Supplementary material

AdViSHE

Assessment of the Validation Status of Health-Economic Decision Models

A. **Validation of the conceptual model (2 questions)**

Part A discusses techniques for validating the conceptual model. A conceptual model describes the underlying system (e.g., progression of disease) using a mathematical, logical, verbal, or graphical representation. Please indicate where the conceptual model and its underlying assumptions are described and justified.

The conceptual model was described in a graphical representation in Figure 1 and Figure 1. Underlying assumptions were described and justified in the Method section.

1. **A1/ Face validity testing (conceptual model): Have experts been asked to judge the appropriateness of the conceptual model?**

   Yes, clinical experts (LW.W, L.X, Y.G) and a statistical expert (JF.X) were asked to judge the appropriateness of the conceptual model within rounds of group discussions. LW.W and L.X are considered clinical experts in the area of gastroenterology. Y.G is considered a sponge cytology tests expert since he has conducted several research on the diagnosis of esophageal cancer using sponge cytology tests. JF.X is considered a statistical expert since she has been in the Statistics Department for many years and has experience in cancer-related statistics.

2. **A2/ Cross validity testing (conceptual model): Has this model been compared to other conceptual models found in the literature or clinical textbooks?**

   No, as to our knowledge, this is the first economic evaluation study for sponge cytology test in esophageal squamous carcinoma (ESCC), and therefore no comparable models are available. However, we did

comparisons between previous economic evaluations for endoscopic ESCC screening and found that the staging of ESCC in our model is consistent in the previous publications(3,4). The surveillance strategy was discriminative from Xia's report(3) as the results of sponge cytology tests were presented as negative or positive and it was therefore impossible to identify healthy individuals, mild esophageal dysplasia, and moderate esophageal dysplasia patients based on cytological results.

B. **Input data validation (2 questions)**

Part B discusses techniques to validate the data serving as input in the model. These techniques are applicable to all types of models commonly used in HE modelling. Please indicate where the description and justification of the following aspects.

We performed related searches on PubMed, MEDLINE, and Embase for related studies. References in the studies were also taken into consideration. Data sources included published economic evaluation studies, randomized controlled trials, cohort studies, background information, and expert opinions. Details are described in the method section.

1. **B1/ Face validity testing (input data): Have experts been asked to judge the appropriateness of the input data?**

   Yes, all input parameters were consulted and confirmed by the authors.

2. **B2/ Model fit testing: When input parameters are based on regression models, have statistical tests been performed?**

   Not applicable as no regression models were adopted in our study.

C. **Validation of the computerized model (4 questions)**

Part C discusses various techniques for validating the model as it is implemented in a software program. If there are any differences between the conceptual model (Part A) and the final computerized model, please indicate where these differences are reported and justified.

Not applicable as there is no difference between the conceptual model and the final model.

1. **C1/ External review: Has the computerized model been examined by modelling experts?**

   Yes, the model structure and calculation were examined by all the corresponding authors in TreeAge Pro 2024 R1.1.

2. **C2/ Extreme value testing: Has the model been run for specific, extreme sets of parameter values in order to detect any coding errors?**

   Yes, specific, extreme sets of parameter values were examined and as no coding errors were found, related outcomes were not reported.

3. **C3/ Testing of traces: Have patients been tracked through the model to determine whether its logic is correct?**

   Yes, but this was not reported as no errors were found.

4. **C4/ Unit testing: Have individual sub-modules of the computerized model been tested?**

   Yes, but this was not reported as no errors were found.

D. **Operational validation (4 questions)**

   Part D discusses techniques used to validate the model outcomes.

1. **D1/ Face validity testing (model outcomes): Have experts been asked to judge the appropriateness of the model outcomes?**

   Yes, all results were discussed and confirmed by the authors.

2. **D2/ Cross validation testing (model outcomes): Have the model outcomes been compared to the outcomes of other models that address similar problems?**

   As limited research on this domain, comparisons were conducted based on published literature with the same intervention or the same disease. Details were described in the discussion section.

3. **D3/ Validation against outcomes using alternative input data: Have the model outcomes been compared to the outcomes obtained when using alternative input data?**

Yes, this was conducted in sensitivity and scenario analyses. Related results have been described in the manuscript.

