Supplementary Online Content

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eAppendix 1. Acknowledgements

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eAppendix 2. Acronyms and Abbreviations

AIDS	acquired immunodeficiency syndrome
anti-HBc	total hepatitis B core antibody
BL/L	Burkitt lymphoma/leukemia
CI	confidence interval
CLL/SLL	chronic/small lymphocytic leukemia/lymphoma
DLBCL	diffuse large B-cell lymphoma
EBER ISH	EBV-encoded RNA *in situ* hybridization
EBV	Epstein-Barr virus
EIA	enzyme immunoassay
ELISA	enzyme-linked immunosorbent assay
ENKTL	extranodal natural killer T-cell lymphoma
ES	effect size
FFPE	formalin-fixed paraffin-embedded
GC	gastric carcinoma/cancer
GI	gastrointestinal
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HCC	hepatocellular carcinoma
HIV	human immunodeficiency virus
HL	Hodgkin lymphoma
HNC	head and neck cancer
H. pylori	*Helicobacter pylori*
HIV	human immunodeficiency virus
HPV	human papillomavirus
HR	high-risk
I^2	index of consistency
IARC	International Agency for Research on Cancer
ICC	intrahepatic cholangiocarcinoma
ICCC	International Classification for Childhood Cancer
ICD	International Classification of Diseases
KSHV	Kaposi sarcoma-associated herpesvirus
LMP-1	latent membrane protein 1
LPL/WM	lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia
MALT	mucosa-associated lymphoid tissue
MCPyV	Merkel cell polyomavirus
MZL	marginal zone lymphoma
NA	not applicable
NCGC	non-cardia gastric cancer
NHANES	National Health and Nutrition Examination Survey
NOS	not otherwise specified
NPC	nasopharyngeal carcinoma
NS	not specified
OR	odds ratio
PAF	population attributable fraction
PWH	people with HIV
Pos	positive
RR	relative risk
RSE	relative standard error
SCC	squamous cell carcinoma
SD	standard deviation
SE	standard error
SEER	Surveillance, Epidemiology, and End Results Program
SES	socioeconomic status
US	United States
WHO	World Health Organization
yrs	years

eAppendix 3. Cancers and Associated *ICD-O-3* Codes

Cancer	*ICD-O-3* codes	Recode used (if applicable) / exclusions
Lymphomas		
Burkitt lymphoma	9687	Children only: ICCC site recode extended
Chronic/small lymphocytic leukemia/lymphoma	9823	Lymphoma subtype recode/WHO 2008
DLBCL NOS	9680	Lymphoma subtype recode/WHO 2008
Lymphoplasmacytic lymphoma	9671	Lymphoma subtype recode/WHO 2008
Marginal zone lymphoma	9699	Lymphoma subtype recode/WHO 2008
Gastric, mucosa-associated lymphoid tissue	C16; 9699	NA
Gastric, DLBCL NOS	C16; 9680	NA
Hodgkin lymphoma	C81	Lymphoma subtype recode/WHO 2008
ENKTL, nasal type	9719	NA
Primary effusion lymphoma	9678	NA
Adult T-cell leukemia/lymphoma	9827	Lymphoma subtype recode/WHO 2008
Head and neck cancers		
Nasopharyngeal carcinoma	C11.0–9; 8010, 8020–1, 8070–3, 8082–3	Children only: ICCC site recode extended
Oropharynx	C01.9, C02.4, C02.8, C05.1–2, C09, C10, C14.2	Excluded: 9050–9055 (mesothelioma), 9140 (Kaposi sarcoma), 9590–9992 (malignant lymphomas)
Oral cavity	C00.3–5, C00.9, C02.0–3, C02.9, C03, C04, C05.0, C05.8–9, C06, C14.8	
Larynx	C32	
Gastrointestinal tract cancers		
Esophageal adenocarcinoma	C15; 8050–83	NA
Hepatocellular carcinoma	C22.0; 8170–5	NA
Intrahepatic bile duct	C22.1	Excluded: 9050–9055, 9140, 9590–9992
Gastric, non-cardia	C16.1–6, proportion of C16.8–9[a]	NA
Gastric carcinoma	C16	Excluded: 9050–9055, 9140, 9590–9992
Anal squamous cell carcinoma	C21.0–2, C21.8; 8050–8076, 8083–4, 8123–4	NA
Genital cancers		
Cervix	C53	Excluded: 9050–9055, 9140, 9590–9992
Penis	C60	
Vagina	C52	
Vulva	C51	
Skin cancers		
Kaposi sarcoma	9140	NA
Merkel cell carcinoma of the skin	C44.0, C44.2–9; 8247	NA

DLBCL = diffuse large B-cell lymphoma, ENKTL = extranodal natural killer T-cell lymphoma, ICCC = International Classification for Childhood Cancer, ICD = International Classification of Diseases, NA = not applicable, NOS = not otherwise specified, WHO = World Health Organization

[a] Non-cardia gastric counts were adjusted by reassigning a proportion of 'overlapping lesion' and 'NOS' gastric carcinoma to non-cardia gastric cancer.

LITERATURE SEARCH

The search shown in **eTable 1** was designed to capture knowledge syntheses (i.e., systematic reviews with or without meta-analyses, scoping reviews, etc.). It included MeSH terms and keywords related to infections and cancers included in this study, and knowledge syntheses, and was limited to records published in English. This search captured 3,604 records of which 353 underwent full-text review.

eTable 1. Search Performed in MEDLINE 1946–January 6, 2023

Individual infections	1.	exp Hepatitis B virus/ or exp Hepatitis B/ or exp Hepatitis C/ or exp Hepacivirus/ or (hepatitis virus* or hepatitis B or hepatitis C or HBV or HCV or hep B or hep C).tw,kf.
	2.	exp Herpesvirus 4, Human/ or exp Epstein-Barr Virus Infections/ or (herpesvirus type 4 or herpesvirus 4 or ebv or hhv4 or hhv-4).tw,kf. or ((epstein-Barr or epstein Barr) adj2 (virus* or viral*)).tw,kf.
	3.	exp HTLV-I Infections/ or exp Human T-lymphotropic virus 1/ or (human T-cell lymphotropic virus or Human T-lymphotropic virus or HTLV-1 or HTLV1).tw,kf.
	4.	exp Herpesvirus 8, Human/ or (human herpesvirus 8 or human herpesvirus type 8 or sarcoma-associated herpesvirus or Kaposi sarcoma-associated herpesvirus or HHV-8 or HHV8 or KSHV).tw,kf. or (Kaposi* adj3 (virus* or viral*)).tw,kf.
	5.	exp Helicobacter/ or exp Helicobacter infection/ or (helicobacter or pylori or pyloridis or HP or campylobacter, H* pylori).tw,kf.
	6.	exp Papillomavirus Infections/ or exp Papillomaviridae/ or (human papillomavirus* or human papilloma virus* or hpv).tw,kf.
	7.	exp HIV Infections/ or exp HIV/ or (hiv or hiv-1 or hiv-2 or hiv1 or hiv2 or hiv infect* or deficiency virus).tw,kf. or (human immun* adj2 (virus* or viral*)).tw,kf.
	8.	exp Merkel cell polyomavirus/ or (merkel cell polyomavirus or MCV or MCPyV).tw,kf. or (merkel adj3 polyomavirus).tw,kf.
	9.	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
Cancer	10.	exp Neoplasms/ or (cancer* or neoplas* or tumor* or tumour* or malignan* or carcinoma* or metasta* or oncolog* or leukemi* or leukaemi* or lymphoma* or myeloma* or sarcoma* or squamous cell* or adenocarcinoma*).tw,kf.
Knowledge syntheses[a]	11.	(meta-analysis or systematic review).pt. or meta-analysis/ or systematic review/ or exp meta-analysis as topic/ or ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf. or ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf. or ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf. or (data synthes* or data extraction* or data abstraction*).ti,ab,kf. or (handsearch* or hand search*).ti,ab,kf. or (met analy* or metanaly*).ti,ab,kf. or (meta regression* or metaregression*).ti,ab,kf. or (meta-analy* or metaanaly* or systematic review*).mp,hw. or (medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw. or (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf.
Limits	12.	9 and 10 and 11
	13.	limit 12 to English
	14.	limit 13 to humans

[a] The knowledge syntheses search terms were adapted from the Canadian Agency for Drugs and Technologies in Health (CADTH) database search filters. Ottawa: CADTH; 2016. [Available from: https://searchfilters.cadth.ca/]

eAppendix 4. Cancer Incidence

Cancer incidence data covering 100% of the US population, including the 50 states, the District of Columbia and Puerto Rico were obtained (due to Hurricane Maria, Puerto Rico's incidence counts are restricted to the first six months of 2017). Cancer was categorized according to ICD-O-3. We used the following coding classifications: ICD-O-3/WHO 2008 for primary sites, lymphoma subsite recode/WHO 2008 for lymphomas, and the ICCC site extended or recode ICD-O-3/WHO 2008 for children. However, the recode could not be used to obtain all the sites required (e.g., subsites of oropharynx or oral cavity). Cancers that did not have a specific histology associated with them (e.g., NCGC, oropharynx, etc.) had the following histologies excluded from their counts: 9050–9055 (mesothelioma), 9140 (Kaposi sarcoma), 9590–9992 (malignant lymphomas).

For the main analysis, the NCGC incidence counts were adjusted by reassigning a proportion of 'overlapping lesion' and NOS GC to NCGC. This proportion was determined by calculating the distribution of cardia (C16.0) versus NCGC (C16.1–16.6) by sex and 5-year age groups and multiplying the proportion that was NCGC by the counts of overlapping lesion and NOS, then adding those counts to the existing NCGC counts. We applied the PAFs to unadjusted NCGC (C16.1–16.6) incidence as a sensitivity analysis. For adults, we reclassified B-cell NOS lymphomas based on distribution of B-cell lymphomas of known histology by sex and 5-year age groups, then applied PAFs for EBV to Burkitt lymphoma, EBV and HCV to DLBCL, and HCV to other non-Hodgkin lymphomas.

eAppendix 5. Multiple Imputation

The imputation model included variables known to be associated with both the infection and missingness, as applicable (i.e., for all three infections: sex, age [missing age at medical examination was imputed using age at interview–last observation carried forward method], education, race, and primary sampling units and strata; HBV infection also included country of birth, intravenous drug use, men who have sex with men, and number of lifetime sexual partners; HCV infection also included injection drug use, receiving a blood transfusion before 1992, HIV diagnosis and anti-HCV antibody result; *H. pylori* infection also included time living in the US, number of people living in the household and family income).[1] We then estimated the prevalence of HBV, HCV and *H. pylori* infection; analyses included the sampling weights provided by NHANES to account for unequal probabilities of selection resulting from the sample design. The recommended variance estimation of Taylor series linearization for variance estimation was used to calculate 95% CIs for the prevalence estimates.[2]

eAppendix 6. Hepatitis B and C Viruses

The general population prevalence estimates for the hepatitis viruses are displayed in **eTables 2 and 3**.

eTable 2. Estimated Prevalence of HBsAg Infection in the US, NHANES Data Collected 1999–2010

Sex-age group (yrs)	Sample				Weighted			Imputed + Weighted	
	Pos no.	Pos %	RSE[a] %	Missing[b] %	Pos %	RSE[a] %	Missing[b] %	Pos %	RSE[a] %
Males									
15–29	12	0.21	28.8	7.8	0.33	32.3	7.9	0.34	32.7
30–39	13	0.58	27.7	6.6	0.51	32.3	5.4	0.55	32.2
40–49	12	0.50	28.8	4.7	0.26	30.3	4.0	0.28	32.2
50–59	22	1.08	21.2	5.1	0.93	22.4	3.6	0.96	21.8
≥60	14	0.32	26.7	5.3	0.28	40.1	4.2	0.31	38.3
Overall	**73**	**0.44**	**11.7**	**6.2**	**0.44**	**14.8**	**7.0**	**0.46**	**6.8**
Females									
15–29	4	0.07	50.0	8.0	0.06	75.4	8.1	0.08	65.1
30–39	10	0.38	31.6	6.0	0.34	30.5	5.2	0.35	30.5
40–49	11	0.43	30.1	5.0	0.28	36.4	4.4	0.30	36.3
50–59	6	0.30	40.8	5.6	0.20	42.4	4.9	0.28	42.4
≥60	13	0.30	27.7	6.3	0.19	33.5	5.3	0.21	33.4
Overall	**44**	**0.25**	**15.1**	**6.6**	**0.20**	**19.2**	**7.5**	**0.23**	**5.4**

HBsAg = hepatitis B surface antigen, NHANES = National Health and Nutrition Examination Survey, Pos = positive, RSE = relative standard error, US = United States, yrs = years

a. The RSE, which is calculated by dividing the estimate's standard error by the estimate itself, RSE's of <30% should be indicated in reporting.[3]

b. Missing refers to individuals who attended the interview and medical examination but do not have a test result for HBsAg infection.

eTable 3. Estimated Prevalence of HCV-RNA Infection in the US, NHANES Data Collected 1999–2010

Sex-age group (yrs)	Sample				Weighted			Imputed + Weighted	
	Pos no.	Pos %	RSE[a] %	Missing[b] %	Pos %	RSE[a] %	Missing[b] %	Pos %	RSE[a] %
Males									
15–29	7	0.12	37.8	7.9	0.24	45.1	7.9	0.26	44.2
30–34	7	0.65	37.7	7.5	0.43	33.5	6.6	0.81	38.1
35–39	18	1.54	23.4	6.4	1.19	23.6	5.2	1.26	22.8
40–44	34	2.78	16.9	6.1	2.67	18.8	5.8	3.47	18.1
45–49	48	4.21	14.1	5.6	3.83	17.3	4.3	4.45	16.8
50–54	45	3.86	14.6	6.6	2.87	17.7	5.5	4.22	18.2
55–59	20	2.38	22.1	6.5	1.62	31.6	4.4	2.14	26.5
60–64	26	2.16	19.4	5.7	1.40	26.5	3.7	1.55	24.6
≥65	15	0.48	25.8	5.8	0.27	29.8	4.8	0.48	26.6
Overall	**220**	**1.32**	**6.7**	**6.8**	**1.36**	**9.2**	**7.5**	**1.76**	**8.7**
Females									
15–29	6	0.10	40.8	8.1	0.09	59.7	8.2	0.10	54.6
30–34	5	0.37	44.6	7.0	0.43	53.9	6.3	0.54	46.6
35–39	12	0.95	28.7	5.5	0.75	34.3	4.8	0.97	32.4
40–44	14	1.08	26.6	5.8	0.83	30.2	5.6	1.34	30.4
45–49	25	2.05	19.8	6.2	1.58	22.2	5.1	2.43	21.4
50–54	19	1.71	22.7	7.2	1.05	30.9	6.5	1.61	29.1
55–59	7	0.81	37.6	5.4	0.35	38.7	4.5	0.73	41.1
60–64	8	0.62	35.2	5.9	0.46	45.3	4.5	0.56	39.0
≥65	11	0.41	27.3	7.1	0.22	48.4	5.9	0.38	33.9
Overall	**107**	**0.62**	**9.6**	**7.0**	**0.55**	**12.4**	**7.9**	**0.82**	**11.7**

HCV = hepatitis C virus, NHANES = National Health and Nutrition Examination Survey, Pos = positive, RSE = relative standard error, US = United States, yrs = years

a. The RSE, which is calculated by dividing the estimate's standard error by the estimate itself, RSE's of <30% should be indicated in reporting.[3]

b. Missing refers to individuals who attended the interview and medical examination but do not have a test result for HCV RNA infection (note, this can include those who tested anti-HCV positive but did not have sufficient volume of sera to be tested for HCV RNA).

eAppendix 7. Hepatocellular Carcinoma

Through inflammation of the liver (cirrhosis), HBV and HCV can cause the major liver cancer histological type – HCC.[4] Additionally, HBV can cause HCC directly through chromosomal integration.[5] Studies reporting a measure of association are detailed in **eTable 4**.

eTable 4. Characteristics of Case-Control Studies on the Association Between HBV or HCV Infection and HCC

Study[a]	Study population	Matching variables	Characteristics of participants	Detection method	Cases		Controls		OR (95% CI)[b]	Adjustment variables & remarks
					n/N	Pos %	n/N	Pos %		
Hassan 2009[6]	Cases: diagnosed HCC GI outpatient clinics at M.D. Anderson Cancer Center Controls: three healthy controls/case non-blood family members of patients recruited from radiology clinic; similar in age, sex, race/ethnicity, education level Recruited: 2000–2006 Diagnosed: 2000–2008	Sex, age group, race	Males: 245 cases; 615 controls Mean age (SE): 62 (0.7) for cases; 60 (NS) for controls	**Anti-HCV** (3rd gen. ELISA)	79/ 347	22.8	6/ 1075	0.6	79.2 (30.6–204.8)	Age, sex, race, educational level, cigarette smoking, alcohol consumption, diabetes mellitus, family history of cancer, HBsAg, anti-HBc
Ognjanovic 2009[7]	Cases: Los Angeles HCC Study (HCC cases were identified through the Los Angeles County Cancer Surveillance Program, a population-based cancer registry) Controls: two neighbourhood controls/case and from Health Care Financing Administration files Diagnosed: 1984–2001 Sera collection: 1992–NS	Sex, age (±5), race	Males: 82 cases; 139 controls Mean age (SD): 60.5 (10.3) for cases; 59.5 (10.7) for controls, range: 18–74 yrs	**Anti-HCV** via ELISA v2 kit, confirmed with RIBA	58/ 120	48.3	1/ 230	0.4	211.0 (40.01–4368)	None OR calculated in OpenEpi
Davila 2005[8]	Cases: HCC in SEER registries also enrolled in Medicare (aged ≥65 yrs) Controls: population-based non-cancer controls aged ≥65 yrs, matched 3:1 to cases on time of diagnosis Recruited: 1994-1999	Frequency matched	Males: 1352 cases; 2248 controls Minimum age for study: 65 Age ≥75: 1139 cases; 3260 controls	ICD-9 codes for **HBV** ICD-09 codes for **HCV** or unspecified hepatitis diagnosed before 1992	182/ 2061 406/ 2061	8.8 19.7	14/ 6183 80/ 6183	0.2 1.3	23.94 (13.65–41.99) 24.42 (17.49–34.11)	Age, sex, race, SEER registry, Medicare/ Medicaid dual enrolment; HCV OR without diabetes

anti-HBc = total hepatitis B core antibody, CI = confidence interval, gen. = generation, GI = gastrointestinal, HBV = hepatitis B virus, HBsAg = hepatitis B surface antigen, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, EIA = enzyme immunoassay, ELISA = enzyme-linked immunoassay, NS = not specified, OR = odds ratio, Pos = positive, RIBA = Recombinant ImmunoBlot Assay, SD = standard deviation, SE = standard error, SEER = Surveillance, Epidemiology, and End Results Program, US = United States, yrs = years

a. Inclusion criteria: hepatitis infection confirmed by serology (HBsAg, anti-HCV [with or without RIBA confirmation], HCV RNA), 10 or more HCC cases, controls without liver disease, US study population.

