THE LANCET
Global Health

Supplementary appendix 2

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Zou Z, Fairley CK, Ong JJ, et al. Domestic HPV vaccine price and economic returns for cervical cancer prevention in China: a cost-effectiveness analysis. *Lancet Glob Health* 2020; **8:** e1335–44.

Supplementary Materials

1. Model structure

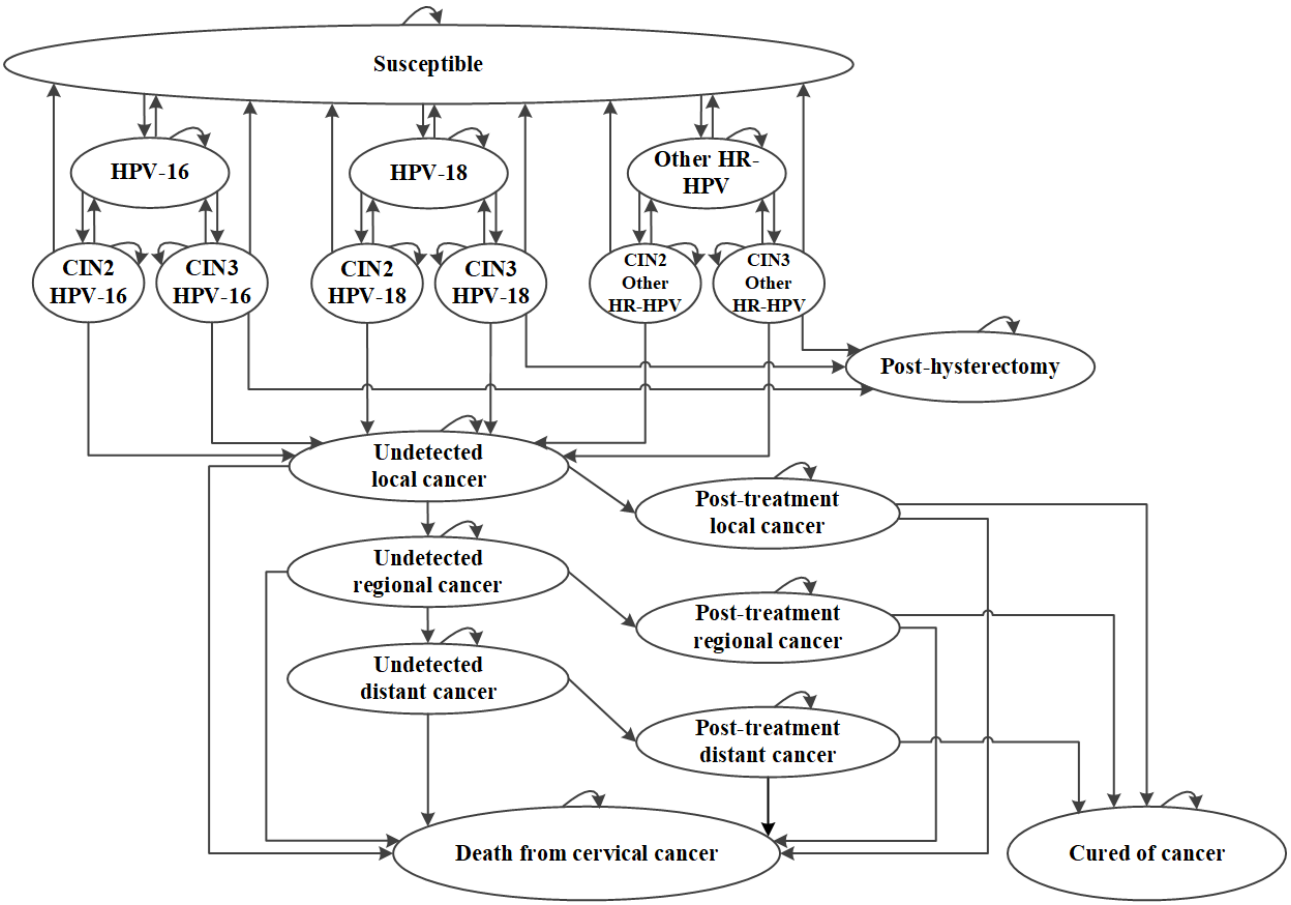


Figure S1 Markov model of cervical cancer natural history

Circles represent health states, and lines with arrowhead represent transitions and their directions. A woman in the susceptible state enters the HPV-16 state if infected with HPV-16 alone or with both HPV-16 and 18, enters the HPV-18 state if infected with HPV-18 alone, or enters the other high-risk HPV state if infected with any other high-risk HPV types (including 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73, 82, and their co-infections) whether with or without the coinfection of HPV-16/18. Women in the CIN2, CIN3, or cancer states can be identified by self-initiated examinations or by the screening, and the diagnosed women are provided with corresponding therapies (Figure S2). A diagnosed woman with CIN3 aged ≥30 years enters the post-hysterectomy state if she selects hysterectomy. Women in any state may suffer a natural background death (the state is not shown here), but women in the cancer states have additional mortality risk due to cervical cancer. A woman in any post-treatment cancer states enters the cured of cancer state if she stays in the current state for ≥ 20 years. Local, regional, and distant cancer states correspond to stage I, II−IV A, and IV B by the International Federation of Obstetrics and Gynaecology staging, respectively. CIN=cervical intraepithelial neoplasia.

Infection with low-risk-HPV was not considered in the model because it does not cause cervical cancer. CIN1 can be

interpreted as a microscopic manifestation of acute HPV infection, and a person with CIN1 is not recommended to receive treatment (same as women infected with HPV but have normal cytology).[1] Therefore, CIN1 was incorporated into the 'HPV infection state' to simplify the model. CIN2 and CIN3 were modelled as non-sequential precancerous states with respective probabilities of progression to cervical cancer due to available observational data, similar to previous studies.[2–5]