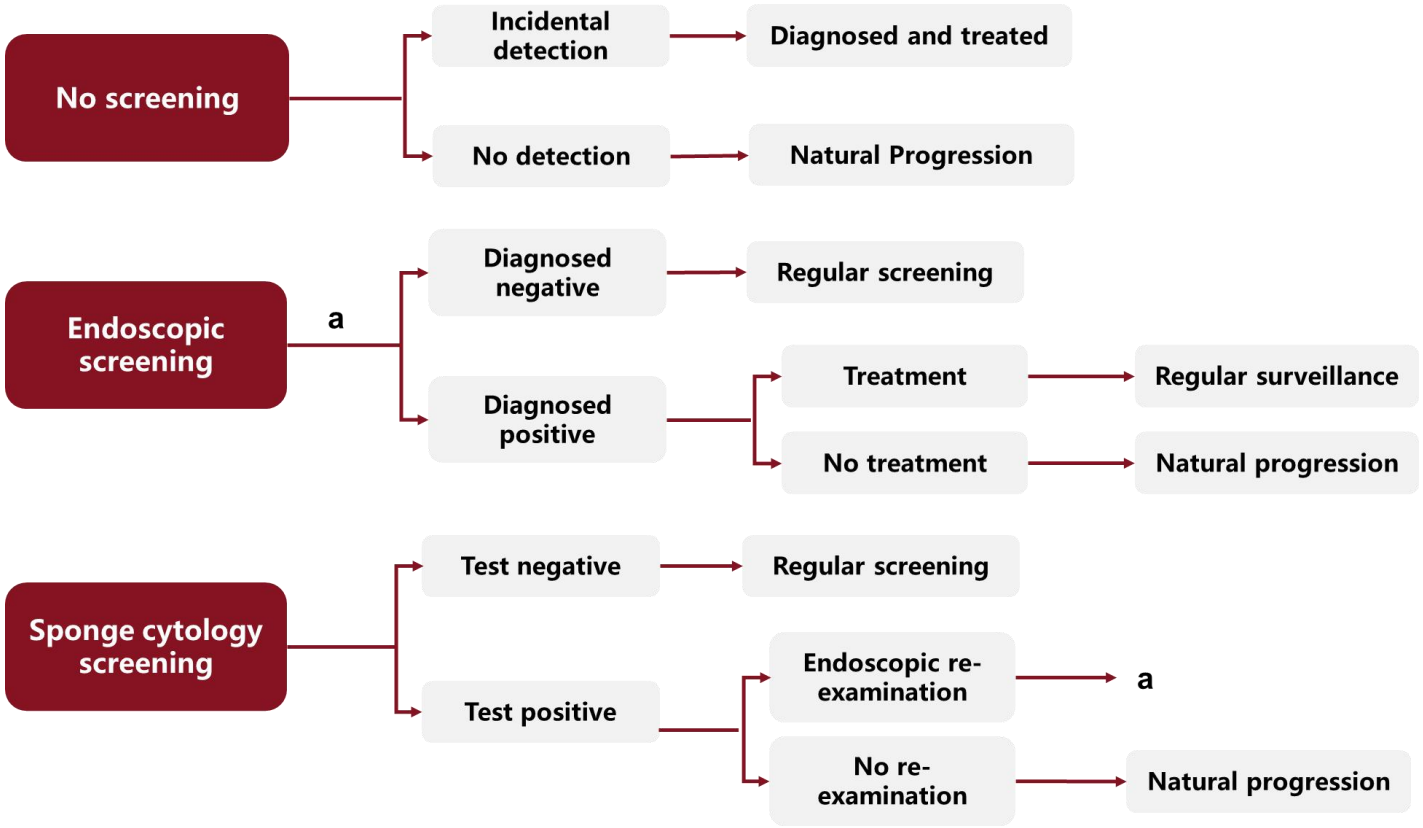
4. **D4/ Validation against empirical data: Have the model outcomes been compared to empirical data?**

   Not applicable.

