CONFIDENTIAL UNTIL PUBLISHED Assessment Group's Addendum

Adjunctive colposcopy technologies for assessing suspected cervical abnormalities: a systematic review with meta-analysis and economic evaluation

July 24th 2017

We report the results of several additional sensitivity and scenario analyses undertaken to address comments received on the main report.

SA8: Uncertainty around the probability to progress from CIN2/3 to cancer

Several commentators considered that the model predictions for new cancer cases appeared high for a screened and actively managed population and raised issues concerning the external validity of the model. Aside from the diagnostic accuracy and effectiveness of the treatments being modelled, the main determinants of cancer risk are the distribution of initial health states and reason for referral (Table 29 p 145 for HPV triage and Table 30 p 146 for HPV primary) and the natural history model and associated transition probabilities (see Table 34 p 149).

The joint distribution of health state and reason for referral for HPV triage was based on outcomes of colposcopy referrals (31,114 samples) from the NHS cervical screening programme 2015-2016. The distribution of initial health states for the HPV primary protocol came from unpublished preliminary results collected in HPV primary pilot sites. Although we noted caution in relation to the lack of completeness and potential selection issues in relation to the HPV primary pilot site data, we consider that both sources represent the most appropriate available evidence.

The natural history data and transition probabilities were derived from a widely used epidemiological model by Kulasingam (2013) which was developed to inform the United States Preventive Services Task Force (USPSTF) on cervical cancer screening. Kulasingam (2013) is an update of the epidemiological model reported by Myers (2000) which was used in the previous economic model developed for DG4. In most cases the parameters and assumptions are exactly the same between Kulasingam (2013) and Myers (2000). The main difference noted by Kulasingam (2013) was: *"the estimate of progression from CIN2-3 to cancer. In the older model, this was estimated to be approximately 4 percent per year. In this model, we have revised the estimate for younger women*

(aged 30 years and younger) to reflect recent analyses that show that progression from CIN3 to cancer is approximately 1 percent per year)."

The Kulasingham (2013) data indicates that age appears to be an important source of heterogeneity (progression rate 4% per annum for age 30+ and 1% age <30). However, since the base-case of our model used a mean age of 36 years (the average age of the population referred for colposcopy), the actual probability applied in the base case was 4% for all women. We therefore undertook an additional sensitivity analysis to further explore the robustness of the base-case results to this source of heterogeneity.

Sensitivity analysis SA8 assumed that the probability to progress from CIN2/3 to cancer was 1% for all women. Results are presented in Tables 2 to 9. As expected, the model predicts a lower number of new cancer cases. Due to the lower incidence of cancer compared to the base-case analyses, the additional value of increased sensitivity (relative to lower specificity) reduces and the ICERs of both DYSIS and ZedScan compared to colposcopy alone increase. However, the ICERs for all referrals (in both types of clinic and under both screening protocols) do not exceed £8500 for DYSIS and £11,500 for ZedScan.

SA9: Impact of age

Considering the impact of age more explicitly within the model appears a more appropriate way to address heterogeneity in parameter inputs. More precisely, the age at which women enter the model has two main implications for cost-effectiveness related to the natural history of the disease and adverse obstetric outcomes. In the model, several parameters of the natural history depend on age. Specifically, women under 35 have higher HPV incidence rates but also higher probabilities of regressing from CIN to clear and a lower probability of progressing from CIN2/3 to cancer (see Table 34 in the report). However, because in the base case analysis women enter the model at 36, this heterogeneity is not fully captured. The second impact of age comes from the modelling of adverse obstetric outcomes. If women enter the model at a younger age, the period during which they can get pregnant will be longer which should logically increase the number of adverse outcomes compared to the base case.

In sensitivity analysis SA9, women's age was drawn from a distribution at the start of the model. The NHS Cervical screening programme 2015-2016 reports the cytology results by age group of 5 years; from there, we derive an age distribution for women referred for colposcopy (Table 1). However, in the absence of a distribution of initial health state and reason for referral by age, the exploration of the impact of age is necessarily limited. Especially, we have to assume that the prevalence of HPV, CIN

lesions and cancer is independent of age: as regards the initial distribution in the model, a 25 years old woman has the same probability than a woman aged 50 to be CIN2/3.