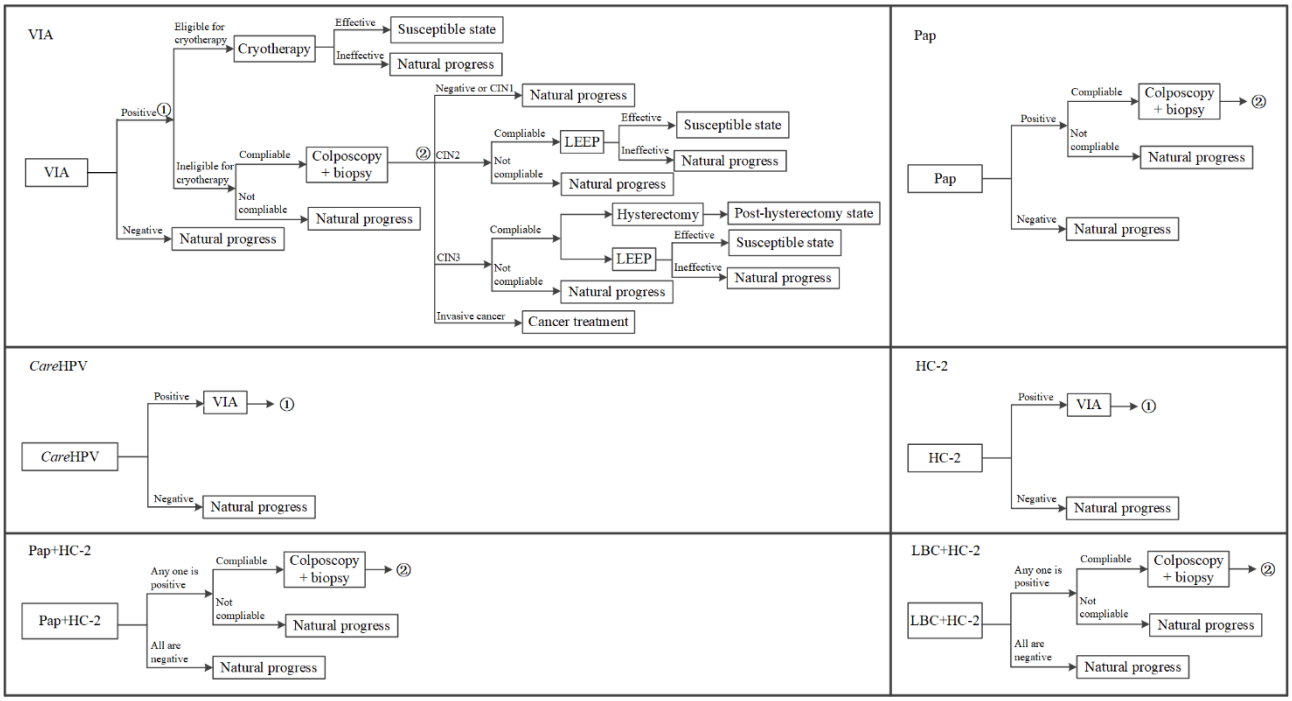


Figure S2 Flowchart of screening, diagnosis, and treatment by various screening methods

VIA=visual inspection with acetic acid. Pap=Papanicolaou test. HC-2=Hybrid Capture-2. LBC=liquid-based cytology. CIN=cervical intraepithelial neoplasia. LEEP=loop electrosurgical excision procedure.

All the screening methods and corresponding diagnosis and treatment procedures were modelled according to the recommendations of the World Health Organization and the Department of Disease Prevention and Control, the National Ministry of Health of China.[6,7] For VIA, *care*HPV, and HC-2 screening strategies, the 'screen-and-treat' approach was assumed to be used: women who are screening-positive and eligible for cryotherapy (i.e., the entire lesion is visible, the squamocolumnar junction is visible, and the lesion does not cover more than 75% of the ectocervix) are treated immediately with cryotherapy; women who are screening-positive but ineligible for cryotherapy are provided further biopsy, and the corresponding treatments are given according to histologically-confirmed results. In the 'screen-and-treat' approach, 'false-positive' identifying women may lead to an additional cryotherapy cost and the loss of quality of life in the year of treatment (if they are eligible for cryotherapy) or additional costs of colposcopy and biopsy (if they are ineligible for cryotherapy). For Pap, Pap+HC-2 and LBC+HC-2 screening strategies, the 'screen, diagnose, and treat' approach was used, that is, the histologically-confirmed diagnosis is necessary prior to any treatment. In this approach, 'false-positive' identifying women may lead to additional costs of colposcopy and biopsy. Noncompliance in screening and treatment was considered in each follow-up visit, and the treatment ineffectiveness was considered for each therapy in our model.

2. Intervention strategies

61 different intervention strategies were investigated in our study, as shown in Table S1.

Table S1 Intervention strategies

	Screening method	Screening frequency	Vaccination
Screening alone	VIA	Once, twice, once every 10 years, once every 5 years, once every 3 years	—
	Pap	Once, twice, once every 10 years, once every 5 years, once every 3 years	—
	*Care*HPV	Once, twice, once every 10 years, once every 5 years, once every 3 years	—
	HC-2	Once, twice, once every 10 years, once every 5 years, once every 3 years	—
	Pap+HC-2	Once, twice, once every 10 years, once every 5 years, once every 3 years	—
	LBC+HC-2	Once, twice, once every 10 years, once every 5 years, once every 3 years	—
Vaccination alone	—	—	Domestic HPV vaccine
Screening and vaccination	VIA	Once, twice, once every 10 years, once every 5 years, once every 3 years	Domestic HPV vaccine
	Pap	Once, twice, once every 10 years, once every 5 years, once every 3 years	Domestic HPV vaccine
	*Care*HPV	Once, twice, once every 10 years, once every 5 years, once every 3 years	Domestic HPV vaccine
	HC-2	Once, twice, once every 10 years, once every 5 years, once every 3 years	Domestic HPV vaccine
	Pap+HC-2	Once, twice, once every 10 years, once every 5 years, once every 3 years	Domestic HPV vaccine
	LBC+HC-2	Once, twice, once every 10 years, once every 5 years, once every 3 years	Domestic HPV vaccine

VIA=visual inspection with acetic acid. Pap=Papanicolaou test. HC-2=Hybrid Capture-2. LBC=liquid-based cytology.

3. Model calibration

The high-risk HPV incidence rate is an important parameter in the Markov model, but there were only a few studies with the relevant data, especially from China. Therefore, the model calibration was conducted to determine the type- and age-specific incidence rates of high-risk HPV infection used in the model.[8,9] This was achieved using the three steps as follows.

First, a wide initial range was provided for each type- and age-specific incidence rate of high-risk HPV infection based on published literature (Table S4),[10,11] to ensure that the actual values were covered in the respective initial ranges. Three types of infection were considered here to correspond to the three HPV states of the Markov model: (1) HPV-16 infection: women infected with HPV-16 alone or with both HPV-16 and 18; (2) HPV-18 infection: women infected with HPV-18 alone; (3) high-risk HPV infection, women infected with any other high-risk HPV types whether with or without the coinfection of HPV-16/18.

Second, multiple calibration targets were established for model calibration, including type- and age-specific prevalence rates of high-risk HPV infection in women and the proportional distributions of different infection types in patients with CIN2, CIN3, and cervical cancer. All calibration targets were assumed to follow a normal distribution, and their point estimates and 95% confidence intervals (CIs) were determined based on published literature.

Only two large sample cross-sectional surveys provided detailed information on age-specific prevalence rates for type-specific HPV infection in general Chinese women. One involved 28,457 women attending screening programs from 10 different regions of Yunnan Province between May 2011 and July 2015 and used Luminex xMAP technology to identify 26 HPV types.[12] The other enrolled 8,944 women attending health examination in Sichuan Province from January to September in 2016 and also used Luminex xMAP technology to identify 27 HPV types.[13] Based on the data from the two surveys, we re-calculated age-specific prevalence rates of the three high-risk HPV infection types and their 95%

CIs after combining the samples for each age group, as shown in Table S2.

