

## Sexually Transmitted Infections

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

Journal:	<i>Sexually Transmitted Infections</i>
Manuscript ID	sextrans-2018-053606.R1
Article Type:	Review
Date Submitted by the Author:	n/a
Complete List of Authors:	Ong, Koh Jun; Public Health England, Centre for Infectious Disease Surveillance and Control Checchi, Marta; Public Health England, HIV & STI Department Burns, Lorna; University of Plymouth, Peninsula Schools of Medicine and Dentistry Pavitt, Charlotte; Public Health England Postma, Maarten; University of Groningen, Department of Pharmacy; University of Groningen, Department of Health Sciences Jit, Mark; PHE, Modelling and Economics Unit; London School of Hygiene & Tropical Medicine, ii. Department of Infectious Disease Epidemiology
Keywords:	HPV, VACCINATION, COST-EFFECTIVENESS, SYSTEMATIC REVIEWS, META-ANALYSIS

SCHOLARONE™  
Manuscripts

## ABSTRACT

### BACKGROUND

Many economic evaluations of human papillomavirus (HPV) vaccination consider multiple disease outcomes in addition to cervical cancer, including anogenital warts, recurrent respiratory papillomatosis, and anal, oropharyngeal, penile, vulvar and vaginal cancers. However, these evaluations mostly derive cost and utility parameters for these outcomes from single studies or informal rapid literature reviews.

### METHODS

We conducted a systematic review of articles up to June 2016 to identify costs and utility estimates admissible for an economic evaluation from a single-payer health care provider's perspective. Meta-analysis was performed for studies that used same utility elicitation tools for similar diseases. Costs were adjusted to 2016/17 US dollars.

### RESULTS

Sixty one papers (35 costs; 24 utilities; 2 costs and utilities) were selected from 10,742 initial records. Cost per case ranges were US\$124–US\$883 (anogenital warts), US\$6,912–US\$52,579 (head and neck cancers), US\$12,936–US\$51,571 (anal cancer), US\$17,524–34,258 (vaginal cancer), US\$14,686–28,502 (vulvar cancer), and US\$9,975–27,629 (penile cancer). Total cost for 14 adult RRP patients was US\$137,601 (1 paper).

Utility per warts episode ranged from 0.651–1 (12 papers, various utility elicitation methods), with pooled mean EQ-5D and EQ-VAS of 0.86 (95% CI 0.85–0.87) and 0.74 (95% CI 0.74–0.75), respectively. Fifteen papers reported utilities in head and neck cancers, with range across studies of 0.29 to 0.94. Mean utility reported ranged from 0.5 to 0.65 (anal cancer; range across studies), 0.59 (0.54–0.64) (vaginal cancer), 0.65 (0.60–0.70) (vulvar cancer), and 0.79 (0.74–0.84) (penile cancer).

## CONCLUSIONS

Differences in values reported from each paper reflect variations in cancer site, disease stages, study population, treatment modality/setting, and utility elicitation methods used. As patient management changes over time, corresponding effects on both costs and utility need to be considered to ensure health economic assumptions are up-to-date and closely reflect the case-mix of patients.

Confidential: For Review Only

**KEY MESSAGES**

- This systematic review identified 61 papers (35 costs; 24 utilities; 2 costs and utilities) reporting economic parameters for HPV-related non-cervical diseases.
- Differences in cost and utility estimates arise from study population, disease stage, cancer type, treatment strategies and country perspective taken.
- Authors of economic evaluations need to consider economic parameter assumptions to ensure they accurately reflect the timing and perspective of the population considered.

Confidential: For Review Only

## INTRODUCTION

Almost a hundred economic evaluations of human papillomavirus (HPV) vaccination had been published by June 2016[1–3]. Initially most of these analyses focused on the health and economic benefits of HPV vaccination in preventing cervical cancer and its precursors, since these were the only cancer outcomes listed in the initial licensure indication for the first two licensed HPV vaccines (the bivalent vaccine Cervarix and the quadrivalent vaccine Gardasil)[4,5]. More recently, evidence has emerged of other diseases that are potentially HPV vaccine-preventable, including recurrent respiratory papillomatosis (RRP) and non-cervical cancers such as vulvar, vaginal, anal, penile, and head and neck cancers[6,7]. Although attributable risk of HPV in each of these non-cervical cancers varies[7], these outcomes are important to incorporate into cost of illness studies of HPV-related diseases and economic evaluation of HPV vaccination for two reasons: (i) they give a comprehensive picture of the (direct and indirect) benefits of introducing HPV vaccination, and (ii) they are the key drivers of comparative evaluations of different strategies for vaccination, such as gender-neutral compared with female-only vaccination and the choice between nonavalent, quadrivalent and bivalent vaccination.

Economic evaluations require input parameters in terms of the costs and disutilities (measured in units such as quality adjusted life years or QALYs) for different disease outcomes. To our knowledge, most published economic evaluations to date have relied on data from the authors' own knowledge or from informal rapid reviews of the literature. Additionally, there exist a number of systematic reviews (without quantitative evidence synthesis) conducted before 2013 covering quality of life for specific diseases such as anogenital warts[8] and head and neck cancers[8–11] but none known of in more recent years covering a wider range of non-cervical HPV-related diseases on both costs and utilities. This gap in the literature may have led to bias in published economic evaluations because they may have failed to consider the entirety of the literature in their parameter estimates.

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

To address this shortcoming, we have conducted a systematic review to compile and summarise costs and quality of life (utility) estimates relevant to HPV-related diseases apart from cervical cancer. We have selected studies that would be admissible for an economic evaluation from the perspective of a single-payer health care provider such as the reference case used by the National Institute for Health and Care Excellence (NICE) in the United Kingdom[12].

Confidential: For Review Only

## METHODS

### Search Methods

A search of the databases Ovid Medline, Embase, Cinahl, Scopus and NHS Economic Evaluations Database was performed in June 2016. The search strategy combined terms for HPV-related diseases with health economics terms. HPV-related disease terms included both free text and, where available, subject headings for the following (ICD-10 codes in parentheses): anogenital warts – AGW (A63.0), recurrent respiratory papillomatosis – RRP (D14), cervical cancer (C53), vulvar cancer (C51), vaginal cancer (C52), anal cancer (C21), penile cancer (C60), oropharyngeal cancer (C09 and C10), oral cavity cancer (C01 to C05) – including cancer of the tonsil, laryngeal cancer (C32), and head and neck cancer as a general term included for completeness, recognising that not all head and neck cancers are HPV-attributed. Health economics terms included terms for health utilities/disutilities, costs, quality of life, quality of life instruments (e.g. EQ-5D) and measurement methods such as time-trade off (TTO) and standard gamble (SG). Results were limited to peer-reviewed full research articles in the English language only. Inclusion criteria covered all papers on HPV-related diseases costs and/or disutilities from high-income countries as defined by the Organisation for Economic Cooperation and Development, stated in Appendix 1[13].

Details of the full search strategies used are provided in Appendix 1.

### Result Screening

Screening was undertaken from September to December 2016. The initial 10,742 articles identified were independently single screened based on titles and abstracts to identify potentially relevant papers (KJO, MC, CP). Allocation decisions at this stage were done leniently, with titles that were uncertain marked for a further round of screening. The 2,785 references selected were entered into another round of single screening (KJO, MC, CP), whereby the results were reconsidered and categorised by type (cost or disutility) and disease area.

1  
2  
3 Although the objective of this systematic review focused on non-cervical diseases, for completeness,  
4 the search strategy and first two stages of single screening included cervical precancer/cancer.  
5  
6 Selected titles for cervical precancer/cancer can be made available to interested researchers.  
7  
8  
9

## 10 **Selection criteria**

11  
12  
13 Once titles from the second single screen had been identified, full-text papers were proportionately  
14 distributed to each reviewer (KJO, MC, CP) for the final round of paper selection and data extraction.  
15  
16 For HPV-related disease management costs we included only papers that took the perspective of a  
17 health care provider from a country with universal healthcare system (either Bismarck-type or  
18 Beveridge-type). For utility estimates, any paper that reported on quality of life loss that was  
19 reported on a scale from 0 to 1 and measured using either an indirect generic utility elicitation tool  
20 such as the EuroQol EQ-5D, or one of the primary/direct methods such as time-trade off or standard  
21 gamble were included. These criteria ensured that selected studies would be admissible for  
22 economic evaluations in most single-payer health care jurisdictions (eg. the NICE reference  
23 case[12]).  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34

## 35 **Data extraction**

36 A standard form to collect the data was created. Relevant data extracted from the papers are  
37 described in Appendix 2.  
38  
39

40  
41  
42 Data extraction was done by one reviewer and checked by a second reviewer, with discrepancies  
43 resolved through discussion.  
44  
45  
46

## 47 **Data synthesis**

48  
49 A descriptive comparison of data extracted from different papers was made. Costs were adjusted to  
50 2016/17 US dollars using the hospital and community health services inflation indices, with foreign  
51 currencies converted to US dollars using historical Bank of England average exchange rates for a  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3 reported year[14,15]. Quality of life values were presented separately for utility score and duration  
4  
5 of disutility, if reported in a paper.  
6

7  
8 Meta-analyses were conducted for AGW utility estimates for papers whereby utility estimates were  
9  
10 generated using standard utility elicitation instruments, such that outcomes measured were  
11  
12 comparable. Meta-analyses were not conducted for utility weights of non-AGW outcomes nor were  
13  
14 they conducted for any cost estimates, given higher heterogeneity in how costs were measured and  
15  
16 the specific disease type and stages considered.  
17

### 18 **Software**

19  
20  
21 References were collected in EndNote and transferred to Eppi-Reviewer 4 software (Thomas J,  
22  
23 Brunton J, Graziosi S, 2010) for screening. Final papers were captured in Mendeley Version 1.15.3.  
24  
25 Data extraction was collated in Microsoft Excel 2010. Meta-analysis was conducted in STATA13.  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**RESULTS**

The initial search strategy identified 10,742 records after deduplication. Screening based on titles and abstracts reduced these to 729 full-text papers that were reviewed. Of these, 61 papers were selected. A PRISMA flow diagram is presented in

Confidential: For Review Only

## FIGURE LEGEND

Figure 1.

### Costs

A total of 37 papers reported non-cervical HPV-related disease management costs[16–52], about half of which reported costs for AGWs[16–35]. Four papers reported costs for more than one disease[26,30,36,37]. Management costs from studies differed by country, disease stages or management settings used, and data collection method.

Figure 2 (Panel A) presents a summary of the various cost per case estimates, where presented, for AGWs. Estimated cost per case of AGW ranged from US\$124 per case in a patient seen for care in Canada[25] to US\$883 per case in Spain[34]. AGW management costs were derived from information collected from case note reviews (13 papers)[18–22,25,26,28,29,31–34], expert opinion (3 papers)[16,24,35], surveillance data (3 papers) [17,23,27] or the literature (1 paper) [30].

Cost per case reported for the various cancers is presented in Figure 2 (Panel B). Six papers reported management cost for anal cancers[30,36–40], but half of these were annual treatment costs[37,39,40] not cost per case. Cost per anal cancer case ranged from US\$12,936 (Italy[30]) to US\$51,571 (Denmark[36]). Twelve reported head and neck cancer treatment costs and differed depending on cancer site and stage[30,37,41–50], with costs ranging from US\$6,912 (Laryngeal cancer, T1 carcinoma, the Netherlands[48]) to US\$52,579 (weighted average costs for cancers of the oral cavity, larynx or oropharynx, the Netherlands[45]). There were four papers each that reported cost for vaginal[26,30,36,37], vulvar[26,30,36,37], and penile[30,36,37,51] cancers, with cost ranges of US\$17,524–34,258, US\$14,686–28,502, and US\$9,975–27,629, respectively. Six papers only presented total spend and/or annual spend for the non-cervical cancers[37,39,40,42,44,52], detailed findings are reported in Appendix 2.

1  
2  
3 One paper reported on total treatment cost covering 14 adult patients seen for RRP care at a clinic in  
4 Glasgow, Scotland, between January 2013 to April 2014 was reported at US\$137,601[52].  
5  
6  
7  
8  
9

## 10 Utilities

11  
12 A total of 25 papers on health-related quality of life were identified (full reference list in Appendix  
13 2)[19,20,53–75]. Two of these covered multiple diseases[53,75]. Fifteen papers covered head and  
14 neck cancers, including oral and laryngeal cancers[53,62–75], whilst another 12 papers reported on  
15 quality of life for AGWs[19,20,53–61,76].  
16  
17  
18  
19

20  
21  
22  
23 Utility per case of AGW ranged from 0.651–1, depending on the method of utility elicitation used.

24  
25 Utility values were generally higher when measured using EQ-5D, compared with Visual Analog Scale  
26 (VAS), TTO, or SG methods used within a single study. Full details of study background and findings  
27 are presented in Appendix 2. Meta-analyses of EQ-5D and EQ-VAS, from nine papers each, found  
28 high heterogeneity (I-squared >90%) in the utility values reported (Figure 3). Pooled mean EQ-5D  
29 and EQ-VAS were 0.86 (95% CI 0.85-0.87) and 0.74 (95% CI 0.74-0.75), respectively.  
30  
31  
32  
33  
34  
35

36  
37 Methods used to elicit utility for HPV-related cancers included EQ-5D, EQ-VAS, HUI3 (Health Utility  
38 Index Mark 3), TTO, SG, SF-36 (Short-Form 36), SF-6D (Short-Form Six-Dimension), and 15D. Utility  
39 estimates for head and neck cancers differed depending on the utility elicitation method used to  
40 generate utility scores, cancer site, patient age, the disease stage at point of completion of the  
41 quality of life questionnaire, and treatment modality. We present summary study details and key  
42 utility output presented in each of these 15 papers on quality of life for HPV-related cancers in Table  
43  
44  
45  
46  
47  
48  
49 1 with further details in Appendix 2.  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**TABLE****Table 1 Summary utility measurement and value ranges for HPV-related non-cervical cancers**

No.	Author, year	Cancer type; notes	Country	n	Utility elicitation instrument used; mean (unless otherwise specified) values and/or ranges reported
1	Aro, 2016[62]	Head and neck	Finland	214	15D; 0.872
2	Govers, 2016[63]	Oral; mean years after treatment range 1.9 (SD 1.4, range 0.4-4.1) to 5.2 (SD 3.2, range 0.4-11.0)	The Netherlands	174	EQ5D; range 0.794 (SE 0.04) to 0.863 (SE 0.05) EQVAS; range 69.7 (SE 3.7) to 79.6 (SE 4.8)
3	Pickard, 2016[64]	Head and neck	US	50	EQ5D; 0.828 EQVAS; 60.8
4	Rettig, 2016[65]	Head and neck; sites include larynx, oral cavity, oropharynx, hypopharynx, nasopharynx,	US	1653	SF6D; range 83.7 (95% CI 82.0, 85.4) to 88.0 (95% CI 86.2, 89.7)

		and nasal cavity/paranasal sinuses			
5	Kent, 2015[66]	Oral cavity and pharynx	US		SF6D; 0.69 (95% CI 0.68, 0.70)
6	Loimu, 2015[67]	Head and neck	Finland	64	15D; range 0.829 (0.12) to 0.886 (0.10)
7	Noel, 2015[68]	Head and neck	Canada		EQ5D; 0.82 (SD 0.18, range -0.07-1.0) EQVAS; 0.76 (SD 0.19, range 0.2-1.0) SG; 0.91 (SD 0.17, range 0.2-1.0) TTO; 0.94 (SD 0.14, range 0.3-1.0) HUI3; 0.75 (SD 0.25, range -0.06-1.0)
8	Pottel, 2015[69]	Head and neck	Belgium	81	EQ5D; median (Q1, Q3) range 0.29 (0.0, 0.76) to 0.66 (0.55, 0.76)
9	Lango, 2014[70]	Head and neck	US	159	EQ5D; median 85 (IQR: 70-90)
10	Nijdam, 2008[71]	Head and neck	The Netherlands	119	EQ5D; median 75
11	Rogers, 2006[72]	Head and neck	UK		EQ5D; 0.75 (SE 0.02; range -0.18 - 1.0) EQVAS; 74 (SE 1)
12	Ringash, 2000[73]	Laryngeal	Canada	84	TTO; 0.878 (SD 0.174; range 0.25 - 1)
13	Downer, 1997[74]	Oral	UK	100	SG; range 0.68 (SD 0.33) to 0.88 (SD 0.20)
14	Marcellusi,	Anal	Italy	26	EQ5D; 0.6 (SD 0.3)

	2015[53]				TTO; range 0.5 (SD 0.26; 95% CI 0.4-0.61) to 0.52 (SD 0.25; 95% CI 0.36-0.67)
		Head and neck; squamous cell carcinoma	Italy	79	EQ5D; 0.8 (SD 0.2) TTO; range 0.69 (SD 0.3; 95% CI 0.62-0.75) to 0.59 (SD 0.3; 95% CI 0.46-0.72)
15	Conway, 2012[75]	Anal	Australia	95	SG; 0.57 (95% CI 0.52 - 0.62); median 0.65 (IQR 0.45 - 0.75)
		Oropharyngeal	Australia	99	SG; 0.58 (95% CI 0.53 - 0.63); median 0.65 (IQR 0.45 - 0.75)
		Vaginal	Australia	98	SG; 0.59 (0.54 - 0.64); median 0.65 (IQR 0.45 - 0.75)
		Vulvar	Australia	98	SG; 0.65 (0.60 - 0.70); median 0.65 (IQR 0.45 - 0.85)
		Penile	Australia	97	SG; 0.79 (0.74 - 0.84); median 0.85 (IQR 0.65 - 1.0)

## DISCUSSION

### Statement of principal findings

This systematic review provides an updated and comprehensive summary of the cost and utility evidence for non-cervical HPV-related diseases that can be used in economic evaluations conducted from the perspective of a national health care provider. There appeared to be high heterogeneity in the papers identified, in terms of disease stages, population studied, treatment modality and setting, as well as utility elicitation methods used. The EuroQoL EQ-5D or EQ-VAS was commonly used in AGWs and in at least half of the non-cervical cancers studies.

