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Systematic review and evidence synthesis of non-cervical human papillomavirus-related disease health systems costs and quality of life estimates

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Appendix 2

Article title.

Systematic review (with meta-analysis) of non-cervical HPV-related disease management costs and quality of life estimates applicable to the English setting.

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Relevant data extracted from the papers

1. Population, HPV-related disease studied, disease stage, country, setting (e.g. hospital, general practices, sexual health clinics), study perspective (e.g. health care payer, patient);
2. For costs, methods for cost measurement (e.g. micro-costing, tariff-based costing), currency and value year, types of costs included and perspective where reported, any discounting applied and discount rates;
3. For utility, instruments used for value elicitation (e.g. EQ-5D scored using country-specific population norms), any information about duration of disutility, including survival/mortality for the HPV-related disease, if reported, perspective (patient or carers) and discounting and discount rates used. Disease-specific quality of life assessment tools used alongside direct/indirect utility elicitation methods were noted but their results were not recorded.

Table 1 Extracts of AGW management costs reported in selected papers, some cost values had been adjusted to 2016/17 US Dollars (US$) for ease of comparison between studies

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
1	Coles, 2016 [1]; United Kingdom; Number of visits and treatment required estimated by GUM clinic experts; resource needs then combined with relevant national tariffs; GBP; 2012; Sanofi Pasteur MSD	Average cost per patient in:							
		England	£265				$343		
		Scotland	£254						
		Wales	£264						
		Northern Ireland	£262						
2	Lanitis, 2012 [2]; United Kingdom; Secondary GUM clinic data from HPA and primary care data from Health Improvement Network; Costs - National Health Service Payment by Results tariff; GBP; 2010; Sanofi Pasteur MSD	Cost per GUM episode	£288						
		cost per treated Genital Wart Episode	£276				$371	$367	$374
			Per episode (£)	Per female episode (£)	Per male episode (£)				
		First attack	291	291	291				
		Recurrent	290	290	290				
		Persistent	271	271	271				
		Primary care	50	53	48				
		Total GW patients	276	273	278				

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
3	Desai, 2011 [3]; England; Cost of care in both GP and GUM clinics considered; unit cost obtained from national tariffs; GBP; 2008; Department of Health		Estimated cost per episode of care for all settings	95% CI (min.)	95% CI (max.)				
		Overall	£113	£104	£121		$157	$145	$169
		Male	£97	£87	£107		$135	$121	$149
		Female	£129	£117	£140		$180	$163	$195
4	Woodhall, 2011 [4]; England and Northern Ireland; Case note review used to identify cost of an episode of care; GBP; 2010; Department of Health	Mean cost per episode of care (£), excluding STI screen		95% CI (min.)	95% CI (max.)				
		All (n = 895)	£94	£84	£104		$126	$113	$140
		Male (n = 494)	£80	£67	£92		$108	$90	$124
		Female (n = 400)	£109	£94	£124		$147	$126	$167
5	Woodhall, 2009 [5]; England; Retrospective case note review of patients diagnosed with AGW attending a York GUM clinic informed treatment cost and duration of an episode of care; US dollars (GBP); 2007; Department of Health	Mean cost of an episode of care		95% CI (min.)	95% CI (max.)				
		Overall (n = 189)	$286 (£139)	$246	$327		$207	$178	$236
		Male (n = 93)	$280	$237	$324		$202	$171	$234
		Female (n = 96)	$292	$254	$331		$211	$184	$239

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
6	Brown, 2006 [6]; United Kingdom; AGW treatment patterns including drugs used, procedures and number of visits were recorded using a standardised questionnaire and completed by six GUM clinic clinicians; Treatment patterns obtained from incidence AGW cases and second and third line treatments for recurrent/persistent cases; Mean event rates used to construct treatment patterns; GUM clinic visit costs estimated based on retrospective chart review of time spent per visit (initial and follow-up); Units of each resource required then combined with literature and UK standard reference price e.g. PSSRU and BNF; GBP; 2003; Sanofi Pasteur MSD	From Table 4							
		incident AGW cost	£10,125,343						
		recurrent AGW cost	£8,282,244						
		persistent AGW cost	£3,994,744						
		incident AGW cases	£76,457						
		recurrent AGW cases	£38,902						
		persistent AGW cases	£16,755						
		incident AGW cost per case	£132						
		recurrent AGW cost per case	£213						
		persistent AGW cost per case	£238						
		average cost per case	£170	Note: Direct sum total spend divided by total cases	-	-	$281		

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
7	Langley, 2004 [7]; England and Wales; Case notes review of 100 males and 100 females seen in each six GUM clinics; four components that make up treatment costs include labour costs, meterial costs, extra costs and indirect costs; Labour costs calculated based on direct observation and discussions with study sites; Material costs included total expenses for materials used to administer treatment; Extra costs included specific tests performed during visits that are on top of specific AGW treatment and included sexual health screens; Indirect costs included remaining departmental expenses; GBP; 2004; Funding source not specified, first author was affiliated with 3M Pharmaceuticals, USA	Aggregate estimate of labour costs, material costs, extra costs, indirect costs - study site average							
		Cost per successful outcome for external GW treatment							
		Male	£222				$355		
		Female	£211				$338		

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
8	Pirotta, 2009 [8]; Australia; Retrospective analysis of national cross-sectional database and standard GP tariff used to estimate cost per GP visit, pathology costs not considered as data not available, hospitalisation costs based on hospital tariff; Database extraction covers period 2000-2007; Australian dollars; 2008-09; Study used data from the BEACH programme funded by the National Prescribing Service Ltd; the Australian government Department of Health and Ageing; AstraZeneca Pty Ltd (Australia); Janssen-Cilag Pty Ltd; Merck, Sharp and Dohme (Australia) Pty Ltd; Roche Products Pty Ltd; Sanofi-Aventis Australia Pty Ltd; the Australian government Department of Veterans' Affairs; and the Department of Employment and Workplace Relations		Cost per case						
		Male	A$251				$170		
		Female	A$386				$261		

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
9	Annemans, 2008 [9]; Belgium; Retrospective analysis of hospital database for year 2004 combined with outpatient data collected using a panel of expert; Euros; 2006; Sanofi Pasteur MSD		Mean total cost, healthcare payer perspective						
		Male	€314				$315		
		Female	€319				$320		
10	Marra, 2008 [10]; Canada; Retrospective data, including physician specialty, hospitalisation, and prescribing data, obtained from all AGWs seen in British Columbia in 1998-2006; Canadian dollars; 2006; Funding source not specified, the authors acknowledged contributions by Dr Marc Brisson, who was employed by Merck Frosst Canada at the time of his contributions		Mean cost	(SD)	Median cost	(IQR)			
		Overall (n=43,586)	190.32	(1,004.21)	71.15	(117.50)	$124	(657)	
		Male	175.67	(1,136.25)	70.32	(104.14)	$115	(743)	
		Female	206.94	(828.90)	72.07	(144.33)	$135	(542)	

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
11	Salo, 2013 [11]; Finland; National registry data provided diagnostic and treatment procedures, hospitalisation, outpatient visit and prescription data, which were combined with national unit costs. Index events were identified during 1999-2008.; Euros; 2010; Funding source not specified, authors reported conflict of interest either through grants or employment from GlaxoSmithKline, Merck&Co. Inc, GSK Biologicals, and/or Sanofi Pasteur MSD		Average undiscounted cost per HPV related AGW	SD	Not clear what overall average cost per case would be				
		Primary health care	€165	75			$190	86	
		Secondary health care	€386	508			$445	585	
		n	4000	women, 70% treated in primary health care					
12	Herse, 2011 [12]; Finland; Registry data over years 2001-2005 was used to estimate average annual AGW cases, their associated procedures and medications. Costs were informed by published costs (Hujanen et al., 2008); 2 cost scenarios presented, min. (where		Total health care cost	Calculated mean cost					
		min. scenario	€2,072,994	€669			$2,079,657	$671	
		max. scenario	€5,602,074	€1,808			$5,620,079	$1,814	