Table S2 Point estimates and 95% confidence intervals (CIs) for age-specific prevalence rates of high-risk HPV infection in general Chinese women, by three infection types

Age group (years)	No. of total	HPV-16[a]		HPV-18[b]		Other high-risk HPV[c]	
		Prevalence	95% CI	Prevalence	95% CI	Prevalence	95% CI
20–25	3,278	0·022	0·013–0·031	0·009	0·006–0·012	0·113	0·102–0·124
26–30	5,423	0·013	0·002–0·023	0·007	0·004–0·011	0·090	0·083–0·098
31–35	6,355	0·016	0·007–0·025	0·004	0·002–0·006	0·081	0·064–0·097
36–40	7,305	0·017	0·011–0·022	0·003	0·001–0·005	0·077	0·071–0·083
41–45	6,232	0·016	0·013–0·019	0·006	0·004–0·008	0·083	0·075–0·090
46–50	4,681	0·011	0·001–0·022	0·003	0·002–0·005	0·083	0·075–0·091
51–55	2,244	0·014	0·009–0·019	0·003	0·000–0·006	0·087	0·067–0·108
≥56	1,883	0·016	0·010–0·022	0·004	0·001–0·007	0·101	0·088–0·115

[a]Infected with HPV-16 alone or with both HPV-16 and 18.
[b]Infected with HPV-18 alone.
[c]Infected with any other high-risk HPV types whether with or without the coinfection of HPV-16/18.

A meta-analysis of 45 PCR-based studies reporting the type-specific HPV distribution among 30,165 HPV-positive Chinese women with various cervical lesions.[14] Based on this report, we determined proportional distributions of the three high-risk HPV infection types and their 95% CIs in Chinese patients with CIN 2, CIN3, and cervical cancer, respectively, as shown in Table S3.

Table S3 Point estimates and 95% confidence intervals (CIs) for proportional distributions of three high-risk HPV infection types in Chinese patients with CIN2, CIN3, and cervical cancer

	HPV-16[a]		HPV-18[b]		Other high-risk HPV[c]	
	Proportion	95% CI	Proportion	95% CI	Proportion	95% CI
CIN2	0·288	0·270–0·306	0·061	0·051–0·070	0·651	0·633–0·670
CIN3	0·413	0·396–0·428	0·044	0·038–0·051	0·543	0·527–0·559
Cervical Cancer	0·551	0·542–0·559	0·106	0·101–0·111	0·343	0·335–0·351

[a]Infected with HPV-16 alone or with both HPV-16 and 18.
[b]Infected with HPV-18 alone.
[c]Infected with any other high-risk HPV types whether with or without the coinfection of HPV-16/18.
CIN=cervical intraepithelial neoplasia.

Third, we identified the 'good-fitting sets' of type- and age-specific incidence rates of high-risk HPV infection, such that the Markov model was able to calibrate satisfactorily to the calibration targets. This step was done using a likelihood-based approach in Matlab software, and a total of 10 million simulations were conducted. In each simulation, one value for each type- and age-specific incidence rate was randomly extracted from a uniform distribution over its initial range and a set of input values was formed. With this set of input values, the Markov model was run to produce the outputs which were compared with the calibration targets and a goodness-of-fit score was calculated by summing the log-likelihoods. In the running of the model, estimated base-case values for all the other transition probability parameters (Table S5) were used. Goodness-of-fit scores were assumed to follow a chi-square distribution with the number of degrees of freedom equal to the number of calibration targets. Based on this distribution, 'good-fitting sets' of type- and age-specific incidence rates of high-risk HPV infection were identified using the likelihood ratio test,

comprising those sets that did not produce a non-inferior fit compared with the best-fitting set (using an alpha level of 5%). The best-fitting set was the set with the lowest goodness-of-fit score whose simulated outputs were closest to the calibration targets (Table S4). A more detailed description of the method can be found in previous articles.[8,9] The best-fitting set was introduced into the Markov model as the base-case values of type- and age-specific incidence rates of high-risk HPV infection and all the good-fitting sets were used in sensitivity analyses.

Table S4 Initial ranges and the best-fitting set of type- and age-specific incidence rates of high-risk HPV infection

HPV type & age group (years)	Initial range	Best-fitting set
HPV-16[a]		
<21	0·00001−0·1	0·019042
21−24	0·00001−0·1	0·026804
25−29	0·00001−0·1	0·011424
30−49	0·00001−0·1	0·00598
≥50	0·00001−0·1	0·010381
HPV-18[b]		
<21	0·00001−0·05	0·007908
21−24	0·00001−0·05	0·02262
25−29	0·00001−0·05	0·00072
30−49	0·00001−0·05	0·00211
≥50	0·00001−0·05	0·003007
Other high-risk HPV[c]		
<21	0·00001−0·5	0·008842
21−24	0·00001−0·5	0·085656
25−29	0·00001−0·5	0·030124
30−49	0·00001−0·5	0·05603
≥50	0·00001−0·5	0·052648

[a]Infected with HPV-16 alone or with both HPV-16 and 18.

[b]Infected with HPV-18 alone.

[c]Infected with any other high-risk HPV types whether with or without the coinfection of HPV-16/18.

For illustrative purposes, we randomly sampled 500 of the good-fitting sets to simulate type- and age-specific prevalence rates of high-risk HPV infection in women and proportional distributions of the three high-risk HPV infection types in patients with CIN2, CIN3, and cervical cancer, respectively. The outputs were compared with the corresponding calibration targets, as shown in Figure S3 and S4.