Whilst the evidence in terms of both costs and utility values appear to be abundant for AGWs, it is less so for other cancers. This may reflect the fact that protection against AGWs is one of the main differentiating factors between the two competing HPV vaccines (quadrivalent and bivalent) on the market until licensure of the nonavalent vaccine in 2015, with several published economic evaluations focusing on the difference in cost-effectiveness between the two vaccines[77].

### Strengths and weaknesses of the study

Many papers did not report a single overall cost or utility estimate for a disease episode. Instead, they reported cost or utility values at different stages of the disease, which means that to obtain a single overall figure over entire disease episode, further details about patient case mix and changes in utility over time are needed. This includes a combination of treatment received at different stages of disease. For example, Kim *et al.*, 2011, reported post-operative management cost for a selective group of head and neck cancer patients who had received surgical resection[43].

In addition, treatment modalities are likely to change over time, with corresponding effects on both treatment costs and quality of life (due to changes in recovery time and patient experience). This



1  
2  
3 means that applying the same methodology to the same group of patients but managed differently  
4  
5 will likely return different costs and utility estimates.  
6  
7

8 The NICE-recommended utility elicitation method is EQ-5D completed by patients and scored using  
9  
10 population norms. This type of evidence is not always available. When alternative utility elicitation  
11  
12 methods are used, such as direct utility elicitation methods, their score can be quite different, as  
13  
14 demonstrated by Noel *et al.*, 2015[68]. In their study, patients with upper aerodigestive tract cancer  
15  
16 completed five direct/indirect utility measures (EQ-5D, VAS, HUI3, standard gamble, and time trade-  
17  
18 off). The authors found that direct utility elicitation methods (SG and TTO) returned higher utility  
19  
20 scores, possibly due to patients being more risk-averse. When the SG method was used in another  
21  
22 study (Conway *et al.*, 2012[75]) completed by general population, the utility score for oropharyngeal  
23  
24 cancers was lower than head and neck cancers scored using SG in Noel *et al.*, 2015[68], although this  
25  
26 could be due to the scenario descriptions used.  
27  
28

### 29 30 **Meaning of the study: possible mechanisms and implications for clinicians or** 31 32 **policymakers** 33

34  
35 This systematic review highlights the importance of understanding the data source used in economic  
36  
37 evaluation, ensuring that health economic assumptions are up-to-date and closely reflect the case-  
38  
39 mix of patients considered in the analysis.  
40  
41

### 42 43 **Unanswered questions and future research** 44

45  
46 During the paper screening and evaluation of eligibility stage, many papers on head and neck  
47  
48 cancers were identified but they often used SF-36 generic utility measures and reported two  
49  
50 summary scores covering physical and mental domains separately. Only four studies[56,59,65,66]  
51  
52 reported a single summary score and were included. To be most applicable to economic evaluations,  
53  
54 mapping exercises are needed to convert SF-36 values to single SF-6D scores specific to a country's  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

population. Future analyses could consider extracting findings from relevant papers and converting to SF-6D scores, especially for diseases with insufficient utility estimates evidence.

Future research can also focus on identifying the duration of disutility to be applied to a disease, since quality of life changes over time, and is an important component of the QALY calculations.

Confidential: For Review Only

## REFERENCES

- 1 Fesenfeld M, Hutubessy R, Jit M. Cost-effectiveness of human papillomavirus vaccination in low and middle income countries : A systematic review. *Vaccine* 2013;**31**:3786–804. doi:10.1016/j.vaccine.2013.06.060
- 2 Marra F, Cloutier K, Oteng B, *et al.* Effectiveness and Cost Effectiveness of Human Papillomavirus Vaccine A Systematic Review. 2009;**27**:127–47.
- 3 Seto K, Marra F, Raymakers A, *et al.* The cost effectiveness of human papillomavirus vaccines: a systematic review. *Drugs* 2012;**72**:715–43. doi:10.2165/11599470-000000000-00000
- 4 Baylor N. October 16, 2009 Approval Letter - Cervarix. *Vaccines, Blood Biol.* 2009.
- 5 Baylor N. June 8, 2006 Approval Letter - Human Papillomavirus Quadrivalent (Types 6, 11, 16, 18) Vaccine, Recombinant. *Vaccines, Blood Biol.* 2006.
- 6 Plummer M, de Martel C, Vignat J, *et al.* Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Glob Heal* 2016;**4**:e609–16.[http://dx.doi.org/10.1016/S2214-109X\(16\)30143-7](http://dx.doi.org/10.1016/S2214-109X(16)30143-7)
- 7 International Agency for Research on Cancer. A Review of Human Carcinogens. Part B: Biological agents / IARC Working Group on the Evaluation of Carginogenic Risks to Humans. Lyon, France: : International Agency for Research on Cancer 2012.  
<http://monographs.iarc.fr/ENG/Monographs/vol100B/>
- 8 Scarbrough Lefebvre C, Krieking G Van, Gonc MA, *et al.* Appraisal of the burden of genital warts from a healthcare and individual patient perspective. *Public Health*

- 1  
2  
3 2011;;464–75. doi:10.1016/j.puhe.2011.01.016  
4  
5  
6 9 Rathod S, Livergant J, Klein J, *et al.* A systematic review of quality of life in head and  
7  
8 neck cancer treated with surgery with or without adjuvant treatment. *Oral Oncol*  
9  
10 2015;**51**:888–900. doi:10.1016/j.oraloncology.2015.07.002  
11  
12  
13  
14 10 Rogers SN, Ahad S, Murphy A. A structured review and theme analysis of papers  
15  
16 published on ‘ quality of life ’ in head and neck cancer : 2000 – 2005. *Oral Oncol*  
17  
18 2007;;843–68. doi:10.1016/j.oraloncology.2007.02.006  
19  
20  
21  
22 11 So WKW, Chan RJ, Chan DNS, *et al.* Quality-of-life among head and neck cancer  
23  
24 survivors at one year after treatment – A systematic review. 2012;;2391–408.  
25  
26 doi:10.1016/j.ejca.2012.04.005  
27  
28  
29  
30 12 National Institute for Health and Care Excellence. Guide to the methods of technology  
31  
32 appraisal 2013. London, United Kingdom: 2013.  
33  
34  
35 13 Organisation for Economic Co-operation and Development. Country Classification  
36  
37 2011. 2011;;14.  
38  
39  
40  
41 14 Curtis L, Burns A. *Unit Costs of Health & Social Care*. Kent, United Kingdom: : Personal  
42  
43 Social Services Research Unit 2016. [http://www.pssru.ac.uk/project-pages/unit-](http://www.pssru.ac.uk/project-pages/unit-costs/2016/)  
44  
45 [costs/2016/](http://www.pssru.ac.uk/project-pages/unit-costs/2016/)  
46  
47  
48 15 Bank of England. Bank of England daily spot exchange rate against Sterling. Bank’s  
49  
50 Publ. Scheme. 2015.<http://www.bankofengland.co.uk/boeapps/iadb/Rates.asp>  
51  
52  
53  
54 16 Coles VAH, Chapman R, Lanitis T, *et al.* The costs of managing genital warts in the UK  
55  
56 by devolved nation: England, Scotland, Wales and Northern Ireland. *Int J STD AIDS*  
57  
58  
59  
60

- 2016;**27**:51–7. doi:10.1177/0956462415573121
- 17 Lanitis T, Carroll S, O’Mahony C, *et al.* The cost of managing genital warts in the UK. *Int J STD AIDS* 2012;**23**:189–94. doi:10.1258/ijsa.2011.011218
- 18 Desai S, Wetten S, Woodhall SC, *et al.* Genital warts and cost of care in England. *Sex Transm Infect* 2011;**87**:464–8. doi:10.1136/sti.2010.048421
- 19 Woodhall SC, Jit M, Soldan K, *et al.* The impact of genital warts: loss of quality of life and cost of treatment in eight sexual health clinics in the UK. *Sex Transm Infect* 2011;**87**:458–63. doi:10.1136/sextrans-2011-050073
- 20 Woodhall SC, Jit M, Cai C, *et al.* Cost of treatment and QALYs lost due to genital warts: Data for the economic evaluation of HPV vaccines in the United Kingdom. *Sex Transm Dis* 2009;**36**:515–21. doi:10.1097/OLQ.0b013e3181a74c2c
- 21 Brown RE, Breugelmans JG, Theodoratou D, *et al.* Costs of detection and treatment of cervical cancer, cervical dysplasia and genital warts in the UK. *Curr Med Res Opin* 2006;**22**:663–70. doi:10.1185/030079906X99972
- 22 Langley PC, White DJ, Drake SM. The costs of treating external genital warts in England and Wales : a treatment pattern analysis. *Int J STD AIDS* 2004;**15**:501–8.
- 23 Pirotta M, Stein AN, Conway EL, *et al.* Genital warts incidence and healthcare resource utilisation in Australia. *Sex Transm Infect* 2010;**86**:181–6. doi:10.1136/sti.2009.040188
- 24 Annemans L, Rémy V, Lamure E, *et al.* Economic burden associated with the management of cervical cancer, cervical dysplasia and genital warts in Belgium. *J Med*

- 1  
2  
3 *Econ* 2008;**11**:135–50. doi:10.3111/13696990801961611  
4  
5  
6 25 Marra F, Ogilvie G, Colley L, *et al.* Epidemiology and costs associated with genital  
7  
8 warts in Canada. *Sex Transm Infect* 2009;**85**:111–5. doi:10.1136/sti.2008.030999  
9  
10  
11 26 Salo H, Leino T, Kilpi T, *et al.* The burden and costs of prevention and management of  
12  
13 genital disease caused by HPV in women: A population-based registry study in  
14  
15 Finland. *Int J Cancer* 2013;**133**:1459–69. doi:10.1002/ijc.28145  
16  
17  
18  
19 27 Herse F, Reissell E. The annual costs associated with human papillomavirus types 6,  
20  
21 11, 16, and 18 infections in Finland. *Scand J Infect Dis* 2011;**43**:209–15.  
22  
23 doi:10.3109/00365548.2010.541492  
24  
25  
26  
27 28 Hillemanns P, Breugelmans JG, Giesecking F, *et al.* Estimation of the incidence of  
28  
29 genital warts and the cost of illness in Germany: A cross-sectional study. *BMC Infect*  
30  
31 *Dis* 2008;**8**:1–10. doi:10.1186/1471-2334-8-76  
32  
33  
34  
35 29 Gianino MM, Delmonte S, Lovato E, *et al.* A retrospective analysis of the costs and  
36  
37 management of genital warts in Italy. *BMC Infect Dis* 2013;**13**:1–9. doi:10.1186/1471-  
38  
39 2334-13-470  
40  
41  
42  
43 30 Baio G, Capone A, Marcellusi A, *et al.* Economic Burden of Human Papillomavirus-  
44  
45 Related Diseases in Italy. *PLoS One* 2012;**7**. doi:10.1371/journal.pone.0049699  
46  
47  
48  
49 31 Merito M, LARGERON N, Cohet C, *et al.* Treatment patterns and associated costs for  
50  
51 genital warts in Italy. *Curr Med Res Opin* 2008;**24**:3175–83.  
52  
53 doi:10.1185/03007990802485694  
54  
55  
56 32 Dee A, Howell F, O'Connor C, *et al.* Determining the cost of genital warts: A study  
57  
58  
59  
60

- 1  
2  
3 from Ireland. *Sex Transm Infect* 2009;**85**:402–3. doi:10.1136/sti.2008.033837  
4  
5
- 6 33 Meijden WI Van Der, Notowicz A, Blog FB, *et al.* A Retrospective Analysis of Costs and  
7  
8 Patterns of Treatment for External Genital Warts in the Netherlands. 2002;**24**:183–96.  
9
- 10  
11 34 Castellsague X, Cohet C, Puig-tintore LM, *et al.* Epidemiology and cost of treatment of  
12  
13 genital warts in Spain. *Eur J Public Health* 2008;**19**:106–10.  
14  
15 doi:10.1093/eurpub/ckn127  
16  
17
- 18  
19 35 Östensson E, Fröberg M, Leval A, *et al.* Cost of Preventing, Managing, and Treating  
20  
21 Human Papillomavirus (HPV)-Related Diseases in Sweden before the Introduction of  
22  
23 Quadrivalent HPV Vaccination. *PLoS One* 2015;:1–15.  
24  
25 doi:10.1371/journal.pone.0139062  
26  
27
- 28  
29 36 Olsen J, Jørgensen TR, Kofoed K, *et al.* Incidence and cost of anal , penile , vaginal and  
30  
31 vulvar cancer in Denmark. Published Online First: 2012. doi:10.1186/1471-2458-12-  
32  
33 1082  
34  
35
- 36  
37 37 Borget I, Abramowitz L, Mathevet P. Economic burden of HPV-related cancers in  
38  
39 France. *Vaccine* 2011;**29**:5245–9. doi:10.1016/j.vaccine.2011.05.018  
40  
41
- 42  
43 38 Keeping ST, Tempest MJ, Stephens SJ, *et al.* The cost of anal cancer in England:  
44  
45 retrospective hospital data analysis and Markov model. *BMC Public Health*  
46  
47 2014;**14**:1123. doi:10.1186/1471-2458-14-1123  
48  
49
- 50  
51 39 Heitland W, Schadlich PK, Chen X, *et al.* Annual cost of hospitalization, inpatient  
52  
53 rehabilitation and sick leave of anal cancer in Germany. *J Med Econ* 2013;**16**:364–71.  
54  
55 doi:10.3111/13696998.2012.759582  
56  
57

- 1  
2  
3 40 Abramowitz L, Remy V, Vainchtock A. Economic burden of anal cancer management  
4  
5 in France. *Rev Epidemiol Sante Publique* 2010;**58**:331–8.  
6  
7  
8 41 van der Linden N, Buter J, Pescott CP, *et al.* Treatments and costs for recurrent and/or  
9  
10 metastatic squamous cell carcinoma of the head and neck in the Netherlands. *Head*  
11  
12 *Neck* 2016;**273**:455–64. doi:10.1007/s00405-015-3495-y  
13  
14  
15  
16 42 Klusmann JP, Schädlich PK, Chen X, *et al.* Annual cost of hospitalization , inpatient  
17  
18 rehabilitation , and sick leave for head and neck cancers in Germany. *Clin Outcomes*  
19  
20 *Res* 2013;**5**:203–13.  
21  
22  
23  
24 43 Kim K, Amonkar MM, Högberg D, *et al.* Economic burden of resected squamous cell  
25  
26 carcinoma of the head and neck in an incident cohort of patients in the UK. *Head*  
27  
28 *Neck Oncol* 2011;**3**:1–10.  
29  
30  
31 44 St Guily JL, Borget I, Vainchtock A, *et al.* Head and neck cancers in France : an analysis  
32  
33 of the hospital medical information system ( PMSI ) database. *Head Neck Oncol*  
34  
35 2010;**2**:1–8.  
36  
37  
38  
39 45 Agthoven M Van, Ineveld BM Van, Boer MF De, *et al.* The costs of head and neck  
40  
41 oncology : primary tumours , recurrent tumours and long-term follow-up. *Eur J*  
42  
43 *Cancer* 2001;**37**:2204–11.  
44  
45  
46  
47 46 Corbridge R, Cox G. The cost of running a multidisciplinary head and neck oncology  
48  
49 service - an audit. *Rev Laryngol Otol Rhinol* 2000;**121**:151–3.  
50  
51  
52 47 Lowry J. Maxillofacial surgery: the economic aspect. *Br J Oral Maxillofac Surg*  
53  
54 1990;**28**:16–9.  
55  
56  
57  
58  
59  
60



