A6. Meta-analyses of studies, median and interquartile range (Q3-Q1) of HR-HPV prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping.

Geographical area	% (95% CI)	Median	IQR (Q3-Q1)
Global	**21% (18 - 24)**	**20%**	**17% (29-12%)**
Sub-Saharan Africa	25% (18 - 32)	26%	18% (35-17%)
Central and South America	22% (16 - 29)	20%	15% (29-14%)
Europe	22% (17 - 28)	20%	17% (32-15%)
Northern America	27% (21 - 32)	24%	9% (29-20%)
Eastern and South-Eastern Asia	10% (7 - 13)	10%	7% (13-6%)

Q1 is the 25th percentile, meaning that 25% of the data falls below the first quartile; Q3 is the 75th percentile, meaning that 75% of the data falls below the third quartile; CI: confidence intervals;

Appendix Table A7. Prevalence of genital HPV infection in men: any HPV, HR-HPV, HPV-16 and HPV-6 by selected variables.

	Any HPV type				HR-HPV				HPV-16				HPV-6			
	N	N Men	HPV prevalence % (95% CI)	p-value[1]	N	N Men	HPV prevalence % (95% CI)	p-value[1]	N	N Men	HPV prevalence % (95% CI)	p-value[1]	N	N Men	HPV prevalence % (95% CI)	p-value[1]
Global	**65**	**44,769**	**31% (27 - 35)**		**56**	**41,617**	**21% (18 - 24)**		**54**	**41,482**	**5% (4 - 7)**		**53**	**41,045**	**4% (3 - 5)**	
Geography																
Eastern and South-Eastern Asia	11	10,335	15% (11 - 21)		10	10,030	10% (7 - 13)		9	10,110	2% (1 - 5)		9	10,110	3% (0 - 10)	
All other regions	54	34,434	34% (30 - 38)		46	31,587	23% (20 - 26)		45	31,372	6% (5 - 7)		44	30,935	4% (3 - 5)	
				p < 0·0001				**p < 0·0001**				**p = 0·005**				p = 0·733
Sample size																
>500	24	34,423	32% (26 - 38)		21	32,710	21% (17 - 26)		22	32,744	5% (4 - 6)		22	32,743	4% (2 - 6)	
<=500	42	10,346	30% (25 - 36)		36	8,907	20% (16 - 24)		33	8,738	6% (4 - 9)		32	8,302	4% (3 - 5)	
				p = 0·651				p = 0·754				p = 0·105				p = 0·939
Risk of bias																
Low	35	29,781	30% (25 - 36)		32	29,066	21% (17 - 25)		28	28,780	5% (4 - 7)		28	28,780	3% (2 - 4)	