Age	Proportion	Source
27	0.364873	
32	0.196887	
37	0.130314	
42	0.104246	
47	0.090919	NHS Cervical screening programme 2015-2016
52	0.061532	
57	0.03243	
62	0.018801	

Table 1 SA9: initial distribution of age for women referred for colposcopy

Results (see Tables 10 to 17) show that including younger women in the model slightly decreases the number of new cancers (from 43 to 40 for 1000 patients for colposcopy alone) but more importantly largely increase the number of adverse obstetric outcomes (from 4 to 8.8 for 1000 patients for colposcopy alone).

DYSIS still dominates colposcopy alone in see and treat clinic and is slightly more costly but also more effective in watchful waiting clinics with an ICER of £126 under HPV triage and £660 under HPV primary. ZedScan still appears to be more costly but also more effective than colposcopy alone, with an ICER ranging from £261 in see and treat clinics to £1316 in watchful waiting clinics under HPV triage (£621 to £2331 under HPV primary). The results of the comparison between DYSIS and ZedScan are globally unchanged compared to the base case.

Sc. 4: Cost of DYSIS do not include optional viewer licence and maintenance package

In the base case analysis, the cost of DYSIS includes the purchase price of the machine (£24,000) as well as the maintenance package offered by the company (£6500), annuitized over 5 years at a 3.5% interest rate. The cost also includes, as an additional yearly cost, the average price of the viewer software licence (£650 for the first year, £500 for the next 4 years). In their comments on the main report, DYSIS Medical Ltd argued that both the maintenance package and the viewer licence were optional and therefore should not be included in DYSIS cost. In response to these comments, we provide a scenario (Sc4) where the cost of DYSIS does not include the price of the viewer licence and where the maintenance cost is equivalent to the one used for colposcopy alone (£1073 per year).

Indeed, we believe it would not be appropriate to consider a scenario where DYSIS does not require any maintenance cost.

In scenario 4, the revised cost per patient for DYSIS is £8.55 (instead of £9.24 in the base case). Since the cost of colposcopy alone and ZedScan as well as secondary outcomes for the three devices are unchanged, we only present the comparison between DYSIS and colposcopy alone and between DYSIS and ZedScan (see Tables 18 to 21).

The impact of the alternative DYSIS cost per patient is very small (the average cost of the DYSIS strategy decreases by about £1) and conclusions are therefore unchanged.

Results

• SA8: Progression from CIN2/3 to Cancer = 1% (annual probability)

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics					
All referrals	Colposcopy alone	779.90	19.21682			
	DYSIS	780.25	19.22269	0.35	0.00588	59
LG referrals	Colposcopy alone	643.37	19.22491			
	DYSIS	659.52	19.22931	16.16	0.00440	3671
HG referrals	Colposcopy alone	1075.70	19.18563			
	DYSIS	1039.67	19.18995	-36.03	0.00432	Dominant
Watchful wai	ting clinics					
All referrals	Colposcopy alone	828.63	19.21366			
	DYSIS	844.68	19.21827	16.05	0.00461	3485
LG referrals	Colposcopy alone	661.78	19.22619			
	DYSIS	684.53	19.23096	22.76	0.00476	4776
HG referrals	Colposcopy alone	1185.82	19.18561			
	DYSIS	1197.97	19.18717	12.14	0.00156	7776

Table 2 SA8, HPV triage – DYSIS vs. colposcopy alone

Table 3 SA8, HPV triage – ZedScan vs. colposcopy alone

	, 0		A	17		
	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics					
All referrals	Colposcopy alone	779.90	19.21682			
	ZedScan	814.38	19.22566	34.48	0.00885	3897
LG referrals	Colposcopy alone	643.37	19.22491			
	ZedScan	704.15	19.23471	60.79	0.00980	6204
HG referrals	Colposcopy alone	1075.70	19.18563			
	ZedScan	1047.78	19.19116	-27.92	0.00553	Dominant
Watchful Wai	ting clinics					
All referrals	Colposcopy alone	828.63	19.21366			
	ZedScan	888.63	19.22104	60.01	0.00737	8140
LG referrals	Colposcopy alone	661.78	19.22619			
	ZedScan	731.60	19.23605	69.82	0.00986	7083
HG referrals	Colposcopy alone	1185.82	19.18561			
	ZedScan	1236.48	19.18735	50.65	0.00174	29,068