b. After the normalizing transformation was performed, the CIs listed in the table may not match those in the forest plot.

eTable 4. Characteristics of case-control studies on the association between HBV or HCV infection and HCC (continued)

Study[a]	Study population	Matching variables	Characteristics of participants	Detection method	Cases		Controls		OR (95% CI)[b]	Adjustment variables & remarks
					n/N	Pos %	n/N	Pos %		
Hassan 2002[9]	Cases: HCC patients diagnosed at The University of Texas M. D. Anderson Cancer Center hospital Controls: histologically confirmed malignant neoplasms other than HCC, which included primary tumors of the GI tract (44.3%), urogenital tract (18.7%), respiratory tract (17.8%), and skin (19.1%) Diagnosed: 1994–1995	2 controls matched for sex, age (5 yrs), year of diagnosis to 1 case	Males: 87 cases; 174 controls Mean age (SD): 59.5 (10.7) for cases; 59.1 (10.9) for controls	**HBsAg** via ELISA	17/115	14.8	2/230	0.9	23.8 (3.9–141.6)	Alcohol consumption, cigarette smoking, diabetes mellitus, anti-HCV (for HBV only), HBsAg (for HCV only)
				Anti-HCV (2nd gen. ELISA) confirmed with RIBA	26/115	22.6	5/230	2.2	14.1 (4.0–49.7)	
Nomura 1996[10]	Nested case-control Cases: American men of Japanese ancestry with HCC, born between 1900-1919 living in Hawaii Controls: males without cancer selected from the cohort Recruited/diagnosed: NS	Age at examination, date of serum collection	All male	**HBsAg**	15/24	62.5	2/72	2.8	43.0 (5.7–325.5)	Not adjusted
				Anti-HCV via EIA and confirmed with RIBA (1st gen.)	0/23	0.0	0/67	0.0	Not computed due to a lack of exposure in cases and controls	
Di Bisceglie 1991[11]	Cases: consecutive HCC patients at Johns Hopkins Oncology Center Controls: patients with other malignant tumors (20% GI tract, 34% respiratory tract, 20% urogenital tract, and 16% breast, 10% neurological or hematological) at same institution Diagnosed: 1987–1988	Not matched	Males: 67 cases; 53 controls Mean (range) age at diagnosis: 52 (10–86) for cases; 55 (18–70) for controls	**HBsAg**	7/99	7.1	0/98 (0.5 added to empty cell)	0.0	11.31 (1.39–335.3)	Not adjusted; 0.5 added to empty cell (HBsAg controls)
				Anti-HCV	13/99	13.1	2/98	2.0	7.20 (1.78–48.22)	

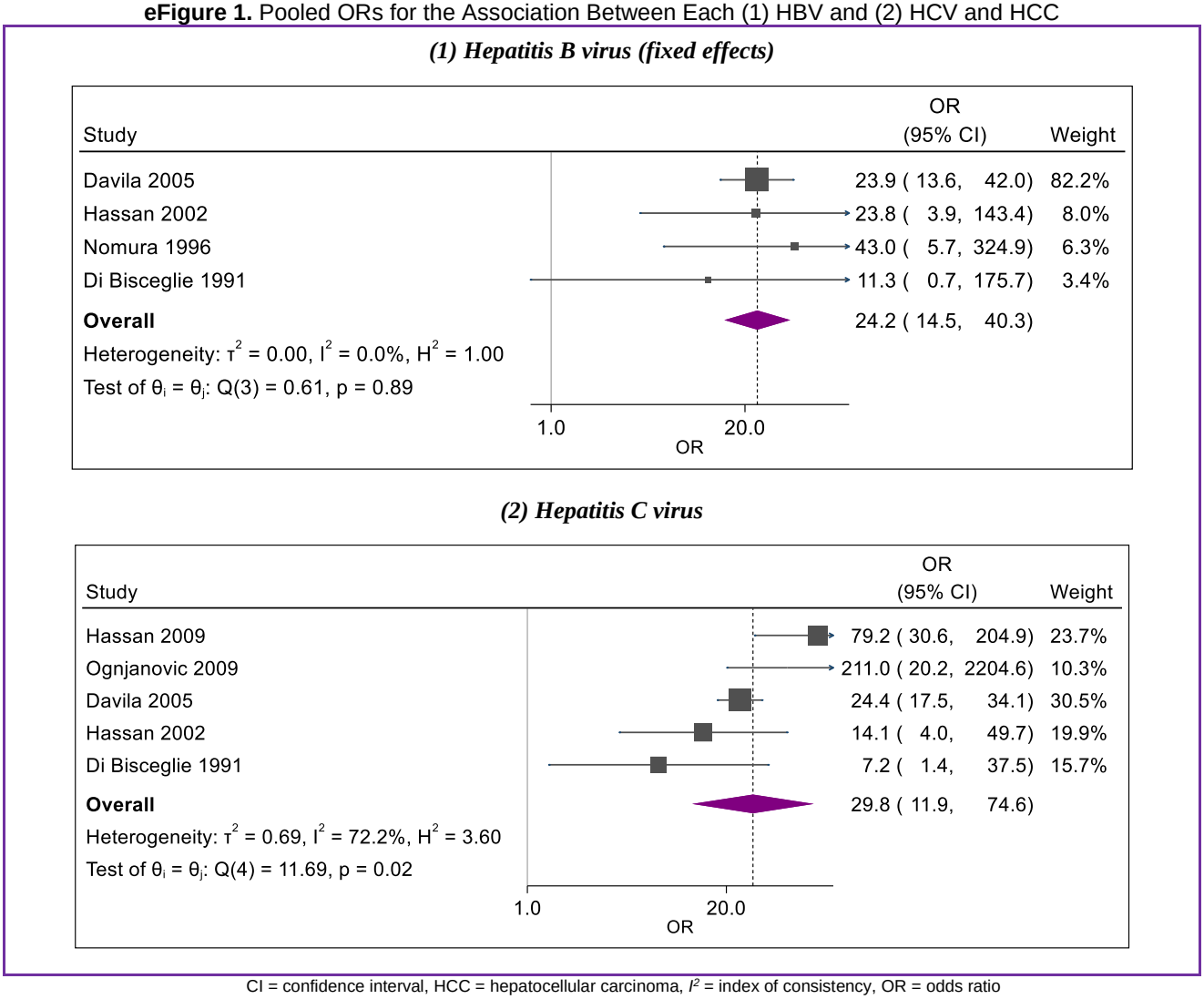
anti-HBc = total hepatitis B core antibody, CI = confidence interval, gen. = generation, GI = gastrointestinal, HBV = Hepatitis B virus, HBsAg = hepatitis B surface antigen, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, EIA = enzyme immunoassay, ELISA = enzyme-linked immunoassay, NS = not specified, OR = odds ratio, Pos = positive, RIBA = Recombinant ImmunoBlot Assay, SD = standard deviation, SE = standard error, SEER = Surveillance, Epidemiology, and End Results Program, US = United States of America, yrs = years

a. Inclusion criteria: hepatitis infection confirmed by serology (HBsAg, anti-HCV [with or without RIBA confirmation], HCV RNA), 10 or more HCC cases, controls without liver disease, US study population.

b. After the normalizing transformation was performed, the CIs listed in the table may not match those in the forest plot.

Pooling four studies reporting on HBV and five studies reporting on HCV gave a pooled OR of 24.2 (CI: 14.5–40.3) for HBV and 29.8 (CI: 11.9–74.6) for HCV (**eFig. 1**).

eFigure 1. Pooled ORs for the Association Between Each (1) HBV and (2) HCV and HCC



CI = confidence interval, HCC = hepatocellular carcinoma, I^2 = index of consistency, OR = odds ratio

The partitioned PAFs for HBV ranged from 1.8–16.0% and for HCV from 2.8–53.1% (**eTable 5**).

eTable 5. HBV and HCV Associated PAFs (%) for HCC, by Age Group and Sex

HCC sex-age group incidence (yrs)	HBV		HCV		Combined HBV-HCV PAF for 2017 %[a]	Partitioned PAFs[a]	
	Prevalence from age group (yrs)	Individual PAF %	Prevalence from age group (yrs)	Individual PAF %		HBV %	HCV %
Males							
20–24	15–29	7.3	15–29	6.9	13.7	7.0	6.6
25–29	15–29	7.3	15–29	6.9	13.7	7.0	6.6
30–34	15–29	7.3	15–29	6.9	13.7	7.0	6.6
35–39	15–29	7.3	15–29	6.9	13.7	7.0	6.6
40–44	30–39	11.4	30–34	19.0	28.2	10.5	17.6
45–49	30–39	11.4	35–39	26.6	35.0	10.5	24.5
50–54	40–49	6.1	40–44	50.0	53.1	5.8	47.3
55–59	40–49	6.1	45–49	56.2	58.9	5.8	53.1
60–64	50–59	18.3	50–54	54.9	63.2	15.8	47.4
65–69	50–59	18.3	55–59	38.1	49.4	16.0	33.4
70–74	≥60	6.7	60–64	30.9	35.5	6.4	29.2
≥75	≥60	6.7	≥60	12.1	17.9	6.4	11.6
Females							
20–24	15–29	1.9	15–29	2.8	4.6	1.8	2.8
25–29	15–29	1.9	15–29	2.8	4.6	1.8	2.8
30–34	15–29	1.9	15–29	2.8	4.6	1.8	2.8
35–39	15–29	1.9	15–29	2.8	4.6	1.8	2.8
40–44	30–39	7.4	30–34	13.6	20.0	7.1	12.9
45–49	30–39	7.4	35–39	21.8	27.6	7.0	20.6
50–54	40–49	6.6	40–44	27.8	32.6	6.2	26.3
55–59	40–49	6.6	45–49	41.2	45.1	6.2	38.9
60–64	50–59	6.1	50–54	31.7	35.9	5.8	30.1
65–69	50–59	6.1	55–59	17.4	22.4	5.8	16.6
70–74	≥60	4.6	60–64	13.9	17.9	4.5	13.4
≥75	≥60	4.6	≥60	9.8	14.0	4.5	9.5

HBV = hepatitis B virus, HCV = hepatitis C virus, HCC = hepatocellular carcinoma, PAF = population attributable fraction, yrs = years

a. The PAFs for HBV and HCV in HCC were combined with this equation: 1 – (1 – HBV PAF) * (1 – HCV PAF) then partitioned by determining the proportion of the summed number of attributable cases.[12]

eAppendix 8. Non-Hodgkin Lymphoma

Since NHLs are a heterogenous group of cancers and studies show that the magnitude of the association between HCV and NHL varies by subtype,[13-15] we utilized subtype specific measures of association. Data arising from the InterLymph Non-Hodgkin Lymphoma Subtypes Project, which pooled data from 11 mostly population-based case-control studies conducted in Australia, Europe and North America were used in the PAF calculations.[13,16] Of the 11 InterLymph studies, six[1] assessed HCV seropositivity via third-generation enzyme-linked immunosorbent assay (ELISA).[16] The overall OR for the association for HCV and NHL was 1.81 (CI: 1.39–2.37). Subtypes that HCV demonstrated a statistically significant association with were included (**eTable 6**). Notably, there were few cases of Burkitt lymphoma/leukemia (BL/L); however, since a similar magnitude of association (OR = 5.2, CI: 1.6–16.8) was also found in another large (33,940 NHL cases overall, 197 BL cases) study conducted in the US, we retained BL/L in the analysis.[14] An OR for HCV and BL/L in those aged <50 years was not calculated by the original study authors; we imputed 0.5 persons to the empty cell and calculated an OR of 1.47 (CI: 0.07–8.03). Since it was not statistically significant, we did not include BL/L among those <50 years in the PAF calculations. With only three cases of Waldenström's macroglobulinemia (the remaining 204 cases were lymphoplasmacytic lymphoma [LPL]), we applied the resulting PAF from LPL/WM to LPL incidence only.

eTable 6. The Association Between HCV Infection and NHL Subtypes as Reported in the InterLymph Study

NHL subtype	Cases		Controls		Adjusted OR (95% CI)	Adjustment variables
	n/N	Pos %	n/N	Pos %		
BL/L: age <50 yrs[17]	0/31	0.0	42/1933	2.2	--	Age, sex, race/ethnicity, & study
BL/L: age ≥50 yrs[17]	3/33	9.1	109/4562	2.4	4.1 (1.1–15.4)	
CLL/SLL[18]	21/994	2.1	95/5354	1.8	2.08 (1.23–3.49)	
DLBCL[19]	63/1654	3.8	152/6898	2.2	Males: 2.17 (1.44–3.26) Females: 1.98 (1.18–3.34)	Age, sex, race/ethnicity, study, SES, history of autoimmune disease, any atopic disorder, blood transfusion, year of first OC use, age at first HT use, 1st degree family history – NHL, BMI as young adult, usual adult BMI, lifetime alcohol consumption, recreational sun exposure, field crop vegetable farmer, sewer & embroiderer, women's hairdresser, driver/material handling equipment operator
LPL/WM[20]	6/207[b]	2.9	95/5354	1.8	2.51 (1.03–6.17)	Age, sex, race/ethnicity, study, Sjögren syndrome, systemic lupus erythematosus, hay fever, usual adult weight, smoking duration, family history of hematological malignancy, & medical occupation
MZL[21]	14/368	3.8	95/5354	1.8	3.04 (1.65–5.60)	Age, sex, race/ethnicity, & study

BL/L = Burkitt lymphoma/leukemia, BMI = body mass index, CLL/SLL = chronic/small lymphocytic leukemia/lymphoma, DLBCL = diffuse large B-cell lymphoma, HCV = hepatitis C virus, HT = hormone therapy, LPL/WM = lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia, MZL = marginal zone lymphoma, NHL = non-Hodgkin lymphoma, Pos = positive, OC = oral contraceptive, SES = socioeconomic status, yrs = years

a. Inclusion criteria: hepatitis infection confirmed by serology (anti-HCV [with or without RIBA confirmation], HCV RNA), 10 or more cases, study population from Western countries.

b. Among the 374 cases enrolled, only three were diagnosed with WM and the remainder LPL.