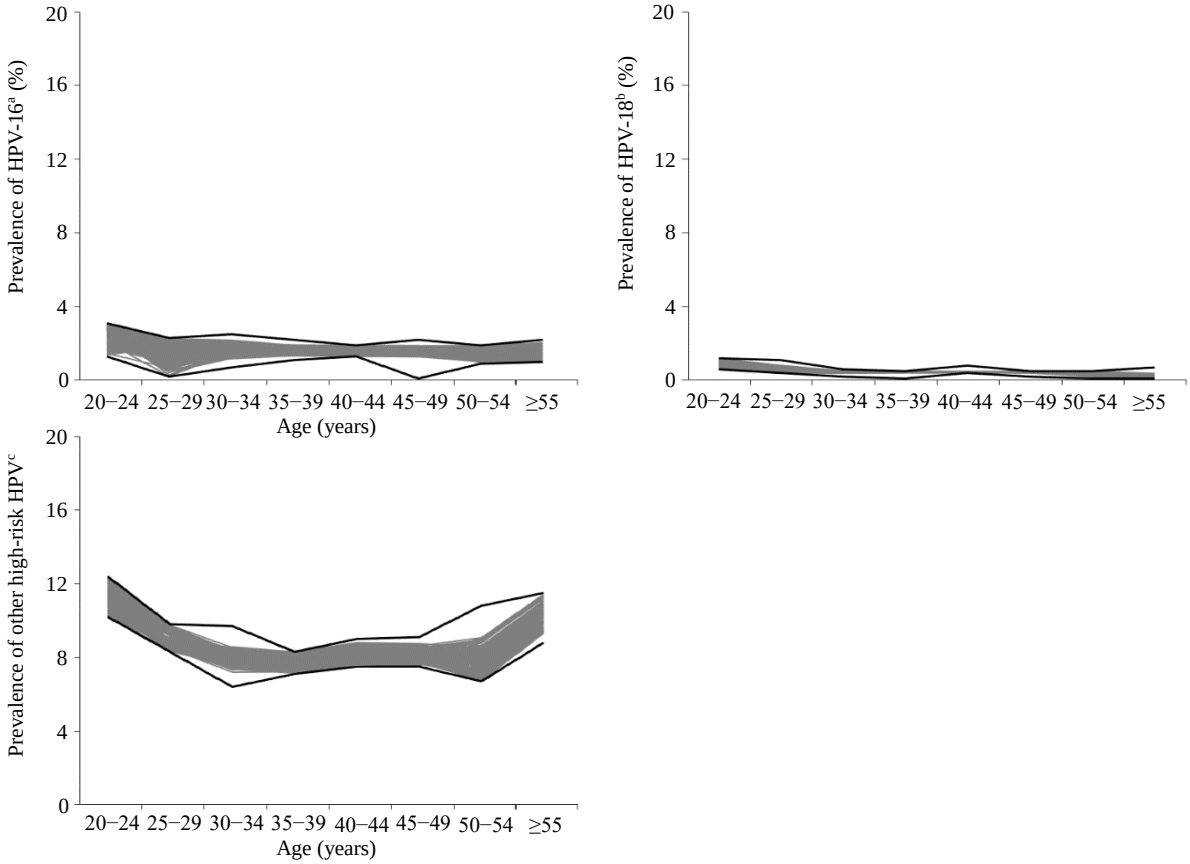
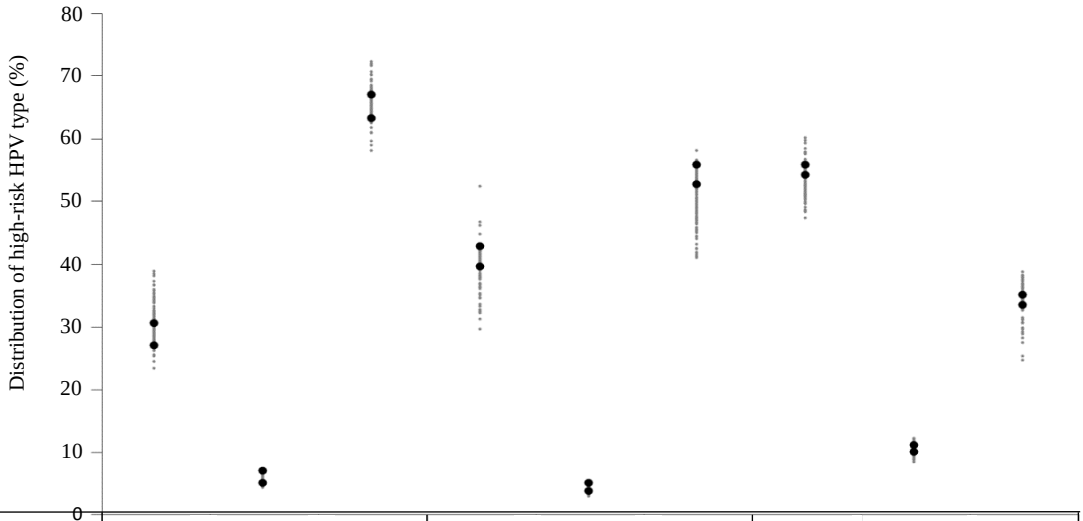


Figure S3 Model outputs of age-specific prevalence rates of high-risk HPV infection in general women, by three infection types

Grey lines represent model outputs resulting from 500 good-fitting sets of type- and age-specific incidence rates of high-risk HPV infection. Bold black lines represent 95% confidence intervals of the corresponding calibration targets. [a]Infected with HPV-16 alone or with both HPV-16 and 18; [b]infected with HPV-18 alone; [c]infected with any other high-risk HPV types whether with or without the coinfection of HPV-16/18.



Percentage of points within 95% CI	CIN2			CIN3			Cervical cancer		
	HPV-16[a]	HPV-18[b]	Other high-risk HPV[c]	HPV-16[a]	HPV-18[b]	Other high-risk HPV[c]	HPV-16[a]	HPV-18[b]	Other high-risk HPV[c]
	91.4	98.2	92.4	88.6	94.8	68.0	76.0	90.2	82.0

Figure S4 Model outputs of proportional distributions of three high-risk HPV infection types in patients with CIN2, CIN3, and cervical cancer

Grey dots represent model outputs resulting from 500 good-fitting sets of type- and age-specific incidence rates of high-risk HPV infection. Bold black dots represent 95% CIs of the corresponding calibration targets. [a]Infected with HPV-16 alone or with both HPV-16 and 18; [b]infected with HPV-18 alone; [c]infected with any other high-risk HPV types whether with or without the coinfection of HPV-16/18. CIN=cervical intraepithelial neoplasia. CI=confidence interval.

4. Model parameters in details

Annual transition probabilities

Annual transition probabilities were derived from published literature of mathematical models and observational studies on the natural history of cervical cancer and were summarized in Table S5. In the model, HPV infection, CIN2, CIN3, and cervical cancer were set as tunnel states to control the transition probabilities which were associated with the duration of infection or duration of stay. All the parameters were adjusted within a wide range in sensitivity analyses to cover the majority of the reported data.

Table S5 Annual transition probabilities used in the model

Parameter	Base-case	Range	Distribution	Reference
HPV infection	..	..	..	..
To susceptible (by infection duration)	..	..	..	Campos et al.[2] Kim et al.[8] Schmeink et al.[11] Zhang et al.[15]
HPV-16: 1 year	0·4002		Uniform (0·2001, 0·6003)	..
2 years	0·3917		Uniform (0·1959, 0·5876)	..
3 years	0·3388	±50%	Uniform (0·1694, 0·5082)	..
4 years	0·3201		Uniform (0·1601, 0·4802)	..
≥5 years	0·2111		Uniform (0·1056, 0·3167)	..
HPV-18: 1 year	0·5987		Uniform (0·2994, 0·8901)	..
2 years	0·5422		Uniform (0·2711, 0·8133)	..
3 years	0·4869	±50%	Uniform (0·2435, 0·7304)	..
4 years	0·2196		Uniform (0·1098, 0·3294)	..
≥5 years	0·2203		Uniform (0·1102, 0·3305)	..
Other high-risk HPV: 1 year	0·5945		Uniform (0·2973, 0·8918)	..
2 years	0·4435	±50%	Uniform (0·2218, 0·6653)	..
3 years	0·4164		Uniform (0·2082, 0·6246)	..
4 years	0·3621		Uniform (0·1811, 0·5432)	..