High	30	14,988	32% (27 - 37)		24	12,551	20% (17 - 25)		26	12,702	6% (4 - 8)		25	12,265	5% (2 - 8)	
				p = 0·765				p = 0·858				p = 0·785				p = 0·300
Studies conducted in STD clinics or equivalent																
No	47	36,841	30% (26 - 34)		43	36,016	20% (17 - 23)		39	35,562	5% (4 - 6)		39	35,562	3% (2 - 5)	
Yes	18	7,928	34% (26 - 42)		13	5,601	24% (17 - 32)		15	5,920	7% (4 - 10)		14	5,483	6% (3 - 9)	
				p = 0·430				p = 0·271				p = 0·211				p = 0·080
Start year of data collection[2]																
Before 2006	30	21,586	28% (22 - 34)		25	20,001	19% (15 - 23)		22	19,504	5% (4 - 6)		21	19,067	3% (2 - 5)	
2006-2013	25	14,418	34% (28 – 40)		21	12,851	22% (17 – 28)		22	13,213	6% (4 - 8)		22	13,213	4% (2 - 5)	
2014 or later	7	8,449	28% (18 - 39)		7	8,449	18% (13 - 24)		7	8,449	4% (1 - 7)		7	8,449	6% (1 - 14)	
				p = 0·338				p = 0·545				p = 0·263				p = 0·628
Method of sampling[3]																
Self-collected	13	5,869	35% (27 - 43)		13	5,869	22% (17 - 27)		11	5,644	7% (5 - 9)		11	5,644	4% (2 - 6)	
Clinician collected	50	38,250	30% (26 - 34)		41	35,098	20% (17 - 23)		41	35,188	5% (4 - 6)		40	34,751	4% (2 - 5)	
				p = 0·257				p = 0·504				p = 0·155				p = 0·750
Anatomic sites sampled																
At least the penile shaft and the glans penis/coronal sulcus sampled	32	30,959	37% (31 - 42)		30	30,331	23% (20 - 28)		30	30,580	7% (5 - 8)		30	30,580	4% (3 - 6)	
Did not collect data from both shaft and glans penis/ coronal sulcus	33	13,810	24% (20 - 30)		26	11,286	17% (14 - 21)		24	10,902	4% (3 -5)		23	10,465	4% (2 - 5)	
				p = 0·001				**p = 0·024**				**p = 0·015**				p = 0·632
Number of HPV types tested for																
8 - 15 types	10	5,854	20% (15 - 25)		5	4,263	20% (14 - 26)		6	5,113	3% (2 - 4)		5	4,676	3% (2 - 5)	
16 - 26 types	17	8,983	25% (18 - 33)		16	8,386	17% (12 - 23)		12	8,005	4% (2 - 6)		12	8,005	4% (2 - 7)	