[1] The six studies were four population-based (region of recruitment and years cases diagnosed): British Columbia (Vancouver & Victoria, Canada; 2000–2004), UCSF1 (San Francisco, US; 1988–1995), SCALE (Denmark & Sweden, 1999–2002), New South Wales (Australian Capital Territory, 2000–2001); one mixed population-based and/or hospital-based: EpiLymph (Spain, France, Germany, Italy, Ireland, Czech Republic; 1998–2004; Italy and Germany were-population-based – the remainder were hospital-based), and one hospital-based: Italy – Aviano-Milan (1983–1992).

eAppendix 9. Intrahepatic Bile Duct Cancer

Pooling four studies reporting on intrahepatic bile duct cancer for each HBV and HCV (**eTable 7**) gave a pooled OR of 3.4 for HBV and 4.5 for HCV (**eFig. 2**).

eTable 7. Characteristics of Case-Control Studies on the Association Between HBV or HCV Infection and Intrahepatic Bile Duct Cancer

Study[a]	Study population	Matching variables	Characteristics of participants, age in yrs (SD)	Detection method	Cases		Controls		OR[b] (95% CI)	Adjustment variables & remarks
					n/N	Pos %	n/N	Pos %		
Petrick 2017[22]	SEER-Medicare database Cases: Medicare beneficiaries enrolled continuously in Medicare Parts A and B for a minimum of three yrs prior to cancer diagnosis with ICC Controls: 5% random sample of Medicare-enrolled beneficiaries residing in the SEER 18 geographic regions and without prior cancer diagnoses Period: 2000–2011	None	Cases: 78.0 (6.5) Controls: 76.6 (7.7)	ICD-9 codes for **HBV**	25/ 2092	1.2	1200/ 323,615	0.4	2.97 (1.97–4.46)	Age, race/ethnicity , geographic region, state buy-in status
				ICD-9 codes for **HCV**	58/ 2092	2.8	2161/ 323,615	0.7	4.67 (3.57–6.11)	
Choi 2016[23]	Cases: patients seen at the Mayo Clinic from 2000–2014 Controls: recruited from the Mayo Clinic Biobank from 2009–2015, which comprises a collection of blood samples & health information from Mayo Clinic patients and other community volunteers (without a history of cancer other than nonmelanoma skin cancer)	Frequency matched 1:2 for age (±5 yrs), sex, race, residence	Cases: 60.6 (13.1) Controls: 61.6 (13.5)	**HBsAg**	10/ 1169	0.9	8/4769	0.2	12.9 (2.69–61.61)	Propensity score adjustment: age, sex, race, obesity, hypertension, diabetes, cerebrovascular accident etc,[c]
				Anti-HCV	23/ 1169	2.0	17/ 4769	0.4	1.95 (0.75–5.11)	
Shaib 2007[24]	Cases: cholangiocarcinoma patients referred to the M.D. Anderson Cancer Center between 1992 and 2002 Controls: randomly selected from an existing database of healthy individuals (genetically unrelated family members, spouses and friends of patients who had cancer other than gastrointestinal cancer) interviewed between 1999–2004 at M.D. Anderson	Frequency matched by gender, ethnicity and age (±5 yrs)	Cases: 59.8 (11.4) Controls: 58.1 (11.4)	**HBsAg**	1/83	1.2	1/236	0.4	2.9 (0.1–236.8)	Race, age, gender, HCV & HBV markers, heavy drinking Lower bound CI was imputed
				Anti-**HCV**	5/83	6.0	2/236	0.8	7.9 (1.3–84.5)	
Shaib 2005[25]	SEER-Medicare database Cases: persons diagnosed no earlier than 1993 and who had two yrs of Medicare data before the date of diagnosis and up to one year after ICC diagnosis or until death Controls: 5% random sample of Medicare-enrolled beneficiaries with no cancer of any type residing in the geographic regions of SEER registries Period: 1993–1999	Yrs of search for risk factors	Cases: 78.7 (6.4) Controls: 76.5 (6.9)	ICD-9 codes for **HBV**	1/625	0.2	181/ 90,834	0.2	0.8 (0.1–5.9)	Age, sex, race, geographic region & Medicare/ Medicaid dual enrollment
				ICD-9 codes for **HCV**	5/625	0.8	161/ 90,834	0.2	5.2 (2.1–12.8)	

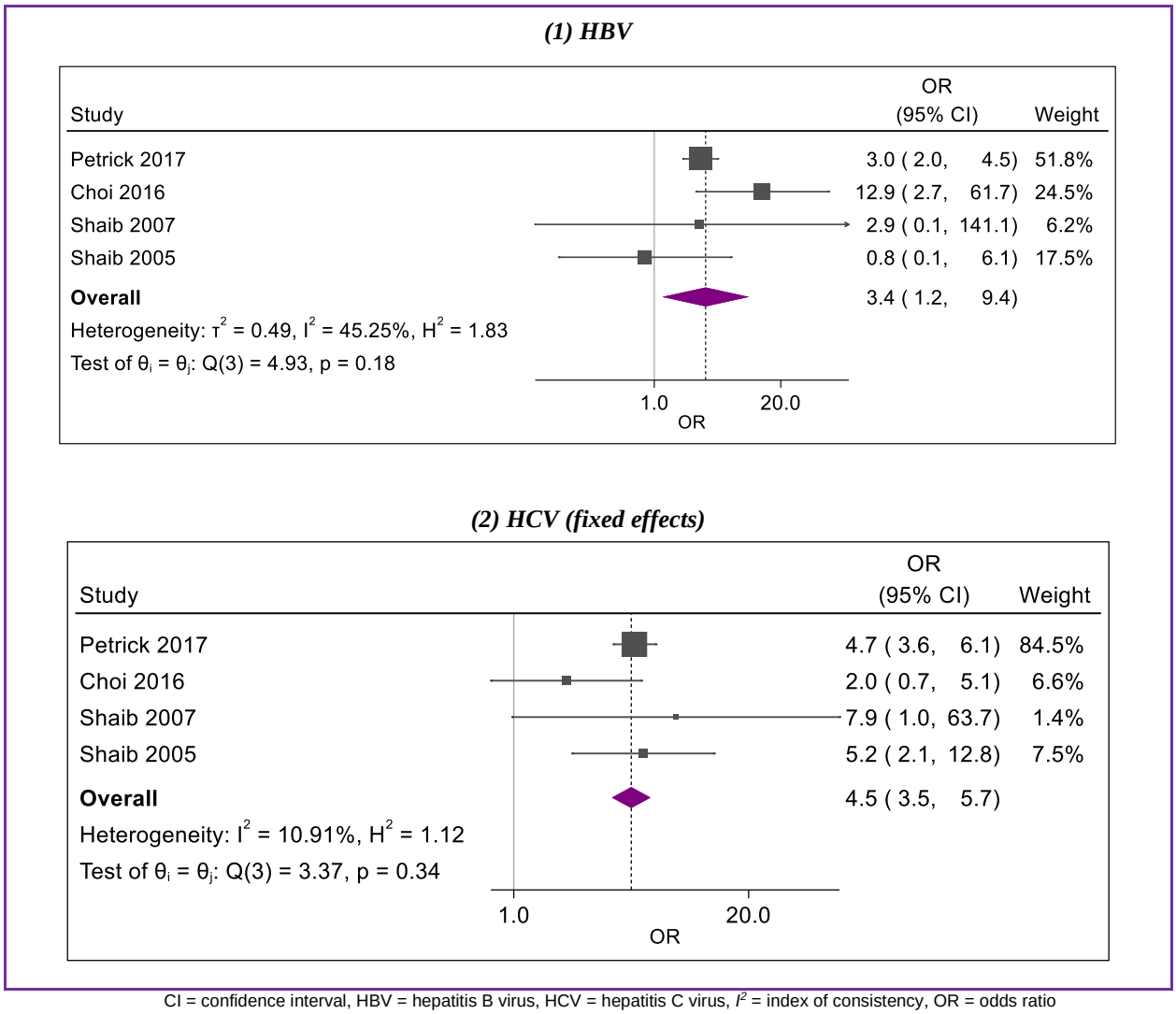
CI = confidence interval, HBV = Hepatitis B virus, HBsAg = hepatitis B surface antigen, HCV = hepatitis C virus, ICC = intrahepatic cholangiocarcinoma, Pos = positive, SD = standard deviation, SEER = Surveillance, Epidemiology, and End Results Program, yrs = years

a. Inclusion criteria: hepatitis infection confirmed by serology (HBsAg, anti-HCV [with or without RIBA confirmation], HCV RNA), 10 or more cases, US study population

b. After the normalizing transformation was performed, the CIs listed in the table may not match those in the forest plot.

c. As well as coronary artery disease, peripheral vascular disease, atrial fibrillation, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, primary sclerosing cholangitis, cirrhosis, inflammatory bowel disease and smoking status

eFigure 2. Pooled ORs for the Association Between Each (1) HBV and (2) HCV and Intrahepatic Bile Duct Cancer



CI = confidence interval, HBV = hepatitis B virus, HCV = hepatitis C virus, I^2 = index of consistency, OR = odds ratio

eAppendix 10. *Helicobacter pylori*

H. pylori is estimated to infect about 50% of the world's population, but the prevalence varies globally, likely reflecting socio-demographic and economic conditions of the regions.[26] Although infection is mostly acquired during childhood, *H. pylori* prevalence increases with age.[27] A decrease in the overall prevalence of *H. pylori* infection has been observed in recent years, with successive generations presenting lower prevalence.[26] The one cycle of the NHANES assessed *H. pylori* serostatus collected data from participants aged ≥3 years, via ELISA from 1999–2000. Equivocal results (representing <2% of results) were categorized as positive (**eTable 8**).

eTable 8. Estimated *H. pylori* Prevalence in the US and PAFs for NCGC

Sex-age Group (yrs)[a]	NHANES estimates from the 1999–2000 cycle									PAF estimates for NCGC for 2017
	Sample				Weighted			Imputed + Weighted		
	Pos no.	Pos %	RSE %	Missing[b] %	Pos %	RSE %	Missing %	Pos %	RSE %	
Males										
10–14	134	23.5	7.6	9.4	15.0	16.9	13.3	14.6	16.5	Not included
15–19	211	32.4	5.7	8.2	16.2	9.9	11.2	16.4	10.8	Not included
20–24	42	27.1	13.2	6.6	19.9	14.9	3.7	20.4	14.5	63.3
25–29	54	35.1	11.0	4.9	28.8	12.1	4.3	28.9	11.8	65.9
30–34	67	43.5	9.2	5.5	31.1	10.2	5.1	31.1	9.7	70.6
35–39	71	43.0	9.0	5.7	27.1	12.6	4.1	27.2	11.9	77.3
40–44	98	52.1	7.0	6.0	35.6	14.6	5.8	34.5	14.7	78.5
45–49	69	51.9	8.4	5.7	29.3	19.0	4.6	29.6	19.1	76.2
50–54	71	52.2	8.2	6.9	37.7	7.4	8.0	37.8	7.9	80.2
55–59	54	50.0	9.6	5.3	37.8	15.2	1.7	38.4	15.3	77.7
60–64	111	56.6	6.3	3.9	38.2	17.7	4.0	38.8	17.7	81.6
65–69	82	50.9	7.7	8.0	35.3	11.4	6.9	36.7	11.2	81.9
70–74	73	50.3	8.2	7.6	37.1	15.5	10.1	36.8	14.8	82.0
75–79	57	55.9	8.8	8.1	43.4	13.7	5.9	44.1	12.9	81.2
80–84	48	51.1	10.1	9.6	50.7	10.9	11.3	51.0	11.7	81.2
≥85	--	--	--	--	--	--	--	--	--	83.8
Overall	**1242**	**39.9**	**2.2**	**7.3**	**29.2**	**4.0**	**6.4**	**29.2**	**4.0**	**80.8**
Females										
10–14	103	17.9	8.9	12.2	9.2	19.7	14.4	9.3	18.9	Not included
15–19	172	27.8	6.5	7.4	16.5	14.4	9.8	17.1	14.5	Not included
20–24	79	33.1	9.2	7.0	20.9	18.3	7.7	20.8	18.2	52.2
25–29	59	28.4	11.0	8.4	20.0	15.1	8.7	19.8	14.8	66.8
30–34	73	34.0	9.5	4.9	27.4	13.7	4.3	27.3	13.1	71.0
35–39	76	40.9	8.8	6.1	26.5	14.6	3.9	27.1	14.8	70.0
40–44	86	47.5	7.8	5.2	26.8	14.2	6.2	27.2	13.8	76.2
45–49	74	43.8	8.7	8.2	29.9	8.7	5.7	30.9	8.7	76.1
50–54	79	48.2	8.1	5.8	37.3	10.9	5.6	38.2	11.1	76.2
55–59	64	55.7	8.3	2.5	38.8	14.1	2.7	38.8	14.0	78.4
60–64	91	50.3	7.4	9.5	38.6	15.3	7.5	39.4	14.6	81.8
65–69	94	59.5	6.6	10.2	46.1	10.4	9.1	45.6	11.0	82.0
70–74	82	57.3	7.2	5.3	49.9	11.0	5.4	49.6	11.4	82.3
75–80	53	54.1	9.3	5.8	48.2	15.3	3.9	48.3	14.9	84.3
80–84	39	40.2	12.4	7.6	30.7	10.9	8.5	32.9	12.5	85.4
≥85	--	--	--	--	--	--	--	--	--	85.0
Overall	**1224**	**36.6**	**2.3**	**7.9**	**28.2**	**4.6**	**7.0**	**28.3**	**4.7**	**81.1**

NHANES = National Health and Nutrition Examination Survey, NCGC = non-cardia gastric cancer, PAF = population attributable fraction, Pos = positive, RSE = relative standard error, US = United States

-- *H. pylori* prevalence among those ≥85 (in 1999–2000) was not calculated because it was not required after applying a latency period.

a. We did not consider *H. pylori* infection prevalence among those aged 3 to 9 (26% did not have a test result).

b. Missing refers to individuals who attended the interview and medical examination but do not have a test result for *H. pylori* infection.

eAppendix 11. Gastric Cancer (Non-Cardia)

This cancer is often classified according to its physical location within the stomach: tumors located in the upper region of the stomach, specifically within 1 to 2 centimeters proximal and 2 centimeters distal to the esophagogastric mucosal junction, are identified as cardia cancers; cancers located in the fundus, body, pyloric antrum or pylorus regions are identified as non-cardia.[28] The latter are the most frequent, accounting for 61% of GC cases diagnosed in the US in 2012 (males: 51.8%, females: 75.5%).[29] *H. pylori* infection is known to increase the risk of NCGC with a reported pooled estimate of 2.81 (CI: 2.14–3.68) considering case-control studies and case-control studies nested within prospective cohorts.[30] The association between *H. pylori* infection and gastric cardia adenocarcinomas remains conflicting. Studies from low gastric cancer risk settings, namely Europe, the US and Australia, generally report null or inverse associations (pooled RR = 0.78, CI: 0.63–0.97), while statistically significant associations have been observed in high-risk settings, namely China, Japan and Korea (pooled RR = 1.98, CI: 1.38–2.83).[30] A recent case-cohort study from China, an area of high *H. pylori* infection endemicity, obtained a statistically significant association (hazard ratio = 3.06, CI: 1.54–6.10).[28] These differences and null associations observed may be explained by the coexistence of two distinct types of cardia GC.[31] One arises from non-atrophic gastric mucosa, associated with acid/bile-induced damage to the distal esophagus, resembling esophageal adenocarcinoma[32] and is likely to have a higher relative frequency in settings with low overall gastric cancer risk. The other is associated with *H. pylori* induced atrophic gastritis,[32] which is etiologically similar to non-cardia tumors and more frequent in populations with a high frequency of gastric cancer. It is possible that *H. pylori* infection may be associated with a small fraction of cardia gastric cancer, however it is difficult to determine the origin of these cancers to obtain an accurate estimate.

In retrospective studies, individuals with GC may test negative following the clearance of infection associated with atrophic gastritis, thus underestimating the prevalence of *H. pylori* infection among cases.[29] As such, only cohort studies or case-control studies nested within prospective cohorts were considered to estimate the association between *H. pylori* infection and NCGC.

The finding that immunoblot is more sensitive than ELISA/ EIA[30] in detecting *H. pylori* necessitated a correction for this potential error.[33] The sensitivity and specificity were extracted, and pooled from two studies that compared ELISA to immunoblot head-to-head.[34,35] A derivation of a formula used to correct measurement error (91% sensitivity and 95% specificity) in the ORs was applied to the five nested case-controls that used EIA or ELISA (**eTable 9**).[36] The corrected and immunoblot studies (**eTable 10**) were pooled with fixed effects due to a lack of heterogeneity (**eFig. 3**).

eTable 9. Characteristics of Studies on the Association Between *H. pylori* Infection Detected Using ELISA or EIA and NCGC

Study[a]	Study population	Follow-up yrs, mean/ median	Matching variables	Characteristics of participants, ages in yrs	Cases		Controls		Unadjusted OR (95% CI)	Corrected OR[b,c] (95% CI)
					n/N	Pos %	n/N	Pos %		
Persson 2011[37]	Swedish cohorts (Swedish Institute for Infectious Disease Control Biobank and Malmö Microbiology Biobank) Recruited: 1968–2001 Diagnosed: 1968–2006	16.5	Sex, age, sera collection year, biobank	Mean (SD; range) age at sera collection: 30.8 (6.1; 16–40) for cases; 30.9 (6.0; 16–40) for controls Mean (SD; range) age at diagnosis: 47.3 (9.4; 25–68)	35/41	85.4	30/81	37.0	9.9 (3.7–26.3)	21.5 (6.1–75.8)
Hansen 2007[31]	Norwegian cohort (Janus Serum Bank Cohort) Recruited: 1972–1986 Diagnosed: 1972–1992	11.9	Sex, age, cohort, sera collection date & study source	Males: 91 cases; 267 controls Median (range) age at sera collection: 45.6 (23.6–63.4) Median (range) age at diagnosis: 55.8 (34.3–68.2)	116/129	89.9	247/376	65.7	4.7 (2.5–8.6)	26.6 (6.5–109.1)
Knekt 2006[38]	Finnish cohort (Finnish Mobile Clinic Health Examination cohort) Recruited: 1968–1972 Diagnosed: 1968–1991	Up to 24	Sex, age, municipality	Males: 120 cases; 231 controls Mean age (SD) at baseline: 68 (14) for cases	176/193	91.2	292/372	78.5	2.8 (1.6–4.9)	66.2 (4.1–1078.6)
Nomura 2002[39]	US cohort of men of Japanese ancestry Recruited: 1967–1977 Diagnosed: 1967–1996	12.7	Age, sera collection date	All men Mean (range) age at diagnosis: 72.5 (50.2–90.3)	231/261	88.5	193/261	73.9	2.7 (1.7–4.3)	7.9 (3.7–16.9)
Parsonnet 1993[40]	US cohort of adult subscribers to the Kaiser Permanente Medical Care Program Recruited: 1964–1969 Diagnosed: 1964–1989	15	Sex, age group, race, sera collection date & study site	Median age at sera collection: 53.6	84/98	85.7	61/98	62.2	3.6 (1.8-7.3)	7.4 (3.1–19.6)

CI = confidence interval, EIA = enzyme immunosorbent assay, ELISA = enzyme-linked immunosorbent assay, NCGC = non-cardia gastric cancer, OR = odds ratio, Pos = positive, SD = standard deviation, US = United States, yrs = years

a. Inclusion criteria: prospective serology collection (~10 years in advance of diagnosis), ELISA or EIA, 10 or more non-cardia gastric cancer cases, North American, European, Australian or New Zealand study populations, data required to correct sensitivity and specificity.

b. Corrected to 91% sensitivity and 95% specificity. ORs were calculated based on the condition maximum likelihood estimates, and CIs were based on Fisher exact tests.

c. After the normalizing transformation was performed, CIs listed in the table may not match those in the forest plot.

eTable 10. Characteristics of Studies on the Association Between *H. pylori* Infection Detected Using Immunoblot and NCGC