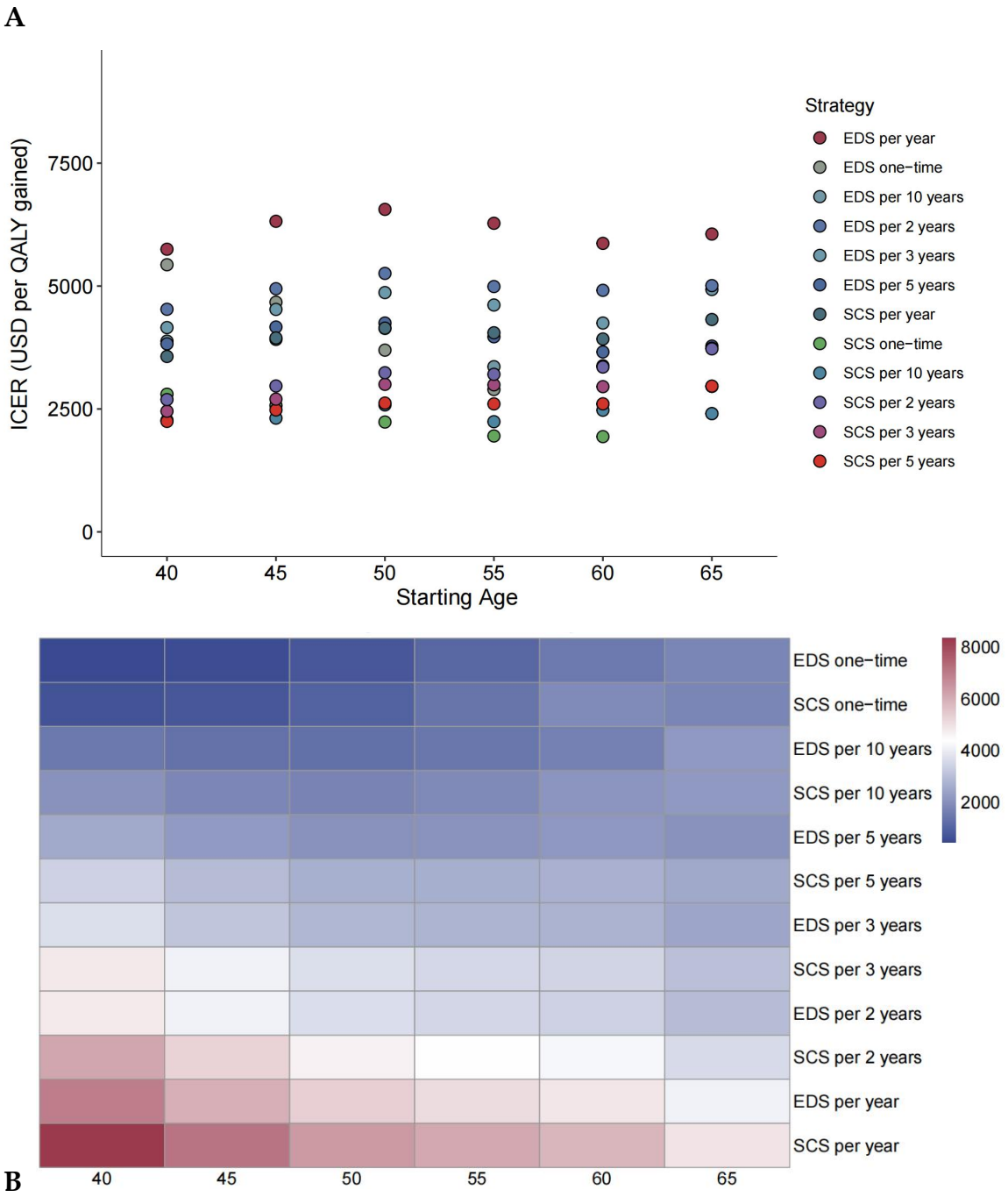
E. **Other validation techniques (1 question)**

1. **E1/ Other validation techniques: Have any other validation techniques been performed?**

   Not applicable.