27 - 50 types	38	29,932	38%	(33 - 43)	35	28,968	22%	(19 - 26)	36	28,364	7%	(5 - 8)	36	28,364	4%	(3 - 6)
				p < 0·0001				p = 0·361				**p < 0·0001**				p = 0·816
Age																
<30 years	47	24,352	32%	(28 - 36)	38	22,189	22%	(19 - 26)	33	19,614	5%	(4 - 6)	-	-	-	-
>=30 years	33	14,831	34%	(28 - 41)	29	14,142	21%	(17 - 25)	22	10,352	4%	(3 - 6)	-	-	-	-
				p = 0·466				p = 0·631				p = 0·647				

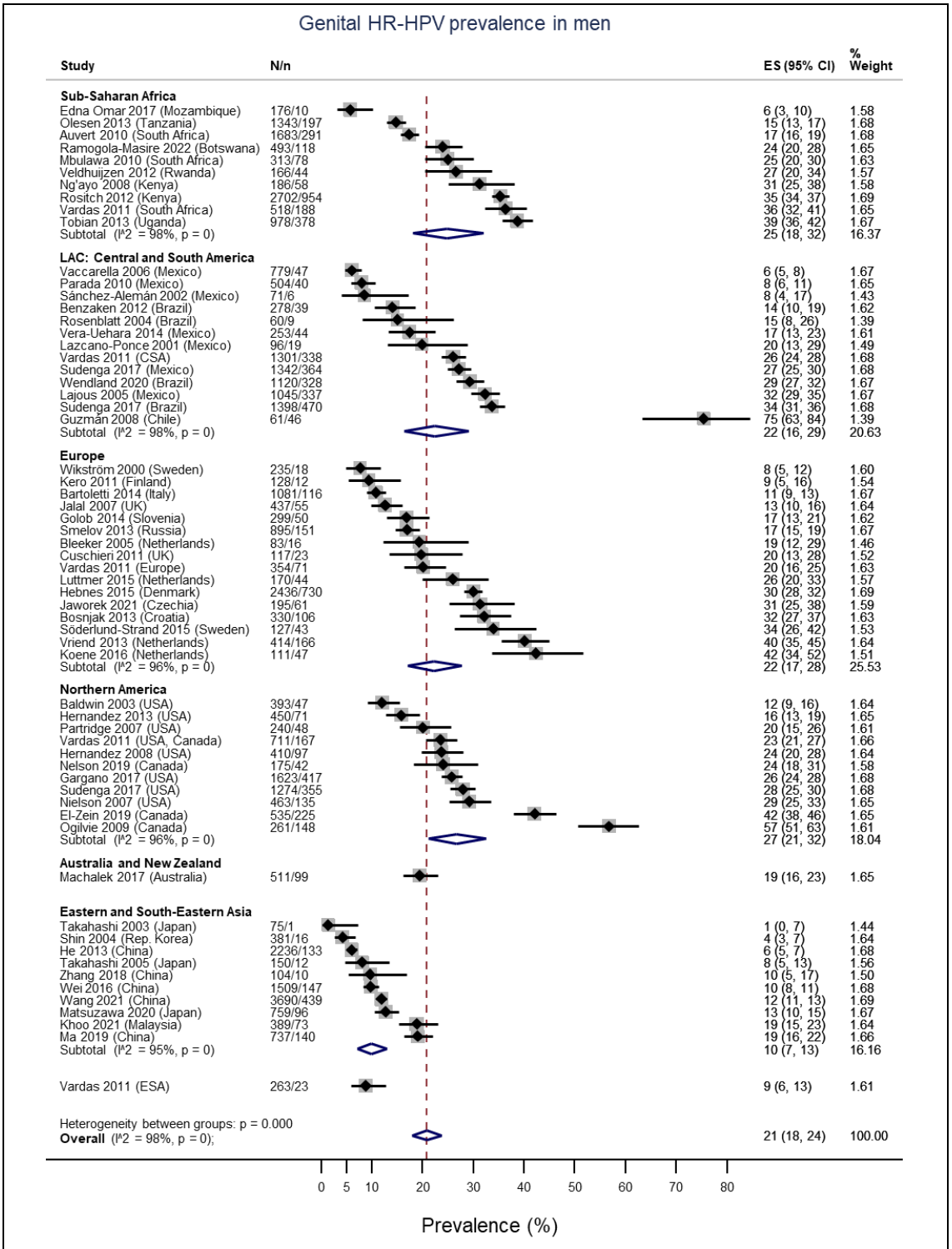
[1]. For heterogeneity between groups within the variable.

[2]. Three studies had no data on when the samples were collected. These were excluded from the analysis (Guzman 2008 (Chile); Kero 2011 (Finland) & Söderlund-Strand 2015 (Sweden))

[3]. Two studies had data for both self and clinician samples. These were excluded from the analysis (Ogilvie 2009 (Canada) & Khoo 2021 (Malaysia))