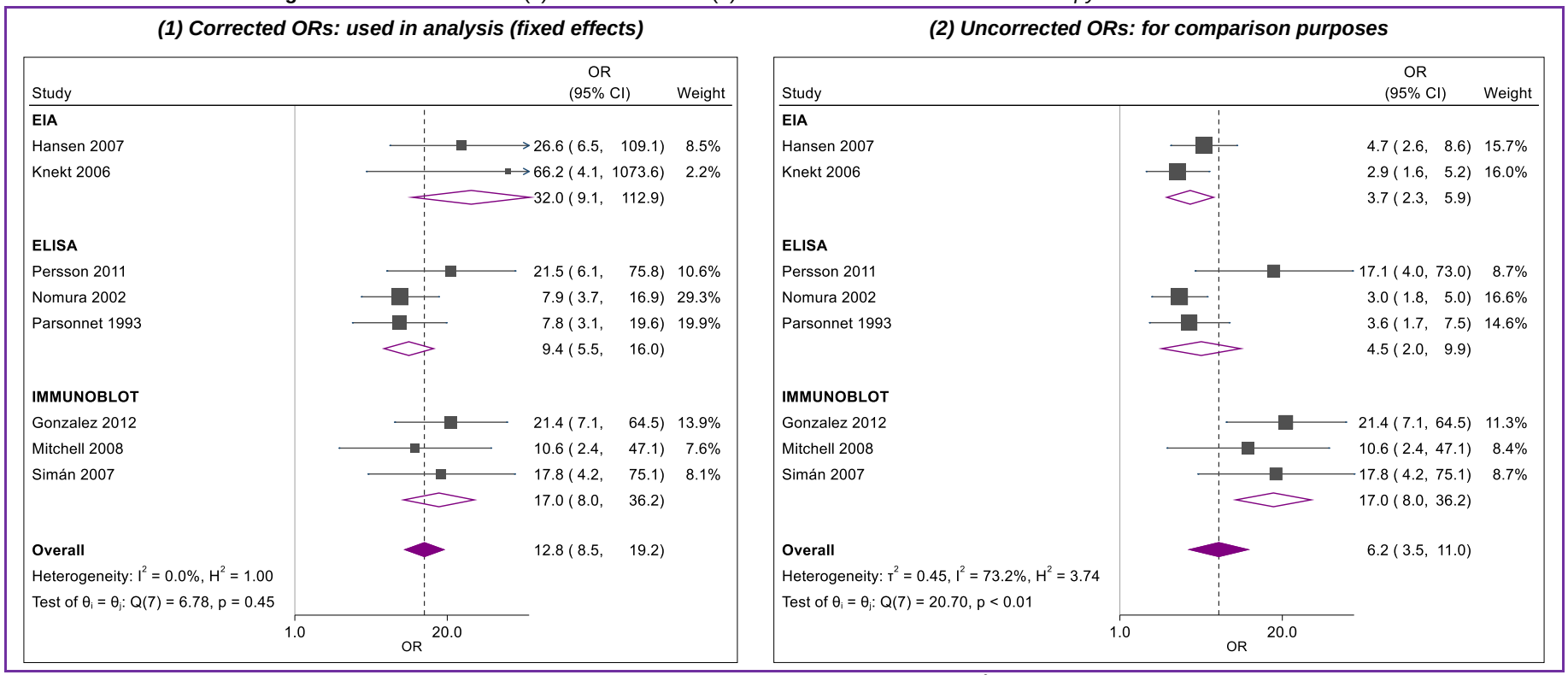
Study[a]	Study population	Follow-up yrs, mean/ median	Matching variables	Characteristics of participants, ages in yrs	Cases		Controls		Adjusted OR[b] (95% CI)	Adjustment variables
					n/N	Pos %	n/N	Pos %		
Gonzalez 2012[34]	10 European countries in the EPIC cohort Recruited: 1992–1998 Diagnosed: 2000–2004	10.7	Sex, age group, study center, date of blood collection	Age range at baseline: 40-65	82/88	93.2	199/338	58.9	21.4 (7.1–64.4)	Smoking status, school level, red & processed meat intake, fruit & vegetable consumption
Mitchell 2008[35]	Australian cohort (Melbourne Collaborative Cohort Study) Recruited: 1990–1994 Diagnosed: 1990–2002	11.6	Sex, age, birth country, sera collection date	Males: 21 cases; 84 controls Median (range) age at baseline: 62 (42–69)	32/34	94.1	85/134	63.4	10.6 (2.4–47.4)	None
Simán 2007[41]	Swedish cohort (Malmö Preventive Medicine) Recruited: 1974–1992 Diagnosed: –2000	Range: 9.2–12.6	Sex, age, sera collection date	Males: 54 cases Mean (range) age at baseline: 50.7 (34.0–60.9)	65/67	97.0	147/250	58.8	17.8 (4.2–74.8)	Occupation, tobacco consumption

CI = confidence interval, EPIC = European Prospective Investigation into Cancer and Nutrition, NCGC = non-cardia gastric cancer, OR = odds ratio, Pos = positive, yrs = years

a. Inclusion criteria: prospective serology collection (~10 yrs in advance of diagnosis), immunoblot detection, 10 or more NCGC cases, North American, European or Australia or New Zealand study populations.

b. After the normalizing transformation was performed, the CIs listed in the table may not match those in the forest plot.

eFigure 3. Pooled Corrected (1) and Uncorrected (2) ORs for the Association Between *H. pylori* and NCGC



CI = confidence interval, EIA = enzyme immunoassay, ELISA = enzyme-linked immunosorbent assay, I^2 = index of consistency, OR = odds ratio

eAppendix 12. Gastric MALT and DLBCL

MALT lymphoma, a type of NHL, is most often diagnosed in the stomach, but can also be found in the lungs, thyroid, skin or soft tissues.[42] A systematic review of published series found that *H. pylori* infection is present in nearly 90% of patients with gastric MALT lymphoma.[43] According to current guidelines, antibiotic therapy against *H. pylori* infection is the first-line of treatment in patients with gastric MALT regardless of stage of disease and prognosis factors.[44,45] In fact, *H. pylori* eradication confers a ~74% remission rate of MALT in Western populations.[43] Even among patients with *H. pylori*-negative gastric MALT, complete remission following eradication therapy is nearly 30%.[46] We identified only one cohort study examining the relationship between *H. pylori* and gastric NHL. This study, conducted by Parsonnet et al., combined data from two cohort studies conducted in Norway and the US,[47] and reported a measure of association (OR = 6.3, CI: 2.0–19.9) for NHL of gastric location. This study included 33 cases matched to four controls by cohort, sex, age and sera collection date.[47] Of the 33 cases, just three cases were gastric MALTs, one case was lymphocytic lymphoma, and the remaining 29 cases were DLBCLs. We opted to utilize the OR for the US cohort (7.9, CI: 1.6–38.1) which included 20 gastric NHL cases and applied it to gastric MALT and DLBCL incidence.

eAppendix 13. Esophageal Adenocarcinoma

Esophageal cancer presents with two major histological types: SCC (morphology codes 8140–8576) that most often arises in the middle third of the esophagus, followed by the lower and the upper third, and adenocarcinoma (morphology codes: 8050–8083) that usually develops in the lower third.[48] In the US, esophageal adenocarcinoma accounted for 55% of esophageal cancer cases diagnosed between 2001 and 2015.[49] *H. pylori* infection is inversely associated with the occurrence of esophageal adenocarcinoma, regardless of other environmental and genetic exposures,[48,50] and the decline in the prevalence of *H. pylori* infection may have contributed to an increase in esophageal adenocarcinoma incidence. The effect of *H. pylori* infection has been evaluated by several meta-analyses reporting results for both esophageal SCC and adenocarcinoma.[51-56] All reported similar results, showing no association between *H. pylori* and esophageal SCC, while for adenocarcinoma a protective effect of *H. pylori* infection was found (OR ≈ 0.5).

The mechanism through which *H. pylori* infection reduces the risk of esophageal adenocarcinoma is not yet clear. Studies have suggested *H. pylori* infection may decrease gastric cancer secretion by acting on parietal cells via bacterial products and cytokines or through mucosal atrophy resulting from chronic inflammation. Consequently, there may be less reflux esophagitis, Barrett's esophagus, and development of esophageal adenocarcinoma.[57,58] However, the association between the absence of *H. pylori* infection and increased gastroesophageal reflux,[59] and whether infection interacts directly with host epithelial cells and/or affects the microbial composition of the esophagus remain unclear.[60] Nevertheless, previous studies have suggested that the association between *H. pylori* infection and esophageal adenocarcinoma may be independent of CagA status and atrophy of the stomach.[57,61,62]

Our search produced six meta-analyses that reported results for the association between *H. pylori* infection and esophageal adenocarcinoma, all reported a protective effect.[51-56] Ten individual studies were conducted in the US.[57,62-70] Studies that did not provide estimates for esophageal adenocarcinoma specifically (i.e., considered esophageal and gastric cardia adenocarcinoma,[64] Barrett's esophagus complicated by dysplasia or adenocarcinoma)[63,70] and/or considered controls with gastrointestinal symptoms or undergoing endoscopy for reasons other than screening (i.e., patients undergoing endoscopy due to achalasia, familial adenomatous polyposis, chronic diarrhea, lower abdominal pain, hemoccult-positive stools, unexplained nausea and vomiting, and unexplained chest pain;[63,70] patients with benign disease and symptoms suggestive of foregut disease;[69] patients undergoing esophagogastroduodenoscopy for classic symptoms of GERD with or without complaints of dysphagia, nocturnal cough, chest pain, nausea, vomiting, or signs of acute or chronic gastrointestinal bleeding;[65] patients with intestinal metaplasia[67] were excluded.[63,70] Four studies met the inclusion criteria (**eTable 11**) and were pooled with fixed effects due to a lack of heterogeneity (**eFig. 4**).

eTable 11. Characteristics of Studies on the Association Between *H. pylori* Infection and Esophageal Adenocarcinoma

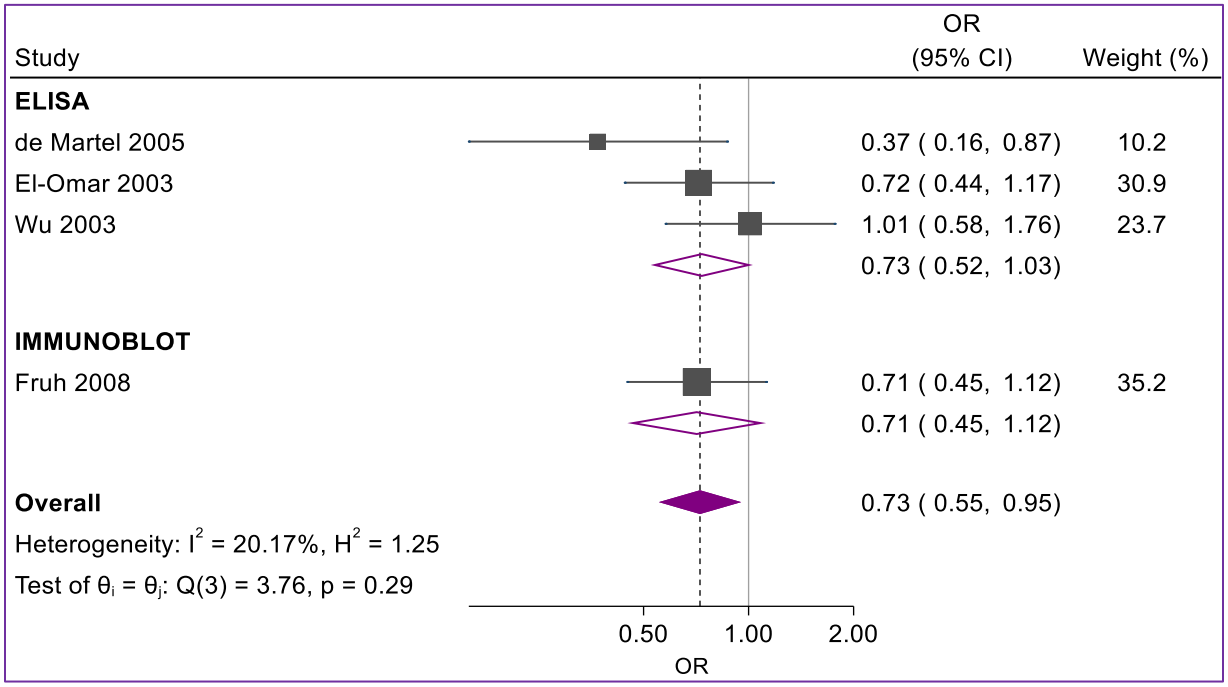
Study[a]	Study population	Matching variables	Characteristics of participants, ages in yrs	Assessment of *H. pylori* infection	Cases		Controls		Adjusted OR (95% CI)[b]	Adjustment variables
					n/N	Pos %	n/N	Pos %		
Fruh 2008[62]	Case-control study Cases: histologically confirmed esophageal adenocarcinoma patients at the Massachusetts General Hospital Controls: selected from healthy GERD-free, non-blood-related family members and friends of other cancer/surgical patients Diagnosed/Recruited: not specified	Sex, age	Males: 88 cases; 88 controls Mean age (SD): 64 (8) for cases; 63 (8) for controls	Serum (Helicoblot)	36/100	36.0	43/101	42.6	0.71 (0.4–1.0)	Adult BMI, smoking status, age, sex
de Martel 2005[57]	Nested case-control study (Kaiser Permanente Medical Care Program) Cases: esophageal adenocarcinoma patients were identified in the cohort and were confirmed by information in the SEER database Controls: randomly selected from the cohort Recruited: 1964–1969 Diagnosed: 1964–2000	Sex, age, race, date & site of sera collection	Males: 41 cases; 121 controls Mean age (SD): 47.9 (10.0) for cases; 47.7 (9.6) for controls	Serum IgG (ELISA)	19/51	37.3	74/150	51.0	0.37 (0.16–0.88)	BMI, cigarette smoking, education
Wu 2003[68]	Case-control study Cases: esophageal adenocarcinoma patients from the Los Angeles County Cancer Surveillance Program (population-based cancer registry) Controls: selected from the neighborhood of residence of the case patient Diagnosed/Recruited: 1992–1997	Sex, age group, race	Males: 73 cases; 261 controls	Serum IgG (ELISA)	49/80	61.2	230/356	64.6	1.01 (0.58–1.77)	Sex, age, education, birthplace, ethnic group, smoking status, BMI
El-Omar 2003[66]	Case-control study Cases: esophageal adenocarcinoma patients from New Jersey and western Washington Controls: population-based controls selected by random-digit dialing and from Health Care Financing Administration files Diagnosed/Recruited: 1993–1995	Sex, age group, study centre	Males: 93 cases; 178 controls Median age: 65 for cases; 66 for controls	Serum IgG (ELISA)	35/108	32.4	84/210	40.0	0.72 (0.44–1.17)	None

BMI = body mass index, CI = confidence interval, ELISA = enzyme-linked immunosorbent assay, GERD = gastroesophageal reflux disease, Pos = positive, OR = odds ratio, SD = standard deviation, SEER = Surveillance, Epidemiology, and End Results, Program, US = United States

a. Inclusion criteria: cohort, nested case-control or case-control studies with *H. pylori* infection confirmed by serology (ELISA, enzyme immunoassay [EIA] or immunoblot), 10 or more esophageal adenocarcinoma cases, controls without gastrointestinal symptoms and not undergoing endoscopy for purposes other than screening, study population from the US.

b. After the normalizing transformation was performed, the CIs listed in the table may not match those in the forest plot.

eFigure 4. Forest Plot of the Association Between *H. pylori* Infection and Esophageal Adenocarcinoma (Fixed Effects)[a,b]



CI = confidence interval, ELISA = enzyme-linked immunosorbent assay, I^2 = index of consistency, OR = odds ratio

a. The study by de Martel and colleagues published in 2005 is a nested case-control where *H. pylori* sera collection occurred prior to adenocarcinoma diagnosis, the remaining studies are case-controls.

b. Pooling the unadjusted ORs from the four studies resulted in a pooled OR of 0.75 (CI: 0.57–0.98).

eAppendix 14. Epstein-Barr Virus

Carcinogenicity is demonstrated by the detection of the EBV viral genome within the tumor cells (i.e., where the EBV genome is translated and transcribed).[71] To detect EBV within cancer tissues, EBER ISH is viewed as the gold standard assay;[4,72] for HL, LMP-1 is comparable to EBER ISH.[72]

eAppendix 15. Burkitt Lymphoma

BL in children (aged 0–19 yrs)

We identified seven studies conducted in the US and Europe (**eTable 12**). The pooled prevalence of EBV was 15.5% (CI: 8.1–23.0%) (**eFig. 5**).