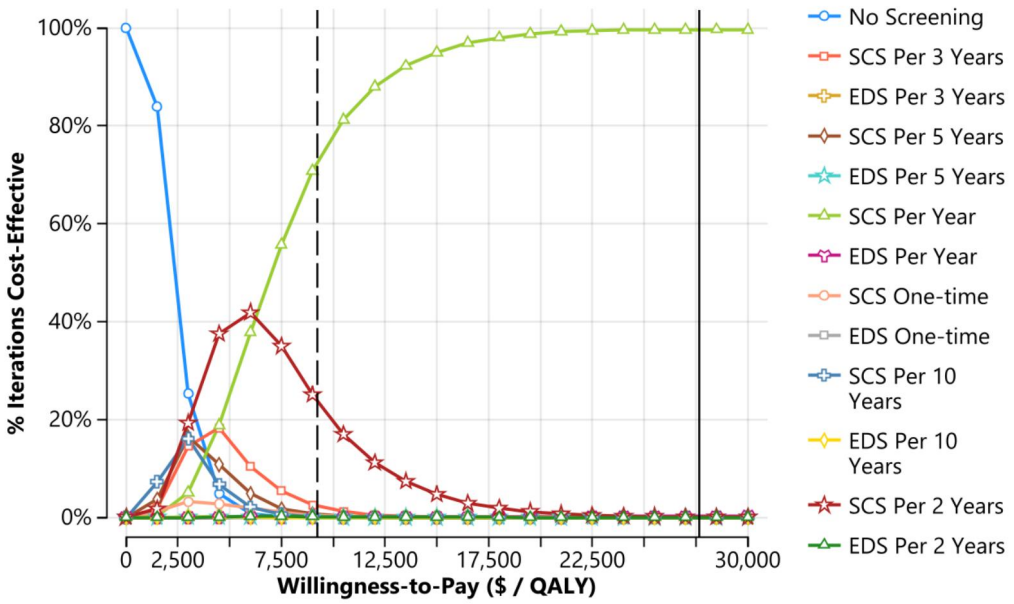


Supplementary Figure 1 Screening pathway of different strategies.



Supplementary Figure 2 Results of scenario analyses. A: Incremental cost-effective ratios (ICERs) for all strategies in different scenario analyses. B: Quality-adjusted life years (QALYs) gained per 100,000 participants in different scenario analyses. QALYs gained and ICERs were computed against no screening strategy for each scenario analysis. QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness; EDS: Endoscopic screening; SCS, sponge cytology

screening.



Supplementary Figure 3 Cost-effectiveness acceptability curve. The dashed vertical black line represents the willingness-to-pay (WTP) threshold of 9217 USD; the solid vertical black line represents the WTP threshold of 27651 USD. EDS: Endoscopic screening; SCS: Sponge cytology screening; QALY: Quality-adjusted life-year.

Supplementary Table 1 Parameters used in scenario analyses

	Scenario 1	**Scenario 2**	**Scenario 3**	**Scenario 4**	**Scenario 5**	**Scenario 6**	**Reference**
Starting age	40	45	50	55	60	65	(1–4)
Cycles	35	30	25	20	15	10	
Prevalence							
mD	0.0116	0.0204	0.0339	0.0535	0.0811	0.1190	

MD	0.0010	0.0022	0.0044	0.0083	0.0146	0.0246
SD/CIS	0.0005	0.0012	0.0028	0.0058	0.0112	0.0205
EEC	0.0002	0.0005	0.0011	0.0023	0.0045	0.0085
AEC	0.0001	0.0002	0.0004	0.0007	0.0014	0.0025

mD: Mild dysplasia; MD: Moderate dysplasia; SD/CIS: Severe dysplasia/carcinoma *in situ*; EEC: Early esophageal cancer; AEC: Advanced esophageal cancer.

Supplementary Table 2 Cost-effectiveness of different screening strategies in the same screening intervals

Strategy	Costs per 100,000 participants (USD)	QALYs per 100,000 participants	Incremental costs per 100,000 participants (USD)	QALYs gained per 100,000 participants	ICERs
One-time					
Spong cytology screening	6,452,020	1,474,672	NA	NA	NA
Endoscopic screening	7,019,587	1,474,458	567,568	-214	Dominated
Per 10 years					
Spong cytology screening	8,691,075	1,475,723	NA	NA	NA
Endoscopic screening	9,716,978	1,475,250	1,025,903	-473	Dominated
Per 5 years					
Spong cytology screening	11,823,542	1,476,865	NA	NA	NA
Endoscopic	13,676,309	1,476,120	1,852,767	-745	Dominated

screening						
Per 3 years						
Spong screening	cytology	15,682,730	1,478,055	NA	NA	NA
Endoscopic screening		18,773,932	1,477,073	3,091,202	-982	Dominated
Per 2 years						
Spong screening	cytology	20,115,833	1,479,177	NA	NA	NA
Endoscopic screening		24,851,313	1,478,033	4,735,480	-1,144	Dominated
Per year						
Spong screening	cytology	32,781,384	1,481,087	NA	NA	NA
Endoscopic screening		42,263,921	1,479,898	9,482,537	-1,189	Dominated

Dominated, negative incremental cost-effectiveness are regarded as dominated. QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness.