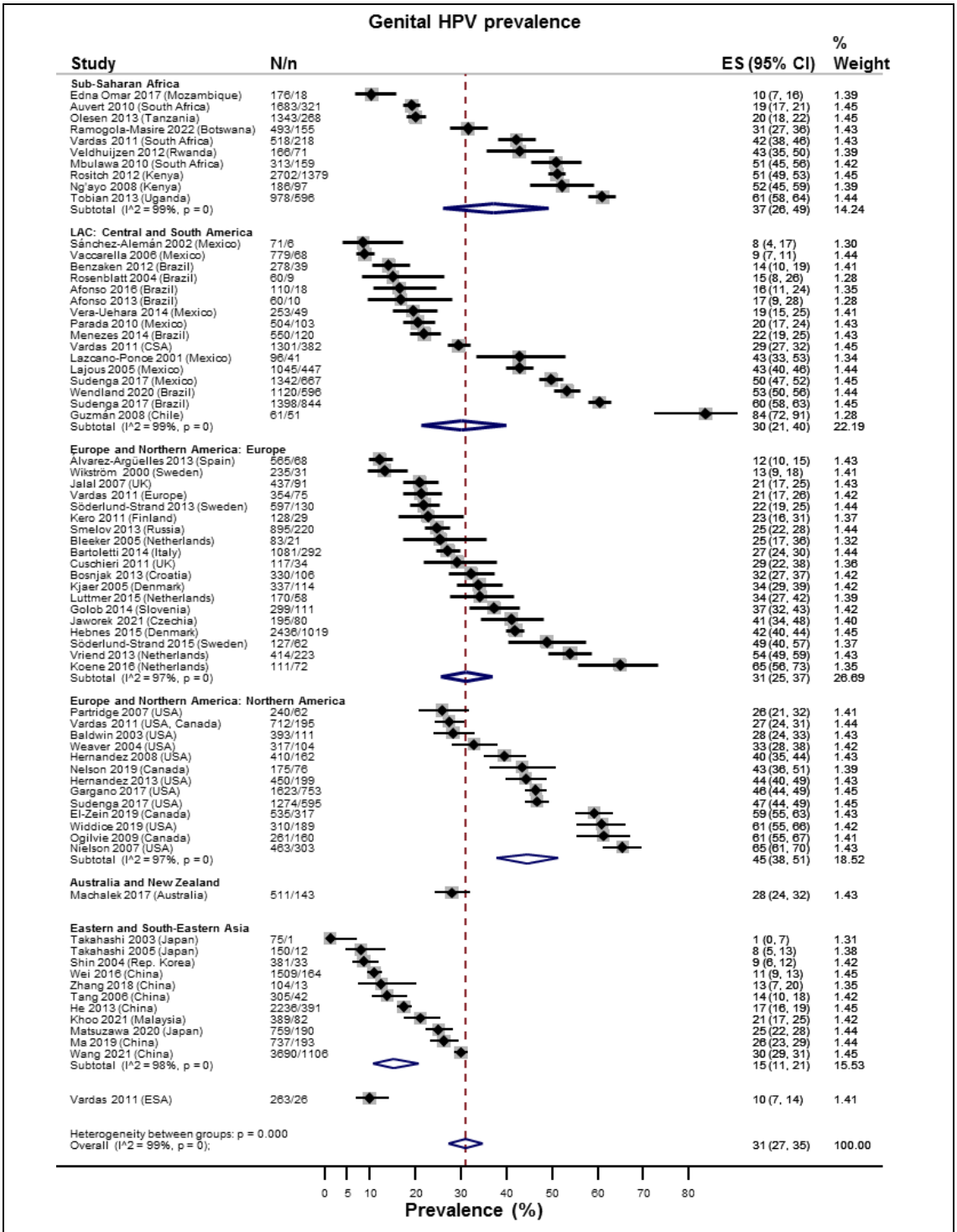
N=number of studies; CI: confidence intervals; HPV: human papillomavirus; HR: high-risk; STI: sexually transmitted infection;

Appendix Figure A1. Meta-analysis of male genital HR-HPV prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping.