- 1  
2  
3 48 van Agthoven M, Heule-Dieleman H, Knegt P, *et al.* Compliance and efficiency before  
4 and after implementation of a clinical practice guideline for laryngeal carcinomas. *Eur*  
5  
6 *Arch Otorhinolaryngol* 2006;**263**:729–37. doi:10.1007/s00405-006-0062-6  
7  
8  
9  
10 49 Zavras A, Andreopoulos N, Katsikeris N, *et al.* Oral cancer treatment costs in Greece  
11 and the effect of advanced disease. *BMC Public Health* 2002;**8**:8–15.  
12  
13  
14  
15 50 Preuss S, Quante G, Semrau R, *et al.* An analysis of surgical complications, morbidity,  
16 and cost calculation in patients undergoing multimodal treatment for operable  
17 oropharyngeal carcinoma. *Laryngoscope* 2007;**117**:101–5.  
18  
19  
20  
21  
22  
23 51 Keeping ST, Tempest MJ, Stephens SJ, *et al.* Penile cancer treatment costs in England.  
24 *BMC Public Health* 2015;**15**:1305. doi:10.1186/s12889-015-2669-2  
25  
26  
27  
28 52 Harrison A, Montgomery J, Macgregor FB. Economic impact of recurrent respiratory  
29 papillomas in a UK adult population. *J Laryngol Otol* 2016;**130**:645–9.  
30  
31  
32  
33  
34  
35  
36  
37 53 Marcellusi A, Capone A, Favato G, *et al.* Health utilities lost and risk factors associated  
38 with HPV-induced diseases in men and women: The HPV Italian collaborative study  
39 group. *Clin Ther* 2015;**37**:156–67. doi:10.1016/j.clinthera.2014.11.002  
40  
41  
42  
43  
44 54 Vriend HJ, Nieuwkerk PT, Sande MAB Van Der. Impact of genital warts on emotional  
45 and sexual well-being differs by gender. *Int J STD AIDS* 2014;**25**:949–55.  
46  
47  
48  
49  
50  
51  
52 55 Dominiak-Felden G, Cohet C, Atrux-Tallau S, *et al.* Impact of human papillomavirus-  
53 related genital diseases on quality of life and psychosocial wellbeing: results of an  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 observational, health-related quality of life study in the UK. *BMC Public Health*  
4  
5 2013;**13**:1065. doi:10.1186/1471-2458-13-1065  
6  
7
- 8 56 Drolet M, Brisson M, Maunsell E, *et al.* The Impact of Anogenital Warts on Health-  
9  
10 Related Quality of Life : A 6-Month Prospective Study. *Sex Transm Dis* 2011;**38**:949–  
11  
12 56. doi:10.1097/OLQ.0b013e3182215512  
13  
14
- 15  
16 57 Mennini FS, Panatto D, Marcellusi A, *et al.* Time trade-off procedure for measuring  
17  
18 health utilities loss with human papillomavirus-induced diseases: A multicenter,  
19  
20 retrospective, observational pilot study in Italy. *Clin Ther* 2011;**33**:1084–95.e4.  
21  
22 doi:10.1016/j.clinthera.2011.06.012  
23  
24
- 25  
26 58 Senecal M, Brisson M, Maunsell E, *et al.* Loss of quality of life associated with genital  
27  
28 warts : baseline analyses from a prospective study. *Sex Transm Infect* 2011;**87**:209–  
29  
30 15. doi:10.1136/sti.2009.039982  
31  
32
- 33  
34 59 Marra C, Ogilvie G, Gastonguay L, *et al.* Patients With Genital Warts Have a Decreased  
35  
36 Quality of Life. *Sex Transm Dis* 2009;**36**:258–60. doi:10.1097/OLQ.0b013e318191a55e  
37  
38
- 39  
40 60 Pirotta M, Ung L, Stein A, *et al.* The psychosocial burden of human papillomavirus  
41  
42 related disease and screening interventions. *Sex Transm Infect* 2009;**85**:508–13.  
43  
44 doi:10.1136/sti.2009.037028  
45  
46
- 47  
48 61 Woodhall S, Ramsey T, Cai C, *et al.* Estimation of the impact of genital warts on  
49  
50 health- related quality of life. *Sex Transm Infect* 2008;**84**:161–6.  
51  
52 doi:10.1136/sti.2007.029512  
53  
54
- 55  
56 62 Aro K, Back L, Loimu V, *et al.* Trends in the 15D health-related quality of life over the  
57  
58  
59  
60

- 1  
2  
3 first year following diagnosis of head and neck cancer. *Eur Arch Otorhinolaryngol*  
4  
5 2016;**273**:2141–50. doi:10.1007/s00405-015-3732-4  
6  
7
- 8 63 Govers T, Schreuder W, Klop W, *et al.* Quality of life after different procedures for  
9  
10 regional control in oral cancer patients: cross-sectional survey. *Clin Otolaryngol*  
11  
12 2016;**41**:228–33.  
13  
14
- 15 64 Pickard AS, Jiang R, Lin H, *et al.* Using Patient-reported Outcomes to Compare  
16  
17 Relative Burden of Cancer : EQ-5D and Functional Assessment of Cancer Therapy-  
18  
19 General in Eleven Types of Cancer. *Clin Ther* 2016;**38**:769–77.  
20  
21 doi:10.1016/j.clinthera.2016.03.009  
22  
23
- 24 65 Rettig E, D’Souza G, Thompson C, *et al.* Health-Related Quality of Life Before and  
25  
26 After Head and Neck Squamous Cell Carcinoma : Analysis of the Surveillance ,  
27  
28 Epidemiology , and End Results – Medicare Health Outcomes Survey Linkage. *Cancer*  
29  
30 2016;**122**:1861–70. doi:10.1002/cncr.30005  
31  
32
- 33 66 Kent E, Ambs A, Mitchell S, *et al.* Health-related quality of life in older adult survivors  
34  
35 of selected cancers: data from the SEER-MHOS linked data resource. *Cancer*  
36  
37 2015;**121**:758–65. doi:10.1002/cncr.29119.  
38  
39
- 40 67 Loimu V, Makitie A, Back L, *et al.* Health-related quality of life of head and neck  
41  
42 cancer patients with successful oncological treatment. *Eur Arch Otorhinolaryngol*  
43  
44 2015;**272**:2415–23. doi:10.1007/s00405-014-3169-1  
45  
46  
47  
48  
49
- 50 68 Noel C, Lee D, Kong Q, *et al.* Comparison of Health State Utility Measures in Patients  
51  
52 with Head and Neck Cancer. *JAMA Otolaryngol Head Neck Surg* 2015;**141**:696–703.  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 69 Pottel L, Lycke M, Boterberg T, *et al.* G-8 indicates overall and quality-adjusted  
4 survival in older head and neck cancer patients treated with curative  
5 radiochemotherapy. *BMC Cancer* 2015;**15**:1–11. doi:10.1186/s12885-015-1800-1  
6  
7  
8  
9  
10 70 Lango MN, Egleston B, Fang C, *et al.* Baseline Health Perceptions , Dysphagia , and  
11 Survival in Patients With Head and Neck Cancer. *Cancer* 2014;**120**:840–7.  
12 doi:10.1002/cncr.28482  
13  
14  
15  
16  
17  
18 71 Nijdam WM, Levendag PC, Noever I, *et al.* Longitudinal changes in quality of life and  
19 costs in long-term survivors of tumors of the oropharynx treated with brachytherapy  
20 or surgery. *Brachytherapy* 2008;**7**:343–50. doi:10.1016/j.brachy.2008.05.001  
21  
22  
23  
24  
25  
26 72 Rogers SN, Miller RD, Ali K, *et al.* Patients' perceived health status following primary  
27 surgery for oral and oropharyngeal cancer. *Int J Oral Maxillofac Surg* 2006;**35**:913–9.  
28 doi:10.1016/j.ijom.2006.07.017  
29  
30  
31  
32  
33  
34 73 Ringash J, Redelmeier D, O'Sullivan B, *et al.* Quality of life and utility in irradiated  
35 laryngeal cancer patients. *Int J Radiat Oncol Biol Phys* 2000;**47**:875–81.  
36  
37  
38  
39 74 Downer M, Jullien J, Speight P. An interim determination of health gain from oral  
40 cancer and precancer screening: 1. obtaining health state utilities. *Community Dent*  
41 *Health* 1997;**14**:139–42.  
42  
43  
44  
45  
46  
47 75 Conway EL, Farmer KC, Lynch WJ, *et al.* Quality of life valuations of HPV-associated  
48 cancer health states by the general population. *Sex Transm Infect* 2012;**88**:517–21.  
49 doi:10.1136/sextrans-2011-050161  
50  
51  
52  
53  
54  
55 76 Shi J, Kang D, Qi S, *et al.* Impact of genital warts on health related quality of life in  
56  
57  
58  
59  
60

1  
2  
3 men and women in mainland China : a multicenter hospital-based cross-sectional  
4  
5 study. *BMC Public Health* 2012;**12**. doi:10.1186/1471-2458-12-153  
6  
7

- 8 77 Suijkerbuijk A, Donken R, Lugnér A, *et al*. The whole story: a systematic review of  
9  
10 economic evaluations of HPV vaccination including non-cervical HPV-associated  
11  
12 diseases. *Expert Rev Vaccines* 2017;**16**:361–75. doi:10.1080/14760584.2017.1256778  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

**FIGURE LEGEND**

**Figure 1 PRISMA flow diagram**

Confidential: For Review Only

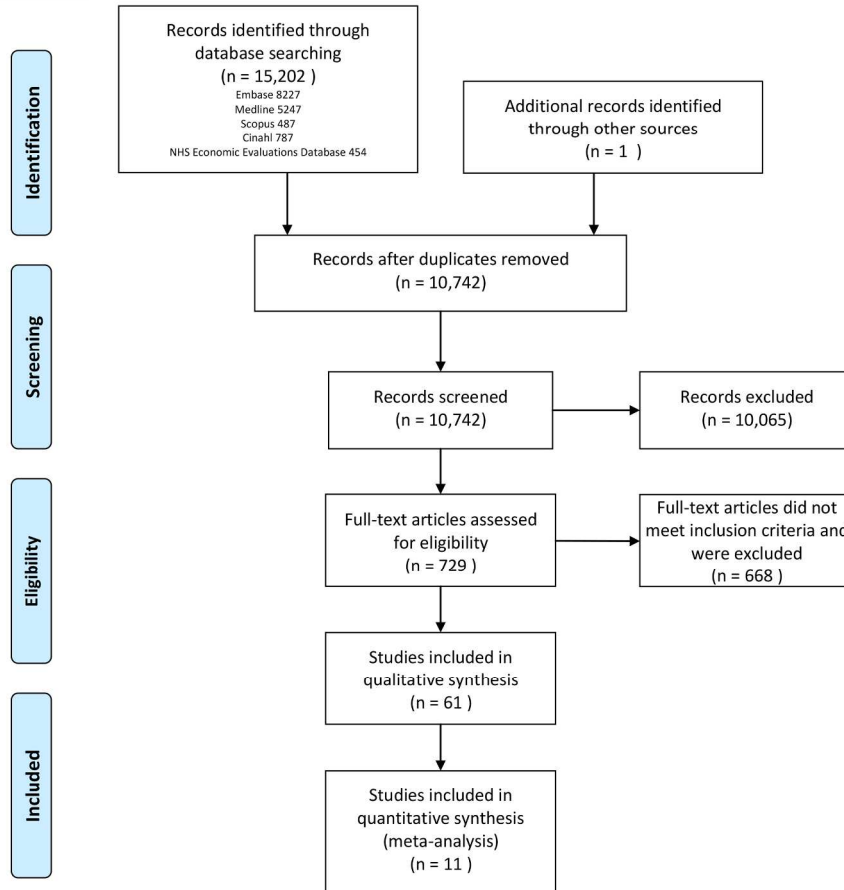
1  
2  
3 **Figure 2 Disease management costs reported in selected papers. Panel A**  
4 **outlines costs reported for anogenital warts (AGWs). Panel B contains an**  
5 **extraction of non-cervical cancer management costs; Panel A: Cost per case**  
6 **of AGWs management as reported in the relevant papers; Note that overall**  
7 **cost per patient is presented where this information is available, otherwise,**  
8 **cost per patient broken down by e.g. gender or new/recurrences presented**  
9 **and these are specified; Herse et al., 2011 not included as they presented**  
10 **minimum and maximum total cost of all patients, not per patient; Cost per**  
11 **patient for resistant cases reported in Hillemanns et al., 2008 not presented on**  
12 **this figure; Panel B: Cost per case of cancer management; Figure only**  
13 **presents cost per patient for their cancer management, excluding where only**  
14 **annual costs were reported or where total cost to the health care system was**  
15 **reported but not per patient cost; Note: H&N=Head and neck; Preuss, 2007,**  
16 **minimum and maximum costs reported for oropharyngeal carcinomas**  
17 **treatment with surgery and postoperative radio(chemo)therapy.**  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 **Figure 3 Forest plots of pooled mean (95% CI) of studies reporting AGW EQ-5D**  
4 **(Panel A) and EQ-VAS (Panel B) utility estimates; Panel A: Pooled AGW EQ-5D**  
5 **utility estimates; Panel B: Pooled AGW EQ-VAS utility estimates. Note: utility**  
6 **estimates for different subgroups within Vriend, 2014[54] and Drolet, 2011[56]**  
7 **were pooled together and the combined mean and 95% CI were subsequently**  
8 **added to utility estimates from the other studies to generate an overall pooled**  
9 **mean and 95% CI.**  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60





### PRISMA 2009 Flow Diagram



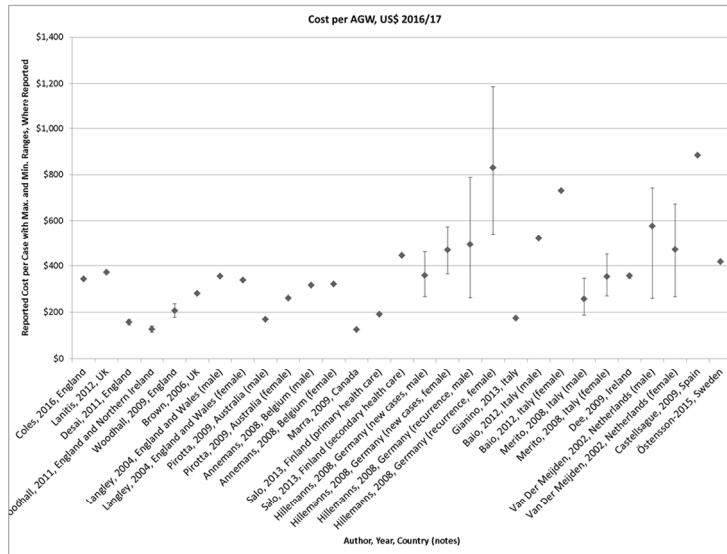
From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).

Figure 1 PRISMA flow diagram

185x248mm (300 x 300 DPI)

Panel A



Panel B

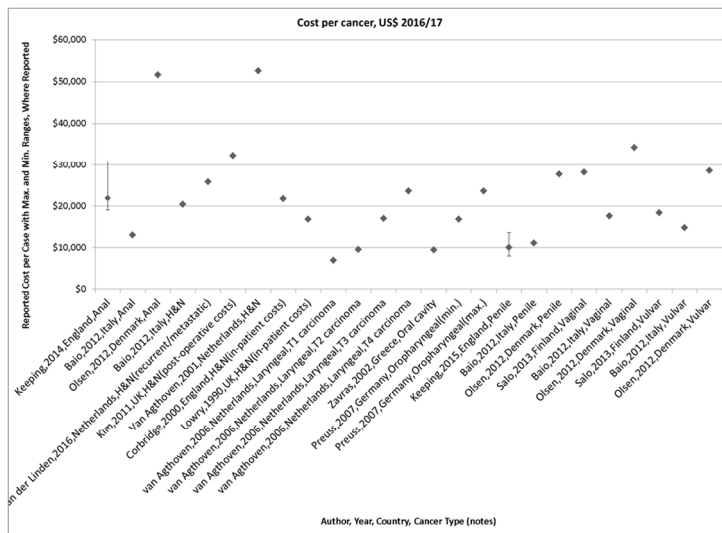


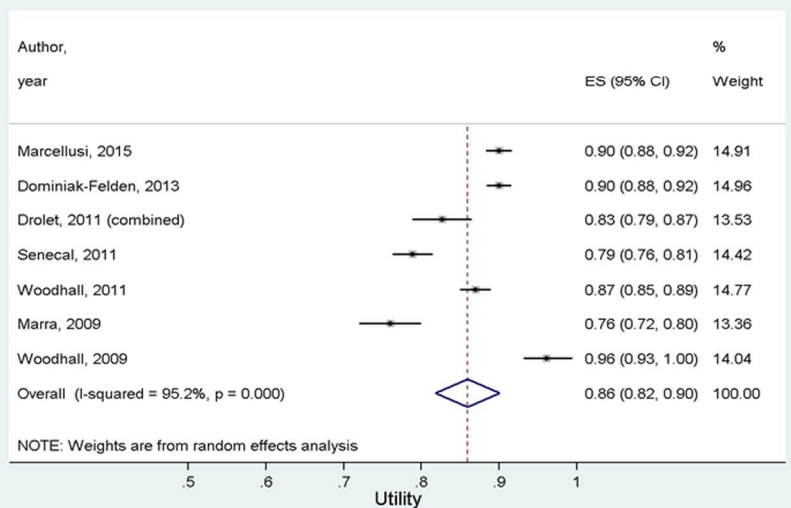
Figure 2 Disease management costs reported in selected papers. Panel A outlines costs reported for anogenital warts (AGWs). Panel B contains an extraction of non-cervical cancer management costs; Panel A: Cost per case of AGWs management as reported in the relevant papers; Note that overall cost per patient is presented where this information is available, otherwise, cost per patient broken down by e.g. gender or new/recurrences presented and these are specified; Herse et al., 2011 not included as they presented minimum and maximum total cost of all patients, not per patient; Cost per patient for resistant cases reported in Hillemanns et al., 2008 not presented on this figure; Panel B: Cost per case of cancer management; Figure only presents cost per patient for their cancer management, excluding where only annual costs were reported or where total cost to the health care system was reported but not per patient cost; Note: H&N=Head and neck; Preuss, 2007, minimum and maximum costs reported for oropharyngeal carcinomas treatment with surgery and postoperative radio(chemo)therapy.