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
	outpatient visit costs were estimated from number of visits recorded and average visit cost) and max. (where all costs in min. scenario included and outpatient procedures done by specialists and primary care costs); estimated 3098 patients in year 2005; Euros; 2006; Sanofi Pasteur MSD								

13	Hillemanns, 2008 [13]; Germany; Specialist physicians retrospectively extracted resource use data over preceding 12 months for AGW patients seen for care between 9 February and 6 April 2005; Resource use data was available for 617 patients (233 males, 384 females), mean age 32.0±10.0 years; Euros; 2004; Sanofi Pasteur MSD		Mean annual direct cost per patient	Range (min.)	Range (max.)				
		New cases							
		Male (n=160)	€315	€235	€407		$358	$267	$461
		Female (n=268)	€414	€322	€506		$469	$365	$574
		Recurrent cases							
		Male (n=37)	€434	€230	€695		$492	$261	$788
		Female (n=55)	€732	€476	€1,047		$829	$539	$1,186
		Resistant cases							
		Male (n=17)	€700	€228	€1,431		$793	$259	$1,622
		Female (n=19)	€1,563	€842	€2,428		$1,771	$954	$2,752

14	Gianino, 2013 [14]; Italy;		Mean cost	±					

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
	Retrospective observational study using outpatient medical records to identify patients who visited 1 STI clinic in Italy; Selected AGW episodes that cleared in 18 months from initial visit; Analyses included 450 episodes (297 males, 153 females); Euros; 2011; Sanofi Pasteur MSD SpA		(diagnosis and treatment)						
		Overall (n=450)	€158	257.77			$175	284	
		Male (n=297)	€157	253.17					
		Female (n=153)	€161	267.3					
15	Baio, 2012 [15]; Italy; Used available secondary data in Italy, identified via literature review, to estimate lifetime cost per case of disease and merged with relative HPV 6, 11, 16, and 18 prevalence data to estimate total HPV-attributable burden; secondary data source for AGW based on Merito et al. (2008); Euros; 2011; No funding to report	Lifetime cost per case							
		Male	€470				$518		
		Female	€663				$730		

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
16	Merito, 2008 [16]; Italy; Retrospective observational study conducted among STI clinic clinicians, resource use data collected via medical chart review, included patients aged 14-64 years with new/recurrent/resistant AGWs in year 2005; Euros; 2005; Sanofi Pasteur MSD SNC (Lyon, France)		Mean annual direct cost per patient	Range (min.)	Range (max.)				
		Male (n=189)	€242	€176	€326		$257	$187	$346
		Female (n=152)	€332	€254	€425		$352	$269	$451
17	Dee, 2009 [17]; Ireland; Prospective resource use data collection over a 3-week period (September to November 2007) in five GUM clinics representing defined urban/rural area mix; total 217 patients had AGWs; Euros; Not reported, assume 2007; Funding source not specified		Average annual cost per AGW patient	Range (min.)	Range (max.)				
		Overall	€335	€326	€344		$356	$346	$366
		Male	€300						
		Female	€366						
18	Van Der Meijden, 2002 [18]; Netherlands;		Average total cost	Range (min.)	Range (max.)				

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
	Retrospective analysis of patient records identified over period 1 January 1998 to 31 December 1999, across largest health care providers in 3 largest cities in the Netherlands (total 3 dermatology clinics); Euros; Unknown, assume 2000; Funding source not specified, last author was affiliated with 3M Pharmaceuticals, USA	Overall (both completed and incomplete episode of care)							
		Male	€190	€155	€228				
		Female	€222	€165	€288				
		Completed episode of care							
		Male	€221	€196	€270				
		Female	€292	€187	€378				
		Incomplete episode of care							
		Male	€147	€64	€199				
		Female	€157	€98	€212				
		Cost per successful outcome							
		Male	€485	€219	€624		$576	$261	$742
		Female	€396	€225	€566		$470	$267	$673
19	Castellsague, 2009 [19]; Spain; Multicentre retrospective observational study covering public providers in six autonomous regions in Spain; Data on resources used to treat AGWs were		Adjusted mean cost per patient	(95% CI lower)	(95% CI upper)				
		NHS perspective							
		Overall	€833				$883		
		Male	€673	€666	€682				
		Female	€1,040	€994	€1,073				
		Societal perspective							

No.	Author, year; Country; Value elicitation method; Currency; Value year; Funding	Reported value					US$ 2016/17	Range min.	Range max.
	retrospectively collected from medical records over 6 months (99 new cases) to 1 year (90 recurrent/resistant AGWs); total 281 patients (128 males, 153 females); mean age 31+/-9 years; Euros; 2005; Sanofi Pasteur MSD	Overall	€1,056						
		Male	€927	€917	€941				
		Female	€1,223	€1,170	€1,265				
20	Östensson, 2015 [20]; Sweden; Annual AGW management and treatment costs estimated from a clinical expert panel, which estimated visits, procedures, and medications used; Euros; 2009; Swedish Cancer Foundation, KI Cancer Strategic Grants, Swedish Research Council, and Stockholm County Council	Total annual cost, Sweden	€9,764,094						
		Total number of AGW cases in 2009, Sweden	28744						
		Calculated average annual cost per AGW	€340				$418		

Table 2 Extracts of non-cervical cancer management costs reported in selected papers, some cost values had been adjusted to 2016/17 US Dollars (US$) for ease of comparison between studies

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
1	Baio, 2012 [15]; Anal, head and neck, penile, vaginal, and vulvar cancer, and RRP; Italy; Euros; 2011; Available Italian secondary data identified from literature review and used to estimate lifetime cost per case of HPV-related diseases; Sources for non-cervical cancer cost estimates derived mainly from Italian standard tariffs; No funding to report	Disease	Lifetime direct costs per incident patient						
		Anal cancer	€11,742				$12,936		
		Head and neck cancer	€18,507				$20,389		
		Vulvar cancer	€13,330				$14,686		
		Vaginal cancer	€15,906				$17,524		
		Penile cancer	€10,048				$11,070		
		RRP	€187,428				$206,489		
2	Olsen, 2012 [21]; Anal, penile, vaginal, and vulvar cancer; Denmark; Euros; 2008; Retrospective data extraction using the Danish national registers to identify anal cancer patients diagnosed in 2004-2007. The authors identified health care resources use for the year prior to diagnosis and for the first, second, and third year after diagnosis. Discounting at 3% per annum was applied to costs incurred in the second and third year after diagnosis. Standard hospital tariffs were used to estimate cost. Regression analysis was used to estimate hospital costs for anal (ICD-10 code C21), penile (C60), vaginal (C52), and vulvar cancers (C51). The paper took the perspective of hospital sector; Sanofi Pasteur MSD		Total hospital cost per patient, including the year before diagnosis	Total hospital cost per patient, excluding the year before diagnosis			Total hospital cost per patient, including the year before diagnosis		
		Anal cancer							
		Overall	€38,289	€34,004			$51,571		
		Male	€41,347	€36,822			$55,690		
		Female	€36,734	€32,590			$49,477		
		Penile cancer	€20,513	€18,275			$27,629		
		Vaginal cancer	€25,435	€21,646			$34,258		
		Vulvar cancer	€21,161	€18,337			$28,502		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
3	Borget, 2011 [22]; Anal, laryngeal, oral cavity, oropharyngeal, penile, pharyngeal, vaginal, and vulvar cancer; France; Euros; 2007; Resource use data extracted from the French national hospital database, outpatient and daily allowance costs were derived from the French National Institute of Cancer report, 2007; Sanofi Pasteur MSD	Cancer type	Annual number of patients hospitalised	Mean annual hospital cost per patient	(SD)				
		Vulvar cancer	1,237	€4,608	(4,183)		$4,896	(4,445)	
		Vaginal cancer	728	€5,512	(4,574)		$5,857	(4,860)	
		Anal cancer	3,711	€5,478	(5,081)		$5,821	(5,399)	
		Penile cancer	678	€3,840	(3,160)		$4,080	(3,358)	
		Oral cavity cancer	10,786	€6,634	(6,530)		$7,049	(6,939)	
		Oropharyngeal cancer	12,232	€6,819	(6,726)		$7,246	(7,147)	
		Pharyngeal cancer	9,718	€6,838	(6,807)		$7,266	(7,233)	
		Laryngeal cancer	9,516	€5,599	(5,668)		$5,950	(6,023)	
4	Keeping, 2014 [23]; Anal cancer; England; GBP; 2010/11; Mathematical model used to illustrate treatment pathway and combined with national tariffs, used to calculate average treatment cost per patient; Hospital Episode Statistics (HES) data used to identify cases of squamous cell anal carcinoma seen for care over period 2006 to 2011 (9 months data in 2010/11). Cost of care			range (min.)	range (max.)				