≥5 years	0·2059		Uniform (0·103, 0·3089)	..
To CIN2 & CIN3 (by infection duration)	..	..	..	Campos et al.[2] Kim et al.[8] Guo et al.[16]
HPV-16: 1 year	0·0262		Uniform (0·0131, 0·0393)	..
2 years	0·0371		Uniform (0·0186, 0·0557)	..
3 years	0·0394	±50%	Uniform (0·0197, 0·0591)	..
4 years	0·0839		Uniform (0·042, 0·1259)	..
≥5 years	0·2144		Uniform (0·1072, 0·3216)	..
HPV-18: 1 year	0·0005		Uniform (0·0003, 0·0008)	..
2 years	0·0024		Uniform (0·0012, 0·0036)	..
3 years	0·0032	±50%	Uniform (0·0016, 0·0048)	..
4 years	0·1093		Uniform (0·0547, 0·164)	..
≥5 years	0·1093		Uniform (0·0547, 0·164)	..
Other high-risk HPV: 1 year	0·0058		Uniform (0·0029, 0·0087)	..
2 years	0·0192		Uniform (0·0096, 0·0288)	..
3 years	0·0395	±50%	Uniform (0·0198, 0·0593)	..
4 years	0·0621		Uniform (0·0311, 0·0932)	..
≥5 years	0·0838		Uniform (0·0419, 0·1257)	..
Proportion of CIN3 in this transition	..	..	..	Campos et al.[2]
HPV-16	0·35	0·3–0·5	Triangular (0·3, 0·35, 0·5)	..
HPV-18/other high-risk HPV	0·2	0·05–0·3	Triangular (0·05, 0·2, 0·3)	..
CIN2	..	..	..	Campos et al.[2] Kim et al.[8]
To susceptible	0·0498	±50%	Triangular (0·0249, 0·0498, 0·0747)	Campos et al.[2] Kim et al.[8]
To HPV infection	0·0498	±50%	Triangular (0·0249, 0·0498, 0·0747)	Campos et al.[2] Kim et al.[8] Myers at al.[17]
To local cancer (by duration of stay)				..
1–5 years	0·0001		Uniform (0·00005, 0·0002)	..
6–10 years	0·0002		Uniform (0·0001, 0·0003)	..
11–20 years	0·0029		Uniform (0·0015, 0·0044)	..
21–30 years	0·0056		Uniform (0·0028, 0·0084)	..
31–34 years	0·0067	±50%	Uniform (0·0034, 0·0101)	..
35–39 years	0·0072		Uniform (0·0036, 0·0108)	..
40–44 years	0·0155		Uniform (0·0078, 0·0233)	..
45–49 years	0·0166		Uniform (0·0083, 0·0249)	..
≥50 years	0·0177		Uniform (0·0089, 0·0266)	..
CIN3	..	..	..	Campos et al.[2] Kim et al.[8]
To susceptible	0·0255	±50%	Triangular (0·0128, 0·0255, 0·0383)	Campos et al.[2] Kim et al.[8]
To HPV infection	0·0255	±50%	Triangular (0·0128, 0·0255, 0·0383)	Campos et al.[2] Kim et al.[8] Myers at al.[17]
To local cancer (by duration of stay)				..
1–5 years	0·0007		Uniform (0·0004, 0·0011)	..
6–10 years	0·0008		Uniform (0·0004, 0·0012)	..
11–20 years	0·0142		Uniform (0·0071, 0·0213)	..
21–30 years	0·0275		Uniform (0·0138, 0·0413)	..
31–34 years	0·0329	±50%	Uniform (0·0165, 0·0494)	..
35–39 years	0·0356		Uniform (0·0178, 0·0534)	..
40–44 years	0·0753		Uniform (0·0377, 0·113)	..
45–49 years	0·0804		Uniform (0·0402, 0·1206)	..
≥50 years	0·0855		Uniform (0·0428, 0·1283)	..
Local cancer	..	..	..	..
To regional cancer	0·2153	±50%	Triangular (0·1077, 0·2153, 0·323)	Campos et al.[2] Kim et al.[8] Wang et al.[18]
To death (by duration of stay after treatment)[a]	..	..	..	Wang et al.[18] Dong et al.[19] Dai et al.[20]
1 year	0·024		Uniform (0·012, 0·036)	..
2–3 years	0·021	±50%	Uniform (0·011, 0·032)	..
4–20 years	0·02		Uniform (0·01, 0·03)	..
Regional cancer	..	..	..	..
To distant cancer	0·262	±50%	Triangular (0·131, 0·262, 0·393)	Campos et al.[2] Kim et al.[8]
To death (by duration of stay after treatment)[a]	..	..	..	Wang et al.[18] Sun et al.[21]
1 year	0·127		Uniform (0·064, 0·191)	..
2–3 years	0·112	±50%	Uniform (0·056, 0·168)	..
4–20 years	0·059		Uniform (0·03, 0·089)	..
Distant cancer	..	..	..	..
To death (by duration of stay after treatment)[a]	..	..	..	Wang et al.[18]
1 year	0·3	±50%	Uniform (0·15, 0·45)	..
2–3 years	0·21		Uniform (0·105, 0·315)	..
4–20 years	0·087		Uniform (0·044, 0·131)	..

[a]Death probability decreases by time after treatment (if the survival time is longer than 20 years, the patient was assumed to be free from cervical cancer-related death). For the undetected cancer states, the death probabilities in the

first year were used until diagnosis. CIN=cervical intraepithelial neoplasia.

Sensitivities and specificities of various screening methods

For each cervical screening method (as detailed in Figure S2), reported sensitivities and specificities were different across studies. To obtain accurate estimates, we reviewed all published studies on the performance of the screening methods from China and conducted a meta-analysis for eligible studies. This literature review was conducted in peer-reviewed research articles published from January 2000 to March 2019 in PubMed, Web of Science, China National Knowledge Infrastructure (CNKI) and Wanfang Data. We used the following keywords in the search strategy: ('cervical cancer' OR 'cervical intraepithelial lesions' OR 'CIN') AND ('screening method' OR 'screening test' OR 'screening approach' OR 'early detection') AND ('comparison' OR 'evaluation' OR 'performance' OR 'accuracy') AND ('China'). These keywords were translated into Chinese terms accordingly when searching the Chinese databases of CNKI and Wanfang Data. Studies evaluating the performance of VIA, Pap, *care*HPV, HC-2 or LBC tests were considered for inclusion. The sample size, the numbers of true positives (TP), false positives (FP), true negatives (TN), and false negatives (FN) were extracted. Sensitivity (Se) [Se = TP / (TP + FN)], specificity (Sp) [Sp = TN / (FP + TN)], and their 95% confidence intervals (95% CIs) were calculated. Pooled sensitivity and specificity estimates were calculated using a random-effects model in Stata Statistical software. Heterogeneity across studies was assessed using the I^2 statistic and the Cochrane Q test. The data extracted from eligible studies were shown in Table S6 and the results of the meta-analysis in Figure S5. The pooled point estimates and the 95% CIs were used as base-case values and sensitivity analysis ranges in our cost-effectiveness analysis, respectively.