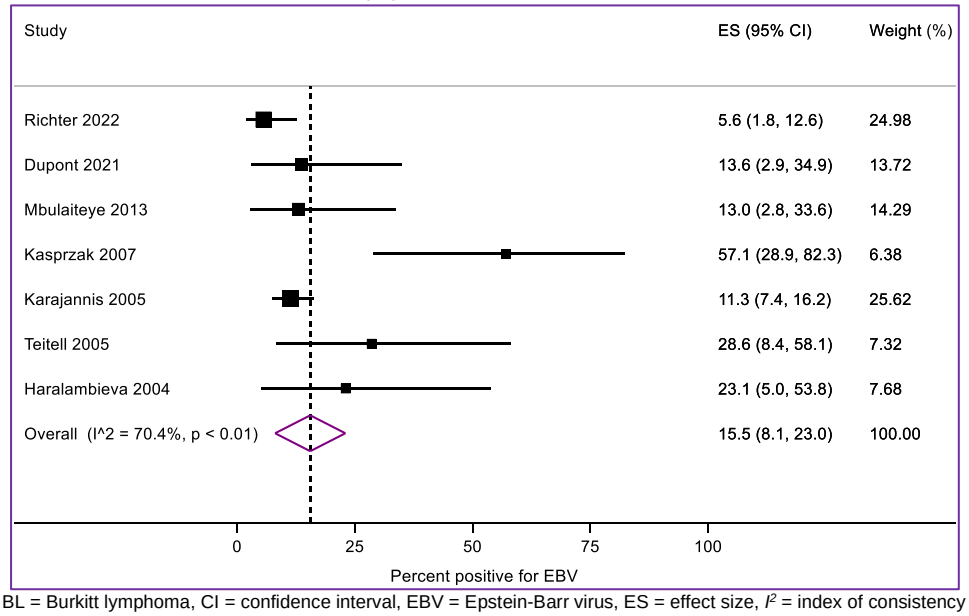
eTable 12. Characteristics of Studies on EBV Prevalence in BLs From Individuals Aged 0–19

Study[a]	Region(s)	Source of cases	Diagnosis dates	Male %	Age range (yrs)	Tested N	Pos %
Richter 2022[73]	Germany	Hematopathology Section & Lymph Node Registry of the University Hospital Schleswig-Holstein, Campus Kiel	2001–2013	86.8	NS	89	5.6
Dupont 2021[74]	Denmark	Danish Registry of Pathology	1980–2018	81.8	3–19	22	13.6
Mbulaiteye 2013[75]	Los Angeles County, Hawaii & Iowa	Residual tissue repositories (population-based) & diagnostic referral centers	1979–2009	91.3	0–19	23	13.0
Kasprzak 2007[76]	Poland	Department of Haematology & Paediatric Oncology	1999–2003	92.9	3–16	14	57.1
Karajannis 2005[77]	Austria, Germany & Switzerland	NHL-BFM (Berlin-Frankfurt-Munster) data center	1990–1998	79.7	1–18	222	11.3
Teitell 2005[78]	France & United Kingdom	Institut Gustave Roussy & Children's Hospital	NS	85.7	2–16	14	28.6
Haralambieva 2004[79]	the Netherlands	Pathology departments & Dutch Childhood Oncology Group	NS	NS	5–13	13	23.1

BL = Burkitt lymphoma, EBV = Epstein-Barr virus, EBER ISH = Epstein-Barr encoding region *in situ* hybridization, NS = Not specified, Pos = positive, yrs = years

[a] Inclusion criteria: tissue specimen tested for EBV, EBER ISH detection, European or North American cases, and 8 or more participants.

eFigure 5. Forest Plot of EBV Prevalence (%) in BL Tumor Tissues Collected From Individuals Aged 0–19



BL = Burkitt lymphoma, CI = confidence interval, EBV = Epstein-Barr virus, ES = effect size, I^2 = index of consistency

BL in adults (aged ≥20 yrs)

We identified two studies conducted in the US that utilized EBER ISH; they were one study by Mbulaiteye and colleagues (2014) of 40 HIV-negative or unknown HIV status cases (11 HIV+ cases excluded by us) diagnosed from 1979–2009 using SEER data collected from Los Angeles County, Hawaii and Iowa, where 27.5% tested EBV positive (including the 11 PWH, 35.3% tested positive).[75] Another study by Naeini and colleagues (2016), tested 27 BL cases of unknown HIV status sent to pathology services in California, and reported that 37.0% tested positive.[80]

Pooling five studies (four conducted in Europe and one in the US)[75,81-84] reporting on EBV prevalence in 118 BLs among PWH, provided prevalence of 50.1% (CI: 34.6–65.6; individual studies not shown). Considering individuals aged 20–59 (since the estimated proportion of BLs occurring among PWH aged ≥60 years was only 2.0% over 1980–2007, we did not consider this age group) an estimated 21.5% of BLs from the most recent period available (2001–2007) were diagnosed among PWH in the US.[85] Weighting the pooled prevalence by HIV status provided EBV prevalence of 35.1%, which is near identical pooled EBV prevalence reported by Mbulaiteye and colleagues that included general and PWH cases. For this reason, we instead opted to use age-group specific EBV prevalence from the Mbulaiteye study which included some HIV+ cases: 55% (aged 20–34), 33% (aged 35–59), 25% (aged ≥60).[75]

eAppendix 16. Hodgkin Lymphoma

HL in children (aged 0–19 yrs)

Pooling six studies providing EBV prevalence for younger versus older children (**eTable 13**), resulted in EBV prevalence of 62.2% for children aged 0–9 and 22.3% for those aged 10–19 years (**eFig. 6**).

HL in adults (aged ≥20 yrs)

Pooling four studies reporting on EBV prevalence in two adult age groups, provided a pooled prevalence of 20.5% in adults aged 15–44 years old and 42.5% in adults aged ≥45 years old (**eFig. S7**). Pooling six studies (two[86,87] conducted in the US and four[88-91] in Europe) reporting on EBV prevalence in 282 HL cases diagnosed among PWH, resulted in prevalence of 92.9%. Using data from the 14 SEER cancer registries (2000–2010), Shiels and colleagues estimated the proportion of HLs among PWH by sex and age group.[92] We utilized the proportion of HL cases estimated to be among PWH by 10-year age groups from age 20 to 69 to partition HL cancer incidence; these proportions were 1.5% (age 20–29), 5.4% (age 30–39), 9.3% (age 40–49), 7.3% (age 50–59), and 1.9% (age 60–69) and applied to males HL incidence counts only.[92]

eTable 13. Characteristics of Studies Reporting on EBV Prevalence in HLs

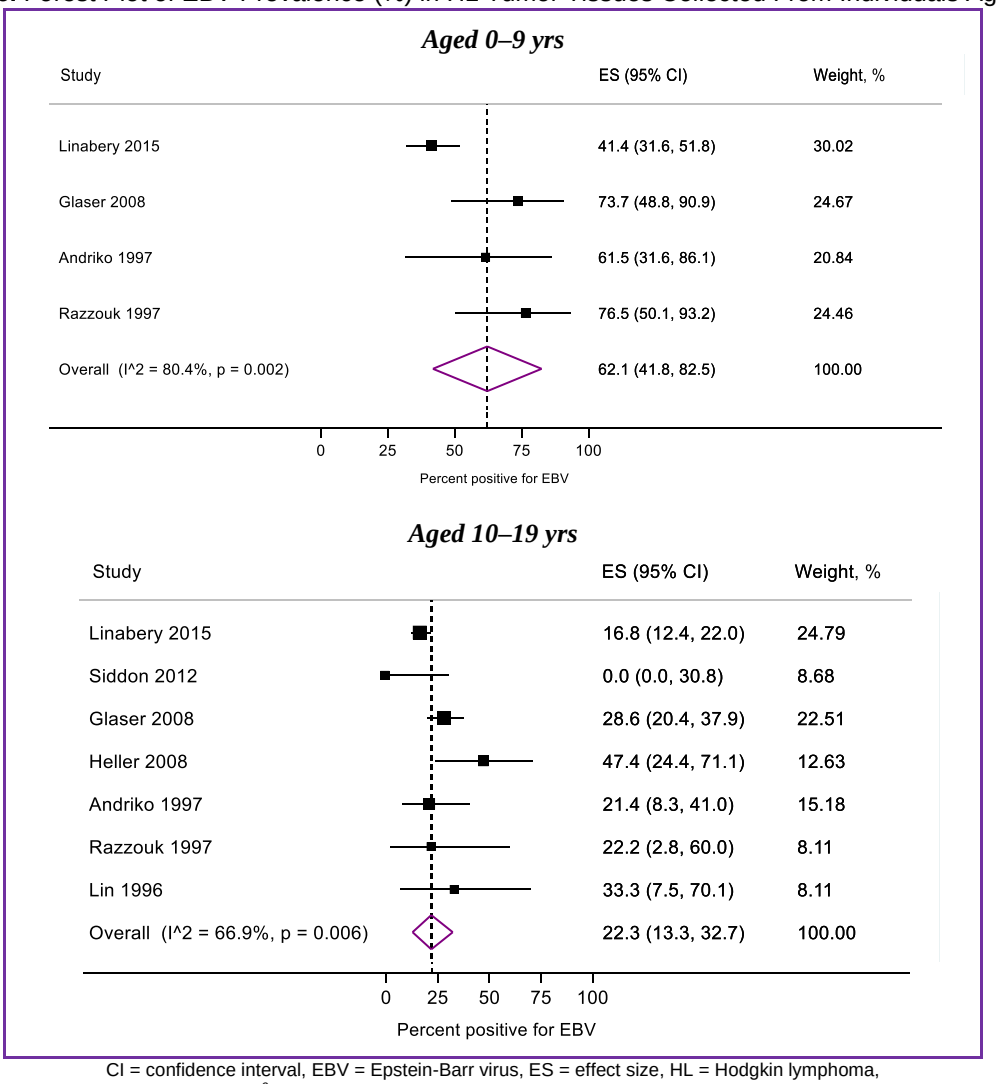
Study[a]	Region(s)	Source of cases	Diagnosis dates	Male %	Detection method(s)	HIV status	Age range (yrs)	Tested N	Pos %
Linabery 2015[93]	US, Puerto Rico & Canada	Children's Oncology Group	1989–2003	NS	EBER ISH	Unknown	0–9 10–14	99 256	41.4 16.8
Siddon 2012[94]	Connecticut	Yale-New Haven Hospital	NS	50.0	EBER ISH	HIV-	10–19	10	0.0
Glaser 2008[95]	California	California Cancer Registry and non-White Los Angeles County residents	1988–1997	NS	EBER ISH, LMP-1	HIV-	0–9 10–19 20–49 ≥50	19 112 650 251	73.7 28.6 20.9 48.6
Heller 2008[96]	New York	Memorial Sloan-Kettering Cancer Center	NS	45.5	EBER ISH	HIV-	10–19	19	47.4
Chang 2004[97]	Massachusetts & Connecticut	Population-based case-control study	1997–2001	57.0	EBER ISH, LMP-1	HIV-	15–44 ≥45	291 108	18.9 38.0
Vasef 2004[98]	Iowa	Pathology department	NS	58.6	EBER ISH, LMP-1	Unknown	15–44	24	25.0
Andriko 1997[99]	Washington, D.C.	Lymphatic Pathology Registry, Armed Force Institute of Pathology	1984–1996	90.9	LMP-1	Unknown	0–9 10–19	13 28	61.5 21.4
Razzouk 1997[100]	Tennessee	St. Jude Children's Research Hospital	NS	42.3	EBER ISH	Unknown	0–9 10–19	17 9	76.5 22.2
Elenitoba-Johnson 1996[101]	Rhode Island	Pathology departments	NS	42.9	LMP-1	Unknown	15–44 ≥45	18 10	33.3 30.0
Lin 1996[102]	Maryland	Clinical Center of National Institutes of Health	1971–1992	NS	EBER ISH	Unknown	10–19	9	33.3
Studies conducted among adults living with HIV									
Besson 2015[88]	France	22 centres: French Cohort of HIV-related lymphomas—French National Agency for Research on AIDS and Viral Hepatitis ANRS-CO16 Lymphovir cohort	2008–2014	86.8	EBER-1 ISH, LMP-1	HIV+	38–48	42	92.9
Hentrich 2012[89]	Austria & Germany	42 institutions in Austria & Germany	2004–2010	92.6	LMP (81%), EBER ISH (4%), PCR (3%), LMP & EBER (4%), method NS (9%)	HIV+	27–70	103	92.2
Glaser 2003[86]	California	California Cancer Registry non-White Los Angeles County residents	1988–1998	100.0	EBER ISH, LMP-1	HIV+	NS	59	89.8
Thompson 2004[87]	D.C.	AIDS Registry of the Armed Forces Institute of Pathology[b]	1984–2000	97.8	LMP	HIV+	21–75	33	97.0
Carbone 1999[90]	Italy	NS	NS	NS	EBER ISH	HIV+	NS	27	92.6
Tirelli 1995[91]	Italy	Division of Pathology at the Centro di Riferimento Oncologico	NS	NS	EBER-1 & EBER-2 ISH, Southern blotting	HIV+	NS	18	77.8

AIDS = acquired immunodeficiency syndrome, D.C. = District of Columbia, EBV = Epstein-Barr virus, EBER ISH = Epstein-Barr encoding region *in situ* hybridization, HIV = human immunodeficiency virus, LMP = latent membrane protein, HL = Hodgkin lymphoma, NS = Not specified, PCR = polymerase chain reaction, Pos = positive, US = United States, yrs = years

a. Inclusion criteria: tissue specimen tested for EBV, EBER ISH detection, North American cases (for HIV+ cases from Europe were also eligible), and 8 or more cases (children) or 10 or more cases (adults), EBV prevalence reported by age-group.

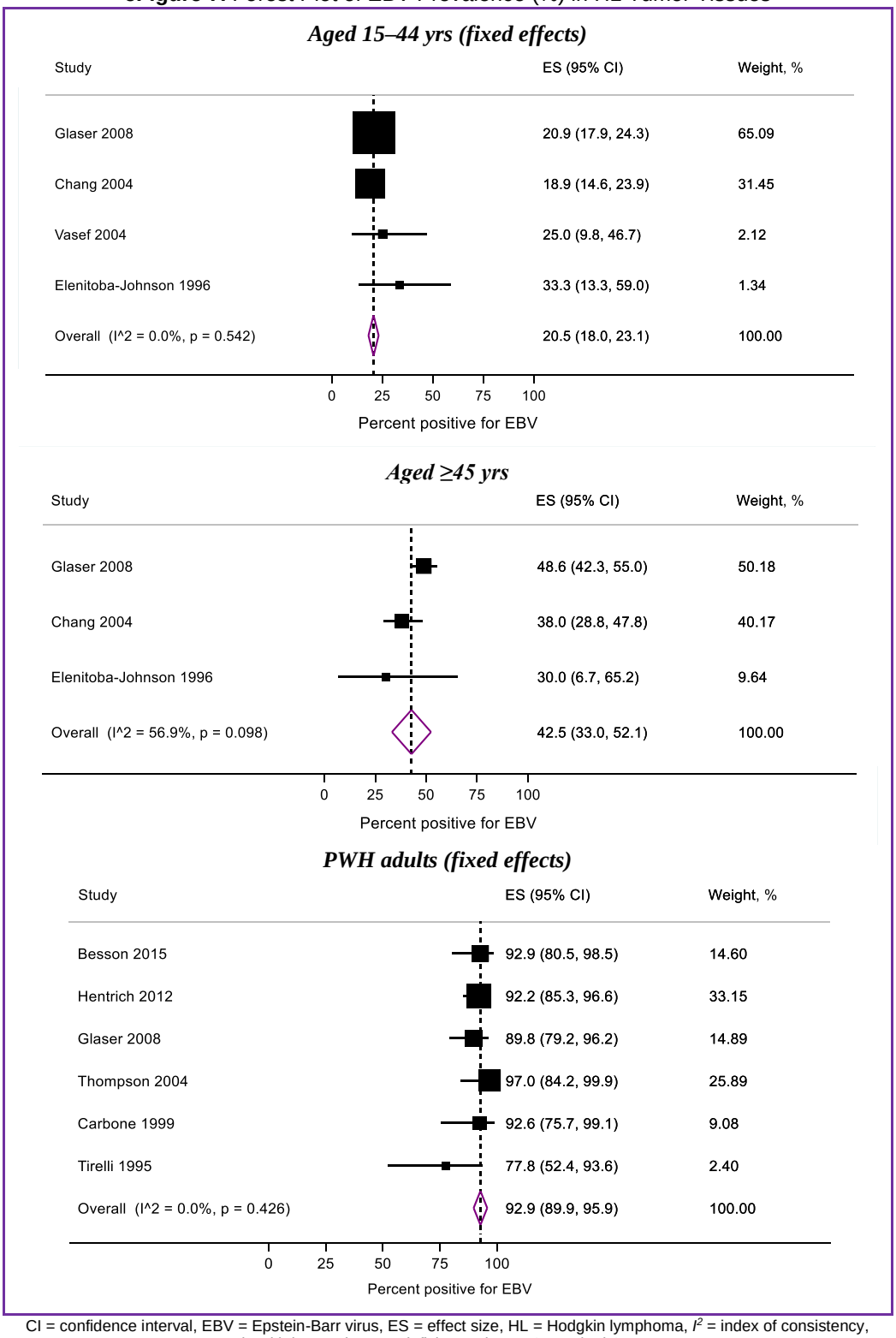
b. 26 cases from civilian sources, 15 cases from Veterans Administration medical centers, four cases from military hospitals.

eFigure 6. Forest Plot of EBV Prevalence (%) in HL Tumor Tissues Collected From Individuals Aged 0–19



CI = confidence interval, EBV = Epstein-Barr virus, ES = effect size, HL = Hodgkin lymphoma, I^2 = index of consistency, US = United States, yrs = years

eFigure 7. Forest Plot of EBV Prevalence (%) in HL Tumor Tissues



CI = confidence interval, EBV = Epstein-Barr virus, ES = effect size, HL = Hodgkin lymphoma, I^2 = index of consistency, PWH = people with human immunodeficiency virus, US = United States, yrs = years

eAppendix 17. Nasopharyngeal Carcinoma

A tumor of the epithelial tissues, NPC, is classified into three main types, keratinizing SCC accounting for 20% of all NPCs and non-keratinizing type accounting for the remaining 80% (further divided into differentiated and undifferentiated).[103] The pooled prevalence of the seven included studies reporting on EBV in NPC was 61.2% (CI: 45.1–77.2%) (**eTable 14, eFig. 8**). For individuals aged 0–19 years old, we identified two eligible studies (Table S14)[104,105] each with eight NPC cases – all EBV positive. Since this was insufficient to perform a meta-analysis, we calculated exact CIs in OpenEpi[106] using a numerator and denominator of eight patients for a prevalence of 100.0% (CI: 63.1–100.0%).