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
	was obtained from national tariffs. A mathematical model, with a Markov model component to simulate disease progression and follow-up based on mode of primary treatment (chemo radiotherapy vs. radiotherapy), was used to calculate costs from diagnosis to follow-up, using data obtained from the Association of Coloproctology of Great Britain and Ireland's anal cancer position statement, supplemented as necessary by expert opinion; Sanofi Pasteur MSD	Average cost of treating a case of invasive anal cancer from referral through to either completion of follow-up or death (not taking into account of future inflation)	£16,281	£14,143	£22,884		$21,884	$19,010	$30,759

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
5	Heitland, 2013 [24]; Anal cancer; Germany; Euros; 2008; Retrospective cross-sectional analysis of five German hospital databases for year 2008, covering hospitalisation, diagnosis-related groups, major treatment category during hospital stay, inpatient rehabilitation and sick leave. The authors considered social insurance payers expenditure reflect direct hospital treatment and inpatient rehabilitation medical costs and did not consider outpatient management costs, patients' co-payments and out-of-pocket expenses. Main diagnosis code was anal cancer (ICD-10 code C21); Sanofi Pasteur MSD, Lyon, France		No. of hospitalisation	Annual cost of anal cancer hospitalisation and inpatient rehabilitation, excluding sick leaves					
		Male	2,238	€11,877,807			$15,998,145		
		Female	3,536	€18,947,967			$25,520,901		
		Sum	5,774	€30,825,774			$41,519,046		
6	Abramowitz, 2010 [25]; Anal cancer; France; Euros; 2007; Retrospective analysis of French hospital database, including private hospital records, of anal cancers in 2006. These were combined with standard public and private hospital tariffs year 2007 and included indirect daily allowances costs paid for by the French social security system. The authors took the perspective of French healthcare-payer; Sanofi Pasteur MSD	Total number of anal cancer patients	3,711						
		Total annual cost (public and private hospital, outpatient, and daily allowances included)	€38,249,981				$40,644,525		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
7	van der Linden, 2016 [26]; Head and neck cancer (recurrent and/or metastatic squamous cell carcinoma); Netherlands; Euros; 2013; Retrospective data collection covering years 2006 to 2013 from six Dutch head and neck treatment centers of recurrent and/or metastatic head and neck squamous cell carcinomas. Data extracted included tumour characteristics, treatment patterns, disease progression, survival, adverse evetns, and resource use. Unit cost data from published literature was used; the Netherlands Organization for Health Research and Development (ZonMw) and Merck B.V.		Mean total cost per patient	±					
		Overall	€24,211	€22,432			$25,822		
8	Klussmann, 2013 [27]; Head and neck cancer; Germany; Euros; 2008; Retrospective cross-sectional analysis of five German hospital databases for year 2008, covering hospital treatment, inpatient rehabilitation and sick leave. The authors considered social insurance payers expenditure reflect direct hospital treatment and inpatient rehabilitation medical costs and did not consider outpatient management costs, patients' co-payments and out-of-pocket expenses. Main diagnosis codes for head and neck cancers included ICD-10 codes C01-C06, C09-C14 and C32; SPMSD	Cancer category, gender (ICD-10 code)	No. of hospitalisation	Annual cost of hospitalisation and inpatient rehabilitation, excluding sick leaves					
		Oral cavity, male (C02-C06)	11,929	€79,091,226			$106,527,487		
		Oral cavity, female (C02-C06)	4,965	€34,177,666			$46,033,689		
		Oropharynx, male (C01, C09-C10)	14,396	€64,387,928			$86,723,706		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
		Oropharynx, female (C01, C09-C10)	4,110	€18,641,573			$25,108,220		
		Pharynx other, male (C11-C13)	10,268	€40,060,755			$53,957,585		
		Pharynx other, female (C11-C13)	1,908	€7,155,015			$9,637,046		
		Other/ill-defined sites in the lip, oral cavity, and pharynx, male (C14)	532	€3,648,316			$4,913,894		
		Other/ill-defined sites in the lip, oral cavity, and pharynx, female (C14)	129	€872,291			$1,174,883		
		Larynx, male (C32)	13,744	€51,615,938			$69,521,190		
		Larynx, female (C32)	1,876	€7,116,289			$9,584,886		
		Total, male	50,869	€238,804,163			$321,643,863		
		Total, female	12,988	€67,962,834			$91,538,725		
		Total, overall	63,857	€306,766,997					