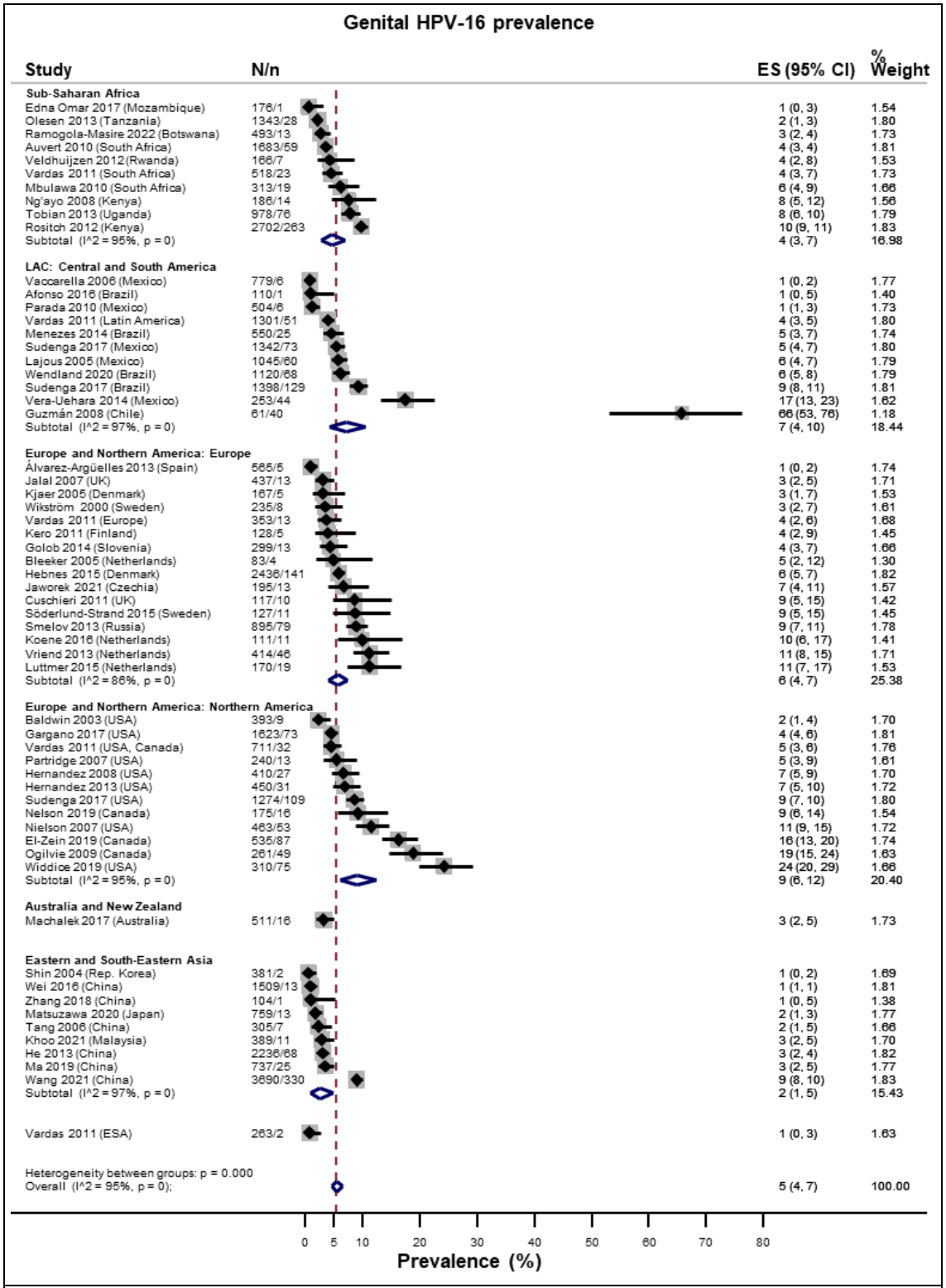
HR: high-risk; N: number of men; n: number of positive HPV men; ES: estimate; HPV: human papillomavirus; Error bars are 95% confidence intervals.
** 56 studies included in the analysis. 50 studies provided an estimate of HR-HPV and for 6 studies we estimated the prevalence.*
Vardas 2011 (Europe) includes Croatia, Finland, Germany, Netherlands, Norway, Portugal, Spain and Sweden. Vardas 2011 (CSA) includes Costa Rica, Mexico, Brazil and Peru; Vardas 2011 (ESA) includes Philippines, Taiwan and Australia; LAC: Latin America and the Caribbean; Rep. Korea: Republic of Korea; UK: United Kingdom; USA: United States of America; Tanzania: United Republic of Tanzania

Appendix Figure A2. Meta-analysis of male genital HPV prevalence (any HPV) by United Nations Sustainable Development Goals regional or sub-regional grouping.