259x419mm (300 x 300 DPI)

Confidential: For Review Only

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## Panel A



## Panel B

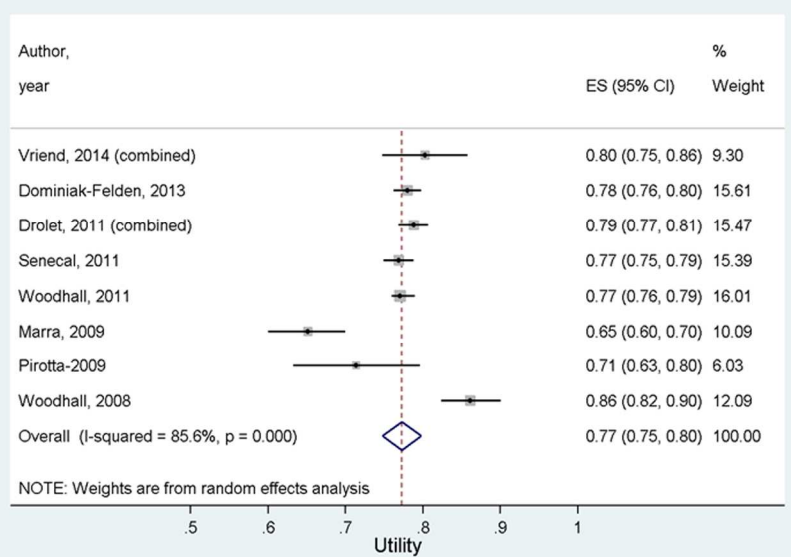


Figure 3 Forest plots of pooled mean (95% CI) of studies reporting AGW EQ-5D (Panel A) and EQ-VAS (Panel B) utility estimates; Panel A: Pooled AGW EQ-5D utility estimates; Panel B: Pooled AGW EQ-VAS utility estimates. Note: utility estimates for different subgroups within Vriend, 2014[54] and Drolet, 2011[56] were pooled together and the combined mean and 95% CI were subsequently added to utility estimates from the other studies to generate an overall pooled mean and 95% CI.

190x274mm (300 x 300 DPI)

## Appendix 1

**Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid  
MEDLINE(R) 1946 to Present**

- 1 Condylomata Acuminata/  
2 (anogenital adj3 (wart\* or polyp\*)).ab,ti.  
3 (genital adj3 (wart\* or polyp\*)).ab,ti.  
4 ((anal or anus) adj3 (wart\* or polyp\*)).ab,ti.  
5 "condyloma\* acuminat\*".ab,ti.  
6 "recurrent respiratory papilloma\*".ab,ti.  
7 RRP.ab,ti.  
8 Uterine Cervical Neoplasms/  
9 (cervi\* adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
10 adenocarcinom\*)).ab,ti.  
11 Vulvar Neoplasms/  
12 (vulva\* adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
13 adenocarcinom\*)).ab,ti.  
14 Vaginal Neoplasms/  
15 (vagina\* adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
16 adenocarcinom\*)).ab,ti.  
17 exp Anus Neoplasms/  
18 ((anal or anus) adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
19 adenocarcinom\*)).ab,ti.  
20 Penile Neoplasms/  
21 ((penile or penis) adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
22 adenocarcinom\*)).ab,ti.  
23 exp "Head and Neck Neoplasms"/  
24 ((oral\* or intra-oral\* or intraoral\* or "intra oral\*" or gingiva\* or orophary\* or mouth\* or tongue\* or tonsil\* or  
25 cheek\* or gum\* or palatal\* or palate\* or "head and neck") adj5 (cancer\* or neoplasm\* or malignan\* or

- 1  
2  
3 tumor\* or tumour\* or carcinom\* or adenocarcinom\*).ab,ti.  
4  
5  
6 ((larynx\* or pharynx\* or vocal cord\* or cordal or glott\* or throat or voice box or subglott\* or supraglott\*) adj5  
7 20 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*).ab,ti.  
8  
9  
10 21 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20  
11  
12 22 Quality-Adjusted Life Years/  
13  
14 23 Quality of Life/  
15  
16 24 "quality of life".ti,kw,kf.  
17  
18 25 (health utilit\* or utilit\* measure\* or utilit\* instrument\*).ab,ti.  
19  
20 26 "Disutilit\*".ab,ti.  
21  
22 27 (QALY\* or DALY\*).ab,ti.  
23  
24 28 (Quality adjusted life year\* or Disability adjusted life year\*).ab,ti.  
25  
26 29 (EQ-5D or EQ5D or EQ-5D-3L or EQ-5D-5L).ab,ti.  
27  
28 30 (SF-12 or SF12).ab,ti.  
29  
30 31 (SF-6D or SF6D).ab,ti.  
31  
32 32 (HUI or "H.U.I").ab,ti.  
33  
34 33 (SF-36 or SF36).ab,ti.  
35  
36 34 time trade off.ab,ti.  
37  
38 35 standard gamble.ab,ti.  
39  
40 41  
41 42 cost\*.ti,ab,kw,kf.  
42  
43  
44 37 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36  
45  
46 (America\* or Australia\* or Austria\* or Belgium or Belgian or Britain or British or Canad\* or Chile or Chilean  
47 or Czech or Denmark or Danish or Estonia\* or Finland or Finnish or France or French or German\* or  
48 Hungary or Hungarian or Iceland\* or Ireland or Irish or Italy or Italian or Japan\* or Korea\* or Luxembourg  
49 38 or Mexico or Mexican or Netherlands or Dutch or New Zealand\* or Norway or Norwegian or Poland or  
50 Polish or Portug\* or Slovak\* or Slovenia\* or Spain or Spanish or Sweden or Swedish or Switzerland or  
51 Swiss or Turkey or Turkish or United Kingdom or United States).ab,hw,in,kf,ti.  
52  
53  
54  
55 39 exp Great Britain/ or Europe/  
56  
57  
58  
59  
60

1  
2  
3  
4 40 (national health service\* or nhs\*).ab,hw,in,kf,ti.

5  
6 (english not ((published or publication\* or translat\* or written or language\* or speak\* or literature or  
7 41 citation\*) adj5 english)).ti,ab.

8  
9 (gb or "g.b." or britain\* or british or uk or "u.k." or united kingdom\* or england\* or ireland\* or irish\* or  
10 42 scotland\* or scottish\* or wales or welsh).ab,hw,in,kf,ti.

11  
12 (bath or "bath's" or birmingham or "birmingham's" or bradford or "bradford's" or brighton or "brighton's" or  
13 bristol or "bristol's" or carlisle\* or "carlisle's" or cambridge or "cambridge's" or canterbury or "canterbury's"  
14 or chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or  
15 "coventry's" or derby or "derby's" or durham or "durham's" or ely or "ely's" or exeter or "exeter's" or  
16 gloucester or "gloucester's" or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or  
17 leeds\* or leicester or "leicester's" or lincoln or "lincoln's" or liverpool or "liverpool's" or london or "london's"  
18 or manchester or "manchester's" or newcastle or "newcastle's" or norwich or "norwich's" or nottingham or  
19 "nottingham's" or oxford or "oxford's" or peterborough or "peterborough's" or plymouth or "plymouth's" or  
20 portsmouth or "portsmouth's" or preston or "preston's" or ripon or "ripon's" or salford or "salford's" or  
21 salisbury or "salisbury's" or sheffield or "sheffield's" or southampton or "southampton's" or st albans or  
22 stoke or "stoke's" or sunderland or "sunderland's" or truro or "truro's" or wakefield or "wakefield's" or wells  
23 or westminster or "westminster's" or winchester or "winchester's" or wolverhampton or "wolverhampton's"  
24 or worcester or "worcester's" or york or "york's").ab,hw,in,kf,ti.

25  
26 (bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st  
27 44 davids or swansea or "swansea's").ab,hw,in,kf,ti.

28  
29 (aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or  
30 45 "glasgow's" or inverness or perth or stirling or "stirling's").ab,hw,in,kf,ti.

31  
32 (armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or  
33 46 derry or "derry's" or newry or "newry's").ab,hw,in,kf,ti.

34  
35  
36 47 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46

37  
38  
39 48 21 and 37 and 47

40  
41 49 limit 48 to english language

42  
43 50 (case reports or clinical conference).pt.

44  
45  
46 51 49 not 50

## Ovid Embase 1974 to 2016 July 05

- 1  
2  
3  
4  
5 1 Condyloma Acuminatum/  
6  
7 2 (anogenital adj3 (wart\* or polyp\*)).ti,ab.  
8  
9 3 (genital adj3 (wart\* or polyp\*)).ti,ab.  
10  
11 4 ((anal or anus) adj3 (wart\* or polyp\*)).ti,ab.  
12  
13 5 "condyloma\* acuminat\*".ti,ab.  
14  
15 6 "recurrent respiratory papilloma\*".ti,ab.  
16  
17 7 RRP.ti,ab.  
18  
19 8 exp uterine cervix cancer/  
20  
21 (cervi\* adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
22  
23 9 adenocarcinom\*)).ti,ab.  
24  
25 10 exp vulva cancer/  
26  
27 (vulva\* adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
28  
29 11 adenocarcinom\*)).ti,ab.  
30  
31 12 exp vagina cancer/  
32  
33 (vagina\* adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
34  
35 13 adenocarcinom\*)).ti,ab.  
36  
37 14 exp anus cancer/  
38  
39 ((anal or anus) adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
40  
41 15 adenocarcinom\*)).ti,ab.  
42  
43 16 exp penis cancer/  
44  
45 ((penile or penis) adj5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or  
46  
47 17 adenocarcinom\*)).ti,ab.  
48  
49 18 exp "head and neck cancer"/  
50  
51 ((oral\* or intra-oral\* or intraoral\* or "intra oral\*" or gingiva\* or orophary\* or mouth\* or tongue\* or tonsil\* or  
52  
53 19 cheek\* or gum\* or palatal\* or palate\* or "head and neck") adj5 (cancer\* or neoplasm\* or malignan\* or  
54  
55 tumor\* or tumour\* or carcinom\* or adenocarcinom\*)).ti,ab.  
56  
57  
58  
59  
60



- 1  
2  
3  
4 20 exp larynx cancer/  
5  
6 ((larynx\* or pharynx\* or vocal cord\* or cordal or glott\* or throat or voice box or subglott\* or supraglott\*) adj5  
7 21 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)).ti,ab.  
8  
9 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or  
10 22 21  
11  
12  
13 23 Cost Utility Analysis/  
14  
15 24 Quality Adjusted Life Year/  
16  
17 25 "Quality of Life"/  
18  
19 26 "quality of life".ti,kw.  
20  
21 27 (health utilit\* or utilit\* measure\* or utilit\* instrument\*).ti,ab.  
22  
23 28 "Disutilit\*".ti,ab.  
24  
25 29 (QALY\* or DALY\*).ti,ab.  
26  
27 30 (Quality adjusted life year\* or Disability adjusted life year\*).ti,ab.  
28  
29 31 (EQ-5D or EQ5D or EQ-5D-3L or EQ-5D-5L).ti,ab.  
30  
31 32 (SF-12 or SF12).ti,ab.  
32  
33 33 (SF-6D or SF6D).ti,ab.  
34  
35 34 (HUI or "H.U.I").ti,ab.  
36  
37 35 (SF-36 or SF36).ti,ab.  
38  
39 36 time trade off.ti,ab.  
40  
41 37 standard gamble.ti,ab.  
42  
43 38 cost\*.ti,ab,kw.  
44  
45 39 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38  
46  
47 (America\* or Australia\* or Austria\* or Belgium or Belgian or Britain or British or Canad\* or Chile or Chilean  
48  
49 or Czech or Denmark or Danish or Estonia\* or Finland or Finnish or France or French or German\* or  
50  
51 Hungary or Hungarian or Iceland\* or Ireland or Irish or Italy or Italian or Japan\* or Korea\* or Luxembourg  
52  
53 or Mexico or Mexican or Netherlands or Dutch or New Zealand\* or Norway or Norwegian or Poland or  
54  
55 Polish or Portug\* or Slovak\* or Slovenia\* or Spain or Spanish or Sweden or Swedish or Switzerland or  
56  
57  
58  
59  
60

Swiss or Turkey or Turkish or United Kingdom or United States).in,ti,hw,ab,ad,kw.

41 United Kingdom/ or europe/ or exp western europe/

42 (national health service\* or nhs\*).in,ti,hw,ab,ad,kw.

43 (english not ((published or publication\* or translat\* or written or language\* or speak\* or literature or citation\*) adj5 english)).ti,ab.

44 (gb or "g.b." or britain\* or british or uk or "u.k." or united kingdom\* or england\* or ireland\* or irish\* or scotland\* or scottish\* or wales or welsh).in,ti,hw,ab,ad,kw.

45 (bath or "bath's" or birmingham or "birmingham's" or bradford or "bradford's" or brighton or "brighton's" or bristol or "bristol's" or Carlisle\* or "Carlisle's" or Cambridge or "Cambridge's" or canterbury or "canterbury's" or Chelmsford or "Chelmsford's" or Chester or "Chester's" or Chichester or "Chichester's" or Coventry or "Coventry's" or derby or "derby's" or Durham or "Durham's" or Ely or "Ely's" or Exeter or "Exeter's" or Gloucester or "Gloucester's" or Hereford or "Hereford's" or Hull or "Hull's" or Lancaster or "Lancaster's" or Leeds\* or Leicester or "Leicester's" or Lincoln or "Lincoln's" or Liverpool or "Liverpool's" or London or "London's" or manchester or "manchester's" or Newcastle or "Newcastle's" or Norwich or "Norwich's" or Nottingham or "Nottingham's" or Oxford or "Oxford's" or Peterborough or "Peterborough's" or Plymouth or "Plymouth's" or Portsmouth or "Portsmouth's" or Preston or "Preston's" or Ripon or "Ripon's" or Salford or "Salford's" or Salisbury or "Salisbury's" or Sheffield or "Sheffield's" or Southampton or "Southampton's" or St Albans or Stoke or "Stoke's" or Sunderland or "Sunderland's" or Truro or "Truro's" or Wakefield or "Wakefield's" or Wells or Westminster or "Westminster's" or Winchester or "Winchester's" or Wolverhampton or "Wolverhampton's" or Worcester or "Worcester's" or York or "York's").in,ti,hw,ab,ad,kw.

46 (Bangor or "Bangor's" or Cardiff or "Cardiff's" or Newport or "Newport's" or St Asaph or "St Asaph's" or St Davids or Swansea or "Swansea's").in,ti,hw,ab,ad,kw.

47 (Aberdeen or "Aberdeen's" or Dundee or "Dundee's" or Edinburgh or "Edinburgh's" or Glasgow or "Glasgow's" or Inverness or Perth or Stirling or "Stirling's").in,ti,hw,ab,ad,kw.

48 (Armagh or "Armagh's" or Belfast or "Belfast's" or Lisburn or "Lisburn's" or Londonderry or "Londonderry's" or Derry or "Derry's" or Newry or "Newry's").in,ti,hw,ab,ad,kw.

49 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48

50 22 and 39 and 49

51 limit 50 to english language

52 ("Conference Abstract" or "conference paper" or "Conference review" or letter or note).pt.

53 51 not 52

## Ebsco Cinahl

- 1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60
- S1 ( anogenital N3 (wart\* or polyp\*) ) OR ( genital N3 (wart\* or polyp\*) ) OR ( (anal or anus) N3 (wart\* or polyp\*) )
- S2 recurrent respiratory papilloma\*
- S3 RRP
- S4 MH "Cervix Neoplasms+"
- S5 cervi\* N5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)
- S6 vulva\* N5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)
- S7 (MH "Vulvar Neoplasms")
- S8 (MH "Vaginal Neoplasms")
- S9 vagina\* N5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)
- S10 (MH "Anus Neoplasms+")
- S11 (anal OR anus) N5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)
- S12 (MH "Penile Neoplasms")
- S13 (penile OR penis) N5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)
- S14 (MH "Head and Neck Neoplasms+")
- S15 (oral\* or intra-oral\* or intraoral\* or "intra oral\*" or gingiva\* or orophary\* or mouth\* or tongue\* or tonsil\* or cheek\* or gum\* or palatal\* or palate\* or "head and neck") N5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)
- S16 (larynx\* OR pharynx\* OR vocal cord\* OR cordal OR glott\* OR throat OR voice box OR subglott\* OR supraglott\*) N5 (cancer\* or neoplasm\* or malignan\* or tumor\* or tumour\* or carcinom\* or adenocarcinom\*)
- S17 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
- S18 (MH "Costs and Cost Analysis")
- S19 (MH "Quality of Life")
- S20 (MH "Quality-Adjusted Life Years")
- S21 TI "quality of life" OR SU "quality of life"
- S22 health utilit\* OR utilit\* measure\* OR utilit\* instrument\*
- S23 disutilit\*
- S24 QALY\* OR DALY\*
- S25 Quality adjusted life year\* OR Disability adjusted life year\*