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
9	Kim, 2011 [28]; head and neck cancer; UK; GBP; 2008/09; Retrospective analysis using Hospital Episode Statistic (HES) data to estimate the post-operative healthcare costs for an incidence cohort of squamous cell carcinoma of the head and neck patients (primary diagnosis in lip, tongue, oral cavity, pharynx or larynx, ICD-10: C00-6, C09-10, C12-4, C32) who underwent surgical resection between 1 July 2003 and 31 March 2008 - mapped healthcare utilization to "national schedule of reference costs 2008-09 for NHS Trusts" and "Unit costs of health & social care 2009"; GlaxoSmithKline	**Mean cost of post-operative healthcare utilisation for resected patients w h&n cancer over 5 years**	£23,212				$32,333		
		Mean cost per year 1st year	£19,778				$27,550		
		Mean cost per year 2nd year	£1,477				$2,057		
		Mean cost per year 3rd year	£847				$1,180		
		Mean cost per year 4th year	£653				$910		
		Mean cost per year 5th year	£455				$634		
		Mean cost of post-operative healthcare utilisation for laryngeal cancer over 5 years	£28,981				$40,369		
		Mean cost of post-operative healthcare utilisation for pharyngeal	£25,827				$35,976		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
		cancer over 5 years							
		Mean cost of post-operative healthcare utilisation for oral cavity cancer over 5 years	£25,311				$35,257		
		Mean cost of post-operative healthcare utilisation for tongue cancer over 5 years	£19,493				$27,153		
		Mean cost of post-operative healthcare utilisation for lip cancer over 5 years	£5,790				$8,065		
		Total cost of post-operative healthcare utilisation for cohort of resected h&n cancer (5 year f/u period)	£255,500,000				$355,900,677		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
10	Lacau, 2010 [29]; Head and neck cancer; France; Euros; Not explicitly stated, assume 2008; Retrospective analysis of the French national hospital database (PMSI) to extract year 2007 number of head and neck cancer patients, recorded from both public and private hospitals. The authors took a healthcare payer perspective. Data extracted included hospital stays, chemotherapy and radiotherapy sessions. Costs were obtained from French official tariffs; Sanofi Pasteur MSD	Cancer type	Annual number of patients	Total annual cost for all patients from payer perspective, including hospital costs, expensive drugs, indirect costs and outpatient costs and excluding rehabilitation costs					
		Oral cavity cancer	10,786	€130,694,253			$176,031,288		
		Salivary glands cancer	1,831	€17,271,550			$23,262,945		
		Oropharyngeal cancer	12,232	€158,722,207			$213,781,968		
		Pharyngeal cancer	9,718	€125,582,771			$169,146,664		
		Laryngeal cancer	9,516	€98,251,871			$132,334,843		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
11	Van Agthoven, 2001 [30]; Head and neck cancer; Netherlands; Euros; 1996; Retrospective analysis of patients with confirmed cancer of the oral cavity, larynx or oropharynx diagnosis between 1994 and 1996, accessing care in the University Hospital Rotterdam and the University Hospital Vrije Universiteit Amsterdam. The authors took an institutional perspective and only direct costs within healthcare, e.g. medical therapy costs. Total medical consumption of all patients were identified via micro-costing method based on a detailed inventory and measurement of resources consumed, combined with financial data, with future costs discounted at 4% per annum. A model was built that covers 10-year disease course, from diagnosis, treatment and follow-up of primary tumours in the first 2 years to treatment and follow-up of recurrences, and deaths, to up to 10 years. Modelled survival data was extracted from the Netherlands Cancer Registry; the Association of University Hospitals (VAZ)	Head and neck cancer site	Average total discounted costs per new patient						
		Oral cavity	€35,541				$58,711		
		Larynx	€26,851				$44,356		
		Oropharynx	€35,642				$58,878		
		Overall (weighted average of the 3 cancer sties studied)	€31,829				$52,579		
12	Corbridge, 2000 [31]; Head and neck cancer; England; GBP; not stated, assume 2000 GBP; Prospective audit of inpatient care cost of 10 patients referred to a head and neck clinic in Oxford. The personnel involved in patient care and materials used were documented. Only inpatient resource use documented, excluded any preoperative assessments as outpatients or day case admissions information not collected.	Average min. total cost of treating a head and neck cancer in-patient	£11,450				$21,683		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
	Post-discharge care, readmissions or post-treatment radiotherapy not accounted for. Audit also excluded patients receiving primary radiotherapy or palliative care; Funding source not specified								
13	Lowry, 1990 [32]; Head and neck cancer; UK; GBP; Not identified, assume 1990; Not specified; Funding source not specified	Overall total cost for resection and reconstruction of head and neck malignancy including presurgical chemotherapy and postoperative radiotherapy	£5,661				$16,784		
14	van Agthoven, 2006 [33]; Laryngeal cancer; Netherlands; Euros; 2003; Retrospective observational study of laryngeal cancer patients in five Dutch university hospitals. Assessment was carried out to evaluate impact of new disease management guideline. Study period covered 1 January 1995 to 30 April 2001. Cost data was from hospital administrative departments and standard Dutch tariffs. The authors took a hospital perspective; Funding	Type of laryngeal cancer	n (post-guideline implementation)	Total treatment cost post-guideline implementation, mean					
		Dysplasia	16	€3,005			$3,502		
		Carcinoma in		€5,136			$5,985		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
	source not specified	situ	23						
		T1 carcinoma	120	€5,931			$6,912		
		T2 carcinoma	104	€8,180			$9,533		
		T3 carcinoma	49	€14,593			$17,006		
		T4 carcinoma	51	€20,229			$23,574		
15	Zavras, 2002 [34]; Oral cavity cancer; Greece; US dollars; 2001; Retrospective analysis of 95 patients diagnosed with squamous cell carcinoma of the oral cavity (ICD-10 code C00.3-C00.9, C01-C06) between 1 January 1993 and 31 December 1999, extracted from medical records and clinic files of the Oral and Maxillofacial Clinic of the Athens General Hospital. Information extracted included length of hospitalisation, treatment, disease stage etc. Prices were obtained from official publications or professional association catalogues or average prices from 3 private hospitals when published sources were unavailable; National Institute of Dental Research funds (NIDCR/NIH, Bethesda, MD.)		Mean treatment cost per patient						
		Overall	$7,450				$9,372		
		Stage I disease	$3,662				$4,607		
		Stage II disease	$5,867				$7,381		
		Stage III disease	$10,316				$12,978		
		Stage IV disease	$11,467				$14,426		
16	Preuss, 2007 [35]; Oropharyngeal carcinomas; Germany; Euros and US dollars; 2006; Retrospective analysis of 211 patients who presented to an otorhinolaryngology department		Euros	US dollars					
		Surgery and	€17,488	$22,097			$16,811		

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
	in Germany between 1992 and 2005. Patients were included if they have histologically confirmed squamous cell carcinoma diagnosis, suitable for curative surgical treatment. Study excluded patients with distant metastases. The authors analysed data on surgical complications, therapeutic morbidity, and treatment costs; Funding source not specified	postoperative radio(chemo)therapy, min.							
		Surgery and postoperative radio(chemo)therapy, max.	€24,631	$30,996			$23,582		
17	Keeping, 2015 [36]; Penile cancer; England; GBP; 2010/11; Hospital Episode Statistics (HES) data used to identify inpatient and outpatient activity associated with penile cancer, covering years 2006/07 to 2010/11 (nine months provisional data for 2010/11). Resource needs combined with 2010/11 national tariffs. A mathematical model with a Markov model was used to estimate treatment cost per patient per case, informed by the European Association of Urologists Treatment Guidelines, modified; Sanofi Pasteur MSD	Table 3: Per patient treatment costs by scenario							
		Scenario	**Cost per Patient**						
			Base Case	**Lower Bound**	**Upper Bound**				
		No inflation, no MFF	£7,421	£5,930	£10,104		$9,975	$7,971	$13,581
		Inflation, no MFF	£7,465	£5,961	£10,156		$10,034	$8,012	$13,651
		No inflation, MFF	8,015	£6,405	£10,913		$10,773	$8,609	$14,668
		Inflation, MFF	8,063	£6,437	£10,968		$10,838	$8,652	$14,742
		(MFF, Market Force Factor)							

No.	Author, year; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value					USD 2016/17	Range min.	Range max.
18	Harrison, 2016 [37]; RRP; Scotland; GBP; 2013/14; Questionnaire used to collect data during routine adult RRP follow-up in a single centre managing RRP in Glasgow, Scotland. Cost data sourced from Scottish Government's Information Services Division. Included 14 patients (6 males and 8 females, mean age at diagnosis 36, range 12 to 66 years old) with active RRP between January 2013 and April 2014; Funding source not specified	Total treatment cost for 14 patients from January 2013 to April 2014	£107,478				$137,601		
19	Salo, 2013 [11]; Vaginal and vulvar cancer; Finland; Euros; 2010; National registry data provided diagnostic and treatment procedures, hospitalisation, outpatient visit and prescription data, which were combined with national unit costs. Index events were identified during 1999-2008 and cancers that were recorded in the Cancer Registry during 1990-1998; Funding source not specified, authors reported conflict of interest either through grants or employment from GlaxoSmithKline, Merck&Co. Inc, GSK Biologicals, and/or Sanofi Pasteur MSD		Average undiscounted cost per HPV related AGW	SD					
		Vaginal cancer	€24,424	26,760			$28,131		
		Vulvar cancer	€15,867	18,346			$18,275		

Table 3 Details of studies reporting utility estimates for anogenital warts (AGWs)