Table S6 Performance of screening methods reported in eligible studies[a]

Author	Sample size	Prevalence of CIN2+, %	Sensitivity (95% CI), %	Specificity (95% CI), %
VIA	..	..	..	..
Qiao et al.[22]	2388	2·9	41·4 (29·9–52·9)	94·5 (93·6–95·4)
Zong et al.[23]	3763	0·6	77·3 (59·8–94·8)	81·2 (79·9–82·5)
Zhao et al.[24]	7421	1·9	47·2 (39·0–55·4)	93·6 (93·0–94·2)
Fei et al.[25]	859	1·8	68·9 (46·2–91·6)	82·8 (80·3–85·3)
Hao et al.[26]	890	1·8	67·2 (44·2–90·2)	78·5 (75·8–81·2)
Pap	..	..	..	..
Zong et al.[23]	3763	0·6	81·8 (65·7–97·9)	98·2 (97·8–98·6)
Fei et al.[25]	859	1·8	25·0 (3·8–46·2)	90·0 (88·0–92·0)
Hao et al.[26]	890	1·8	27·8 (5·8–49·8)	87·5 (85·3–89·7)
Tang et al.[27]	3800	2·1	26·3 (16·7–35·9)	88·4 (87·4–89·4)
*Care*HPV	..	..	..	..
Qiao et al.[22]	2388	2·9	84·3 (75·8–92·8)	87·5 (86·2–88·8)
Zhao et al.[24]	7421	1·9	82·6 (76·4–88·8)	86·9 (86·1–87·7)
Zhang et al.[28]	444	12·4	90·9 (83·3–98·5)	82·0 (78·2–85·8)
HC-2	..	..	..	..
Qiao et al.[22]	2388	2·9	97·1 (93·2–100·0)	85·6 (84·2–87·0)
Zong et al.[23]	3763	0·6	90·9 (78·9–100·0)	89·4 (88·4–90·4)
Zhao et al.[24]	7421	1·9	91·7 (87·2–96·2)	83·6 (82·7–84·5)
Fei et al.[25]	859	1·8	87·5 (71·3–100·0)	77·3 (74·5–80·1)
Tang et al.[27]	3800	2·1	86·3 (78·8–93·8)	77·5 (76·2–78·8)
LBC	..	..	..	..
Qiao et al.[22]	2388	2·9	85·3 (77·0–93·6)	97·0 (96·3–97·7)

Fei et al.[25]	859	1·8	81·3 (62·2–100·0)	97·3 (96·2–98·4)
Hao et al.[26]	890	1·8	79·6 (59·9–99·3)	91·2 (89·3–93·1)
Tang et al.[27]	3800	2·1	80·0 (71·2–88·8)	96·5 (95·9–97·1)

[a]All eligible studies assessed the performance of cervical cancer screening methods based on the detection of CIN2+ on histology. VIA=visual inspection with acetic acid. Pap=Papanicolaou test. HC-2=Hybrid Capture-2. LBC=liquid-based cytology. CIN=cervical intraepithelial neoplasia. CI=confidence interval.

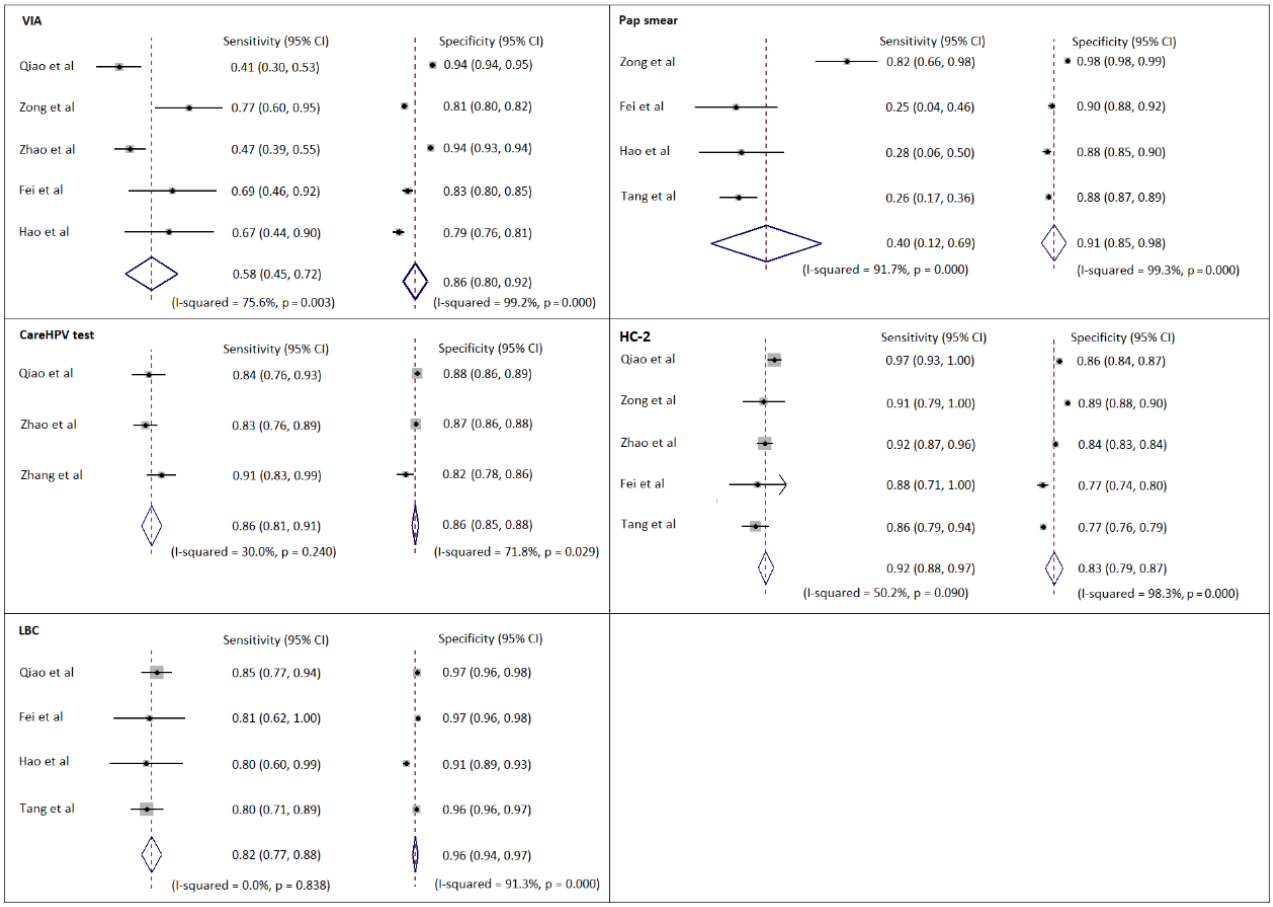


Figure S5 Meta-analysis of the performance of various cervical cancer screening methods

VIA=visual inspection with acetic acid. Pap=Papanicolaou test. HC-2=Hybrid Capture-2. LBC=liquid-based cytology.