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER				
See and Treat	See and Treat clinics									
All referrals	DYSIS	780.25	19.22269							
	ZedScan	814.38	19.22566	34.13	0.00297	11,483				
LG referrals	DYSIS	659.52	19.22931							
	ZedScan	704.15	19.23471	44.63	0.00540	8270				
HG referrals	DYSIS	1039.67	19.18995							
	ZedScan	1047.78	19.19116	8.11	0.00121	6694				
Watchful Wai	ting clinics		•		•	•				
All referrals	DYSIS	844.68	19.21827							
	ZedScan	888.63	19.22104	43.95	0.00277	15,894				
LG referrals	DYSIS	684.53	19.23096							
	ZedScan	731.60	19.23605	47.06	0.00509	9242				
HG referrals	DYSIS	1197.97	19.18717							
	ZedScan	1236.48	19.18735	38.51	0.00018	212,622				

Table 4 SA8, HPV triage – ZedScan vs. DYSIS

	Strategy	Missed CIN2+	Develop Cancer	Die from cancer	LLETZ	Unnecessary treatment (Clear, HPV)	Unnecessary treatment (CIN1)	Unnecessary diagnostic biopsy	Pre- term delivery
See and T	reat clinics								
All referrals	Colposcopy alone	70	12	3.0	480	9	18	140	4.0
	DYSIS	30	10	2.5	511	22	39	230	4.4
	ZedScan	3	8	2.3	531	31	52	292	4.8
LG referrals	Colposcopy alone	93	14	2.9	295	6	18	133	1.4
	DYSIS	39	11	2.3	331	16	40	246	1.8
	ZedScan	4	10	2.0	354	22	52	324	2.1
HG referrals	Colposcopy alone	22	8	3.3	882	15	16	150	10.0
	DYSIS	9	6	3.0	904	35	37	193	10.3
	ZedScan	1	6	2.8	918	49	50	221	10.5
Watchful	Waiting clinics	5	-						
All referrals	Colposcopy alone	70	13	3.1	463	0	0	148	4.0
	DYSIS	30	11	2.7	476	0	0	253	4.1
	ZedScan	3	9	2.5	485	0	0	326	4.3
LG referrals	Colposcopy alone	93	15	3.0	279	0	0	139	1.3
	DYSIS	39	12	2.6	297	0	0	262	1.7
	ZedScan	4	11	2.2	310	0	0	349	2.0
HG referrals	Colposcopy alone	23	8	3.3	865	0	0	164	9.5
	DYSIS	10	7	3.1	867	0	0	231	9.4
	ZedScan	1	7	3.1	868	0	0	277	9.5

Table 5 SA8 - Secondary outcomes, base case (per 1,000 women referred)

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics				•	
All referrals	Colposcopy alone	759.95	19.20797			
	DYSIS	762.71	19.21179	2.75	0.00382	721
LG referrals	Colposcopy alone	626.40	19.23303			
	DYSIS	643.87	19.23514	17.47	0.00211	8295
HG referrals	Colposcopy alone	1075.27	19.18172			
	DYSIS	1039.91	19.18282	-35.36	0.00110	Dominant
Watchful wait	ting clinics					
All referrals	Colposcopy alone	804.67	19.21040			
	DYSIS	824.81	19.21289	20.15	0.00249	8078
LG referrals	Colposcopy alone	642.51	19.22947			
	DYSIS	664.16	19.23481	21.64	0.00534	4055
HG referrals	Colposcopy alone	1183.50	19.17997			
	DYSIS	1197.10	19.17835	13.60	-0.00163	Dominated

Table 6 SA8, HPV primary - DYSIS vs. colposcopy alone

Table 7 SA8, HPV primary – ZedScan vs. colposcopy alone

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics		•			
All referrals	Colposcopy alone	759.95	19.20797			
	ZedScan	799.77	19.21576	39.82	0.00779	5110
LG referrals	Colposcopy alone	626.40	19.23303			
	ZedScan	695.24	19.23832	68.84	0.00529	13012
HG referrals	Colposcopy alone	1075.27	19.18172			
	ZedScan	1049.66	19.18575	-25.60	0.00402	Dominant
Watchful Wai	ting clinics					
All referrals	Colposcopy alone	804.67	19.21040			
	ZedScan	870.61	19.21633	65.94	0.00594	11,107
LG referrals	Colposcopy alone	642.51	19.22947			
	ZedScan	716.84	19.23768	74.32	0.00821	9057
HG referrals	Colposcopy alone	1183.50	19.17997			
	ZedScan	1237.14	19.17949	53.64	-0.00048	Dominated