- 1  
2  
3 S26 EQ-5D OR EQ5D OR EQ-5D-3L OR EQ-5D-5L  
4  
5 S27 SF-12 OR SF12  
6  
7 S28 SF-6D OR SF6D  
8  
9 S29 HUI or "H.U.I."  
10  
11 S30 SF-36 OR SF36  
12  
13 S31 time trade off  
14  
15 S32 standard gamble  
16  
17 S33 cost\*  
18  
19 S34 S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR  
20 S30 OR S31 OR S32 OR S33  
21  
22 S35 America\* or Australia\* or Austria\* or Belgium or Belgian or Britain or British or Canad\* or Chile or  
23 Chilean or Czech or Denmark or Danish or Estonia\* or Finland or Finnish or France or French or German\* or  
24 Hungary or Hungarian or Iceland\* or Ireland or Irish or Italy or Italian or Japan\* or Korea\* or Luxembourg or  
25 Mexico or Mexican or Netherlands or Dutch or New Zealand\* or Norway or Norwegian or Poland or Polish or  
26 Portug\* or Slovak\* or Slovenia\* or Spain or Spanish or Sweden or Swedish or Switzerland or Swiss or Turkey or  
27 Turkish or United Kingdom or United States  
28  
29 S36 (MH "United Kingdom+")  
30  
31 S37 national health service\* or nhs\*  
32  
33 S38 gb or "g.b." or britain\* or british or uk or "u.k." or united kingdom\* or england\* or ireland\* or irish\* or  
34 scotland\* or scottish\* or wales or welsh  
35  
36 S39 bath or "bath's" or birmingham or "birmingham's" or bradford or "bradford's" or brighton or "brighton's" or  
37 bristol or "bristol's" or carlisle\* or "carlisle's" or cambridge or "cambridge's" or canterbury or "canterbury's" or  
38 chelmsford or "chelmsford's" or chester or "chester's" or chichester or "chichester's" or coventry or "coventry's" or  
39 derby or "derby's" or durham or "durham's" or ely or "ely's" or exeter or "exeter's" or gloucester or "gloucester's"  
40 or hereford or "hereford's" or hull or "hull's" or lancaster or "lancaster's" or leeds\* or leicester or "leicester's" or  
41 lincoln or "lincoln's" or liverpool or "liverpool's" or london or "london's" or manchester or "manchester's" or  
42 newcastle or "newcastle's" or norwich or "norwich's" or nottingham or "nottingham's" or oxford or "oxford's" or  
43 peterborough or "peterborough's" or plymouth or "plymouth's" or portsmouth or "portsmouth's" or preston or  
44 "preston's" or ripon or "ripon's" or salford or "salford's" or salisbury or "salisbury's" or sheffield or "sheffield's" or  
45 southampton or "southampton's" or st albans or stoke or "stoke's" or sunderland or "sunderland's" or truro or  
46 "truro's" or wakefield or "wakefield's" or wells or westminster or "westminster's" or winchester or "winchester's" or  
47 wolverhampton or "wolverhampton's" or worcester or "worcester's" or york or "york's"  
48  
49 S40 bangor or "bangor's" or cardiff or "cardiff's" or newport or "newport's" or st asaph or "st asaph's" or st  
50 davids or swansea or "swansea's"  
51  
52 S41 aberdeen or "aberdeen's" or dundee or "dundee's" or edinburgh or "edinburgh's" or glasgow or  
53 "glasgow's" or inverness or perth or stirling or "stirling's"  
54  
55 S42 armagh or "armagh's" or belfast or "belfast's" or lisburn or "lisburn's" or londonderry or "londonderry's" or  
56 derry or "derry's" or newry or "newry's"  
57  
58 S43 (MH "Europe")  
59  
60 S44 S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43  
S45 S17 AND S34 AND S44

## Scopus

( TITLE-ABS-KEY ( ( anogenital OR genital OR anal OR anus ) W/3 ( wart\* OR polyp\* ) ) OR TITLE-ABS-KEY ( "condyloma\* acuminat\*" ) OR TITLE-ABS-KEY ( "recurrent respiratory papilloma\*" ) ) OR ( TITLE-ABS-KEY ( ( cervi\* OR vulva\* OR vagina\* OR anal OR anus OR penile OR penis OR oral\* OR intra-oral\* OR intraoral\* OR "intra oral\*" OR gingiva\* OR orophary\* OR phary\* OR mouth\* OR tongue\* OR tonsil\* OR cheek\* OR gum\* OR palatal\* OR palate\* OR "head and neck" OR larynx\* OR pharynx\* OR "vocal cord\*" OR cordal OR glott\* OR throat OR "voice box" OR subglott\* OR supraglott\* ) W/5 ( cancer\* OR neoplasm\* OR malignan\* OR tumor\* OR tumour\* OR carcinom\* OR adenocarcinom\* ) ) )

AND

( TITLE-ABS-KEY ( cost\* ) OR TITLE-ABS-KEY ( "health utilit\*" OR "utilit\* measure\*" OR "utilit\* instrument\*" ) OR TITLE-ABS-KEY ( disutilit\* OR qaly\* OR qaly\* OR "Quality adjusted life year\*" OR "Disability adjusted life year\*" ) OR TITLE-ABS-KEY ( eq-5d OR eq5d OR eq-5d-3l OR eq-5d-5l OR sf-12 OR sf12 OR sf-6d OR sf6d OR sf-36 OR sf36 OR hui OR "H.U.I." ) OR TITLE-ABS-KEY ( "time trade off" OR "standard gamble" ) OR TITLE ( "quality or life" ) OR KEY ( "quality of life" ) )

AND

( TITLE-ABS-KEY ( america\* OR australia\* OR austria\* OR belgium OR belgian OR britain OR british OR canad\* OR chile OR chilean OR czech OR denmark OR danish OR estonia\* OR finland OR finnish OR france OR french OR german\* OR hungary OR hungarian OR iceland\* OR ireland OR irish OR italy OR italian OR japan\* OR korea\* OR luxembourg OR mexico OR mexican OR netherlands OR dutch OR "New Zealand\*" OR norway OR norwegian OR poland OR polish OR portug\* OR slovak\* OR slovenia\* OR spain OR spanish OR sweden OR swedish OR switzerland OR swiss OR turkey OR turkish OR "United Kingdom" OR "United States" OR europe ) OR AFFIL ( america\* OR australia\* OR austria\* OR belgium OR belgian OR britain OR british OR canad\* OR chile OR chilean OR czech OR denmark OR danish OR estonia\* OR finland OR finnish OR france OR french OR german\* OR hungary OR hungarian OR iceland\* OR ireland OR irish OR italy OR italian OR japan\* OR korea\* OR luxembourg OR mexico OR mexican OR netherlands OR dutch OR "New Zealand\*" OR norway OR norwegian OR poland OR polish OR portug\* OR slovak\* OR slovenia\* OR spain OR spanish OR sweden OR swedish OR switzerland OR swiss OR turkey OR turkish OR "United Kingdom" OR "United States" OR europe ) ) OR ( TITLE-ABS-KEY ( gb OR "g.b." OR britain\* OR british OR uk OR "u.k." OR "united kingdom\*" OR england\* OR ireland\* OR irish\* OR scotland\* OR scottish\* OR wales OR welsh OR "national health service\*" OR nhs\* ) OR AFFIL ( gb OR "g.b." OR britain\* OR british OR uk OR "u.k." OR "united kingdom\*" OR england\* OR ireland\* OR irish\* OR scotland\* OR scottish\* OR wales OR welsh OR "national health service\*" OR nhs\* ) ) OR ( TITLE-ABS-KEY ( bath\* OR birmingham\* OR bradford\* OR brighton\* OR bristol\* OR Carlisle\* OR cambridge\* OR canterbury\* OR chelmsford\* OR chester\* OR chichester\* OR coventry\* OR derby\* OR durham\* OR ely\* OR exeter\* OR gloucester\* OR hereford\* OR hull\* OR lancaster\* OR leeds OR leicester\* OR lincoln\* OR liverpool\* OR london\* OR manchester\* OR newcastle\* OR norwich\* OR nottingham\* OR oxford\* OR peterborough\* OR plymouth\* OR portsmouth\* OR preston\* OR ripon\* OR salford\* OR salisbury\* OR sheffield\* OR southampton\* OR albans\* OR stoke\* OR sunderland\* OR truro\* OR wakefield\* OR wells OR westminster\* OR winchester\* OR wolverhampton\* OR worcester\* OR york\* ) OR AFFIL ( bath\* OR birmingham\* OR bradford\* OR brighton\* OR bristol\* OR Carlisle\* OR cambridge\* OR canterbury\* OR chelmsford\* OR chester\* OR chichester\* OR coventry\* OR derby\* OR durham\* OR ely\* OR exeter\* OR gloucester\* OR hereford\* OR hull\* OR lancaster\* OR leeds OR leicester\* OR lincoln\* OR liverpool\* OR london\* OR manchester\* OR newcastle\* OR norwich\* OR nottingham\* OR oxford\* OR peterborough\* OR plymouth\* OR portsmouth\* OR preston\* OR ripon\* OR salford\* OR salisbury\* OR sheffield\* OR southampton\* OR albans\* OR stoke\* OR sunderland\* OR truro\* OR wakefield\* OR wells OR westminster\* OR winchester\* OR wolverhampton\* OR worcester\* OR york\* ) ) OR ( TITLE-ABS-KEY ( bangor\* OR cardiff\* OR newport\* OR st "st asaph\*" OR "st davids" OR swansea\* OR aberdeen\* OR dundee\* OR edinburgh\* OR glasgow\* OR inverness OR perth\* OR stirling\* OR armagh\* OR belfast\* OR lisburn\* OR londonderry\* OR derry\* OR newry\* ) OR AFFIL ( bangor\* OR cardiff\* OR newport\* OR st "st asaph\*" OR "st davids" OR swansea\* OR aberdeen\* OR dundee\* OR edinburgh\* OR glasgow\* OR inverness OR perth\* OR stirling\* OR armagh\* OR belfast\* OR lisburn\* OR londonderry\* OR derry\* OR newry\* ) )

1  
2  
3 AND NOT INDEX ( Medline OR embase ) AND ( LIMIT-TO ( LANGUAGE , "English" ) ) AND ( EXCLUDE ( DOCTYPE , "cp" ) )  
4  
5  
6

7 **NHS EED via Cochrane Library**

- 8  
9 #1 MeSH descriptor: [Condylomata Acuminata] explode all trees  
10  
11 #2 "recurrent respiratory papilloma\*"  
12  
13 #3 MeSH descriptor: [Uterine Cervical Neoplasms] explode all trees  
14  
15 #4 MeSH descriptor: [Vulvar Neoplasms] explode all trees  
16  
17 #5 MeSH descriptor: [Vaginal Neoplasms] explode all trees  
18  
19 #6 MeSH descriptor: [Anus Neoplasms] explode all trees  
20  
21 #7 MeSH descriptor: [Penile Neoplasms] explode all trees  
22  
23 #8 MeSH descriptor: [Head and Neck Neoplasms] explode all trees  
24  
25 #9 {or #1-#8}

**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.

*Author information:*

Koh Jun Ong, Marta Checchi, Lorna Burns, Charlotte Pavitt, Maarten Postma, Mark Jit

Confidential: For Review Only

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

**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; <a href="#">Sanofi Pasteur MSD</a>	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; <a href="#">Sanofi Pasteur MSD</a>	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; <a href="#">Department of Health</a>	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; <a href="#">Department of Health</a>	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; <a href="#">Department of Health</a>	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		

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

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, material 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; <u>Funding source not specified, first author was affiliated with 3M Pharmaceuticals, USA</u>	Aggregate estimate of labour costs, material costs, extra costs, indirect costs - study site average							
		<b>Cost per successful outcome for external GW treatment</b>							
		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; <a href="#">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</a>	Cost per case							
		Male	A\$251				\$170		
		Female	A\$386				\$261		

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

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; <a href="#">Sanofi Pasteur MSD</a>	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; <a href="#">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</a>	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; <a href="#">Funding source not specified, authors reported conflict of interest either through grants or employment from GlaxoSmithKline, Merck&amp;Co. Inc, GSK Biologicals, and/or Sanofi Pasteur MSD</a>	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	

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

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; <a href="#">Sanofi Pasteur MSD</a>								

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; <a href="#">Sanofi Pasteur MSD</a>		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; <a href="#">Sanofi Pasteur MSD SpA</a>	(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; <a href="#">No funding to report</a>	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; <a href="#">Sanofi Pasteur MSD SNC (Lyon, France)</a>		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; <a href="#">Funding source not specified</a>		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						

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

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; <a href="#">Sanofi</a> <a href="#">Pasteur MSD</a>	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; <a href="#">Swedish Cancer Foundation</a> , <a href="#">KI Cancer Strategic Grants</a> , <a href="#">Swedish Research Council</a> , and <a href="#">Stockholm County Council</a>	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, <del>country</del> ; 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; <u>No funding to report-</u>	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; <u>Sanofi Pasteur MSD-</u>		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, <del>country</del> ; 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; <a href="#">Sanofi Pasteur MSD</a> .	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, <del>country</del> ; 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; <a href="#">Sanofi Pasteur MSD</a> .	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, <del>country</del> ; 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); <a href="#">Sanofi Pasteur MSD, Lyon, France-</a>		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; <a href="#">Sanofi Pasteur MSD-</a>	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, <del>country</del> ; 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 events, and resource use. Unit cost data from published literature was used; <a href="#">the Netherlands Organization for Health Research and Development (ZonMw) and Merck B.V.</a>	Overall	Mean total cost per patient	±		€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; <a href="#">SPMSD</a>	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

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

No.	Author, year, <del>country</del> ; 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, <del>country</del> ; 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"; <a href="#">GlaxoSmithKline</a>	<b>Mean cost of post-operative healthcare utilisation for resected patients w h&amp;n cancer over 5 years</b>	£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		
		<b>Mean cost of post-operative healthcare utilisation for laryngeal cancer over 5 years</b>	£28,981			\$40,369		
		<b>Mean cost of post-operative healthcare utilisation for pharyngeal</b>	£25,827			\$35,976		

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

No.	Author, year, <del>country</del> ; Disease; Country; Currency; Value year; Value elicitation method; <u>Funding</u>	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, <del>country</del> ; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value				USD 2016/17	Range min.	Range max.
10	Lacau <del>_z</del> 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; <a href="#">Sanofi Pasteur MSD</a> ;	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		

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

No.	Author, year, <del>country</del> ; 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; <a href="#">the Association of University Hospitals (VAZ)</a> -.	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, <del>country</del> ; 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; <u>Funding source not specified</u>							
13	Lowry, 1990 [32]; Head and neck cancer; UK; GBP; Not identified, assume 1990; Not specified; <u>Funding source not specified</u>	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; <u>Funding</u>	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, <del>country</del> ; Disease; Country; Currency; Value year; Value elicitation method; Funding	Reported value				USD 2016/17	Range min.	Range max.
	<a href="#">source not specified.</a>	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; <a href="#">National Institute of Dental Research funds (NIDCR/NIH, Bethesda, MD.)</a> .-		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, <del>country</del> ; 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							
		<b>Scenario</b>	<b>Cost per Patient</b>						
			<b>Base Case</b>	<b>Lower Bound</b>	<b>Upper Bound</b>				
		<b>No inflation, no MFF</b>	£7,421	£5,930	£10,104		\$9,975	\$7,971	\$13,581
		<b>Inflation, no MFF</b>	£7,465	£5,961	£10,156		\$10,034	\$8,012	\$13,651
		<b>No inflation, MFF</b>	8,015	£6,405	£10,913		\$10,773	\$8,609	\$14,668
		<b>Inflation, MFF</b>	8,063	£6,437	£10,968		\$10,838	\$8,652	\$14,742
		(MFF, Market Force Factor)							

No.	Author, year, <del>country</del> ; Disease; Country; Currency; Value year; Value elicitation method; <b>Funding</b>	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; <b>Funding source not specified.</b>	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 <u>individually linked to health care registers</u> provided diagnostic and treatment procedures, hospitalisations, outpatient visits and prescription data, <u>as well as diagnostic and treatment procedures by private providers.</u> <u>These which</u> were combined with national unit costs. <u>Cancers recorded in the Cancer Registry in 1990-2008 were included; index events were identified during 1999-2008 and cancers that were recorded in the Cancer Registry during 1990-1998; Funding source not specified; some authors reported conflicts of interest either through grants or employment from GlaxoSmithKline, Merck&amp;Co. Inc, GSK Biologicals, and/or Sanofi Pasteur MSD.</u>		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)**

No.	Author, year, Country; Utility elicitation method; Study details; Funding	Results				
1	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 of Education, University and Scientific Research-		n	Mean age (SD)	Mean (SD) EQ-5D utility for patients with AGW	Mean (SD and 95% CI) TTO utility for patients with AGW
		AGW overall	132	33.1 (10.2)	0.9 (0.1)	0.78 (SD 0.27; 95% CI 0.73-0.82)
		Males	74	35.7 (10.2)	0.9 (0.1)	0.83 (95% CI: 0.77-0.88)
		Females	58	29.7 (9.3)	1 (0.1)	0.71 (95% CI: 0.64-0.79)
2	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, therefore not possible to calculate single utility score using population norms; No specific funding received-				EQ-VAS score from	
		45 women			75.3% (95% CI: 70.3-80.2)	
		34 heterosexual men			83.7% (95% CI: 79.3-88.2)	
		14 MSM			82.1 (95% CI: 75.4-88.9)	
3	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-				EQ-5D score adjusted by age and sex (SD)	vs population norm 0.89, p = 0.633
		VAS score adjusted by age and sex (SD)			0.9 (0.13)	
					78% (14.8%)	vs UK general population 85%
					EQ-5D score (crude)	VAS score (crude)
		Men			0.89 (SD 0.17)	79 (SD: 15.5)
		Women			0.84 (SD 0.16)	75 (SD: 19.3)