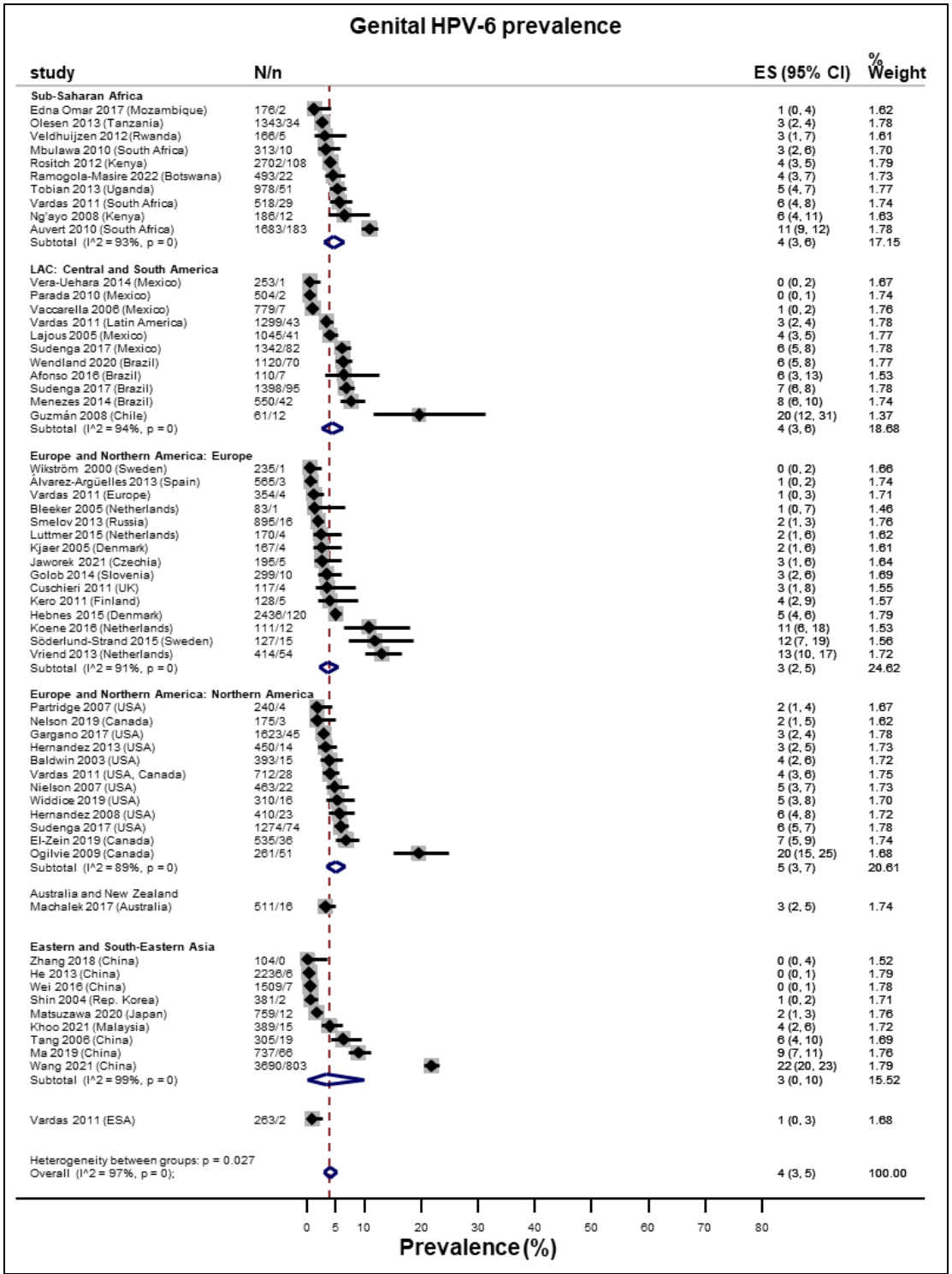
** 62 studies provided an estimate of any HPV and for 3 studies we estimated the prevalence. Vardas 2011 (Europe) includes Croatia, Finland, Germany, Netherlands, Norway, Portugal, Spain, and Sweden. Vardas 2011 (CSA) includes Costa Rica, Mexico, Brazil, and Peru; Vardas 2011 (ESA) includes Philippines, Taiwan, and Australia; LAC: Latin America and the Caribbean; Rep. Korea: Republic of Korea; UK: United Kingdom; USA: United States of America; Tanzania: United Republic of Tanzania; Error bars are 95% confidence intervals.*