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics					
All referrals	DYSIS	762.71	19.21179			
	ZedScan	799.77	19.21576	37.07	0.00398	9325
LG referrals	DYSIS	643.87	19.23514			
	ZedScan	695.24	19.23832	51.37	0.00318	16,130
HG referrals	DYSIS	1039.91	19.18282			
	ZedScan	1049.66	19.18575	9.75	0.00293	3330
Watchful Wai	ting clinics			•	•	
All referrals	DYSIS	824.81	19.21289			
	ZedScan	870.61	19.21633	45.79	0.00344	13,303
LG referrals	DYSIS	664.16	19.23481			
	ZedScan	716.84	19.23768	52.68	0.00287	18,360
HG referrals	DYSIS	1197.10	19.17835			
	ZedScan	1237.14	19.17949	40.04	0.00114	35,039

Table 8 SA8, HPV primary protocol – ZedScan vs. DYSIS

	Strategy	Missed CIN2+	Develop Cancer	Die from cancer	LLETZ	Unnecessary treatment (Clear, HPV)	Unnecessary treatment (CIN1)	Unnecessary diagnostic biopsy	Pre- term delivery
See and T	reat clinics								
All referrals	Colposcopy alone	85	9	2.5	457	8	14	165	3.9
	DYSIS	34	7	2.0	486	20	30	297	4.2
	ZedScan	4	6	1.7	503	28	40	387	4.4
LG referrals	Colposcopy alone	105	10	2.1	278	6	14	165	1.3
	DYSIS	43	8	1.6	310	15	31	324	1.6
	ZedScan	5	6	1.2	329	21	40	434	2.0
HG referrals	Colposcopy alone	31	6.1	3.3	885	14	14	163	10.0
	DYSIS	12	5.2	3.0	905	33	31	231	10.2
	ZedScan	1	4.6	2.9	918	46	42	277	10.4
Watchful	Waiting clinics	5							
All referrals	Colposcopy alone	84	10	2.5	444	0	0	172	3.8
	DYSIS	35	8	2.2	458	0	0	317	4.0
	ZedScan	4	6	1.9	466	0	0	417	4.1
LG referrals	Colposcopy alone	106	11	2.2	266	0	0	171	1.3
	DYSIS	44	8	1.7	283	0	0	339	1.6
	ZedScan	5	7	1.4	295	0	0	455	1.9
HG referrals	Colposcopy alone	31	6	3.3	871	0	0	177	9.6
	DYSIS	13	6	3.1	873	0	0	268	9.5
	ZedScan	1	5	3.0	874	0	0	331	9.5

Table 9 HPV primary protocol - Secondary outcomes, base case (per 1,000 women referred)

• SA9: Age distribution from NHS statistics 2015-2016

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics					
All referrals	Colposcopy alone	961.33	18.99018			
	DYSIS	946.82	19.00384	-14.51	0.01366	Dominant
LG referrals	Colposcopy alone	787.81	18.98179			
	DYSIS	778.94	19.00245	-8.87	0.02066	Dominant
HG referrals	Colposcopy alone	1334.11	18.95948			
	DYSIS	1296.20	18.96579	-37.92	0.00631	Dominant
Watchful wait	ting clinics					
All referrals	Colposcopy alone	1004.60	18.97208			
	DYSIS	1006.42	18.98650	1.82	0.01442	126
LG referrals	Colposcopy alone	800.64	18.98353			
	DYSIS	800.45	19.00461	-0.19	0.02108	Dominant
HG referrals	Colposcopy alone	1434.50	18.95879			
	DYSIS	1441.58	18.96781	7.08	0.00902	785