No.	Author, year, Country; Utility elicitation method; Study details; Funding	Results																																															
4	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-	<b>Overall VAS score</b>		65.2 ± 22.0																																													
		<b>Mean (SD) EQ-5D based on UK preference weight</b>																																															
		<b>Overall</b>		0.826 (0.201)																																													
		<b>Male</b>		0.856 (0.185)																																													
		<b>Female</b>		0.802 (0.210)																																													
5	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.-	<table border="1"> <thead> <tr> <th></th> <th>EQ-5D total score</th> <th>VAS</th> <th>SF-6D</th> </tr> </thead> <tbody> <tr> <td><b>Men</b></td> <td></td> <td></td> <td></td> </tr> <tr> <td><i>Norm mean</i></td> <td>89.1</td> <td>82.3</td> <td>NA</td> </tr> <tr> <td><i>All AGW cases at recruitment, n=127, mean (95% CI)</i></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><i>AGW cleared at end of 6 months follow-up, n=47, mean (95% CI)</i></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><i>AGW persisted at end of 6 months follow-up, n=80, mean (95% CI)</i></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><b>Women</b></td> <td></td> <td></td> <td></td> </tr> <tr> <td><i>Norm mean</i></td> <td>88.6</td> <td>83.2</td> <td>NA</td> </tr> <tr> <td><i>All AGW cases at recruitment, n=145, mean (95% CI)</i></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><i>AGW cleared at end of 6 months follow-up, n=87, mean (95% CI)</i></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><i>AGW persisted at end of 6 months follow-up, n=58, mean (95% CI)</i></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> </tbody> </table> <p>Median duration of an AGW episode, n=51 incident cases: 125 days Average QALY loss per AGW case: 0.017 to 0.041</p>					EQ-5D total score	VAS	SF-6D	<b>Men</b>				<i>Norm mean</i>	89.1	82.3	NA	<i>All AGW cases at recruitment, n=127, mean (95% CI)</i>	81.0 (77.4-84.5)	77.6 (74.9-80.2)	74.2 (72.0-76.5)	<i>AGW cleared at end of 6 months follow-up, n=47, mean (95% CI)</i>	86.1 (79.8-92.3)	81.6 (76.8-86.5)	77.5 (73.2-81.8)	<i>AGW persisted at end of 6 months follow-up, n=80, mean (95% CI)</i>	83.8 (78.5-89.1)	78.7 (75.8-81.6)	73.8 (70.3-77.4)	<b>Women</b>				<i>Norm mean</i>	88.6	83.2	NA	<i>All AGW cases at recruitment, n=145, mean (95% CI)</i>	77.4 (74.0-80.8)	76.4 (73.9-78.9)	71.0 (69.0-73.0)	<i>AGW cleared at end of 6 months follow-up, n=87, mean (95% CI)</i>	89.3 (84.6-94.0)	82.1 (78.6-85.7)	76.7 (73.8-79.4)	<i>AGW persisted at end of 6 months follow-up, n=58, mean (95% CI)</i>	79.6 (73.4-84.7)	78.1 (73.5-82.8)	71.5 (67.8-75.2)
	EQ-5D total score	VAS	SF-6D																																														
<b>Men</b>																																																	
<i>Norm mean</i>	89.1	82.3	NA																																														
<i>All AGW cases at recruitment, n=127, mean (95% CI)</i>	81.0 (77.4-84.5)	77.6 (74.9-80.2)	74.2 (72.0-76.5)																																														
<i>AGW cleared at end of 6 months follow-up, n=47, mean (95% CI)</i>	86.1 (79.8-92.3)	81.6 (76.8-86.5)	77.5 (73.2-81.8)																																														
<i>AGW persisted at end of 6 months follow-up, n=80, mean (95% CI)</i>	83.8 (78.5-89.1)	78.7 (75.8-81.6)	73.8 (70.3-77.4)																																														
<b>Women</b>																																																	
<i>Norm mean</i>	88.6	83.2	NA																																														
<i>All AGW cases at recruitment, n=145, mean (95% CI)</i>	77.4 (74.0-80.8)	76.4 (73.9-78.9)	71.0 (69.0-73.0)																																														
<i>AGW cleared at end of 6 months follow-up, n=87, mean (95% CI)</i>	89.3 (84.6-94.0)	82.1 (78.6-85.7)	76.7 (73.8-79.4)																																														
<i>AGW persisted at end of 6 months follow-up, n=58, mean (95% CI)</i>	79.6 (73.4-84.7)	78.1 (73.5-82.8)	71.5 (67.8-75.2)																																														

No.	Author, year, Country; Utility elicitation method; Study details; Funding	Results																																						
6	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; <a href="#">Italian Ministry of Education, University and Scientific Research in Italy</a>	<table border="1"> <thead> <tr> <th data-bbox="848 367 1230 428">Mean (SD) baseline EQ-5D utility in all women with HPV-related diseases</th> <td colspan="3" data-bbox="1236 367 1927 428">0.93 (0.10)</td> </tr> <tr> <th data-bbox="848 433 1230 464"></th> <td colspan="3" data-bbox="1236 433 1927 464">Mean (SD) TTO utility</td> </tr> <tr> <th data-bbox="848 469 1230 500">AGW</th> <td colspan="3" data-bbox="1236 469 1927 500">0.71 (0.35)</td> </tr> </thead> </table>			Mean (SD) baseline EQ-5D utility in all women with HPV-related diseases	0.93 (0.10)				Mean (SD) TTO utility			AGW	0.71 (0.35)																										
Mean (SD) baseline EQ-5D utility in all women with HPV-related diseases	0.93 (0.10)																																							
	Mean (SD) TTO utility																																							
AGW	0.71 (0.35)																																							
7	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; <a href="#">Merck Frosst Canada Ltd.</a>	<table border="1"> <thead> <tr> <th data-bbox="848 566 1360 597"></th> <th colspan="3" data-bbox="1367 566 1927 597">Mean (95% CI)</th> </tr> </thead> <tbody> <tr> <td data-bbox="848 602 1360 633">EQ-5D score (AGW patients)</td> <td colspan="3" data-bbox="1367 602 1927 633">0.789 (0.763-0.815)</td> </tr> <tr> <td data-bbox="848 638 1360 669">EQ-5D disutility vs Canadian norm</td> <td colspan="3" data-bbox="1367 638 1927 669">9.9 (7.3-12.5)</td> </tr> <tr> <td data-bbox="848 673 1360 704">EQ-5D disutility vs Canadian norm (males)</td> <td colspan="3" data-bbox="1367 673 1927 704">7.8 (4.1-11.5)</td> </tr> <tr> <td data-bbox="848 709 1360 740">EQ-5D disutility vs Canadian norm (females)</td> <td colspan="3" data-bbox="1367 709 1927 740">11.7 (8.3-15.2)</td> </tr> <tr> <td data-bbox="848 745 1360 776">EQ-VAS score (AGW patients)</td> <td colspan="3" data-bbox="1367 745 1927 776">0.769 (0.749-0.788)</td> </tr> <tr> <td data-bbox="848 781 1360 812">EQ-VAS disutility vs Canadian norm</td> <td colspan="3" data-bbox="1367 781 1927 812">6 (4.1-7.9)</td> </tr> <tr> <td data-bbox="848 816 1360 847">EQ-VAS disutility vs Canadian norm (males)</td> <td colspan="3" data-bbox="1367 816 1927 847">4.8 (2.0-7.5)</td> </tr> <tr> <td data-bbox="848 852 1360 883">EQ-VAS disutility vs Canadian norm (females)</td> <td colspan="3" data-bbox="1367 852 1927 883">7 (4.4-9.6)</td> </tr> </tbody> </table>				Mean (95% CI)			EQ-5D score (AGW patients)	0.789 (0.763-0.815)			EQ-5D disutility vs Canadian norm	9.9 (7.3-12.5)			EQ-5D disutility vs Canadian norm (males)	7.8 (4.1-11.5)			EQ-5D disutility vs Canadian norm (females)	11.7 (8.3-15.2)			EQ-VAS score (AGW patients)	0.769 (0.749-0.788)			EQ-VAS disutility vs Canadian norm	6 (4.1-7.9)			EQ-VAS disutility vs Canadian norm (males)	4.8 (2.0-7.5)			EQ-VAS disutility vs Canadian norm (females)	7 (4.4-9.6)		
	Mean (95% CI)																																							
EQ-5D score (AGW patients)	0.789 (0.763-0.815)																																							
EQ-5D disutility vs Canadian norm	9.9 (7.3-12.5)																																							
EQ-5D disutility vs Canadian norm (males)	7.8 (4.1-11.5)																																							
EQ-5D disutility vs Canadian norm (females)	11.7 (8.3-15.2)																																							
EQ-VAS score (AGW patients)	0.769 (0.749-0.788)																																							
EQ-VAS disutility vs Canadian norm	6 (4.1-7.9)																																							
EQ-VAS disutility vs Canadian norm (males)	4.8 (2.0-7.5)																																							
EQ-VAS disutility vs Canadian norm (females)	7 (4.4-9.6)																																							
8	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; <a href="#">Department of Health</a>	<table border="1"> <thead> <tr> <th data-bbox="848 935 1230 966"></th> <th data-bbox="1236 935 1444 966">All (95% CI)</th> <th data-bbox="1451 935 1659 966">Male (95% CI)</th> <th data-bbox="1665 935 1927 966">Female (95% CI)</th> </tr> </thead> <tbody> <tr> <td data-bbox="848 971 1230 1002">EQ-5D index</td> <td data-bbox="1236 971 1444 1002">0.87 (0.85-0.89)</td> <td data-bbox="1451 971 1659 1002">0.88 (0.86-0.9)</td> <td data-bbox="1665 971 1927 1002">0.87 (0.83-0.9)</td> </tr> <tr> <td data-bbox="848 1006 1230 1037">EQ-VAS</td> <td data-bbox="1236 1006 1444 1037">77 (76-79)</td> <td data-bbox="1451 1006 1659 1037">79 (77-80)</td> <td data-bbox="1665 1006 1927 1037">75 (71-78)</td> </tr> <tr> <td data-bbox="848 1042 1230 1073">EQ-5D disutility</td> <td data-bbox="1236 1042 1444 1073">0.056 (0.038-0.074)</td> <td data-bbox="1451 1042 1659 1073">0.043 (0.021-0.065)</td> <td data-bbox="1665 1042 1927 1073">0.063 (0.029-0.097)</td> </tr> <tr> <td data-bbox="848 1078 1230 1109">Duration episode of care (days)</td> <td data-bbox="1236 1078 1444 1109">36 (27-46)</td> <td data-bbox="1451 1078 1659 1109">35 (20-51)</td> <td data-bbox="1665 1078 1927 1109">37 (20-53)</td> </tr> <tr> <td data-bbox="848 1114 1230 1144">Prescription/recovery time (days)</td> <td data-bbox="1236 1114 1444 1144">36 (36-40)</td> <td data-bbox="1451 1114 1659 1144">39 (34-44)</td> <td data-bbox="1665 1114 1927 1144">37 (41-43)</td> </tr> <tr> <td data-bbox="848 1149 1230 1203">Time to attendance (days) at clinic after noticing GW</td> <td data-bbox="1236 1149 1444 1203">111 (88-135)</td> <td data-bbox="1451 1149 1659 1203">144 (112-174)</td> <td data-bbox="1665 1149 1927 1203">69 (48-90)</td> </tr> <tr> <td data-bbox="848 1208 1230 1239">Mean QALY loss (days)</td> <td data-bbox="1236 1208 1444 1239">6.6 (2.9-11.3)</td> <td data-bbox="1451 1208 1659 1239">6.6 (0.8-14.9)</td> <td data-bbox="1665 1208 1927 1239">6.5 (2.9-11.2)</td> </tr> </tbody> </table>				All (95% CI)	Male (95% CI)	Female (95% CI)	EQ-5D index	0.87 (0.85-0.89)	0.88 (0.86-0.9)	0.87 (0.83-0.9)	EQ-VAS	77 (76-79)	79 (77-80)	75 (71-78)	EQ-5D disutility	0.056 (0.038-0.074)	0.043 (0.021-0.065)	0.063 (0.029-0.097)	Duration episode of care (days)	36 (27-46)	35 (20-51)	37 (20-53)	Prescription/recovery time (days)	36 (36-40)	39 (34-44)	37 (41-43)	Time to attendance (days) at clinic after noticing GW	111 (88-135)	144 (112-174)	69 (48-90)	Mean QALY loss (days)	6.6 (2.9-11.3)	6.6 (0.8-14.9)	6.5 (2.9-11.2)				
	All (95% CI)	Male (95% CI)	Female (95% CI)																																					
EQ-5D index	0.87 (0.85-0.89)	0.88 (0.86-0.9)	0.87 (0.83-0.9)																																					
EQ-VAS	77 (76-79)	79 (77-80)	75 (71-78)																																					
EQ-5D disutility	0.056 (0.038-0.074)	0.043 (0.021-0.065)	0.063 (0.029-0.097)																																					
Duration episode of care (days)	36 (27-46)	35 (20-51)	37 (20-53)																																					
Prescription/recovery time (days)	36 (36-40)	39 (34-44)	37 (41-43)																																					
Time to attendance (days) at clinic after noticing GW	111 (88-135)	144 (112-174)	69 (48-90)																																					
Mean QALY loss (days)	6.6 (2.9-11.3)	6.6 (0.8-14.9)	6.5 (2.9-11.2)																																					

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

No.	Author, year, Country; Utility elicitation method; Study details; Funding	Results													
9	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; <a href="#">Funding source not specified</a> .	<table border="1"> <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>	Mean EQ-5D utility score	0.76 (SD: 0.19; 95% CI: 0.72-0.8)	Mean EQ-5D VAS score	65.1 (SD: 21.2; 95% CI: 60-70)	Mean SF-6D utility score	0.74 (SD: 0.13; 95% CI: 0.71-0.77)							
Mean EQ-5D utility score	0.76 (SD: 0.19; 95% CI: 0.72-0.8)														
Mean EQ-5D VAS score	65.1 (SD: 21.2; 95% CI: 60-70)														
Mean SF-6D utility score	0.74 (SD: 0.13; 95% CI: 0.71-0.77)														
10	Pirota, 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; <a href="#">CSL Limited</a> .	<table border="1"> <tr> <td></td> <td>Mean</td> </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>		Mean	EuroQoL VAS, observed value	68.9 (SD: 21.4)	Multivariate analysis (adjusted for age, ethnicity, and current partner)	71.4 (95% CI: 63.3-79.6)							
	Mean														
EuroQoL VAS, observed value	68.9 (SD: 21.4)														
Multivariate analysis (adjusted for age, ethnicity, and current partner)	71.4 (95% CI: 63.3-79.6)														
11	Woodhall, 2009, England [5]; EQ-5D (note: disutility value presented); 189 patients attending the York STD clinic in 2006/07; <a href="#">Department of Health</a>	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).													
12	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; <a href="#">Department of Health</a> .	<table border="1"> <thead> <tr> <th></th> <th>Unadjusted mean EQ-5D index score</th> <th>Unadjusted mean EQ-VAS score</th> </tr> </thead> <tbody> <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&lt;0.001), based on 70 cases; male cases lower by 10.9 (95% CI 5.7-15.5; p&lt;0.001); female cases lower by 19.9 (95% CI 11.7-26.2; p&lt;0.001)</td> </tr> </tbody> </table>			Unadjusted mean EQ-5D index score	Unadjusted mean EQ-VAS score	Cases	0.9	72	Controls (UK norms)	0.91	86	Note	Age and sex adjusted mean EQ-5D index score 0.039 points lower (95% CI 0.005-0.078; p=0.02)	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)
	Unadjusted mean EQ-5D index score	Unadjusted mean EQ-VAS score													
Cases	0.9	72													
Controls (UK norms)	0.91	86													
Note	Age and sex adjusted mean EQ-5D index score 0.039 points lower (95% CI 0.005-0.078; p=0.02)	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)													

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

No.	Author, year, Disease; Country; Utility elicitation method; Study details; Funding	Results					
			15D utility				
1	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						
		Population	0.911				
		Patients	0.872				
		Baseline	0.872	p-value vs baseline			
		3 months	0.839	p < 0.001			
		6 months	0.857	p = 0.001			
		12 months	0.852	p = 0.003			
2	Govers, 2016, Oral cancers, 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	Patient subgroup	n	Mean age (SD, range)	Mean time after treatment in years (SD, range)	Mean (SE) EQ-5D-3L utility score, adjusted for age, gender, and time since treatment (p-value 0.700)	Mean (SE) EQ-VAS score, adjusted for age, gender, and time since treatment (p-value 0.234)
		watchful waiting (WW)	26	71.4 (11.4, 54.8-91.6)	4.8 (1.8, 2.3-9.2)	0.804 (0.04)	69.7 (3.7)
		sentinel lymph node biopsy (SLNB)	19	63.6 (9.4, 44.9-80.2)	1.9 (1.4, 0.4-4.1)	0.863 (0.05)	79.6 (4.8)
		supraomohyoid neck dissection (SOHND)	109	62.7 (12.2, 29.5-84.6)	5.2 (2.6, 1.6-12.2)	0.834 (0.02)	76.1 (1.8)
		modified radical neck dissection (MRND)	27	64.8 (10.6, 40.5-96.5)	5.2 (3.2, 0.4-11.0)	0.794 (0.04)	71.5 (3.3)