<table>
<tr><th>No.</th><th>Author, year;Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>1</td><td>Marcellusi, 2015; Italy [38]; TTO and EQ-5D; 465 patients with confirmed diagnosis of HPV-related disease e.g. anal cancer, head and neck cancer, or AGW, mean age 44.0 (SD 16.3) years and 135 controls, mean age 44.0 (SD 13.2) years enrolled over 31 October 2008 to 31 July 2012. EQ-5D source, EuroQol, the Netherlands; Sanofi Pasteur MSD, Italy and partly funded by the Italian Ministry o fEducation, University and Scientific Research</td><td>
<table>
<tr><th></th><th>n</th><th>Mean age (SD)</th><th>Mean (SD) EQ-5D utility for patients with AGW</th><th>Mean (SD and 95% CI) TTO utility for patients with AGW</th></tr>
<tr><td>AGW overall</td><td>132</td><td>33.1 (10.2)</td><td>0.9 (0.1)</td><td>0.78 (SD 0.27; 95% CI 0.73-0.82)</td></tr>
<tr><td>Males</td><td>74</td><td>35.7 (10.2)</td><td>0.9 (0.1)</td><td>0.83 (95% CI: 0.77-0.88)</td></tr>
<tr><td>Females</td><td>58</td><td>29.7 (9.3)</td><td>1 (0.1)</td><td>0.71 (95% CI: 0.64-0.79)</td></tr>
</table>
</td></tr>
<tr><td>2</td><td>Vriend, 2014; The Netherlands [39]; EQ-5D-3L, EQ-VAS, and genital wart-specific CECA-10 tool; Patients attending 9 STI clinics in the Netherlands for first or recurrent AGW episode between February and August 2012 were eligible for recruitment. Single EQ-5D utility not reported, although figure with percentage of patients reporting some of severe problems with each of the five EQ-5D dimensions were presented, separately for women, men, and MSM. Actual proportions not stratified by some problems or severe problems not available, thefore not possible to calculate single utility score using population norms; No specific funding received</td><td>
<table>
<tr><th></th><th>EQ-VAS score from</th></tr>
<tr><td>45 women</td><td>75.3% (95% CI: 70.3-80.2)</td></tr>
<tr><td>34 heterosexual men</td><td>83.7% (95% CI: 79.3-88.2)</td></tr>
<tr><td>14 MSM</td><td>82.1 (95% CI: 75.4-88.9)</td></tr>
</table>
</td></tr>
<tr><td>3</td><td>Dominiak-Felden, 2013; UK [40]; EQ-5D; For AGW, participants were men and women clinic attendees who were either seen for first or recurrent AGW (n = 186) or had a history of AGW more than 6 months before (n = 62) recruitment period between May 2008 and March 2009; Sanofi Pasteur MSD</td><td>
<table>
<tr><td>EQ-5D score adjusted by age and sex (SD)</td><td>0.9 (0.13)</td><td>vs population norm 0.89, p = 0.633</td></tr>
<tr><td>VAS score adjusted by age and sex (SD)</td><td>78% (14.8%)</td><td>vs UK general population 85%</td></tr>
<tr><td></td><td>EQ-5D score (crude)</td><td>VAS score (crude)</td></tr>
<tr><td>Men</td><td>0.89 (SD 0.17)</td><td>79 (SD: 15.5)</td></tr>
<tr><td>Women</td><td>0.84 (SD 0.16)</td><td>75 (SD: 19.3)</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>No.</th><th>Author, year;Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>4</td><td>Shi, 2012; China [41]; EQ-5D-3L, Chinese version, and EQ-VAS; EQ-5D index scores calculated using UK, US, and Japan population norms; 1,358 GW patients (612 men, 746 women) enrolled between July 2007 to July 2008 from 18 clinics across China were included in the analysis, with a mean age of 32.0 ± 10.6 years; MSD China</td><td>
<table>
<tr><td>Overall VAS score</td><td>65.2 ± 22.0</td></tr>
<tr><td></td><td>Mean (SD) EQ-5D based on UK preference weight</td></tr>
<tr><td>Overall</td><td>0.826 (0.201)</td></tr>
<tr><td>Male</td><td>0.856 (0.185)</td></tr>
<tr><td>Female</td><td>0.802 (0.210)</td></tr>
</table>
</td></tr>
<tr><td>5</td><td>Drolet, 2011; Canada [42]; EQ-5D, VAS, SF-6D; 272 patients with first or recurrent AGW between September 2006 and February 2008 recruited. EuroQol, SF-12, short Spielberg State-Trait Anxiety Inventory, and HPV impact profile measured at recruitment, and 2 and 6 months later. British scoring system used to translate health states of study participants into EQ-5D utility scores; Merck Frosst Canada Ltd.</td><td>
<table>
<tr><th></th><th>EQ-5D total score</th><th>VAS</th><th>SF-6D</th></tr>
<tr><td>Men</td><td></td><td></td><td></td></tr>
<tr><td>Norm mean</td><td>89.1</td><td>82.3</td><td>NA</td></tr>
<tr><td>All AGW cases at recruitment, n=127, mean (95% CI)</td><td>81.0 (77.4-84.5)</td><td>77.6 (74.9–80.2)</td><td>74.2 (72.0–76.5)</td></tr>
<tr><td>AGW cleared at end of 6 months follow-up, n=47, mean (95% CI)</td><td>86.1 (79.8–92.3)</td><td>81.6 (76.8–86.5)</td><td>77.5 (73.2–81.8)</td></tr>
<tr><td>AGW persisted at end of 6 months follow-up, n=80, mean (95% CI)</td><td>83.8 (78.5–89.1)</td><td>78.7 (75.8–81.6)</td><td>73.8 (70.3–77.4)</td></tr>
<tr><td>Women</td><td></td><td></td><td></td></tr>
<tr><td>Norm mean</td><td>88.6</td><td>83.2</td><td>NA</td></tr>
<tr><td>All AGW cases at recruitment, n=145, mean (95% CI)</td><td>77.4 (74.0-80.8)</td><td>76.4 (73.9–78.9)</td><td>71.0 (69.0–73.0)</td></tr>
<tr><td>AGW cleared at end of 6 months follow-up, n=87, mean (95% CI)</td><td>89.3 (84.6-94.0)</td><td>82.1 (78.6–85.7)</td><td>76.7 (73.8–79.4)</td></tr>
<tr><td>AGW persisted at end of 6 months follow-up, n=58, mean (95% CI)</td><td>79.6 (73.4-84.7)</td><td>78.1 (73.5–82.8)</td><td>71.5 (67.8–75.2)</td></tr>
</table>
Median duration of an AGW episode, n=51 incident cases: 125 days
Average QALY loss per AGW case: 0.017 to 0.041
</td></tr>
</table>