Table 10 SA9, HPV triage – DYSIS vs. colposcopy alone

Table 11 SA9, HPV triage – ZedScan vs. colposcopy alone

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics					
All referrals	Colposcopy alone	961.33	18.99018			
	ZedScan	967.83	19.01509	6.50	0.02492	261
LG referrals	Colposcopy alone	787.81	18.98179			
	ZedScan	809.95	19.01761	22.14	0.03583	618
HG referrals	Colposcopy alone	1334.11	18.95948			
	ZedScan	1301.15	18.96653	-32.97	0.00705	Dominant
Watchful Wai	ting clinics					
All referrals	Colposcopy alone	1004.60	18.97208			
	ZedScan	1036.05	18.99598	31.45	0.02389	1316
LG referrals	Colposcopy alone	800.64	18.98353			
	ZedScan	834.37	19.01692	33.73	0.03339	1010
HG referrals	Colposcopy alone	1434.50	18.95879			
	ZedScan	1474.80	18.97160	40.30	0.01281	3146

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics					
All referrals	DYSIS	946.82	19.00384			
	ZedScan	967.83	19.01509	21.02	0.01125	1868
LG referrals	DYSIS	778.94	19.00245			
	ZedScan	809.95	19.01761	31.01	0.01516	2045
HG referrals	DYSIS	1296.20	18.96579			
	ZedScan	1301.15	18.96653	4.95	0.00074	6726
Watchful Wai	ting clinics		•	•		
All referrals	DYSIS	1006.42	18.98650			
	ZedScan	1036.05	18.99598	29.63	0.00948	3127
LG referrals	DYSIS	800.45	19.00461			
	ZedScan	834.37	19.01692	33.92	0.01231	2755
HG referrals	DYSIS	1441.58	18.96781			
	ZedScan	1474.80	18.97160	33.22	0.00379	8767

Table 12 SA9, HPV triage – ZedScan vs. DYSIS

	Strategy	Missed CIN2+	Develop Cancer	Die from cancer	LLETZ	Unnecessary treatment (Clear, HPV)	Unnecessary treatment (CIN1)	Unnecessary diagnostic biopsy	Pre- term delivery
See and T	reat clinics								
All referrals	Colposcopy alone	66	39.8	8.9	441	9	17	138	8.8
	DYSIS	28	32.0	7.1	478	22	37	228	9.8
	ZedScan	3	27.0	6.1	501	31	48	291	10.3
LG referrals	Colposcopy alone	87	47.6	9.8	245	6	17	131	3.2
	DYSIS	37	37.7	7.7	286	15	36	243	4.1
	ZedScan	4	31.4	6.6	312	22	47	322	4.8
HG referrals	Colposcopy alone	20	24.1	6.8	872	15	17	152	20.8
	DYSIS	8	20.8	6.0	896	35	37	196	21.4
	ZedScan	1	18.8	5.6	911	49	51	223	21.8
Watchful	Waiting clinics	5							
All referrals	Colposcopy alone	66	41.4	9.3	426	0	0	147	8.5
	DYSIS	29	34.8	7.9	443	0	0	251	9.0
	ZedScan	3	30.5	6.9	455	0	0	325	9.4
LG referrals	Colposcopy alone	87	48.9	10.1	229	0	0	137	3.0
	DYSIS	38	40.3	8.3	253	0	0	260	3.8
	ZedScan	4	34.8	7.3	270	0	0	346	4.4
HG referrals	Colposcopy alone	20	25.0	7	855	0	0	166	19.9
	DYSIS	9	22.7	6	857	0	0	233	19.9
	ZedScan	1	21.7	6	858	0	0	280	19.9

Table 13 SA9 - Secondary outcomes, base case (per 1,000 women referred)

	<u> </u>			<u> </u>		
	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER
See and Treat	clinics					
All referrals	Colposcopy alone	911.44	18.98603			
	DYSIS	898.15	19.00011	-13.29	0.01408	Dominant
LG referrals	Colposcopy alone	736.99	18.99048			
	DYSIS	733.68	19.01248	-3.31	0.02200	Dominant
HG referrals	Colposcopy alone	1321.61	18.95540			
	DYSIS	1283.91	18.96235	-37.69	0.00694	Dominant
Watchful wai	ting clinics					
All referrals	Colposcopy alone	946.06	18.98287			
	DYSIS	952.02	18.99191	5.97	0.00903	660
LG referrals	Colposcopy alone	748.94	18.99404			
	DYSIS	749.42	19.01595	0.48	0.02191	22
HG referrals	Colposcopy alone	1431.97	18.95319			
	DYSIS	1440.03	18.95462	8.05	0.00144	5603