No.	Author, year, <u>c</u> ; <u>Disease</u> ; <u>Country</u> ; Utility elicitation method; <u>Study details</u> ; <u>Funding</u>	Results																																																								
3	<p>Pickard, 2016, <u>c</u>; Head and neck <u>cancer</u>; 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); <u>Funding support for the original study was provided by 11 pharmaceutical companies-</u></p>	<table border="1"> <thead> <tr> <th></th> <th>Mean (SD)</th> </tr> </thead> <tbody> <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> </tbody> </table>						Mean (SD)	Unadjusted EQ-5D	0.76 (0.15)	EQ-5D index scores, adjusted for age and sex	0.828	Unadjusted EQ-VAS	61.8 (21.7)	EQ-VAS, adjusted for age and sex	60.8																																										
	Mean (SD)																																																									
Unadjusted EQ-5D	0.76 (0.15)																																																									
EQ-5D index scores, adjusted for age and sex	0.828																																																									
Unadjusted EQ-VAS	61.8 (21.7)																																																									
EQ-VAS, adjusted for age and sex	60.8																																																									
4	<p>Rettig, 2016, <u>c</u>; Head and neck <u>cancer</u>, 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; <u>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</u></p>	<table border="1"> <thead> <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> </thead> <tbody> <tr> <td></td> <td>Overall, n = 1,653</td> <td>&lt;2 Year Survivors, n = 296</td> <td>2-5 Year Survivors, n = 209</td> <td>&gt;5-Year Survivors, n = 1,081</td> </tr> <tr> <td><b>Time interval prediagnosis</b></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><b>Time interval postdiagnosis</b></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> </tbody> </table>	Time	HRQOL Score (95% CI)	HRQOL Score (95% CI)	HRQOL Score (95% CI)	HRQOL Score (95% CI)		Overall, n = 1,653	<2 Year Survivors, n = 296	2-5 Year Survivors, n = 209	>5-Year Survivors, n = 1,081	<b>Time interval prediagnosis</b>					5 y (Baseline)	92.3 (89.3, 95.2)	87.3 (92.7, 91.9)	92.8 (85.1, 100.5)	96.4 (91.8, 100.9)	2 y	90.2 (88.4, 92.0)	86.3 (83.4, 89.2)	89.8 (85.3, 94.2)	94.5 (91.9, 97.1)	Diagnosis: 0 y	85.0 (83.4, 86.6)	73.9 (70.3, 77.6)	82.9 (79.0, 86.9)	91.5 (89.4, 93.5)	<b>Time interval postdiagnosis</b>					13 mo	83.7 (82.0, 85.4)	69.7 (62.8, 76.7)	79.9 (76.1, 83.7)	90.1 (87.9, 92.2)	2 years	84.1 (82.4, 85.8)	63.8 (35.9, 91.7)	78.0 (73.6, 82.5)	89.2 (87.2, 91.2)	5 years	88.0 (86.2, 89.7)		52.1 (14.9, 89.3)	88.6 (86.8, 90.3)	10 years	84.6 (81.6, 87.6)			84.2 (81.4, 87.1)	<p>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.</p>
Time	HRQOL Score (95% CI)	HRQOL Score (95% CI)	HRQOL Score (95% CI)	HRQOL Score (95% CI)																																																						
	Overall, n = 1,653	<2 Year Survivors, n = 296	2-5 Year Survivors, n = 209	>5-Year Survivors, n = 1,081																																																						
<b>Time interval prediagnosis</b>																																																										
5 y (Baseline)	92.3 (89.3, 95.2)	87.3 (92.7, 91.9)	92.8 (85.1, 100.5)	96.4 (91.8, 100.9)																																																						
2 y	90.2 (88.4, 92.0)	86.3 (83.4, 89.2)	89.8 (85.3, 94.2)	94.5 (91.9, 97.1)																																																						
Diagnosis: 0 y	85.0 (83.4, 86.6)	73.9 (70.3, 77.6)	82.9 (79.0, 86.9)	91.5 (89.4, 93.5)																																																						
<b>Time interval postdiagnosis</b>																																																										
13 mo	83.7 (82.0, 85.4)	69.7 (62.8, 76.7)	79.9 (76.1, 83.7)	90.1 (87.9, 92.2)																																																						
2 years	84.1 (82.4, 85.8)	63.8 (35.9, 91.7)	78.0 (73.6, 82.5)	89.2 (87.2, 91.2)																																																						
5 years	88.0 (86.2, 89.7)		52.1 (14.9, 89.3)	88.6 (86.8, 90.3)																																																						
10 years	84.6 (81.6, 87.6)			84.2 (81.4, 87.1)																																																						



No.	Author, year, <u>c</u> ; <u>Disease</u> ; <u>Country</u> ; <u>Utility elicitation method</u> ; <u>Study details</u> ; <u>Funding</u>	Results																
5	Kent, 2015; <u>c</u> ; <u>Oral cavity and pharyngeal cancers</u> ; <u>US</u> [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; <u>Last author received grants from the NIA and the NIMHD</u> .	<table border="1"> <tr> <td data-bbox="848 435 1201 475">Mean SF-6D/VR-6D (95% CI)</td> <td data-bbox="1201 435 1642 475">0.69 (0.68, 0.70)</td> </tr> </table>		Mean SF-6D/VR-6D (95% CI)	0.69 (0.68, 0.70)													
Mean SF-6D/VR-6D (95% CI)	0.69 (0.68, 0.70)																	
6	Loimu, 2015; <u>c</u> ; <u>Head and neck cancer</u> ; <u>Finland</u> [53]; 15D; Prospective cohort study of 64 patients with laryngeal, pharyngeal or nasal cavity carcinoma treated with definitive (chemo) radiotherapy between 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; <u>The Helsinki University Central Hospital Research Funds</u> .	<table border="1"> <thead> <tr> <th data-bbox="848 630 991 686"></th> <th data-bbox="991 630 1453 686">Mean 15D score, all patients, n = 64</th> <th data-bbox="1453 630 1915 686">Compared with 15D of standardised Finnish general population</th> </tr> </thead> <tbody> <tr> <td data-bbox="848 686 991 743"><b>Baseline</b></td> <td data-bbox="991 686 1453 743">0.886 (0.10)</td> <td data-bbox="1453 686 1915 743">Difference not statistically significant or in clinically important manner</td> </tr> <tr> <td data-bbox="848 743 991 800"><b>3 months</b></td> <td data-bbox="991 743 1453 800">0.829 (0.12)</td> <td data-bbox="1453 743 1915 800"></td> </tr> <tr> <td data-bbox="848 800 991 857"><b>6 months</b></td> <td data-bbox="991 800 1453 857">0.860 (0.12)</td> <td data-bbox="1453 800 1915 857"></td> </tr> <tr> <td data-bbox="848 857 991 914"><b>12 months</b></td> <td data-bbox="991 857 1453 914">0.862 (0.14)</td> <td data-bbox="1453 857 1915 914">Difference not statistically significant or in clinically important manner</td> </tr> </tbody> </table>			Mean 15D score, all patients, n = 64	Compared with 15D of standardised Finnish general population	<b>Baseline</b>	0.886 (0.10)	Difference not statistically significant or in clinically important manner	<b>3 months</b>	0.829 (0.12)		<b>6 months</b>	0.860 (0.12)		<b>12 months</b>	0.862 (0.14)	Difference not statistically significant or in clinically important manner
	Mean 15D score, all patients, n = 64	Compared with 15D of standardised Finnish general population																
<b>Baseline</b>	0.886 (0.10)	Difference not statistically significant or in clinically important manner																
<b>3 months</b>	0.829 (0.12)																	
<b>6 months</b>	0.860 (0.12)																	
<b>12 months</b>	0.862 (0.14)	Difference not statistically significant or in clinically important manner																
7	Noel, 2015; <u>c</u> ; <u>Head and neck cancer</u> ; <u>Canada</u> [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); <u>Funding source not specified</u>	<table border="1"> <tr> <td data-bbox="848 963 1201 1003"><b>EQ-5D</b></td> <td data-bbox="1201 963 1642 1003">0.82 (SD: 0.18, range: -0.07-1.0)</td> </tr> <tr> <td data-bbox="848 1003 1201 1044"><b>SG</b></td> <td data-bbox="1201 1003 1642 1044">0.91 (SD: 0.17, range: 0.2-1.0)</td> </tr> <tr> <td data-bbox="848 1044 1201 1084"><b>TTO</b></td> <td data-bbox="1201 1044 1642 1084">0.94 (SD: 0.14, range: 0.3-1.0)</td> </tr> <tr> <td data-bbox="848 1084 1201 1125"><b>VAS</b></td> <td data-bbox="1201 1084 1642 1125">0.76 (SD: 0.19, range: 0.2-1.0)</td> </tr> <tr> <td data-bbox="848 1125 1201 1166"><b>HUI3</b></td> <td data-bbox="1201 1125 1642 1166">0.75 (SD: 0.25, range: -0.06-1.0)</td> </tr> </table>		<b>EQ-5D</b>	0.82 (SD: 0.18, range: -0.07-1.0)	<b>SG</b>	0.91 (SD: 0.17, range: 0.2-1.0)	<b>TTO</b>	0.94 (SD: 0.14, range: 0.3-1.0)	<b>VAS</b>	0.76 (SD: 0.19, range: 0.2-1.0)	<b>HUI3</b>	0.75 (SD: 0.25, range: -0.06-1.0)					
<b>EQ-5D</b>	0.82 (SD: 0.18, range: -0.07-1.0)																	
<b>SG</b>	0.91 (SD: 0.17, range: 0.2-1.0)																	
<b>TTO</b>	0.94 (SD: 0.14, range: 0.3-1.0)																	
<b>VAS</b>	0.76 (SD: 0.19, range: 0.2-1.0)																	
<b>HUI3</b>	0.75 (SD: 0.25, range: -0.06-1.0)																	

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

No.	Author, year, <del>c</del> ; Disease; Country; Utility elicitation method; Study details; Funding	Results																	
8	<p>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; <a href="#">the Belgian Federal Government, National Cancer Plan-</a></p>	<p>EQ-5D complete for 81 patients Post-treatment EQ-5D postal response was 90%</p> <table border="1"> <thead> <tr> <th colspan="2">General median (Q1, Q3) EQ-5D index score</th> </tr> </thead> <tbody> <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> </tbody> </table> <p>Vulnerable patients showed significantly lower EQ-5D index scores compared to fit patients, before, during, and after treatment start (p&lt;0.05)</p>	General median (Q1, Q3) EQ-5D index score		Prior to treatment start	0.66 (0.55, 0.76)	Week-4 (mid-therapy)	0.42 (0.26, 0.73)	Month-2 (end of treatment)	0.66 (0.29, 0.76)	Month-5	0.66 (0.27, 0.76)	Month-12	0.64 (0.0, 0.76)	Month-24	0.29 (0.0, 0.76)	Month-36	0.0 (0.0, 0.67)	
General median (Q1, Q3) EQ-5D index score																			
Prior to treatment start	0.66 (0.55, 0.76)																		
Week-4 (mid-therapy)	0.42 (0.26, 0.73)																		
Month-2 (end of treatment)	0.66 (0.29, 0.76)																		
Month-5	0.66 (0.27, 0.76)																		
Month-12	0.64 (0.0, 0.76)																		
Month-24	0.29 (0.0, 0.76)																		
Month-36	0.0 (0.0, 0.67)																		
9	<p>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); <a href="#">the American Cancer Society-</a></p>	<table border="1"> <tr> <td>Median EQ-5D utility value</td> <td>85 (IQR: 70-90)</td> </tr> </table>	Median EQ-5D utility value	85 (IQR: 70-90)															
Median EQ-5D utility value	85 (IQR: 70-90)																		
10	<p>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&amp;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; <a href="#">Funding source not specified-</a></p>	<table border="1"> <thead> <tr> <th colspan="2">Median value</th> </tr> </thead> <tbody> <tr> <td>EQ5D values, same for both brachytherapy group (n = 75) and surgery group (n = 44), p=0.87</td> <td>75</td> </tr> </tbody> </table>	Median value		EQ5D values, same for both brachytherapy group (n = 75) and surgery group (n = 44), p=0.87	75													
Median value																			
EQ5D values, same for both brachytherapy group (n = 75) and surgery group (n = 44), p=0.87	75																		

No.	Author, year, <del>c</del> ; Disease; Country; Utility elicitation method; Study details; Funding	Results					
11	Rogers, 2006, <del>r</del> ; Head and neck, <del>r</del> 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; <del>Funding source not specified</del>	<b>EQ5D mean utility (health index)</b>		0.75 (SE: 0.02; range: -0.18 to 1.0)			
		<b>Overall mean EQ-VAS</b>		74 (SE: 1)			
12	Ringash, 2000; Laryngeal cancer, <del>r</del> 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 questionnaire 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; questionnaire administered via structured personal interview; <del>Funding source not specified</del>				<b>Mean (SD; range)</b>		
		<b>TTO, n=112</b>			0.914 (0.156; 0.25 to 1)		
		<b>TTO, excluding patients who claimed they had or did not want perfect health, n=84</b>			0.878 (0.174; 0.25 to 1)		
13	Downer, 1997, <del>r</del> ; Oral cancers; 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; <del>Funding source not specified</del>	<b>Health state</b>		<b>Mean utility value (SD)</b>			
		Precancer		0.92 (0.18)			
		Stage 1 cancer		0.88 (0.20)			
		Stage 2+ cancer		0.68 (0.33)			
14	Marcellusi, 2015, <del>r</del> ; 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; <del>Sanofi Pasteur MSD, Italy and partly funded by the Italian Ministry of Education, University and Scientific Research</del>	<b>Patients with</b>		<b>Overall n</b>	<b>Mean EQ-5D utility (SD)</b>	<b>Mean EQ-5D utility (SD), males</b>	<b>Mean EQ-5D utility (SD), females</b>
		anal cancer		26	0.6 (0.3)	0.7 (0.2)	0.4 (0.3)
		anal cancer, controls		10	0.9 (0.1)	0.9 (0.1)	0.9 (0.1)

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

No.	Author, year, <u>c</u> ; <u>Disease</u> ; <u>Country</u> ; Utility elicitation method; Study details; <u>Funding</u>	Results																												
		head and neck squamous cell carcinoma	79	0.8 (0.2)	0.8 (0.2)	0.7 (0.2)																								
		head and neck squamous cell carcinoma, controls	20	0.9 (0.3)	1 (0.1)	0.8 (0.3)																								
		<b>Patients with</b>		<b>Mean TTO utility (SD; 95% CI)</b>	<b>Mean TTO utility (SD), males</b>	<b>Mean TTO utility (SD), females</b>																								
		anal cancer		0.5 (0.26; 0.4-0.61)	0.48 (0.24)	0.54 (0.31)																								
		anal cancer, controls		0.52 (0.25; 0.36-0.67)																										
		head and neck squamous cell carcinoma		0.69 (0.3; 0.62-0.75)	0.7 (0.32)	0.64 (0.21)																								
		head and neck squamous cell carcinoma, controls		0.59 (0.3; 0.46-0.72)																										
15	Conway, 2012, <u>r</u> ; Anal, oropharyngeal, vaginal, vulvar, penile, Australia [61]; <u>SG</u> ; 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; <u>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-</u>	<table border="1"> <thead> <tr> <th data-bbox="840 901 1113 950">Scenario</th> <th data-bbox="1113 901 1197 950">N</th> <th data-bbox="1197 901 1480 950">Mean (95% CI)</th> <th data-bbox="1480 901 1711 950">Median (IQR)</th> </tr> </thead> <tbody> <tr> <td data-bbox="840 950 1113 982">Anal cancer</td> <td data-bbox="1113 950 1197 982">95</td> <td data-bbox="1197 950 1480 982">0.57 (0.52 to 0.62)</td> <td data-bbox="1480 950 1711 982">0.65 (0.45 to 0.75)</td> </tr> <tr> <td data-bbox="840 982 1113 1015">Oropharyngeal cancer</td> <td data-bbox="1113 982 1197 1015">99</td> <td data-bbox="1197 982 1480 1015">0.58 (0.53 to 0.63)</td> <td data-bbox="1480 982 1711 1015">0.65 (0.45 to 0.75)</td> </tr> <tr> <td data-bbox="840 1015 1113 1047">Vaginal cancer</td> <td data-bbox="1113 1015 1197 1047">98</td> <td data-bbox="1197 1015 1480 1047">0.59 (0.54 to 0.64)</td> <td data-bbox="1480 1015 1711 1047">0.65 (0.45 to 0.75)</td> </tr> <tr> <td data-bbox="840 1047 1113 1079">Vulvar cancer</td> <td data-bbox="1113 1047 1197 1079">98</td> <td data-bbox="1197 1047 1480 1079">0.65 (0.60 to 0.70)</td> <td data-bbox="1480 1047 1711 1079">0.65 (0.45 to 0.85)</td> </tr> <tr> <td data-bbox="840 1079 1113 1120">Penile cancer</td> <td data-bbox="1113 1079 1197 1120">97</td> <td data-bbox="1197 1079 1480 1120">0.79 (0.74 to 0.84)</td> <td data-bbox="1480 1079 1711 1120">0.85 (0.65 to 1.0)</td> </tr> </tbody> </table>					Scenario	N	Mean (95% CI)	Median (IQR)	Anal cancer	95	0.57 (0.52 to 0.62)	0.65 (0.45 to 0.75)	Oropharyngeal cancer	99	0.58 (0.53 to 0.63)	0.65 (0.45 to 0.75)	Vaginal cancer	98	0.59 (0.54 to 0.64)	0.65 (0.45 to 0.75)	Vulvar cancer	98	0.65 (0.60 to 0.70)	0.65 (0.45 to 0.85)	Penile cancer	97	0.79 (0.74 to 0.84)	0.85 (0.65 to 1.0)
Scenario	N	Mean (95% CI)	Median (IQR)																											
Anal cancer	95	0.57 (0.52 to 0.62)	0.65 (0.45 to 0.75)																											
Oropharyngeal cancer	99	0.58 (0.53 to 0.63)	0.65 (0.45 to 0.75)																											
Vaginal cancer	98	0.59 (0.54 to 0.64)	0.65 (0.45 to 0.75)																											
Vulvar cancer	98	0.65 (0.60 to 0.70)	0.65 (0.45 to 0.85)																											
Penile cancer	97	0.79 (0.74 to 0.84)	0.85 (0.65 to 1.0)																											