Appendix Figure A3. Meta-analysis of male genital HPV-16 prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping.



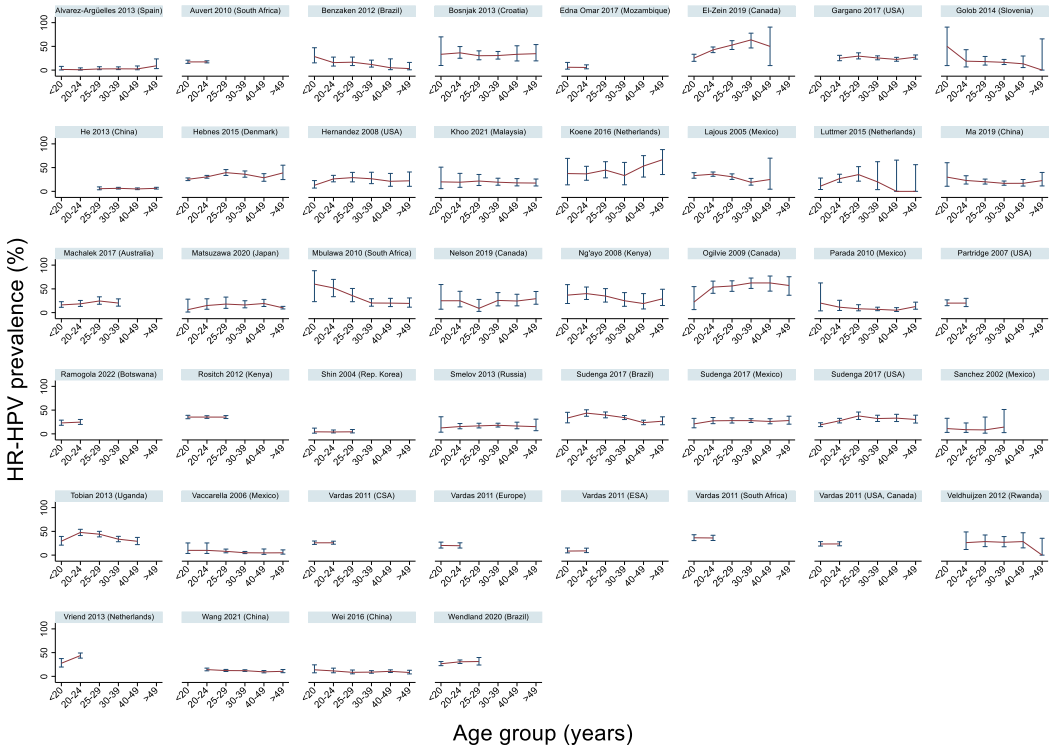
** 54 studies included in the analysis. Vardas 2011 (Europe) includes Croatia, Finland, Germany, Netherlands, Norway, Portugal, Spain, and Sweden. Vardas 2011 (CSA) includes Costa Rica, Mexico, Brazil, and Peru; Vardas 2011 (ESA) includes Philippines, Taiwan, and Australia; LAC: Latin America and the Caribbean; Rep. Korea: Republic of Korea; UK: United Kingdom; USA: United States of America; Tanzania: United Republic of Tanzania; Error bars are 95% confidence intervals. Error bars are 95% confidence intervals.*