Supplementary Table 3 Cost-effectiveness of different screening intervals under certain screening strategies

Strategy	Costs per 100,000 participants (USD)	QALYs per 100,000 participants	Incremental costs per 100,000 participants (USD)	QALYs gained per 100,000 participants	ICERs
Sponge cytology screening					
One-time	6,452,020	1,474,672	NA	NA	NA
Per 10 years	8,691,075	1,475,723	2,239,055	1,051	2130
Per 5 years	11,823,542	1,476,865	3,132,467	1,142	2743
Per 3 years	15,682,730	1,478,055	3,859,188	1,190	3244
Per 2 years	20,115,833	1,479,177	4,433,104	1,122	3950
Per year	32,781,384	1,481,087	12,665,550	1,910	6630
Endoscopic screening					
One-time	7,019,587	1,474,458	NA	NA	NA
Per 10 years	9,716,978	1,475,250	2,697,391	792	3407
Per 5 years	13,676,309	1,476,120	3,959,331	870	4551
Per 3 years	18,773,932	1,477,073	5,097,623	953	5350
Per 2 years	24,851,313	1,478,033	6,077,381	961	6325
Per year	42,263,921	1,479,898	17,412,607	1,864	9340

Incremental cost-effectiveness are calculated against the next optimal alternative. QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness.

Supplementary Table 4 Cost-effectiveness of different strategies with varying participation rates of sponge cytology screening

Participation rate of SCS	**0.28**			**0.42**			**0.56**			**0.7**			**0.84**		
Outcomes / Strategy	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERS**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**
No screening	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA
EDS one-time	70	14.7446	Dominated	70	14.7446	Dominated	70	14.7446	Dominated	70	14.7446	Dominated	70	14.7446	4671
SCS one-time	55	14.7434	2269	60	14.7451	2463	65	14.7467	2571	69	14.7484	2639	74	14.7501	759
EDS per 10 years	97	14.7525	Dominated	97	14.7525	Dominated	97	14.7525	Dominated	97	14.7525	6754	97	14.7525	9366
SCS per 10 years	66	14.7488	2168	77	14.7531	2259	87	14.7572	2313	97	14.7613	2353	108	14.7653	2385

EDS per 5 years	137	14.7612	Dominated	137	14.7612	Dominated	137	14.7612	Dominated	137	14.7612	Dominated	137	14.7612	Dominated
SCS per 5 years	82	14.7552	2571	100	14.7621	2653	118	14.7686	2743	136	14.7748	2842	153	14.7806	2952
EDS per 3 years	188	14.7707	Dominated	188	14.7707	Dominated	188	14.7707	Dominated	188	14.7707	Dominated	188	14.7707	Dominated
SCS per 3 years	103	14.7626	2806	131	14.7721	3006	157	14.7805	3244	182	14.7880	3528	207	14.7946	3870
EDS per 2 years	249	14.7803	Dominated	249	14.7803	Dominated	249	14.7803	Dominated	249	14.7803	Dominated	249	14.7803	Dominated
SCS per 2 years	128	14.7708	3017	166	14.7823	3422	201	14.7918	3950	236	14.7995	4644	269	14.8058	5572
EDS per year	423	14.7990	22996	423	14.7990	Dominated	423	14.7990	Dominated	423	14.7990	Dominated	423	14.7990	Dominated
SCS per year	196	14.7891	3734	263	14.8022	4882	328	14.8109	6630	394	14.8164	9373	462	14.8197	13885

Costs are given in USD. Dominated, negative incremental cost-effective ratios (ICERs) are regarded as dominated. ICERs are calculated among all strategies.QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness; EDS: Endoscopic screening; SCS: Sponge cytology screening

Supplementary Table 5 Cost-effectiveness of different strategies with varying specificity of endoscopy

Specificity of endoscopy	**0.59**			**0.6925**			**0.7950**			**0.8975**			**1**		
Outcomes / Strategy	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**
No Screening	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA
SCS One-Time	65	14.7467	2571.0094	65	14.7467	2571.0094	65	14.7467	2571.0094	65	14.7467	2571.0094	65	14.7467	2571.0094
EDS One-Time	70	14.7445	Dominated	70	14.7445	Dominated	70	14.7446	Dominated	70	14.7446	Dominated	70	14.7446	Dominated
SCS Per 10 Years	87	14.7572	2313.4309	87	14.7572	2313.4309	87	14.7572	2313.4309	87	14.7572	2313.4309	87	14.7572	2313.4309
EDS Per 10 Years	97	14.7520	Dominated	97	14.7521	Dominated	97	14.7522	Dominated	97	14.7524	Dominated	97	14.7525	Dominated
SCS Per 5	118	14.7	2743.2	118	14.7	2743.2	118	14.7	2743.2	118	14.7	2743.2	118	14.7	2743.2