eTable 14. Characteristics of Studies Reporting on EBV Prevalence in NPC Cases

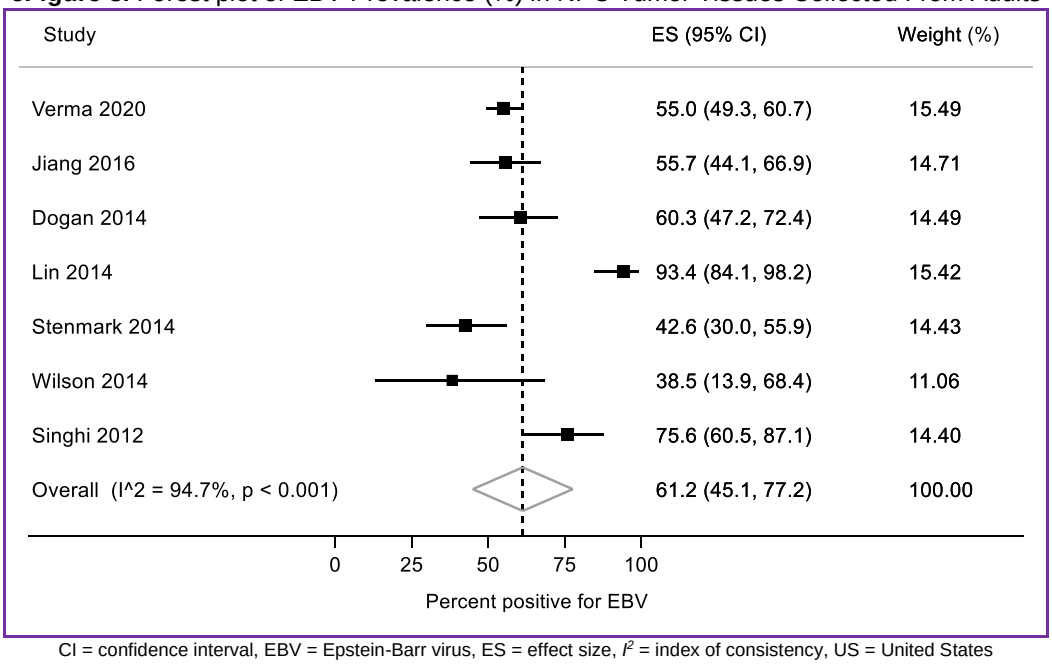
Study[a]	Region	Source of cases	Diagnosis dates	Male %	Mean/ median age	Non-keratinizing %	Tested N	Pos %
Studies conducted among adults (aged ≥20 yrs)								
Verma 2020[107]	New York	Memorial Sloan-Kettering Cancer Center	1998–2017	72.0	52.0	86.0	307	55.0
Jiang 2016[108]	Texas	M.D. Anderson Cancer Center	2000–2014	70.9	51.4	79.7	79	55.7
Dogan 2014[109]	Pennsyl-vania & Washington	University of Pittsburgh Medical Center, Virginia Mason Medical Center	1981–2012	69.8	53.0	85.7	63	60.3
Lin 2014[110]	California	Stanford University	1993–2010	75.4	45	NS	61	93.4
Stenmark 2014[111]	Michigan	University of Michigan	1985–2011	65.6	54.3	72.1	61	42.6
Wilson 2014[112]	Virginia	University of Virginia	2002–2013	NS	NS	76.9	13	38.5
Singhi 2012[113]	Maryland	Johns Hopkins Hospital	1985–2010	80.0	42.0	100.0	45	75.6
Studies conducted among children (aged 0–19 yrs)								
Polychronopoulou 2004[105]	Greece	Aghia Sophia Children's Hospital	1987–2001	NS	NS	100.0	8	100.0
Mertens 1997[104]	Germany	Institute of Pathology, University of Kiel	1992–NS	NS	NS	100.0	8	100.0

EBER ISH = Epstein-Barr encoding region *in situ* hybridization, EBV = Epstein-Barr virus, NPC = nasopharyngeal carcinoma, NS = not specified, yrs = years

a. Inclusion criteria: tissue specimens from 10 of more cases tested for EBV, EBER ISH detection, conducted in the US, cases aged 15 and older.

b. EBV positivity was reported for two periods of diagnoses: 1956–1977 and 1981–2012, cases from the first diagnoses period were excluded because they occurred 61 to 40 yrs before year the PAFs were applied to (2017).

eFigure 8. Forest plot of EBV Prevalence (%) in NPC Tumor Tissues Collected From Adults



CI = confidence interval, EBV = Epstein-Barr virus, ES = effect size, I^2 = index of consistency, US = United States

eAppendix 18. Extranodal Natural Killer T-Cell Lymphoma – Nasal Type

EBV is detected in virtually all cases of ENKTL – nasal type and considered part of the diagnostic criteria for that cancer.[114-117] A study conducted at the University of Texas M.D. Anderson Cancer Center, reported that all 73 ENKTL – nasal type cases identified and tested, were EBER ISH positive.[116] All 186 ENKTL – nasal type cases diagnosed in the US in 2017 were attributed to EBV.

eAppendix 19. Diffuse Large B-Cell Lymphoma

DLBCL, the most common subtype of NHL, has an average age of onset of mid-60s.[118] Studies meeting the inclusion criteria were published from 1996–2021, and all but one study reported on the HIV or the general immune status of cases thereby allowing us to calculate separate PAFs by HIV status (**eTable 15**). Pooling 13 studies conducted in HIV negative populations and one study (Naeini 2016,[80] where HIV status was not reported) yielded EBV prevalence of 4.9% (**eFig. 9**). The pooled prevalence of EBV in DLBCLs diagnosed among PWH was substantially higher at 45.7%. Utilizing estimated proportions of DLBCLs occurring in males with HIV (10.4% among those aged 0–29, 15.7% among those 30–59),[85] we partitioned the cancer incidence data and applied the pooled PAFs (4.9% and then 45.7% for PWH).

eTable 15. Characteristics of Studies Reporting on EBV Prevalence in DLBCL Cases

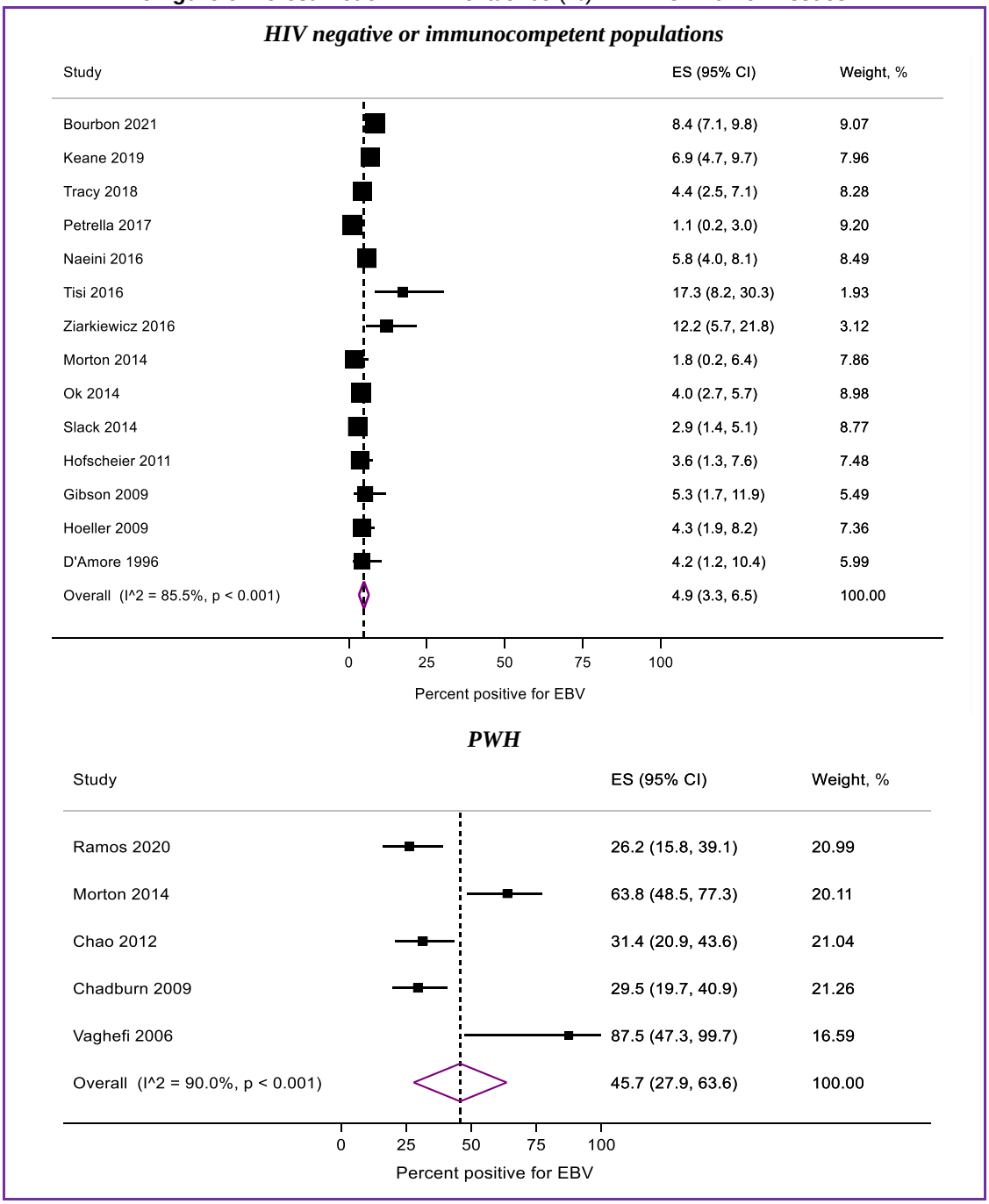
Study[a]	Region(s)	Source of cases	Diagnosis dates	Male %	Mean/ median age (yrs, range)	HIV status[b]	EBV positivity cut-off, %	Tested N	Pos %
Studies conducted among immunocompetent or HIV negative populations									
Bourbon 2021[119]	France	Hematopathology Department of Lyon-Sud University Hospital	2006–2019	NS	NS	IC	NS	1645	8.4
Keane 2019[120]	Australia & New Zealand	Princess Alexandra Hospital, Canberra Hospital, Royal North Shore Hospital, Australasian Leukaemia and Lymphoma Group Discovery Centre	2003–2014	40.0	NS (18–90)	IC	NS	433	6.9
Tracy 2018[121]	Iowa & Minnesota	University of Iowa or Mayo Clinic Rochester	2002–2012	59.4	63 (20–89)	HIV-	≥30	362	4.4
Petrella 2017[122]	Belgium, France, Switzerland	Lymphoma Study Association trial LNH03-6B	2003–2012	68.4	70 (60–80)	HIV-	NS	285	1.1
Naeini 2016[80]	California	Clarient Pathology Services/ Neogenomics	2008–2015	57.0	67 (11–96)	NS	≥10	567	5.8
Tisi 2016[123]	Italy	Catholic University of the Sacred Heart, Rome	2006–2013	NS	NS	HIV-	NS	52	17.3
Ziarkiewicz 2016[124]	Poland	Medical University of Warsaw	1994–2011	50.0	63.5 (23–86)	IC	>5	74	12.2
Morton 2014[125]	California	Los Angeles Residual Tissue Repository	1977–2003	48.3	NS	HIV-	"All or nearly all"	111	1.8
Ok 2014[126]	"Western countries"	International DLBCL Rituximab-CHOP Consortium Program Study	NS	57.5	63 (16–95)	HIV-	≥10	703	4.0
Slack 2014[127]	Canada	British Columbia Cancer Agency	1999–2006	63.3	64 (16–92)	IC	"Majority of tumor cells"	385	2.9
Hofscheier 2011[128]	Germany	Institute of Pathology, Tubingen	2000–2009	NS	72 (51–92)	IC	"Majority of tumor cells"	169	3.6
Gibson 2009[129]	Ohio	Department of Clinical Pathology, Cleveland Clinic	2002–2007	NS	NS (60–NS)	IC	NS	95	5.3
Hoeller 2009[130]	Austria, Italy & Switzerland	Pathology at the University Hospitals of Basel, Switzerland; Bologna, Italy; Innsbruck, Austria; & the Triemli Hospital, Zurich, Switzerland	NS	52.5	NS (50–93)	HIV-	≥10	188	4.3
D'Amore 1996[131]	Denmark	Danish Lymphoma Study Group (LYFO Registry)	1983–NS	NS	NS	IC	NS	95	4.2
Studies conducted among people with HIV									
Ramos 2020[132]	US	Many study sites (Randomized controlled trial)	2012–2017	NS	NS	HIV+	NS	61	26.2
Morton 2014[13]	California	Los Angeles Residual Tissue Repository	1977–2003	100.0	NS	HIV+	"All or nearly all"	47	63.8
Chao 2012[133]	California	Kaiser Permanente Southern and Northern California Health Plans	1996–2007	91.4	NS	HIV+	≥75	70	31.4
Chadburn 2009[134]	California, Florida, Illinois, Massachusetts, New Jersey, New York, Ohio	Clinical trials AMC010 (45 pts) & AMC034 (36 pts)	NS	86.5	41	HIV+	"Majority of neoplastic cells"	78	29.5
Vaghefi 2006[135]	France	NS	1984–2002	NS	NS	HIV+	NS	8	87.5

DLBCL = diffuse large B-cell lymphoma, EBV = Epstein-Barr virus, HIV = human immunodeficiency virus, IC = immunocompetent, NS = not specified, Pos = positive, pts = patients, US = United States, yrs = years

a. Inclusion criteria: tissue specimens from 10 of more cases tested for EBV, EBER ISH detection, conducted in Canada, Europe or the US, cases aged 15 and older.

b. In addition to excluding HIV+ cases, some studies (reported as IC) made additional exclusions based on immune status (e.g., excluding organ transplant recipients).

eFigure 9. Forest Plot of EBV Prevalence (%) in DLBCL Tumor Tissues



CI = confidence interval, DLBCL = diffuse large B-cell lymphoma, EBV = Epstein-Barr virus, ES = effect size, PWH = people with human immunodeficiency virus, I^2 = index of consistency

eAppendix 20. Gastric Carcinoma

The association between EBV and GC was first reported in a case of lymphoepithelial-like gastric carcinoma,[136] and afterwards, the association was observed in gastric adenocarcinoma.[137] Since then, several meta-analyses have addressed the prevalence of EBV in GC.[138-142] The most recent systematic review by Tavakoli and colleagues, including studies from 26 countries, estimated a pooled prevalence of EBV infection (via EBER ISH detection) among GC patients of 8.77% (CI: 7.73–9.92%).[143]

We identified seven studies conducted in the US (**eTable 16**), where the pooled prevalence of EBV was 13.6% for males and 1.9% for females (**eFig. 10**). After combining these calculated PAFs with those for *H. pylori*, the final PAFs were 12.8% (8.3–17.8%) for males and 1.8% (0.3–4.1%) for females.

eTable 16. Characteristics of Studies Reporting on EBV Prevalence in GC Cases

Study[a]	Region	Source of cases	Diagnosis dates	Mean/ median age in yrs	Males		Females	
					Tested N	Pos %	Tested N	Pos %
Kim 2019[144]	New York	Memorial Sloan Kettering Cancer Center	2006–2016	68.0	24	20.8	19	5.3
Ma 2016[145]	Pennsylvania	University of Pittsburgh Medical Center	2004–2015	73.0	25	24.0	19	5.3
Truong 2009[146]	Texas	University of Texas M. D. Anderson Cancer Center	1987–2006	EBV+: 60.0 EBV-: 67.0	147	7.5	88	1.1
Grogg 2003[147]	Minnesota	Mayo Clinic	1990–1998	68.4	69[b]	5.8	38	0.0
Vo 2002[148]	Texas, Louisiana, Minnesota	Touro Infirmary, St Luke's Baptist Hospital, Audie Murphy Memorial Veterans Administration Hospital	NS	EBV+: 66.5 EBV-: 68.3	78	14.1	30	0.0
Shibata 1993[149]	Hawaii	Japan-Hawaii Cancer Study	1965–NS	EBV+: 69.5 EBV-: 69.1	99	14.1	88	5.7
Shibata 1992[137]	Los Angeles	LAC+USC Medical Center, Hospital of the Good Samaritan[c]	NS	NS	99	21.2	39	2.6