Table 14 SA9, HPV primary - DYSIS vs. colposcopy alone

Table 15 SA9, HPV primary – ZedScan vs. colposcopy alone

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER				
See and Treat clinics										
All referrals	Colposcopy alone	911.44	18.98603							
	ZedScan	924.38	19.00685	12.94	0.02082	621				
LG referrals	Colposcopy alone	736.99	18.99048							
	ZedScan	768.85	19.02084	31.86	0.03036	1050				
HG referrals	Colposcopy alone	1321.61	18.95540							
	ZedScan	1293.61	18.96504	-28.00	0.00964	Dominant				
Watchful Wai	ting clinics									
All referrals	Colposcopy alone	946.06	18.98287							
	ZedScan	987.62	19.00071	41.56	0.01783	2331				
LG referrals	Colposcopy alone	748.94	18.99404							
	ZedScan	785.46	19.02320	36.52	0.02915	1253				
HG referrals	Colposcopy alone	1431.97	18.95319							
	ZedScan	1474.96	18.95947	42.99	0.00628	6842				

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER				
See and Treat clinics										
All referrals	DYSIS	898.15	19.00011							
	ZedScan	924.38	19.00685	26.22	0.00674	3891				
LG referrals	DYSIS	733.68	19.01248							
	ZedScan	768.85	19.02084	35.17	0.00836	4207				
HG referrals	DYSIS	1283.91	18.96235							
	ZedScan	1293.61	18.96504	9.69	0.00270	3594				
Watchful Wai	ting clinics		•	•	•					
All referrals	DYSIS	952.02	18.99191							
	ZedScan	987.62	19.00071	35.59	0.00880	4045				
LG referrals	DYSIS	749.42	19.01595							
	ZedScan	785.46	19.02320	36.04	0.00725	4972				
HG referrals	DYSIS	1440.03	18.95462							
	ZedScan	1474.96	18.95947	34.94	0.00485	7210				

Table 16 SA9, HPV primary protocol – ZedScan vs. DYSIS

	Strategy	Missed CIN2+	Develop Cancer	Die from cancer	LLETZ	Unnecessary treatment (Clear, HPV)	Unnecessary treatment (CIN1)	Unnecessary diagnostic biopsy	Pre- term delivery
See and T	reat clinics								
All referrals	Colposcopy alone	77	31	6.8	426	8	13	165	8.5
	DYSIS	31	24	5.2	458	21	29	296	9.2
	ZedScan	3	19	4.4	478	29	38	388	9.6
LG referrals	Colposcopy alone	97	36	7.1	236	6	13	163	3.3
	DYSIS	40	27	5.4	273	15	28	320	4.0
	ZedScan	4	22	4.3	295	21	36	431	4.6
HG referrals	Colposcopy alone	28	20	6.0	877	14	14	166	20.7
	DYSIS	11	17	5.3	899	33	31	235	21.3
	ZedScan	1	15	5.0	913	47	42	282	21.7
Watchful	Waiting clinics	5							
All referrals	Colposcopy alone	77	32	7.0	412	0	0	172	8.1
	DYSIS	32	26	5.6	428	0	0	317	8.7
	ZedScan	3	22	4.9	440	0	0	419	8.9
LG referrals	Colposcopy alone	99	37	7.4	224	0	0	169	3.0
	DYSIS	41	29	5.7	247	0	0	337	3.7
	ZedScan	4	24	4.7	262	0	0	455	4.1
HG referrals	Colposcopy alone	28	21	6.3	861	0	0	181	20.3
	DYSIS	11	18	5.8	864	0	0	274	20.2
	ZedScan	1	17	5.5	866	0	0	338	20.2

Table 17 SA9, HPV primary protocol - Secondary outcomes, base case (per 1,000 women referred)