## References

- 1 Coles VAH, Chapman R, Lanitis T, *et al.* The costs of managing genital warts in the UK by devolved nation: England, Scotland, Wales and Northern Ireland. *Int J STD AIDS* 2016;**27**:51–7. doi:10.1177/0956462415573121
- 2 Lanitis T, Carroll S, O'Mahony C, *et al.* The cost of managing genital warts in the UK. *Int J STD AIDS* 2012;**23**:189–94. doi:10.1258/ijsa.2011.011218
- 3 Desai S, Wetten S, Woodhall SC, *et al.* Genital warts and cost of care in England. *Sex Transm Infect* 2011;**87**:464–8. doi:10.1136/sti.2010.048421
- 4 Woodhall SC, Jit M, Soldan K, *et al.* The impact of genital warts: loss of quality of life and cost of treatment in eight sexual health clinics in the UK. *Sex Transm Infect* 2011;**87**:458–63. doi:10.1136/sextrans-2011-050073
- 5 Woodhall SC, Jit M, Cai C, *et al.* Cost of treatment and QALYs lost due to genital warts: Data for the economic evaluation of HPV vaccines in the United Kingdom. *Sex Transm Dis* 2009;**36**:515–21. doi:10.1097/OLQ.0b013e3181a74c2c
- 6 Brown RE, Breugelmans JG, Theodoratou D, *et al.* Costs of detection and treatment of cervical cancer, cervical dysplasia and genital warts in the UK. *Curr Med Res Opin* 2006;**22**:663–70. doi:10.1185/030079906X99972
- 7 Langley PC, White DJ, Drake SM. The costs of treating external genital warts in England and Wales : a treatment pattern analysis. *Int J STD AIDS* 2004;**15**:501–8.
- 8 Pirotta M, Stein AN, Conway EL, *et al.* Genital warts incidence and healthcare resource utilisation in Australia. *Sex Transm Infect* 2010;**86**:181–6. doi:10.1136/sti.2009.040188
- 9 Annemans L, Rémy V, Lamure E, *et al.* Economic burden associated with the management of cervical cancer, cervical dysplasia and genital warts in Belgium. *J Med Econ* 2008;**11**:135–50. doi:10.3111/13696990801961611
- 10 Marra F, Ogilvie G, Colley L, *et al.* Epidemiology and costs associated with genital warts in Canada. *Sex Transm Infect* 2009;**85**:111–5. doi:10.1136/sti.2008.030999
- 11 Salo H, Leino T, Kilpi T, *et al.* The burden and costs of prevention and management of genital disease caused by HPV in women: A population-based registry study in Finland. *Int J Cancer* 2013;**133**:1459–69. doi:10.1002/ijc.28145
- 12 Herse F, Reissell E. The annual costs associated with human papillomavirus types 6, 11, 16, and 18 infections in Finland. *Scand J Infect Dis* 2011;**43**:209–15. doi:10.3109/00365548.2010.541492
- 13 Hillemanns P, Breugelmans JG, Gieseck F, *et al.* Estimation of the incidence of genital warts and the cost of illness in Germany: A cross-sectional study. *BMC Infect Dis* 2008;**8**:1–10. doi:10.1186/1471-2334-8-76

- 1  
2  
3  
4  
5 14 Gianino MM, Delmonte S, Lovato E, *et al.* A retrospective analysis of the costs and management of genital warts in Italy. *BMC Infect Dis* 2013;**13**:1–9.  
6 doi:10.1186/1471-2334-13-470  
7  
8 15 Baio G, Capone A, Marcellusi A, *et al.* Economic Burden of Human Papillomavirus-Related Diseases in Italy. *PLoS One* 2012;**7**.  
9 doi:10.1371/journal.pone.0049699  
10  
11 16 Merito M, LARGERON N, Cohet C, *et al.* Treatment patterns and associated costs for genital warts in Italy. *Curr Med Res Opin* 2008;**24**:3175–83.  
12 doi:10.1185/03007990802485694  
13  
14 17 Dee A, Howell F, O'Connor C, *et al.* Determining the cost of genital warts: A study from Ireland. *Sex Transm Infect* 2009;**85**:402–3.  
15 doi:10.1136/sti.2008.033837  
16  
17 18 Meijden WI Van Der, Notowicz A, Blog FB, *et al.* A Retrospective Analysis of Costs and Patterns of Treatment for External Genital Warts in the  
18 Netherlands. 2002;**24**:183–96.  
19  
20 19 Castellsague X, Cohet C, Puig-tintore LM, *et al.* Epidemiology and cost of treatment of genital warts in Spain. *Eur J Public Health* 2008;**19**:106–10.  
21 doi:10.1093/eurpub/ckn127  
22  
23 20 Östensson E, Fröberg M, Leval A, *et al.* Cost of Preventing, Managing, and Treating Human Papillomavirus (HPV)-Related Diseases in Sweden before  
24 the Introduction of Quadrivalent HPV Vaccination. *PLoS One* 2015;**1–15**. doi:10.1371/journal.pone.0139062  
25  
26 21 Olsen J, Jørgensen TR, Kofoed K, *et al.* Incidence and cost of anal , penile , vaginal and vulvar cancer in Denmark. Published Online First: 2012.  
27 doi:10.1186/1471-2458-12-1082  
28  
29 22 Borget I, Abramowitz L, Mathevet P. Economic burden of HPV-related cancers in France. *Vaccine* 2011;**29**:5245–9. doi:10.1016/j.vaccine.2011.05.018  
30  
31 23 Keeping ST, Tempest MJ, Stephens SJ, *et al.* The cost of anal cancer in England: retrospective hospital data analysis and Markov model. *BMC Public*  
32 *Health* 2014;**14**:1123. doi:10.1186/1471-2458-14-1123  
33  
34 24 Heitland W, Schädlich PK, Chen X, *et al.* Annual cost of hospitalization, inpatient rehabilitation and sick leave of anal cancer in Germany. *J Med Econ*  
35 2013;**16**:364–71. doi:10.3111/13696998.2012.759582  
36  
37 25 Abramowitz L, Remy V, Vainchtock A. Economic burden of anal cancer management in France. *Rev Epidemiol Sante Publique* 2010;**58**:331–8.  
38  
39 26 van der Linden N, Buter J, Pescott CP, *et al.* Treatments and costs for recurrent and/or metastatic squamous cell carcinoma of the head and neck in  
40 the Netherlands. *Head Neck* 2016;**273**:455–64. doi:10.1007/s00405-015-3495-y  
41  
42 27 Klussmann JP, Schädlich PK, Chen X, *et al.* Annual cost of hospitalization , inpatient rehabilitation , and sick leave for head and neck cancers in  
43  
44  
45  
46  
47

- 1  
2  
3  
4  
5 Germany. *Clin Outcomes Res* 2013;**5**:203–13.
- 6  
7 28 Kim K, Amonkar MM, Högberg D, *et al.* Economic burden of resected squamous cell carcinoma of the head and neck in an incident cohort of patients  
8 in the UK. *Head Neck Oncol* 2011;**3**:1–10.
- 9  
10 29 St Guily JL, Borget I, Vainchtock A, *et al.* Head and neck cancers in France : an analysis of the hospital medical information system ( PMSI ) database.  
11 *Head Neck Oncol* 2010;**2**:1–8.
- 12  
13 30 Agthoven M Van, Ineveld BM Van, Boer MF De, *et al.* The costs of head and neck oncology : primary tumours , recurrent tumours and long-term  
14 follow-up. *Eur J Cancer* 2001;**37**:2204–11.
- 15  
16 31 Corbridge R, Cox G. The cost of running a multidisciplinary head and neck oncology service - an audit. *Rev Laryngol Otol Rhinol* 2000;**121**:151–3.
- 17  
18 32 Lowry J. Maxillofacial surgery: the economic aspect. *Br J Oral Maxillofac Surg* 1990;**28**:16–9.
- 19  
20 33 van Agthoven M, Heule-Dieleman H, Knegt P, *et al.* Compliance and efficiency before and after implementation of a clinical practice guideline for  
21 laryngeal carcinomas. *Eur Arch Otorhinolaryngol* 2006;**263**:729–37. doi:10.1007/s00405-006-0062-6
- 22  
23 34 Zavras A, Andreopoulos N, Katsikeris N, *et al.* Oral cancer treatment costs in Greece and the effect of advanced disease. *BMC Public Health* 2002;**8**:8–  
24 15.
- 25  
26 35 Preuss S, Quante G, Semrau R, *et al.* An analysis of surgical complications, morbidity, and cost calculation in patients undergoing multimodal  
27 treatment for operable oropharyngeal carcinoma. *Laryngoscope* 2007;**117**:101–5.
- 28  
29 36 Keeping ST, Tempest MJ, Stephens SJ, *et al.* Penile cancer treatment costs in England. *BMC Public Health* 2015;**15**:1305. doi:10.1186/s12889-015-  
30 2669-2
- 31  
32 37 Harrison A, Montgomery J, Macgregor FB. Economic impact of recurrent respiratory papillomas in a UK adult population. *J Laryngol Otol*  
33 2016;**130**:645–9. doi:10.1017/S0022215116001201
- 34  
35 38 Marcellusi A, Capone A, Favato G, *et al.* Health utilities lost and risk factors associated with HPV-induced diseases in men and women: The HPV  
36 Italian collaborative study group. *Clin Ther* 2015;**37**:156–67. doi:10.1016/j.clinthera.2014.11.002
- 37  
38 39 Vriend HJ, Nieuwkerk PT, Sande MAB Van Der. Impact of genital warts on emotional and sexual well-being differs by gender. *Int J STD AIDS*  
39 2014;**25**:949–55. doi:10.1177/0956462414526706
- 40  
41 40 Dominiak-Felden G, Cohet C, Atrux-Tallau S, *et al.* Impact of human papillomavirus-related genital diseases on quality of life and psychosocial  
42 wellbeing: results of an observational, health-related quality of life study in the UK. *BMC Public Health* 2013;**13**:1065. doi:10.1186/1471-2458-13-  
43  
44  
45  
46  
47

- 1  
2  
3  
4  
5 1065  
6  
7 41 Shi J, Kang D, Qi S, *et al.* Impact of genital warts on health related quality of life in men and women in mainland China : a multicenter hospital-based  
8 cross-sectional study. *BMC Public Health* 2012;**12**. doi:10.1186/1471-2458-12-153  
9  
10 42 Drolet M, Brisson M, Maunsell E, *et al.* The Impact of Anogenital Warts on Health-Related Quality of Life : A 6-Month Prospective Study. *Sex Transm*  
11 *Dis* 2011;**38**:949–56. doi:10.1097/OLQ.0b013e3182215512  
12  
13 43 Mennini FS, Panatto D, Marcellusi A, *et al.* Time trade-off procedure for measuring health utilities loss with human papillomavirus-induced diseases:  
14 A multicenter, retrospective, observational pilot study in Italy. *Clin Ther* 2011;**33**:1084–95.e4. doi:10.1016/j.clinthera.2011.06.012  
15  
16 44 Senecal M, Brisson M, Maunsell E, *et al.* Loss of quality of life associated with genital warts : baseline analyses from a prospective study. *Sex Transm*  
17 *Infect* 2011;**87**:209–15. doi:10.1136/sti.2009.039982  
18  
19 45 Marra C, Ogilvie G, Gastonguay L, *et al.* Patients With Genital Warts Have a Decreased Quality of Life. *Sex Transm Dis* 2009;**36**:258–60.  
20 doi:10.1097/OLQ.0b013e318191a55e  
21  
22 46 Pirotta M, Ung L, Stein A, *et al.* The psychosocial burden of human papillomavirus related disease and screening interventions. *Sex Transm Infect*  
23 2009;**85**:508–13. doi:10.1136/sti.2009.037028  
24  
25 47 Woodhall S, Ramsey T, Cai C, *et al.* Estimation of the impact of genital warts on health- related quality of life. *Sex Transm Infect* 2008;**84**:161–6.  
26 doi:10.1136/sti.2007.029512  
27  
28 48 Aro K, Back L, Loimu V, *et al.* Trends in the 15D health-related quality of life over the first year following diagnosis of head and neck cancer. *Eur Arch*  
29 *Otorhinolaryngol* 2016;**273**:2141–50. doi:10.1007/s00405-015-3732-4  
30  
31 49 Govers T, Schreuder W, Klop W, *et al.* Quality of life after different procedures for regional control in oral cancer patients: cross-sectional survey. *Clin*  
32 *Otolaryngol* 2016;**41**:228–33.  
33  
34 50 Pickard AS, Jiang R, Lin H, *et al.* Using Patient-reported Outcomes to Compare Relative Burden of Cancer : EQ-5D and Functional Assessment of  
35 Cancer Therapy-General in Eleven Types of Cancer. *Clin Ther* 2016;**38**:769–77. doi:10.1016/j.clinthera.2016.03.009  
36  
37 51 Rettig E, D’Souza G, Thompson C, *et al.* Health-Related Quality of Life Before and After Head and Neck Squamous Cell Carcinoma : Analysis of the  
38 Surveillance , Epidemiology , and End Results – Medicare Health Outcomes Survey Linkage. *Cancer* 2016;**122**:1861–70. doi:10.1002/cncr.30005  
39  
40 52 Kent E, Ambs A, Mitchell S, *et al.* Health-related quality of life in older adult survivors of selected cancers: data from the SEER-MHOS linked data  
41 resource. *Cancer* 2015;**121**:758–65. doi:10.1002/cncr.29119.  
42  
43  
44  
45  
46  
47



- 1  
2  
3  
4  
5 53 Loimu V, Makitie A, Back L, *et al.* Health-related quality of life of head and neck cancer patients with successful oncological treatment. *Eur Arch Otorhinolaryngol* 2015;**272**:2415–23. doi:10.1007/s00405-014-3169-1
- 6  
7  
8 54 Noel C, Lee D, Kong Q, *et al.* Comparison of Health State Utility Measures in Patients with Head and Neck Cancer. *JAMA Otolaryngol Head Neck Surg* 2015;**141**:696–703.
- 9  
10  
11 55 Pottel L, Lycke M, Boterberg T, *et al.* G-8 indicates overall and quality-adjusted survival in older head and neck cancer patients treated with curative radiochemotherapy. *BMC Cancer* 2015;**15**:1–11. doi:10.1186/s12885-015-1800-1
- 12  
13 56 Lango MN, Egleston B, Fang C, *et al.* Baseline Health Perceptions , Dysphagia , and Survival in Patients With Head and Neck Cancer. *Cancer* 2014;**120**:840–7. doi:10.1002/cncr.28482
- 14  
15  
16 57 Nijdam WM, Levendag PC, Noever I, *et al.* Longitudinal changes in quality of life and costs in long-term survivors of tumors of the oropharynx treated with brachytherapy or surgery. *Brachytherapy* 2008;**7**:343–50. doi:10.1016/j.brachy.2008.05.001
- 17  
18 58 Rogers SN, Miller RD, Ali K, *et al.* Patients' perceived health status following primary surgery for oral and oropharyngeal cancer. *Int J Oral Maxillofac Surg* 2006;**35**:913–9. doi:10.1016/j.ijom.2006.07.017
- 19  
20  
21 59 Ringash J, Redelmeier D, O'Sullivan B, *et al.* Quality of life and utility in irradiated laryngeal cancer patients. *Int J Radiat Oncol Biol Phys* 2000;**47**:875–81.
- 22  
23  
24 60 Downer M, Jullien J, Speight P. An interim determination of health gain from oral cancer and precancer screening: 1. obtaining health state utilities. *Community Dent Health* 1997;**14**:139–42.
- 25  
26  
27 61 Conway EL, Farmer KC, Lynch WJ, *et al.* Quality of life valuations of HPV-associated cancer health states by the general population. *Sex Transm Infect* 2012;**88**:517–21. doi:10.1136/sextrans-2011-050161
- 28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

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

Confidential: For Review Only

**WORD COUNT, EXCLUDING TITLE PAGE, ABSTRACT, REFERENCES, FIGURES AND TABLES.**

Abstract	298 of 300 max.
Main text	2,261 of 3,000 max.
Number of figures and tables	3 Figures and 1 Table

**KEYWORDS**

HPV  
 VACCINATION  
 COST-EFFECTIVENESS  
 SYSTEMATIC REVIEWS  
 META-ANALYSIS

**AUTHORS' CONTRIBUTIONS**

KJO, MJP, and MJ conceived and planned the systematic review. LB conducted the systematic literature searches. KJO, MC, and CP, carried out sifting and data extraction of the systematic literature search results. KJO conducted the meta-analysis and took the lead in writing the manuscript, with guidance from MJP and MJ. All authors provided critical feedback on the manuscript.

**CORRESPONDING AUTHOR STATEMENT**

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in STI and any other BMJPG products and sub-licences such use and exploit all subsidiary rights, as set out in our licence

<http://group.bmj.com/products/journals/instructions-for-authors/licence-forms>

**ACKNOWLEDGEMENT**

We thank Kate Soldan, Consultant Epidemiologist, Public Health England, for her helpful review and suggestions of the manuscript.

We thank Anh Tran, Knowledge and Evidence Specialist, Public Health England, for her assistance with clarifying the systematic review searches.

We thank colleagues within the National Infection Service, Public Health England, specifically Ross Harris, Sara Croxford, Yoon Choi, Allen Lin, and Natasha Ratna, for their guidance and suggestions on meta-analysis.

**DISCLAIMERS**

The views expressed in the submitted article are the authors' own and not an official position of the institution or funder.

**SOURCE(S) OF SUPPORT**

MJ reports grants from National Institute for Health Research, during the conduct of the study. MP reports grants and personal fees from various pharmaceutical companies, outside the submitted work and holds 2% stocks of Ingress Health. KJO, MC, and MJ are employees of Public Health England whilst LB and CP were employees are Public Health England during initial periods of this work. The views expressed are those of the authors and not necessarily those of the NHS (England), the NIHR, the Department of Health (England) or Public Health England.

**CONFLICT OF INTEREST DECLARATION**

MJ reports grants from National Institute for Health Research, during the conduct of the study. MP reports grants and personal fees from various pharmaceutical companies, outside the submitted work and holds 2% stocks of Ingress Health. All other authors have nothing to disclose.

Confidential: For Review Only