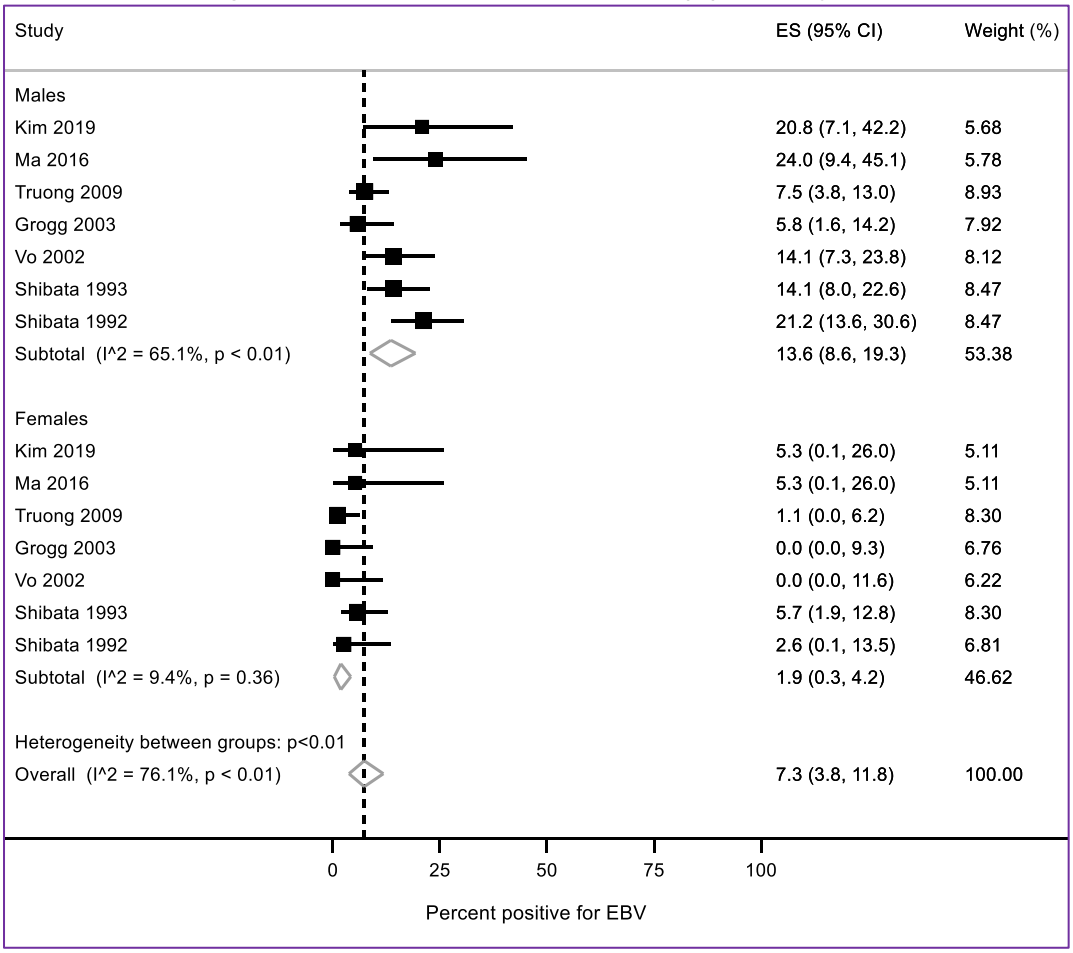
EBER ISH = Epstein-Barr encoding region *in situ* hybridization, EBV = Epstein-Barr virus, GC = gastric carcinoma, NS = not specified, Pos = positive, US = United States, yrs = years

a. Inclusion criteria: tissue specimens from 10 of more cases tested for EBV, EBER ISH detection, conducted in the US, cases aged 15 and older, EBV prevalence reported by sex.

b. Removed three cases of known EBV-positive gastric carcinoma who were added to the series from the consultation files.

c. Cases positive for EBV sequences via PCR were then studied by ISH.

eFigure 10. Forest Plot of EBV Prevalence (%) in GC, by Sex



CI = confidence interval, EBV = Epstein-Barr virus, ES = effect size, GC = gastric carcinoma, I^2 = index of consistency

eAppendix 21. Human Papillomavirus

The most recent monograph (volume 100B) classified HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59 as Group 1 carcinogens.[4] HPV68 is considered 'probably' carcinogenic (Group 2A), and several HPV types (26, 30, 34, 53, 66, 67, 69, 70, 73, 82, 85, 97) as 'possibly' carcinogenic (Group 2B).[4] Persistent HPV infection is the strongest risk factor for anal, penile, vaginal and vulvar cancers, with virtually all cervical cancers being caused by HPV infection.[150]

eAppendix 22. Anal SCC

After combining five studies (**eTable S17**) that met our inclusion criteria, the pooled prevalence of HR-HPV in anal SCCs was 90.2% for males and 96.3% for females (**eFig. 11**). We found that 100% of anal SCCs among PWH were attributable to HR-HPV. This finding is supported by studies conducted in Europe (not shown); Kreuter and colleagues (2010) found HR-HPV in all nine HIV+ males diagnosed with anal SCCs from 2003 to 2009 in Germany;[151] Arana (2015) et al. reported that among 14 HIV+ males and five HIV+ females diagnosed with anal SCC in France from 2007 to 2009, all were HR-HPV+.[152] It has been estimated that 32.5% of anal SCCs in males and 3.0% in females were diagnosed in PWH in the US from 2001 to 2015.[153] Only two of the five included studies reported HPV results by HIV status; among these two studies, 31.9% of cases were PWH. We assumed that proportion of cases that are PWH in studies where the HIV status of cases was not reported (Herfs 2017,[154] Alemany 2015,[155] Steinau 2013[156]) would be similar to that among the two studies (Zhu 2021[157] and Meyer 2013[158]) where HIV status was reported. For this reason, we combined all studies/cases to get PAFs for each males and females.

eTable 17. Characteristics of Studies Reporting on HR-HPV Prevalence in Invasive Anal SCCs, by Sex and HIV Status

7.5	Region(s)	Source of cases	Diagnosis dates	Histology	Detection methods HR-HPV types tested for[b]	Specimen	HIV status	Males		Females	
								Tested N	Pos %	Tested N	Pos %
Zhu 2021[157]	Massachusetts	Pathology archives	2000–2020	SCC	PCR, MGP, HPV GP5/GP6, L1 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	FFPE	HIV- HIV+	34 12	64.7 100.0	70 0	88.6 NA
Herfs 2017[154]	Little Rock (Arkansas), Boston (Massachusetts)	Pathology archives	2001–2015	SCC	PCR-RT 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	FFPE	Unknown (14/154 HIV+)	23	91.3	27	88.9
Alemany 2015[155]	Multiple	Pathology archives	1999–2009	SCC	SPF-10 PCR, DEIA, $LiPA_{25}$ 16, 18, 31, 33, 34, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70, 73	FFPE	Unknown	35	88.6	57	100.0
Meyer 2013[158]	New York	Surgical pathology files	1997–2009	SCC	SPF-10 PCR, DEIA, $LiPA_{25}$ 16, 18, 31, 33, 35, 39, 45, 51, 56, 58, 59, 66, 68, 73	NS	HIV- HIV+	13 10	100.0 100.0	17 2	100.0 100.0
Steinau 2013[156]	Florida, Hawaii, Iowa, Kentucky, Louisiana, Michigan, California	Cancer registries, tissue repositories	1995–2005	133 SCC, 2 other[c]	PCR, LA, INNO-LiPA 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	FFPE	Unknown	48	91.7	87	96.6

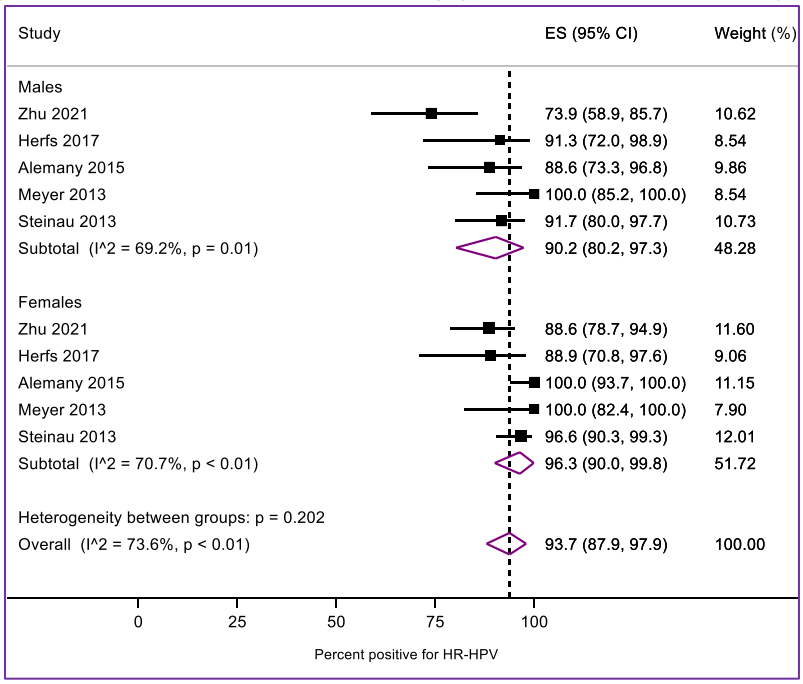
FFPE = formalin-fixed paraffin-embedded, HIV = human immunodeficiency virus, HPV = human papillomavirus, HR = high-risk, LA = Linear Array, MGP = modified general primer, NA = not applicable, NS = not specified,
PCR = polymerase chain reaction, Pos = positive, RT = "RealTime", SCC = squamous cell carcinoma, US = United States

a. Inclusion criteria: invasive anal SCC tissue specimens, PCR detection, 10 or more cases, US-based study population, published after 1995, data stratified by sex or available upon request.

b. HR-HPV types included: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 26, 30, 34, 53, 66, 67, 69, 70, 73, 82, 85, 97.

c. We excluded 11 adenocarcinomas by removing five cases from males and six from females; 2/11 adenocarcinomas were HPV+ and one positive case was removed from each sex.

eFigure 11. Forest Plot of the Prevalence (%) of HR-HPV in Anal SCC, by Sex[a]



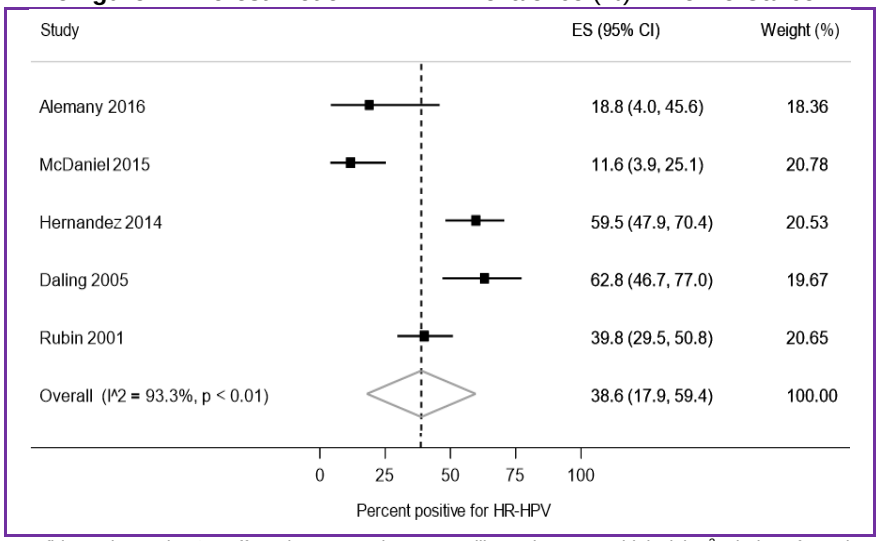
CI = confidence interval, HIV = human immunodeficiency virus, HR-HPV = high-risk human papillomavirus, I^2 = index of consistency, SCC = squamous cell carcinoma

[a] The figures include those positive for HIV (e.g., Zhu 2021 included 34 HIV negative and 12 HIV positive males).

eAppendix 23. Penile Cancer

Pooling five studies (**eTable S18** and **eFig. 12**) meeting the inclusion criteria provided a prevalence in cases of 38.6% (CI: 17.9–59.4%).

eFigure 12. Forest Plot of HR-HPV Prevalence (%) in Penile Cancer



CI = confidence interval, ES = effect size, HPV = human papillomavirus, HR = high-risk, I^2 = index of consistency

eTable 18. Characteristics of Studies Reporting on HR-HPV Prevalence in Penile Cancers

Study[a]	Region(s)	Source of cases	Diagnosis dates	Histology	Detection methods HR-HPV types genotyped[b]	Specimen	HIV status	Tested N	Pos %
Alemany 2016[159]	Hawaii[c], Iowa	Pathology archives	1994–2004	NS	SPF-10, DEIA, LiPA$_{25}$, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59	FFPE	Unknown	16	18.8
McDaniel 2015[160]	Michigan	Pathology archives	2005–2013	SCC	GP5+/GP6+, MY09/MY11, CP, 16, 33	FFPE	Unknown	43	11.6
Hernandez 2014[161]	California, Florida, Hawaii[c], Iowa, Kentucky, Louisiana, Michigan	Population-based cancer registries, residual tissue repositories	1998–2005	NS (majority SCC)	PCR, LA, INNO-LiPA$_{25}$, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	FFPE	Unknown	79	59.5
Daling 2005[162]	Washington	Population-based cancer registry	1979–1998	NS	PCR-MY09/MY11, L1, 16, 18, 31, 33, 35, 45	PE	Unknown	43	62.8
Rubin 2001[163]	Connecticut, Michigan, New York, Texas	Pathology archives	NS	SCC	PCR SPF-10, LiPA$_{25}$, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 70	FFPE	Unknown	88	39.8

CP = consensus primers, FFPE = formalin-fixed paraffin-embedded, HIV = human immunodeficiency virus, HPV = human papillomavirus, HR = high-risk, LA = linear array, NS = not specified, PCR = polymerase chain reaction, PE = paraffin-embedded, Pos = positive, SCC = squamous cell carcinoma

a. Inclusion criteria: invasive penile cancers tissue specimens, PCR detection, 10 or more cases, North American study population, published after 1995.

b. HR-HPV types included: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 26, 30, 34, 53, 66, 67, 69, 70, 73, 82, 85, 97.

a. Three cases overlapped.

eAppendix 24. Vaginal Cancer

Two studies met our inclusion criteria (**eTable S19**). The pooled prevalence of HR-HPV types in invasive vaginal cancers was 72.2% (CI: 62.8–81.7%), where the Sinno 2014 study received a weight of 74.7% and the Daling 2002 study a weight of 25.3% (forest plot not shown).

eTable 19. Characteristics of Studies Reporting on HR-HPV[a] Prevalence in Vaginal Cancers

Study[a]	Region(s)	Source of cases	Diagnosis dates	Histology	HIV status	Detection methods HR-HPV types tested[b]	Spec-imen	Tested N	Pos % (95% CI)
Sinno 2014[164]	California, Florida, Hawaii, Kentucky, Louisiana, Iowa, Michigan	Population-based cancer registries, residual tissue repositories	1994–2005	NS (86% SCC)	Unknown	LA, INNO-LiPA 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 68, 70, 73, 82	FFPE	60	75.0 (62.1–85.3)
Daling 2002[165]	Washington	Population-based cancer registry	1981–1998	SCC	Unknown	PCR-L1, MY09/MY11 16, 18/45, 31	PE	25	64.0 (42.5–82.0)

FFPE = formalin-fixed paraffin-embedded, HIV = human immunodeficiency virus, HPV = human papillomavirus, HR = high-risk, LA = linear array, NS = not specified, PCR = polymerase chain reaction, PE= paraffin-embedded, Pos = positive, SCC = squamous cell carcinoma, US = United States

a. Inclusion criteria: invasive vaginal cancer tissue specimens, PCR detection, 10 or more cases, North American study population, published after 1995.

b. HR-HPV types included: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 26, 30, 34, 53, 66, 67, 69, 70, 73, 82, 85, 97.

eAppendix 25. Vulvar Cancer

Since HPV is more prevalent in vulvar cancers diagnosed among younger women, and vulvar cancer incidence is higher among older women,[166] HR-HPV prevalence was analyzed by age group (**eTable S20**). The pooled prevalence of HR-HPV in cases was 74.4% for women aged <50 years and 45.7% for women aged ≥50 years old (**eFig. 13**).

eTable 20. Characteristics of Studies Reporting on the Prevalence of HR- HPV in Vulvar Cancer Cases, by Age Group

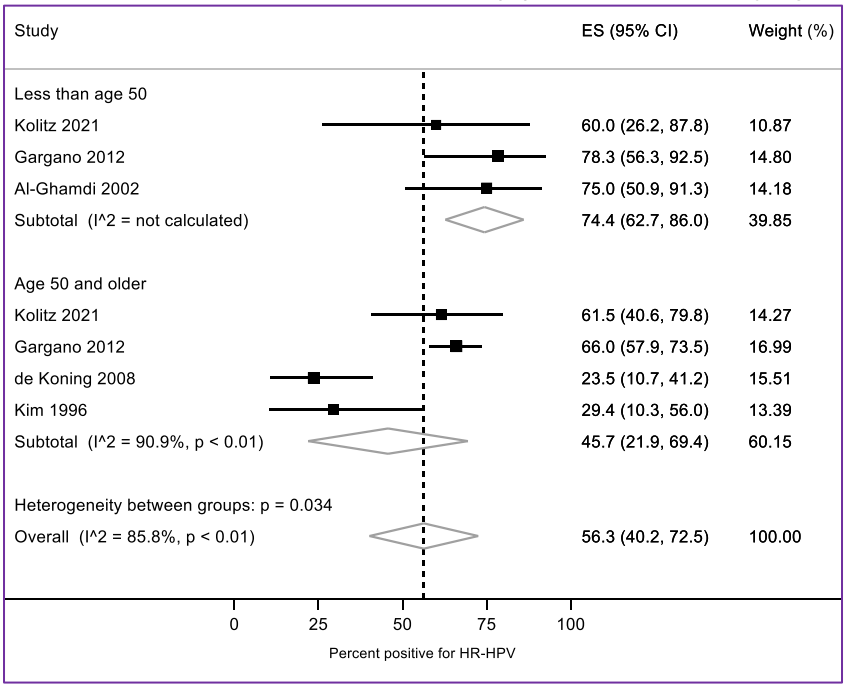
Study[a]	Region(s)	Source of cases	Diagnosis dates	Histology	HIV	Detection methods HR-HPV[b] types tested	Specimen	Age <50 yrs		Age ≥50 yrs	
								Tested N	Pos %	Tested N	Pos %
Kolitz 2021[167]	Texas	Pathology archives	2010–2020	SCC	None	Consensus PCR-L1, NS	FFPE	10	60.0	26	61.5
Gargano 2012[168]	California, Florida, Hawaii, Iowa Kentucky, Louisiana, Michigan	Population-based cancer registries, residual tissue repositories	1995–2005	NS	Unknown	LA, INNO-LiPA 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68	FFPE	23	78.3	153	66.0
de Koning 2008[169]	New York	Pathology department	1990–2005	SCC	Unknown	SPF-10, $LiPA_{25}$ 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 70	PE	--		34	23.5
Al-Ghamdi 2002[170]	British Columbia, Yukon, Canada	Population-based cancer registry	1970–1998	SCC	One HIV+	PCR-MY09/MY11, PCR-GP5/GP6, TS 16, 18	FFPE	20	75.0	--	
Kim 1996[171]	Maryland, Florida	Pathology archives	1989–1994	SCC	Unknown	PCR-MY09/MY11, PCR-L1, TS, Sequencing 16, 18	Fresh	--		17	29.4