5. Model reliability

We examined the model reliability by allowing the Markov model to run in the absence of any interventions and compare the model outputs of age-specific incidence and mortality rates of detected cervical cancer, as well as five- and ten-year cumulative risk of CIN2+ by type-specific HPV (16/18/other high-risk) infection with reported data. A total of 500 sets of cervical cancer natural history parameters were randomly sampled and introduced into the Markov model to simulate the model outputs. Annual transition probabilities in Table S5 were sampled according to their respective distributions, and type- and age-specific incidence rates of high-risk HPV infection from all the good-fitting sets. The outputs of age-specific incidence and mortality rates of detected cervical cancer were compared with the reported incidence and mortality by China Cancer Registry in 2015. The outputs of five- and ten-year cumulative risk of CIN2+ by type-specific HPV (16/18/other high-risk) infection were compared with the reported data from a population-based

cohort study in China.[29] Figure S6 and Figure S7 demonstrated good agreement between simulated and reported data.

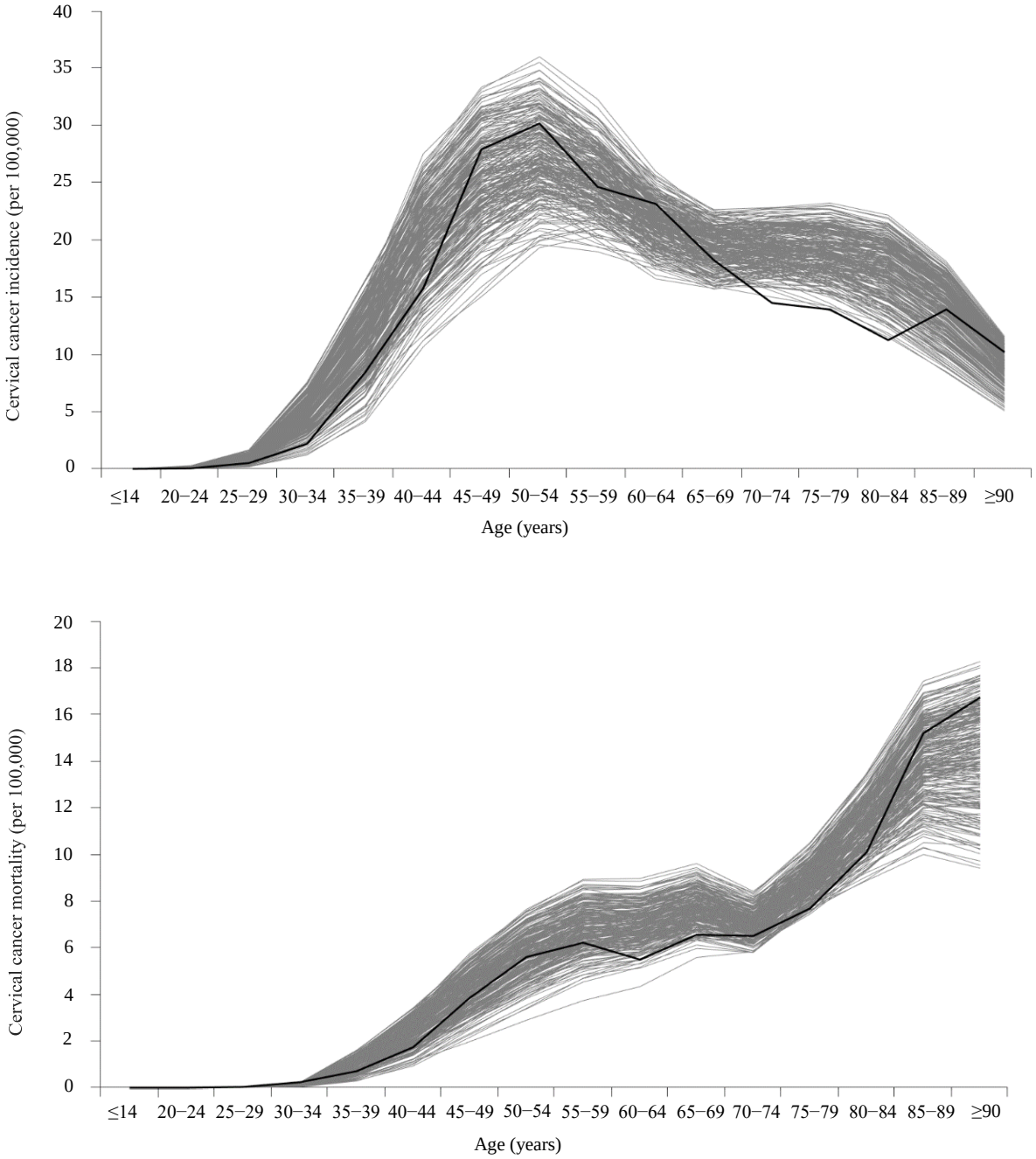


Figure S6 Age-specific cervical cancer incidence and mortality rates in China

Grey lines represent model outputs of 500 simulations. Black lines represent the data reported by China Cancer Registry in 2015.