• Sc4: DYSIS cost do not include viewer licence or the optional maintenance package, maintenance cost are equivalent to colposcopy alone

ruble to be i, in v thage "Dibib vs. corposeopy alone								
Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER			
See and Treat clinics								
Colposcopy alone	903.28	19.16500						
DYSIS	871.15	19.18516	-32.13	0.02016	Dominant			
Colposcopy alone	793.97	19.16330						
DYSIS	769.47	19.18794	-24.51	0.02464	Dominant			
Colposcopy alone	1139.13	19.16122						
DYSIS	1090.21	19.17156	-48.92	0.01034	Dominant			
ting clinics	•							
Colposcopy alone	953.02	19.16286						
DYSIS	939.92	19.18194	-13.09	0.01908	Dominant			
Colposcopy alone	812.85	19.16283						
DYSIS	798.22	19.18601	-14.63	0.02318	Dominant			
Colposcopy alone	1252.07	19.16008						
DYSIS	1254.17	19.16580	2.10	0.00571	367			
	Strategy clinics Colposcopy alone DYSIS Colposcopy alone DYSIS Colposcopy alone DYSIS ing clinics Colposcopy alone DYSIS Colposcopy alone DYSIS Colposcopy alone DYSIS	Strategy Cost clinics 903.28 DYSIS 871.15 Colposcopy alone 903.97 DYSIS 769.47 Colposcopy alone 1139.13 DYSIS 1090.21 ing clinics 939.92 Colposcopy alone 953.02 DYSIS 939.92 Colposcopy alone 812.85 DYSIS 798.22 Colposcopy alone 1252.07 DYSIS 1254.17	StrategyCostQALYsclinics903.2819.16500DYSIS871.1519.18516Colposcopy alone793.9719.16330DYSIS769.4719.18794Colposcopy alone1139.1319.16122DYSIS1090.2119.17156ing clinics1090.2119.16286DYSIS939.9219.18194Colposcopy alone812.8519.16283DYSIS798.2219.18004Colposcopy alone812.8519.16283DYSIS798.2219.16008DYSIS1252.0719.16008DYSIS1254.1719.16580	StrategyCostQALYsIncr. costColposcopy alone903.2819.16500DYSIS871.1519.18516-32.13Colposcopy alone793.9719.16330DYSIS769.4719.18794-24.51Colposcopy alone1139.1319.16122DYSIS1090.2119.17156-48.92ing clinics939.9219.18194-13.09Colposcopy alone812.8519.16283DYSIS798.2219.18601-14.63Colposcopy alone1252.0719.160082.10	StrategyCostQALYsIncr. costIncr. QALYsclinics903.2819.16500Incr. QALYsDYSIS871.1519.18516-32.130.02016Colposcopy alone793.9719.16330Incr. QALYsDYSIS769.4719.18794-24.510.02464Colposcopy alone1139.1319.16122Incr. QALYsDYSIS769.4719.18794-24.510.02464Colposcopy alone1139.1319.16122Incr. QALYsDYSIS1090.2119.17156-48.920.01034ing clinicsIncr. QALYsIncr. QALYsIncr. QALYsColposcopy alone953.0219.16122Incr. QALYsDYSIS939.9219.18194-13.090.01908Colposcopy alone812.8519.16283Incr. QALYsDYSIS798.2219.18601-14.630.02318Colposcopy alone1252.0719.16008Incr. QALYsDYSIS1254.1719.165802.100.00571			

Table 18 Sc4, HPV triage – DYSIS vs. colposcopy alone

Table 19 Sc4, HPV triage – ZedScan vs. DYSIS

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER				
See and Treat clinics										
All referrals	DYSIS	871.15	19.18516							
	ZedScan	885.91	19.19901	14.76	0.01385	1066				
LG referrals	DYSIS	769.47	19.18794							
	ZedScan	789.30	19.20307	19.83	0.01514	1310				
HG referrals	DYSIS	1090.21	19.17156							
	ZedScan	1091.97	19.17651	1.76	0.00495	356				
Watchful Wai	ting clinics									
All referrals	DYSIS	939.92	19.18194							
	ZedScan	965.87	19.19363	25.95	0.01170	2218				
LG referrals	DYSIS	798.22	19.18601							
	ZedScan	823.19	19.20082	24.97	0.01481	1686				
HG referrals	DYSIS	1254.17	19.16580							
	ZedScan	1288.82	19.16911	34.65	0.00332	10,448				

Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER			
See and Treat clinics								
Colposcopy alone	850.08	19.17506						
DYSIS	824.13	19.19120	-25.95	0.01614	Dominant			
Colposcopy alone	732.33	19.19008						
DYSIS	714.12	19.20787	-18.21	0.01779	Dominant			
Colposcopy alone	1126.93	19.16192						
DYSIS	1078.51	19.16774	-48.42	0.00581	Dominant			
ting clinics	•							
Colposcopy alone	894.41	19.17511						
DYSIS	887.50	19.18937	-6.91	0.01426	Dominant			
Colposcopy alone	748.86	19.18496						
DYSIS	736.70	19.20646	-12.16	0.02150	Dominant			
Colposcopy alone	1236.94	19.15863						
DYSIS	1239.14	19.16234	2.20	0.00371	594			
	Strategy clinics Colposcopy alone DYSIS Colposcopy alone DYSIS Colposcopy alone DYSIS ting clinics Colposcopy alone DYSIS Colposcopy alone DYSIS Colposcopy alone DYSIS	StrategyCostclinicsColposcopy alone850.08DYSIS824.13Colposcopy alone732.33DYSIS714.12Colposcopy alone1126.93DYSIS1078.51ting clinics1078.51Colposcopy alone894.41DYSIS887.50Colposcopy alone748.86DYSIS736.70Colposcopy alone1236.94DYSIS1239.14	StrategyCostQALYsclinicsColposcopy alone850.0819.17506DYSIS824.1319.19120Colposcopy alone732.3319.19008DYSIS714.1219.20787Colposcopy alone1126.9319.16192DYSIS1078.5119.16192DYSIS1078.5119.16774ting clinics1919.17511DYSIS887.5019.18937Colposcopy alone748.8619.18496DYSIS736.7019.20646Colposcopy alone1236.9419.15863DYSIS1239.1419.16234	Strategy Cost QALYs Incr. cost clinics Incr. cost Incr. cost Colposcopy alone 850.08 19.17506 Incr. cost DYSIS 824.13 19.19120 -25.95 Colposcopy alone 732.33 19.19008 Incr. cost DYSIS 714.12 19.20787 -18.21 Colposcopy alone 1126.93 19.16192 Incr. cost DYSIS 1078.51 19.16774 -48.42 ting clinics Incr. cost Incr. cost Incr. cost Colposcopy alone 1126.93 19.16192 Incr. cost DYSIS 1078.51 19.16774 -48.42 ting clinics Incr. cost Incr. cost Colposcopy alone 894.41 19.17511 Incr. cost DYSIS 887.50 19.18937 -6.91 Colposcopy alone 748.86 19.18496 Incr. cost DYSIS 736.70 19.20646 -12.16 Colposcopy alone 1236.94 19.15863 <	StrategyCostQALYsIncr. costIncr. QALYsclinicsColposcopy alone850.0819.17506DYSIS824.1319.19120-25.950.01614Colposcopy alone732.3319.19008DYSIS714.1219.20787-18.210.01779Colposcopy alone1126.9319.16192DYSIS1078.5119.16774-48.420.00581ting clinicsColposcopy alone894.4119.17511DYSIS887.5019.18937-6.910.01426Colposcopy alone748.8619.18496DYSIS736.7019.20646-12.160.02150Colposcopy alone1236.9419.15863DYSIS1239.1419.162342.200.00371			

Table 20 Sc4, HPV primary – DYSIS vs. colposcopy alone

Table 21 Sc4, HPV primary protocol – ZedScan vs. DYSIS

	Strategy	Cost	QALYs	Incr. cost	Incr. QALYs	ICER				
See and Treat clinics										
All referrals	DYSIS	824.13	19.19120							
	ZedScan	844.41	19.20206	20.28	0.01085	1869				
LG referrals	DYSIS	714.12	19.20787							
	ZedScan	744.85	19.22007	30.73	0.01220	2518				
HG referrals	DYSIS	1078.51	19.16774							
	ZedScan	1082.27	19.17347	3.76	0.00574	655				
Watchful Wai	ting clinics	•	•	•	•					
All referrals	DYSIS	887.50	19.18937							
	ZedScan	918.78	19.19977	31.28	0.01040	3008				
LG referrals	DYSIS	736.70	19.20646							
	ZedScan	770.26	19.21984	33.56	0.01338	2508				
HG referrals	DYSIS	1239.14	19.16234							
	ZedScan	1276.58	19.16668	37.44	0.00434	8617				