FFPE = formalin-fixed paraffin-embedded, HIV = human immunodeficiency virus, HPV = human papillomavirus, HR = high-risk, LA = linear array, NS = not specified, PE = paraffin-embedded, PCR = polymerase chain reaction, Pos = positive, SCC = squamous cell carcinoma, TS = type-specific, US = United States, yrs = years

a. Inclusion criteria: invasive vulvar cancers tissue specimens, PCR detection, 10 or more cases, North American study population, published after 1995, data stratified by age or available upon request.

b. HR-HPV types included: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 26, 30, 34, 53, 66, 67, 69, 70, 73, 82, 85, 97.

eFigure 13. Forest Plot for HR-HPV Prevalence (%) in Vulvar Cancer, by Age Group



CI = confidence interval, HR-HPV = high-risk human papillomaviruses, I^2 = index of consistency

eAppendix 26. Head and Neck Cancers

When attributing HNCs to HPV detection of the oncoproteins E6 and E7 is recognized as the gold standard,[172,173] because they are produced by HR-HPVs and must be present for viral replication to occur. We only considered the prevalence of HPV16 as the association between HNCs and HPV is most established for this type. Twenty-one studies met the inclusion criteria (**eTable S21**). The PAFs were 60.3% for the oropharynx (**eFig. 14**), 7.9% for the oral cavity (**eFig. 15**) and 12.7% for the larynx (**eFig. 16**).

eTable 21. Characteristics of Studies Reporting on HPV16 Prevalence Detected via E6 and/or E7 in HNCs

Study[a]	Region[b]	Diagnosis dates	Detection method(s)	Specimen	Anatomical site					
					Oropharynx		Oral cavity		Larynx	
					Tested N	Pos[c] %	Tested N	Pos[c] %	Tested N	Pos[c] %
Lewis 2021[174]	Tennessee	2000–2018	qRT-PCR E6/E7	FFPE	259	81.9	--		--	
Mazul 2016[175]	North Carolina	2002–2006	TS-PCR E7	FFPE	238	63.4	--		--	
Hooper 2015[176]	Oregon	--	PCR-E6, E7	FF	44	68.2	24	8.3	19	0.0
Zandberg 2015[177]	Maryland	1992–2007	PCR-E6	FFPE	194	34.5	--		--	
Isayeva 2014[178]	Alabama	2004–2012	RT-PCR E6/E7	PE	102	48.0	--		--	
Lingen 2013[179] [d]	California, Illinois, Ohio, Ontario (CA)	2005–2011	qRT-PCR E6 or 7	FFPE	--		409	3.7	--	
Walline 2013[180]	Michigan	2001-2011	PCR-E6	FFPE	208	78.8	104	4.8	--	
Jordan 2012[181]	California, Illinois, Ohio, Ontario (CA)	2000–2009	qPCR E6	FFPE	235	62.1	--		--	
Stephen 2012[182]	Michigan	1999–2005	qRT-PCR E6	FFPE	--		--		77	27.3
Chaturvedi 2011[183]	Hawaii, Iowa, Los Angeles, California	1984–2004	qRT-PCR E6	FFPE	216	35.2	--		--	
Schlecht 2011[184]	New York	NS	TS-PCR E6/E7	FF, PE	23	52.2	29	27.6	27	18.5
Agoston 2010[185]	Massachu-setts	NS	PCR-E7	FFPE	126	58.7	--		--	
Kingma 2010[186]	Oklahoma & Montana	2005–2007	RT-PCR-E6	FFPE	61	49.2				
Jo 2009[187]	California	2000–2003	PCR-E7	FF, FFPE	14	92.9	--		--	
Settle 2009[188]	Maryland	1995–2006	PCR-E6	PE	--		28	10.7	55	7.3
Tezal 2009[189]	New York	1999–2005	TS-PCR E6	PE	30	70.0	--		--	
Cohen 2008[190]	Pennsylvania	1996–2001	TS-PCR E7	PE	35	68.6	--		--	
Liang 2008[191]	Minnesota	2004–2006	TS-PCR E6	FF	--		51	2.0	--	
Worden 2008[192]	Michigan	NS	RT-PCR E6	NS	42	64.3	--		--	
Zhao 2005[193]	Maryland	1984–2002	RT-PCR E6/E7	Frozen	26	57.7	38	15.8	16	18.8
Strome 2002[194]	Minnesota	1987–1995	TS-PCR E6	PE	52	40.4	--		--	

CA = Canada, FF = fresh-frozen, FFPE = formalin-fixed paraffin embedded, HNCs = head and neck cancers, HPV = human papillomavirus, NS = not specified, PE = paraffin embedded, PCR = polymerase chain reaction, Pos = positive, qRT-PCR = real-time quantitative reverse transcription, RT = real-time, TS = type-specific, US = United states

-- Indicates the cancer was not included in the original study or that it overlapped with another included study.

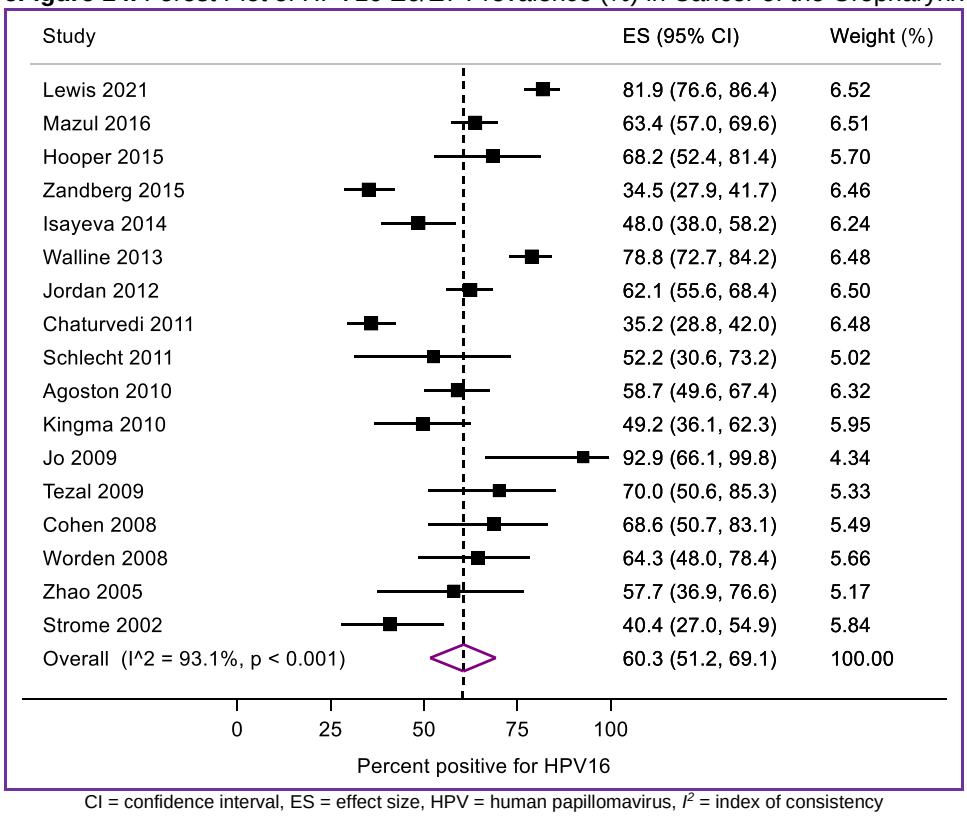
a. Inclusion criteria: site specific results (e.g., base versus oral tongue), detection in cancer tissue, invasive and untreated cancer, detection with E6 and/or E7 for HPV16, did not test specimens for E6/7 based on previous HPV results, North American study population, and published in 2000 or later.

b. Only cases from Chaturvedi et al.'s 2011 study originated from population-based cancer registries, the remaining studies cases came from clinics, hospitals, and pathology departments.

c. Tested positive for E6 and/or E7.

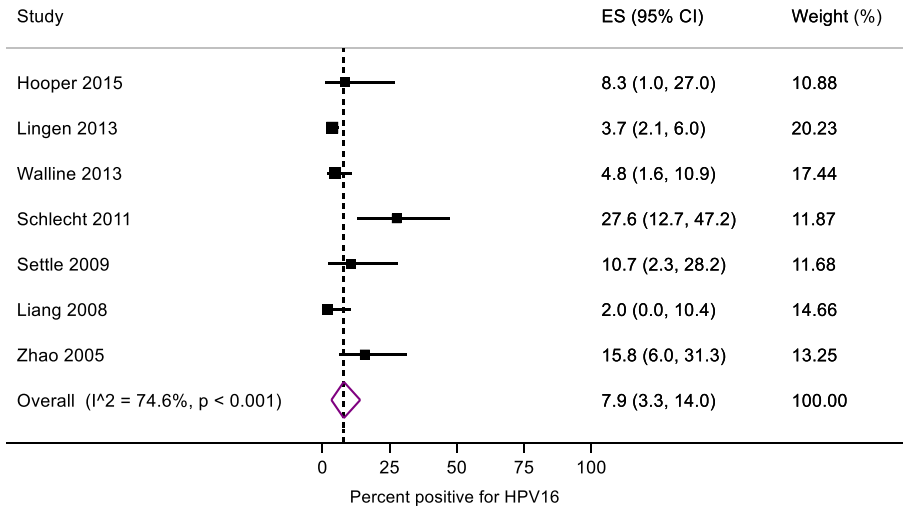
d. Lingen 2013 included four *in situ* cases.

eFigure 14. Forest Plot of HPV16 E6/E7 Prevalence (%) in Cancer of the Oropharynx



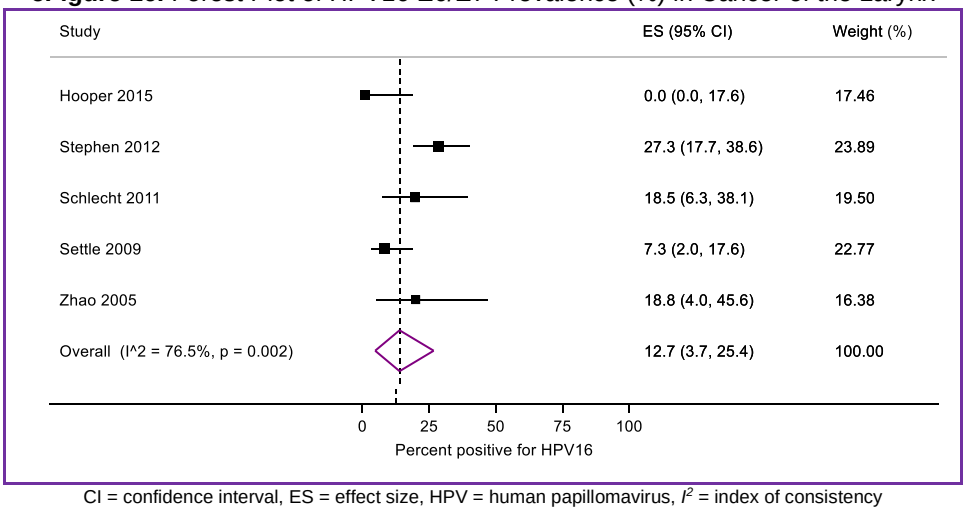
CI = confidence interval, ES = effect size, HPV = human papillomavirus, I^2 = index of consistency

eFigure 15. Forest Plot of HPV16 E6/E7 Prevalence (%) in Cancer of the Oral Cavity



CI = confidence interval, ES = effect size, HPV = human papillomavirus, I^2 = index of consistency

eFigure 16. Forest Plot of HPV16 E6/E7 Prevalence (%) in Cancer of the Larynx



CI = confidence interval, ES = effect size, HPV = human papillomavirus, I^2 = index of consistency

eAppendix 27. Merkel Cell Polyomavirus

MCPyV a small double-stranded DNA virus, is named after skin cells called Merkel cells because these skin cells are believed to be the primary target for this virus. The discovery of the MCPyV genome in Merkel cell carcinoma biopsies in 2008,[195] prompted IARC to evaluate MCPyV in February 2012.[196] MCPyV is prevalent but remains dormant for the vast majority of people infected.

eAppendix 28. Merkel Cell Carcinoma of the Skin

This cancer is a rare and aggressive neuroendocrine tumor of the skin. Merkel cell carcinoma is marked by the uncontrolled growth of Merkel cells (cells responsible for sensation). Most often, Merkel cell carcinoma develops in sun-exposed areas of the body. Risk factors for Merkel cell carcinoma include older age, fair skin, history of intensive sun exposure, and a weaker immune system. The eleven studies meeting the inclusion criteria reported MCPyV prevalence in Merkel cell carcinoma ranging from 25.0–100.0% (**eTable S22**). The pooled prevalence of MCPyV in Merkel cell carcinoma was 70.3% (**eFig. 17**).

eTable 22. Characteristics of Studies Reporting on MCPyV Prevalence in Merkel Cell Carcinoma of the Skin

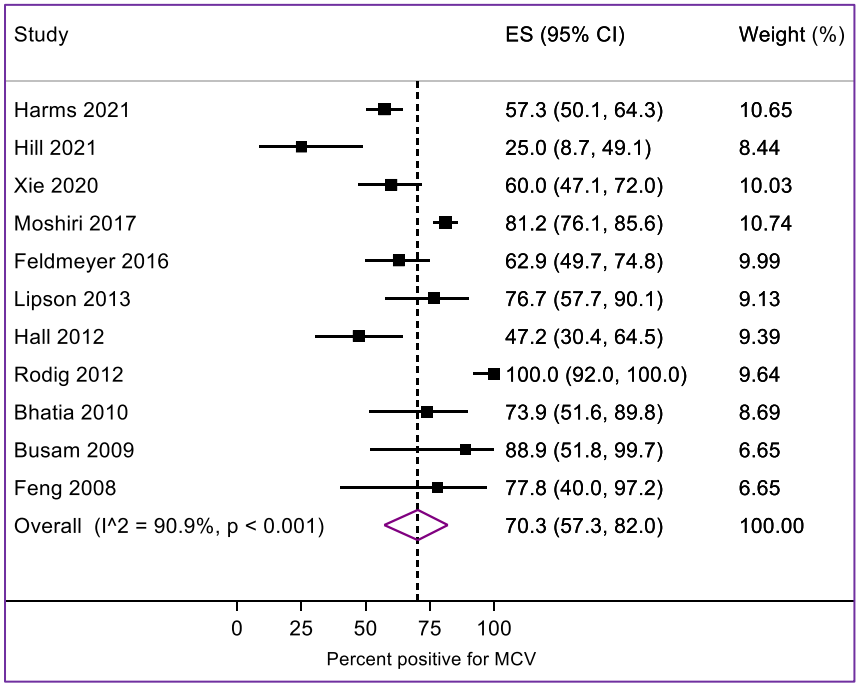
Study[a]	Source of cases	Diagnosis dates	Male %	Median age (in yrs)	Specimen	Detection method(s)	Tested N	Pos %
Harms 2021[197]	Michigan Medicine Cutaneous Oncology Database; Cutaneous Oncology Program database, and Pathology laboratory information systems	1999–2019	65.8	74	FFPE	IHC (CM2B4), ISH (T, ST, LT), RT qPCR (LT2)	199	57.3
Hill 2021[198]	University of Pennsylvania and Marshfield clinic	1996–2012	56.3	73	FFPE	Nested qPCR; OneStep RT-PCR system	20	25.0
Xie 2020[199]	Mayo Clinic	NS	67.7	73	FFPE	IHC (MCPyV large T-antigen)	65	60.0
Moshiri 2017[200]	University of Washington	1980–2015	62.8	71	FFPE	IHC (CM2B4 and Ab3), RT qPCR (Large T, Small T, VP 2)	282[b]	81.2
Feldmeyer 2016[201]	University of Texas MD Anderson Cancer Center	2002–2015	72.6	71	FFPE	IHC (MCPyV T-antigen)	62	62.9
Lipson 2013[202]	Johns Hopkins Hospital surgical pathology archives	2000–2011	65.3	65	FFPE	RT qPCR (VP1, LT3)	30	76.7
Hall 2012[203]	University of California, San Francisco Dermatopathology Service	1996–2010	41.7	77	NS	IHC (CM2B4)	36	47.2
Rodig 2012[204]	Referral specialty clinic	NS	63.6	74	FFPE	RT qPCR (LT2, Set 6, 7, 9, LT3)	44	100.0
Bhatia 2010[205]	Ohio State University Medical Center	1994–2007	73.9	77	FFPE	qPCR (MCPvV, EU375804)	23	73.9
Busam 2009[206]	Memorial Sloan-Kettering Cancer Center	NS	66.7	80	Frozen	RT qPCR (T primer sets)	9	88.9
Feng 2008[195]	Cooperative Human Tissue Network (US)	NS	88.9	58	Frozen	PCR (VP1), nested PCR (VP1-2), PCR-Southern hybridization	9	77.8

FFPE = formalin-fixed paraffin embedded, HPV = human papillomavirus, IHC = immunohistochemistry, ISH = *in situ* hybridization, MCPyV = Merkel cell polyomavirus, NS = not specified, PCR = polymerase chain reaction, Pos = positive, qRT-PCR = real-time quantitative reverse transcription, RT = real-time, US = United states, yrs = years

a. Inclusion criteria: Merkel cell carcinoma tissues (adjacent tissues excluded) arising from ≥8 cancer cases, results presented per person not tissue (if multiple specimens collected), detection via PCR, IHC and/or ISH, US study population.

b. Included 40 recurrent cases.

eFigure 17. Forest Plot of MCPyV Prevalence (%) in Merkel Cell Carcinoma of the Skin



CI = confidence interval, ES = effect size, I^2 = index of consistency, MCPyV = Merkel cell polyomavirus

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