<table>
<tr><th>No.</th><th>Author, year;Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>6</td><td>Mennini, 2011; Italy [43]; TTO and EQ-5D (only at baseline); 36 patients with histologically confirmed CIN2-3 diagnosis eligible, identified between June 2007 and October 2008. Patient given pathologic condition, which included AGWs, to elicit their TTO utility value. EQ-5D-3L used to assess patients' health status at baseline; Italian Ministry of Education, University and Scientific Research in Italy</td><td>
<table>
<tr><td>Mean (SD) baseline EQ-5D utility in all women with HPV-related diseases</td><td>0.93 (0.10)</td></tr>
<tr><td></td><td>Mean (SD) TTO utility</td></tr>
<tr><td>AGW</td><td>0.71 (0.35)</td></tr>
</table>
</td></tr>
<tr><td>7</td><td>Senecal, 2011; Canada [44]; EQ-5D and EQ-VAS; Patients with first or recurrent AGW episode recruited between September 2006 and February 2008 across Canada. Data complete for 270 of 330 AGW patients recruited at diagnosis or follow-up for a first or recurrent episode. Questionnaire completed at recruitment, 2 and 6 months later. Mean age: 33.7 years (men); 29.5 years (women). EQ-5D values calculated based on Canadian population norms data, with additional analysis using US population norms; Merck Frosst Canada Ltd.</td><td>
<table>
<tr><td></td><td>Mean (95% CI)</td></tr>
<tr><td>EQ-5D score (AGW patients)</td><td>0.789 (0.763-0.815)</td></tr>
<tr><td>EQ-5D disutility vs Canadian norm</td><td>9.9 (7.3-12.5)</td></tr>
<tr><td>EQ-5D disutility vs Canadian norm (males)</td><td>7.8 (4.1-11.5)</td></tr>
<tr><td>EQ-5D disutility vs Canadian norm (females)</td><td>11.7 (8.3-15.2)</td></tr>
<tr><td>EQ-VAS score (AGW patients)</td><td>0.769 (0.749-0.788)</td></tr>
<tr><td>EQ-VAS disutility vs Canadian norm</td><td>6 (4.1-7.9)</td></tr>
<tr><td>EQ-VAS disutility vs Canadian norm (males)</td><td>4.8 (2.0-7.5)</td></tr>
<tr><td>EQ-VAS disutility vs Canadian norm (females)</td><td>7 (4.4-9.6)</td></tr>
</table>
</td></tr>
<tr><td>8</td><td>Woodhall, 2011; England and Northern Ireland [4]; EQ-5D-3L and EQ-VAS; 895 patients from a convenience sample of seven sexual health clinics in England and one in Northern Ireland. data collection took place between August 2009 and February 2010. Those who consented to follow-up were given another set of questionnaire two weeks after baseline visit. Utility values calculated based on UK population norms; Department of Health</td><td>
<table>
<tr><td></td><td>All (95% CI)</td><td>Male (95% CI)</td><td>Female (95% CI)</td></tr>
<tr><td>EQ-5D index</td><td>0.87 (0.85-0.89)</td><td>0.88 (0.86-0.9)</td><td>0.87 (0.83-0.9)</td></tr>
<tr><td>EQ-VAS</td><td>77 (76-79)</td><td>79 (77-80)</td><td>75 (71-78)</td></tr>
<tr><td>EQ-5D disutility</td><td>0.056 (0.038-0.074)</td><td>0.043 (0.021-0.065)</td><td>0.063 (0.029-0.097)</td></tr>
<tr><td>Duration episode of care (days)</td><td>36 (27-46)</td><td>35 (20-51)</td><td>37 (20-53)</td></tr>
<tr><td>Prescription/recovery time (days)</td><td>36 (36-40)</td><td>39 (34-44)</td><td>37 (41-43)</td></tr>
<tr><td>Time to attendance (days) at clinic after noticing GW</td><td>111 (88-135)</td><td>144 (112-174)</td><td>69 (48-90)</td></tr>
<tr><td>Mean QALY loss (days)</td><td>6.6 (2.9-11.3)</td><td>6.6 (0.8-14.9)</td><td>6.5 (2.9-11.2)</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>No.</th><th>Author, year;Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>9</td><td>Marra, 2009; Canada [45]; EQ-5D and SF-6D; 75 participants (52% female) with history of AGWs recruited using newspaper advertisements and completed QoL questionnaires considering health state when having AGWs. mean age 40 (SD 11.4) years. Scoring algorithm used UK-based York scoring system; Funding source not specified</td><td><table>
<tr><td>Mean EQ-5D utility score</td><td>0.76 (SD: 0.19; 95% CI: 0.72-0.8)</td></tr>
<tr><td>Mean EQ-5D VAS score</td><td>65.1 (SD: 21.2; 95% CI: 60-70)</td></tr>
<tr><td>Mean SF-6D utility score</td><td>0.74 (SD: 0.13; 95% CI: 0.71-0.77)</td></tr>
</table></td></tr>
<tr><td>10</td><td>Pirotta, 2009; Australia [46]; EuroQoL VAS, HPV Impact Profile (HIP) and the Sheehan Disability Score (SDS); One group of study participants (n = 40) was women with AGW seen in a sexual health clinic in Melbourne in year 2006. Mean age (SD) for this group was 24 (5) years; CSL Limited</td><td><table>
<tr><th></th><th>Mean</th></tr>
<tr><td>EuroQoL VAS, observed value</td><td>68.9 (SD: 21.4)</td></tr>
<tr><td>Multivariate analysis (adjusted for age, ethnicity, and current partner)</td><td>71.4 (95% CI: 63.3-79.6)</td></tr>
</table></td></tr>
<tr><td>11</td><td>Woodhall, 2009; England [5]; EQ-5D (note: disutility value presented); 189 patients attending the York STD clinic in 2006/07; Department of Health</td><td>EQ-5D disutility for 18-30 year olds
Estimated loss of QALYs ranged from 0.0045 (95% CI: 0.0014–0.0078) to 0.023 (95% CI: 0.0072– 0.039).</td></tr>
<tr><td>12</td><td>Woodhall, 2008; England [47]; EQ-5D and EQ-VAS; 81 York GUM attendees (43 men, 38 women, mean age 26 years) recruited over 3-month period; Department of Health</td><td><table>
<tr><th></th><th>Unadjusted mean EQ-5D index score</th><th>Unadjusted mean EQ-VAS score</th></tr>
<tr><td>Cases</td><td>0.9</td><td>72</td></tr>
<tr><td>Controls (UK norms)</td><td>0.91</td><td>86</td></tr>
<tr><td>Note</td><td>Age and sex adjusted mean EQ-5D index score 0.039 points lower (95% CI 0.005-0.078; p=0.02)</td><td>Age adjusted EQ-VAS, average difference lower by 13.9 (95% CI 9.9-17.6; p<0.001), based on 70 cases; male cases lower by 10.9 (95% CI 5.7-15.5; p<0.001); female cases lower by 19.9 (95% CI 11.7-26.2; p<0.001)</td></tr>
</table></td></tr>
</table>

Table 4 Summary details of papers reporting utility values for HPV-related cancers