Years				686	315		686	315		686	315		686	315		686	315
EDS Per Years		5	137	14.7602	Dominated	137	14.7604	Dominated	137	14.7607	Dominated	137	14.7609	Dominated	137	14.7612	Dominated
SCS Per Years		3	157	14.7805	3243.632	157	14.7805	3243.632	157	14.7805	3243.632	157	14.7805	3243.632	157	14.7805	3243.632
EDS Per Years		3	189	14.7693	Dominated	188	14.7696	Dominated	188	14.7700	Dominated	188	14.7704	Dominated	188	14.7707	Dominated
SCS Per Years		2	201	14.7918	3950.0487	201	14.7918	3950.0487	201	14.7918	3950.0487	201	14.7918	3950.0487	201	14.7918	3950.0487
EDS Per Years		2	250	14.7785	Dominated	250	14.7790	Dominated	249	14.7794	Dominated	249	14.7799	Dominated	249	14.7803	Dominated
SCS Per Year			328	14.8109	6630.4570	328	14.8109	6630.4570	328	14.8109	6630.4570	328	14.8109	6630.4570	328	14.8109	6630.4570
EDS Per Year			426	14.7968	Dominated	425	14.7973	Dominated	425	14.7979	Dominated	424	14.7984	Dominated	423	14.7990	Dominated

Costs are given in USD. Dominated, negative incremental cost-effective ratios (ICERs) are regarded as dominated. ICERs are calculated among all strategies.QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness; EDS: Endoscopic screening; SCS: Sponge cytology screening

Supplementary Table 6 Cost-effectiveness of different strategies with varying sensitivity of endoscopy

Sensitivity of endoscopy	**0.88**			**0.91**			**0.94**			**0.97**			**1**		
Outcomes / Strategy	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**	**Costs**	**QALYs**	**ICERs**
No Screening	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA	45	14.7393	NA
SCS One-Time	60	14.7454	2374.9595	61	14.7457	2433.0252	62	14.7460	2484.4157	63	14.7464	2530.1387	65	14.7467	2571.0094
EDS One-Time	65	14.7432	Dominated	67	14.7436	Dominated	68	14.7439	Dominated	69	14.7442	Dominated	70	14.7446	Dominated
SCS Per 10 Years	82	14.7554	2283.0910	83	14.7558	2291.9842	85	14.7563	2299.9498	86	14.7568	2307.0735	87	14.7572	2313.4309
EDS Per 10 Years	92	14.7507	Dominated	93	14.7511	Dominated	95	14.7516	Dominated	96	14.7520	Dominated	97	14.7525	Dominated
SCS Per 5 Years	113	14.7664	2831.8949	115	14.7670	2809.2013	116	14.7676	2786.8700	117	14.7681	2764.8850	118	14.7686	2743.2315
EDS Per 5	132	14.7	Domin	133	14.7	Domin	134	14.7	Domin	136	14.7	Domin	137	14.7	Domin

Years		590	ated		596	ated		601	ated		607	ated		612	ated
SCS Per 3 Years	153	14.7783	3300.6327	154	14.7789	3285.8237	155	14.7794	3271.4008	156	14.7800	3257.3513	157	14.7805	3243.6632
EDS Per 3 Years	183	14.7683	Dominated	184	14.7689	Dominated	185	14.7695	Dominated	187	14.7701	Dominated	188	14.7707	Dominated
SCS Per 2 Years	198	14.7897	3951.2070	199	14.7902	3950.0424	199	14.7908	3949.4663	200	14.7913	3949.4707	201	14.7918	3950.0487
EDS Per 2 Years	244	14.7779	Dominated	245	14.7785	Dominated	246	14.7791	Dominated	247	14.7797	Dominated	249	14.7803	Dominated
SCS Per Year	326	14.8098	6401.9769	327	14.8101	6456.9622	327	14.8103	6513.3668	327	14.8106	6571.1962	328	14.8109	6630.4570
EDS Per Year	420	14.7972	Dominated	425	14.7973	Dominated	425	14.7979	Dominated	424	14.7984	Dominated	423	14.7990	Dominated

Costs are given in USD. Dominated, negative incremental cost-effective ratios (ICERs) are regarded as dominated. ICERs are calculated among all strategies.QALY: Quality-adjusted life year; ICER: Incremental cost-effectiveness; EDS: Endoscopic screening; SCS: Sponge cytology screening.

Reference

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