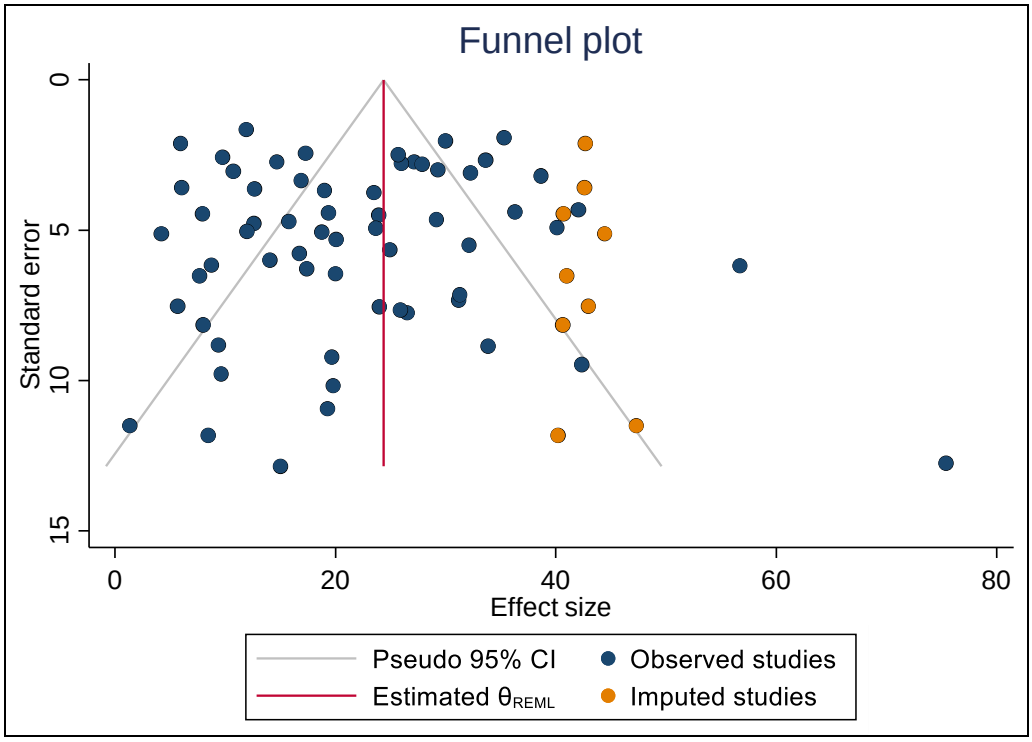
Appendix Figure A4. Meta-analysis of male genital HPV-6 prevalence by United Nations Sustainable Development Goals regional or sub-regional grouping.



** 53 studies included in the analysis. Vardas 2011 (Europe) includes Croatia, Finland, Germany, Netherlands, Norway, Portugal, Spain, and Sweden. Vardas 2011 (CSA) includes Costa Rica, Mexico, Brazil, and Peru; Vardas 2011 (ESA) includes Philippines, Taiwan, and Australia; LAC: Latin America and the Caribbean; Rep. Korea: Republic of Korea; UK: United Kingdom; USA: United States of America; Tanzania: United Republic of Tanzania; Error bars are 95% confidence intervals. Error bars are 95% confidence intervals.*

Appendix Figure A5. Age-specific prevalence of HR-HPV infection in men for the studies with data by age.



** Vardas 2011 (CSA) includes Costa Rica, Mexico, Brazil, and Peru; Vardas 2011 (ESA) includes Philippines, Taiwan, and Australia. Vardas 2011 (Europe) includes Croatia, Finland, Germany, Netherlands, Norway, Portugal, Spain, and Sweden. Error bars are 95% confidence intervals. Graphs are presented in alphabetical order by first author. USA: United States of America; Error bars are 95% confidence intervals.*

Appendix Figure A6. Funnel plot for HR-HPV prevalence by study.