<table>
<tr><th>No.</th><th>Author, year; Disease; Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>1</td><td>Aro, 2016; Head and neck cancer; Finland [48]; 15D; 214 patients treated for head and neck malignancy during years 2007-2013 at their institution completed the 15D questionnaire; the Helsinki University Hospital Research Funds</td><td>
<table>
<tr><th></th><th>15D utility</th><th></th></tr>
<tr><td>Population</td><td>0.911</td><td></td></tr>
<tr><td>Patients</td><td>0.872</td><td></td></tr>
<tr><td>Baseline</td><td>0.872</td><td>p-value vs baseline</td></tr>
<tr><td>3 months</td><td>0.839</td><td>p < 0.001</td></tr>
<tr><td>6 months</td><td>0.857</td><td>p = 0.001</td></tr>
<tr><td>12 months</td><td>0.852</td><td>p = 0.003</td></tr>
</table>
</td></tr>
<tr><td>2</td><td>Govers, 2016; Oral cancer; The Netherlands [49]; EQ-5D-3L, EQ-VAS, and shoulder disability questionnaire (SDQ); 174 patients with early stage (T1-2) oral cavity squamous cell carcinoma between 2001 and 2013 completed EQ-5D-3L, EQ-VAS, and SDQ. EQ-5D-3L converted to utility values using the Dutch tariff; None declared</td><td>
<table>
<tr><th>Patient subgroup</th><th>n</th><th>Mean age (SD, range)</th><th>Mean time after treatment in years (SD, range)</th><th>Mean (SE) EQ-5D-3L utility score, adjusted for age, gender, and time since treatment (p-value 0.700)</th><th>Mean (SE) EQ-VAS score, adjusted for age, gender, and time since treatment (p-value 0.234)</th></tr>
<tr><td>watchful waiting (WW)</td><td>26</td><td>71.4 (11.4, 54.8-91.6)</td><td>4.8 (1.8, 2.3-9.2)</td><td>0.804 (0.04)</td><td>69.7 (3.7)</td></tr>
<tr><td>sentinel lymph node biopsy (SLNB)</td><td>19</td><td>63.6 (9.4, 44.9-80.2)</td><td>1.9 (1.4, 0.4-4.1)</td><td>0.863 (0.05)</td><td>79.6 (4.8)</td></tr>
<tr><td>supraomohyoid neck dissection (SOHND)</td><td>109</td><td>62.7 (12.2, 29.5-84.6)</td><td>5.2 (2.6, 1.6-12.2)</td><td>0.834 (0.02)</td><td>76.1 (1.8)</td></tr>
<tr><td>modified radical neck dissection (MRND)</td><td>27</td><td>64.8 (10.6, 40.5-96.5)</td><td>5.2 (3.2, 0.4-11.0)</td><td>0.794 (0.04)</td><td>71.5 (3.3)</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>No.</th><th>Author, year; Disease; Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>3</td><td>Pickard, 2016; Head and neck cancer; US [50]; EQ-5D-3L (utility values calculated using US preference-based algorithm), EQ-VAS, and Functional Assessment of Cancer Therapy-General (FACT-G); Retrospective analysis on cross-sectional clinical trial data that included cancer patients participating in a US-based multicentre study. 50 cancer patients were recruited for each tumour site studied, which included head/neck. All patients had received at least 2 cycles or at least 1 month of chemotherapy. Mean age 56.0 (SD: 9.2); Funding support for the original study was provided by 11 pharmaceutical companies</td><td>
<table>
<tr><th></th><th>Mean (SD)</th></tr>
<tr><td>Unadjusted EQ-5D</td><td>0.76 (0.15)</td></tr>
<tr><td>EQ-5D index scores, adjusted for age and sex</td><td>0.828</td></tr>
<tr><td>Unadjusted EQ-VAS</td><td>61.8 (21.7)</td></tr>
<tr><td>EQ-VAS, adjusted for age and sex</td><td>60.8</td></tr>
</table>
</td></tr>
<tr><td>4</td><td>Rettig, 2016; Head and neck cancer, sites include larynx, oral cavity, oropharynx, hypopharynx, nasopharynx, and nasal cavity/paranasal sinuses, US [51]; SF-36 to single score; Health-related quality of life (HRQOL) in individuals aged 65+ with head and neck squamous cell carcinoma who participated in the linked Surveillance, Epidemiology, and End Results-Medicare Health Outcomes Survey (SEER-MHOS) database from 1998 to 2005 was extracted. Data included surveys assessing HRQOL from 5 years prediagnosis to 10 years postdiagnosis. HRQOL was measured using SF-36, with the physical component summary and the mental component summary scores combined to generate single HRQOL summary score; n = 1,653; National Institute of Dental and Craniofacial Research/National Institutes of Health Research Training in Otolaryngology grant, with statistical support provided in part by the Johns Hopkins Institute for Clinical and Translational Research</td><td>
<table>
<tr><th>Time</th><th>HRQOL Score (95% CI)</th><th>HRQOL Score (95% CI)</th><th>HRQOL Score (95% CI)</th><th>HRQOL Score (95% CI)</th></tr>
<tr><td></td><td>Overall, n = 1,653</td><td><2 Year Survivors, n = 296</td><td>2-5 Year Survivors, n = 209</td><td>>5-Year Survivors, n = 1,081</td></tr>
<tr><td>Time interval prediagnosis</td><td></td><td></td><td></td><td></td></tr>
<tr><td>5 y (Baseline)</td><td>92.3 (89.3, 95.2)</td><td>87.3 (92.7, 91.9)</td><td>92.8 (85.1, 100.5)</td><td>96.4 (91.8, 100.9)</td></tr>
<tr><td>2 y</td><td>90.2 (88.4, 92.0)</td><td>86.3 (83.4, 89.2)</td><td>89.8 (85.3, 94.2)</td><td>94.5 (91.9, 97.1)</td></tr>
<tr><td>Diagnosis: 0 y</td><td>85.0 (83.4, 86.6)</td><td>73.9 (70.3, 77.6)</td><td>82.9 (79.0, 86.9)</td><td>91.5 (89.4, 93.5)</td></tr>
<tr><td>Time interval postdiagnosis</td><td></td><td></td><td></td><td></td></tr>
<tr><td>13 mo</td><td>83.7 (82.0, 85.4)</td><td>69.7 (62.8, 76.7)</td><td>79.9 (76.1, 83.7)</td><td>90.1 (87.9, 92.2)</td></tr>
<tr><td>2 years</td><td>84.1 (82.4, 85.8)</td><td>63.8 (35.9, 91.7)</td><td>78.0 (73.6, 82.5)</td><td>89.2 (87.2, 91.2)</td></tr>
<tr><td>5 years</td><td>88.0 (86.2, 89.7)</td><td></td><td>52.1 (14.9, 89.3)</td><td>88.6 (86.8, 90.3)</td></tr>
<tr><td>10 years</td><td>84.6 (81.6, 87.6)</td><td></td><td></td><td>84.2 (81.4, 87.1)</td></tr>
<tr><td colspan="5">Note: Overall, HRQOL was not significantly different for oropharyngeal squamous cell carcinoma (OPSCC) patients vs non-OPSCC patients. Higher prediagnosis HRQOL quartile was not significantly associated with improved survival in 131 OPSCC patients with prediagnosis data (HR, 0.95; p = 0.32). HRQOL recovery to baseline after treatment not observed after stratification by survival group. No chemotherapy data and limited surgery data available, treatment-related HRQOL changes could not be fully examined.</td></tr>
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<table>
<tr><th>No.</th><th>Author, year; Disease; Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>5</td><td>Kent, 2015; Oral cavity and pharyngeal cancers; US [52]; SF-6D calculated from SF-36 data; VR-6D calculated from the Veterans RAND 12-item Health Survey (VR-12); Data derived from the Surveillance Epidemiology and End Results (SEER) national cancer registry system linked with the Medicare Health Outcomes Survey (MHOS), covering 10 cohorts from 1998 to 2009. Included patients with oral cavity and pharyngeal cancers in their primary diagnoses. SF-36 used to measure quality of life in the first 6 cohorts, VR-12 used in cohorts 7-10; Last author received grants from the NIA and the NIMHD</td><td><table><tr><td>Mean SF-6D/VR-6D (95% CI)</td><td>0.69 (0.68, 0.70)</td></tr></table></td></tr>
<tr><td>6</td><td>Loimu, 2015; Head and neck cancer; Finland [53]; 15D; Prospective cohort study of 64 patients with laryngeal, pharyngeal or nasal cavity carcinoma treated with definitive (chemo) radiotherapy betwee November 2007-July 2012 completed 15D health-related quality of life (HRQoL) questionnaire; HRQoL measured at baseline, 3, 6, 12 months after treatment onset. 75% males, mean age 61.6 (range: 40-81) years; The Helsinki University Central Hospital Research Funds</td><td><table><tr><th></th><th>Mean 15D score, all patients, n = 64</th><th>Compared with 15D of standardised Finnish general population</th></tr><tr><td>Baseline</td><td>0.886 (0.10)</td><td>Difference not statistically significant or in clinically important manner</td></tr><tr><td>3 months</td><td>0.829 (0.12)</td><td></td></tr><tr><td>6 months</td><td>0.860 (0.12)</td><td></td></tr><tr><td>12 months</td><td>0.862 (0.14)</td><td>Difference not statistically significant or in clinically important manner</td></tr></table></td></tr>
<tr><td>7</td><td>Noel, 2015; Head and neck cancer; Canada [54]; SG, TTO, VAS, EQ-5D-5L, Health Utilities Index Mark 3 (HUI3); Cross-sectional study of 100 upper aerodigestive tract squamous cell carcinoma patients with minimum 3 months follow-up after surgery or radiotherapy treatment completion with no recurrence or metastatic disease, recruited from 1 August to 31 October 2014. 75% male, mean age 61 (range 31-92); Funding source not specified</td><td><table><tr><td>EQ-5D</td><td>0.82 (SD: 0.18, range: -0.07-1.0)</td></tr><tr><td>SG</td><td>0.91 (SD: 0.17, range: 0.2-1.0)</td></tr><tr><td>TTO</td><td>0.94 (SD: 0.14, range: 0.3-1.0)</td></tr><tr><td>VAS</td><td>0.76 (SD: 0.19, range: 0.2-1.0)</td></tr><tr><td>HUI3</td><td>0.75 (SD: 0.25, range: -0.06-1.0)</td></tr></table></td></tr>
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<table>
<tr><th>No.</th><th>Author, year; Disease; Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>8</td><td>Pottel, 2015; Head and neck cancer; Belgium [55]; EQ-5D, Vulnerable Elders Survey-13 (VES-13), Geriatric-8 (G-8) questionnaire, and comprehensive geriatric assessment (CGA); This was an observational, multicentre, prospective study. Head and neck cancer patients aged 65+ years, eligible for curative primary or adjuvant radiotherapy, with or without concomitant systemic therapy, excluding tumours of the parotid gland or nasal cavity and paranasal sinuses, were recruited from January 2010 to April 2012. EQ-5D self-completed or through patient interview at week-0 and week-4; postal EQ-5D at month-2, 5, 12, 24, and 36 after treatment start. EQ-5D index scores followed that developed by Cleemput obtained from 548 Flemish (Belgian) respondents; the Belgian Federal Government, National Cancer Plan</td><td>EQ-5D complete for 81 patients
Post-treatment EQ-5D postal response was 90%
<table><tr><th></th><th>General median (Q1, Q3) EQ-5D index score</th></tr><tr><td>Prior to treatment start</td><td>0.66 (0.55, 0.76)</td></tr><tr><td>Week-4 (mid-therapy)</td><td>0.42 (0.26, 0.73)</td></tr><tr><td>Month-2 (end of treatment)</td><td>0.66 (0.29, 0.76)</td></tr><tr><td>Month-5</td><td>0.66 (0.27, 0.76)</td></tr><tr><td>Month-12</td><td>0.64 (0.0, 0.76)</td></tr><tr><td>Month-24</td><td>0.29 (0.0, 0.76)</td></tr><tr><td>Month-36</td><td>0.0 (0.0, 0.67)</td></tr></table>Vulnerable patients showed significantly lower EQ-5D index scores compared to fit patients, before, during, and after treatment start ($p<0.05$)</td></tr>
<tr><td>9</td><td>Lango, 2014; Head and neck cancer; US [56]; EQ-5D-3L, Swal-QOL; Study recruited 159 patients newly diagnosed head and neck squamous cell carcinoma (HNSCC) with no history of prior treatment for head and neck cancer, no evidence of distant metastases, and were treated with curative intent. Recruitment period was from December 2006 to December 2012. 80% males, median patient age: 60 (range: 32-85); the American Cancer Society</td><td><table><tr><td>Median EQ-5D utility value</td><td>85 (IQR: 70-90)</td></tr></table></td></tr>
<tr><td>10</td><td>Nijdam, 2008; Head and neck cancer; The Netherlands [57]; EQ-5D, performance status scale (PSS) for head and neck cancer patients, European Organization for Research and Treatment of Cancer (EORTC)-QoL questionnaire (QLQ-C30), EORTC Head and Neck (H&N35) module, and VASxero specific for xerostomia-related issues; All patients with tumours of the tonsillar fossa, soft palate, or base of tongue, and between 2 to 10 years alive with no evidence of diseases were eligible for a quality of life survey conducted in 2003 and again in 2005, the latter included EQ-5D questionnaire; Funding source not specified</td><td><table><tr><th></th><th>Median value</th></tr><tr><td>EQ5D values, same for both brachytherapy group (n = 75) and surgery group (n = 44), p=0.87</td><td>75</td></tr></table></td></tr>
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<table>
<tr><th>No.</th><th>Author, year; Disease; Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td>11</td><td>Rogers, 2006; Head and neck cancer; UK [58]; EQ-5D, EQ-VAS, and University of Washington Quality of Life Questionnaire Version 4 (UW-QOL V4); This was a cross-sectional postal survey conducted in 2004 of patients treated for oral/oropharyngeal squamous cell carcinoma by primary surgery between 1992 to 2003. EQ-5D utility score calculated using UK value set. Mean age 65 (SD: 12); 224 completed questionnaires; Funding source not specified</td><td>
<table>
<tr><td>EQ5D mean utility (health index)</td><td>0.75 (SE: 0.02; range: -0.18 to 1.0)</td></tr>
<tr><td>Overall mean EQ-VAS</td><td>74 (SE: 1)</td></tr>
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</td></tr>
<tr><td>12</td><td>Ringash, 2000;, Laryngeal cancer; Canada [59]; TTO, patient completed; 114 laryngeal cancer patients treated mainly with primary radiotherapy and seen in follow-up between May and November 1998 complete TTO utility measure and the Functional Assessment of Cancer Therapy Head and Neck quetionnaire Version 4 (FACT-H&N). For the TTO, patients considered a given period of time in current health state and decided what period of time perfect health would be of equal value; questionnaired administered via structured personal interview; Funding source not specified</td><td>
<table>
<tr><td></td><td>Mean (SD; range)</td></tr>
<tr><td>TTO, n=112</td><td>0.914 (0.156; 0.25 to 1)</td></tr>
<tr><td>TTO, excluding patients who claimed they had or did not want perfect health, n=84</td><td>0.878 (0.174; 0.25 to 1)</td></tr>
</table>
</td></tr>
<tr><td>13</td><td>Downer, 1997; Oral ; UK [60]; SG; A convenience sample of 100 staff members of a commercial company, excluding those with relatives or friends with oral cancer or who had medical knowledge of the disease, completed SG questionnaire. Three health states descriptions were considered, these were oral precancer, early oral cancer, and late oral cancer. 62% of respondents were male. Mean age 49.81 years; Funding source not specified</td><td>
<table>
<tr><td>Health state</td><td>Mean utility value (SD)</td></tr>
<tr><td>Precancer</td><td>0.92 (0.18)</td></tr>
<tr><td>Stage 1 cancer</td><td>0.88 (0.20)</td></tr>
<tr><td>Stage 2+ cancer</td><td>0.68 (0.33)</td></tr>
</table>
</td></tr>
<tr><td>14</td><td>Marcellusi, 2015; AGW, anal, head and neck, Italy; TTO and EQ-5D [38]; 465 patients, mean age 44.0 (SD 16.3) years and 135 controls, mean age 44.0 (SD 13.2) years enrolled over 31 October 2008 to 31 July 2012; Sanofi Pasteur MSD, Italy and partly funded by the Italian Ministry o fEducation, University and Scientific Research</td><td>
<table>
<tr><td>Patients with</td><td>Overall n</td><td>Mean EQ-5D utility (SD)</td><td>Mean EQ-5D utility (SD), males</td><td>Mean EQ-5D utility (SD), females</td></tr>
<tr><td>anal cancer</td><td>26</td><td>0.6 (0.3)</td><td>0.7 (0.2)</td><td>0.4 (0.3)</td></tr>
<tr><td>anal cancer, controls</td><td>10</td><td>0.9 (0.1)</td><td>0.9 (0.1)</td><td>0.9 (0.1)</td></tr>
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<table>
<tr><th>No.</th><th>Author, year; Disease; Country; Utility elicitation method; Study details; Funding</th><th>Results</th></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>head and neck squamous cell carcinoma</td><td>79</td><td>0.8 (0.2)</td><td>0.8 (0.2)</td><td>0.7 (0.2)</td></tr>
<tr><td>head and neck squamous cell carcinoma, controls</td><td>20</td><td>0.9 (0.3)</td><td>1 (0.1)</td><td>0.8 (0.3)</td></tr>
<tr><td>Patients with</td><td></td><td>Mean TTO utility (SD; 95% CI)</td><td>Mean TTO utility (SD), males</td><td>Mean TTO utility (SD), females</td></tr>
<tr><td>anal cancer</td><td></td><td>0.5 (0.26; 0.4-0.61)</td><td>0.48 (0.24)</td><td>0.54 (0.31)</td></tr>
<tr><td>anal cancer, controls</td><td></td><td>0.52 (0.25; 0.36-0.67)</td><td></td><td></td></tr>
<tr><td>head and neck squamous cell carcinoma</td><td></td><td>0.69 (0.3; 0.62-0.75)</td><td>0.7 (0.32)</td><td>0.64 (0.21)</td></tr>
<tr><td>head and neck squamous cell carcinoma, controls</td><td></td><td>0.59 (0.3; 0.46-0.72)</td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>15</td><td>Conway, 2012; Anal, oropharyngeal, vaginal, vulvar, penile, Australia [61]; SG; 99 general population participants (54% male) given SG scenarios of HPV-associated cancer health states, focusing on longer term health states, starting after the initial treatment effects had resolved to 5 years after diagnosis. Since morbidity of longer term health states is related to treatment modality, health state descriptions considered most common cancer stages at diagnosis, recommended treatment for relevant cancer stages, and common long-term consequences; Funded by CSL Biotherapies, a subsidiary of CSL Limited, which is a financial beneficiary of sales of Gardasil and Cervarix; CSL Biotherapies distributes Gardasil in Australia and New Zealand</td><td>
<table>
<tr><th>Scenario</th><th>N</th><th>Mean (95% CI)</th><th>Median (IQR)</th></tr>
<tr><td>Anal cancer</td><td>95</td><td>0.57 (0.52 to 0.62)</td><td>0.65 (0.45 to 0.75)</td></tr>
<tr><td>Oropharyngeal cancer</td><td>99</td><td>0.58 (0.53 to 0.63)</td><td>0.65 (0.45 to 0.75)</td></tr>
<tr><td>Vaginal cancer</td><td>98</td><td>0.59 (0.54 to 0.64)</td><td>0.65 (0.45 to 0.75)</td></tr>
<tr><td>Vulvar cancer</td><td>98</td><td>0.65 (0.60 to 0.70)</td><td>0.65 (0.45 to 0.85)</td></tr>
<tr><td>Penile cancer</td><td>97</td><td>0.79 (0.74 to 0.84)</td><td>0.85 (0.65 to 1.0)</td></tr>
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