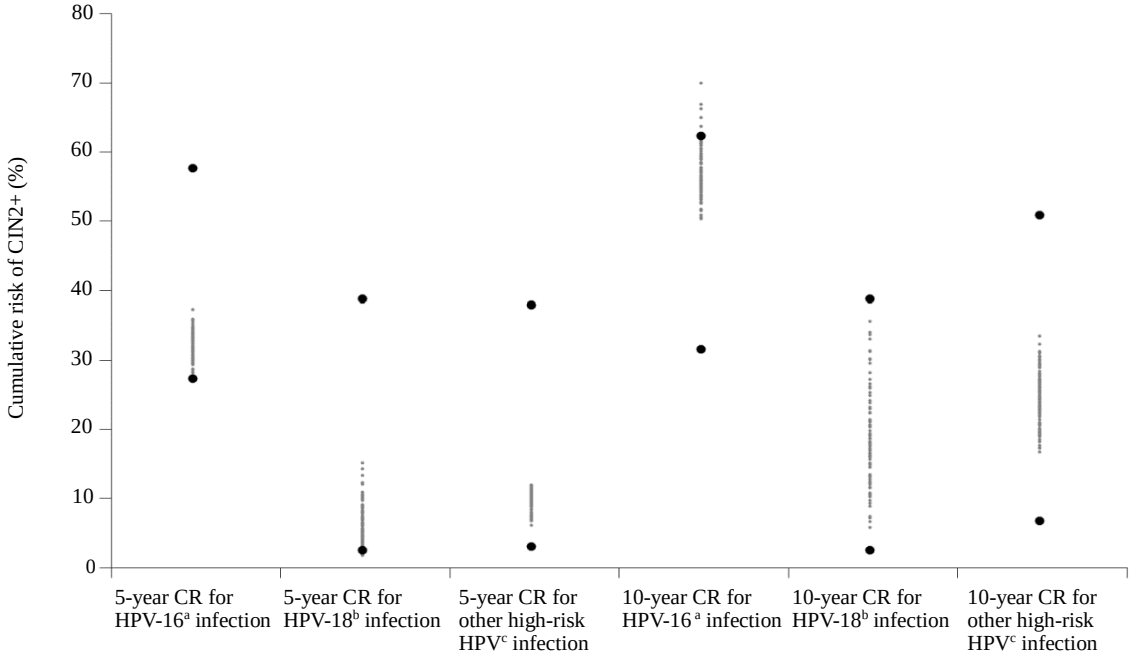


Figure S7 Five- and ten-year cumulative risk of CIN2+ by type-specific HPV (16/18/other high-risk) infection

Grey dots represent model outputs of 500 simulations. Bold black dots represent 95% confidence intervals of the corresponding data from a population-based cohort study in China.[29] [a]Infected with HPV-16 alone or with both HPV-16 and 18; [b]infected with HPV-18 alone; [c]infected with any other high-risk HPV types whether with or without the coinfection of HPV-16/18. CIN=cervical intraepithelial neoplasia. CR=cumulative risk.

6. Determining the optimal age for 'once per lifetime' cervical cancer screening

The optimal age for once per lifetime cervical cancer screening should be the age at which women have the highest prevalence of cervical precancerous lesions and undetected cervical cancers. Therefore, we ran the Markov model with estimated base-case values for all the cervical cancer natural history parameters to simulate this prevalence in women at different ages (30, 35, 40, 45, 50, and 55 years), respectively, in the 'no intervention' scenario. As shown in Table S7, the highest prevalence was identified when the designated initial cohort of 100,000 schoolgirls aged 9−14 years progressed to an average age of 35 years.

Table S7 The simulated prevalence of cervical precancerous lesions and undetected cervical cancers in women at different ages, in the 'no intervention' scenario (100,000 cohort members)

Age (years)	Number of screening targets[a]	Number of cervical lesions				Prevalence of CIN2, CIN3, and undetected cervical cancer (%)
		CIN2	CIN3	Undetected cervical cancer	Total	
30	99,539	2,792	1,234	7	4,033	4·052
35	99,374	2,701	1,310	16	4,076	4·102
40	99,131	2,505	1,267	32	3,804	3·837
45	98,688	2,408	1,220	48	3,676	3·725
50	97,857	2,340	1,169	58	3,567	3·645
55	96,542	2,337	1,142	58	3,537	3·664

[a]The total number of individuals, excluding cases of death, post-treatment cervical cancer, cured of cervical cancer, and hysterectomy. CIN=cervical intraepithelial neoplasia.

7. Results in details

Intervention strategy investment and population impacts

Table S8 reported the QALYs and costs of each strategy, as well as the incremental costs and incremental QALYs of intervention strategies compared to the no intervention scenario in a designated cohort of 100,000 schoolgirls over a lifetime horizon.

Table S8 Incremental QALYs and incremental costs of intervention strategies versus 'no intervention' (100,000 cohort members)[a]

Strategy			QALYs	Incremental QALYs	Costs (US$, thousand)	Incremental costs (US$, thousand)
Screening method	Screening frequency	Vaccination				
No	..	No	2914379·1	..	2,081	..
VIA	Once	No	2914578·5	199·4	1,985	-97
	Twice		2914669·6	290·6	1,974	-107
	Once every 10 years		2914741·6	362·5	2,019	-62
	Once every 5 years		2914847·4	468·3	2,210	129
	Once every 3 years		2914891·8	512·7	2,590	509
Pap	Once	No	2914486·7	107·7	2,257	176
	Twice		2914551·2	172·1	2,401	319
	Once every 10 years		2914603·7	224·6	2,613	532
	Once every 5 years		2914725·6	346·5	3,137	1,055
	Once every 3 years		2914824·0	445·0	3,901	1,820
*Care*HPV	Once	No	2914674·5	295·4	2,068	-14
	Twice		2914776·5	397·4	2,188	106
	Once every 10 years		2914853·9	474·8	2,407	326
	Once every 5 years		2914923·4	544·3	3,092	1,010
	Once every 3 years		2914933·7	554·7	4,114	2,032
HC-2	Once	No	2914696·1	317·0	3,014	933
	Twice		2914796·0	417·0	3,855	1,774
	Once every 10 years		2914871·7	492·6	4,967	2,886
	Once every 5 years		2914925·8	546·7	7,884	5,803
	Once every 3 years		2914926·4	547·3	11,880	9,799
Pap+HC-2	Once	No	2914632·4	253·3	3,407	1,326
	Twice		2914739·9	360·8	4,465	2,384
	Once every 10 years		2914820·3	441·2	5,843	3,762
	Once every 5 years		2914928·4	549·3	9,337	7,255
	Once every 3 years		2914973·5	594·5	14,097	12,016
LBC+HC-2	Once	No	2914641·2	262·1	3,866	1,784
	Twice		2914749·6	370·6	5,268	3,187
	Once every 10 years		2914830·5	451·4	7,074	4,993
	Once every 5 years		2914935·0	556·0	11,635	9,553
	Once every 3 years		2914977·0	597·9	17,819	15,737
No	..	Yes	2915011·0	631·9	8,223	6,142
VIA	Once	Yes	2915118·8	739·7	8,238	6,157
	Twice		2915171·2	792·1	8,278	6,196
	Once every 10 years		2915209·9	830·8	8,364	6,282
	Once every 5 years		2915264·9	885·9	8,621	6,539
	Once every 3 years		2915282·5	903·5	9,037	6,956
Pap	Once	Yes	2915070·2	691·1	8,450	6,368
	Twice		2915107·9	728·9	8,622	6,541
	Once every 10 years		2915137·7	758·6	8,856	6,775
	Once every 5 years		2915207·6	828·5	9,435	7,353
	Once every 3 years		2915263·7	884·6	10,244	8,162
*Care*HPV	Once	Yes	2915171·6	792·5	8,373	6,291
	Twice		2915231·4	852·3	8,548	6,466
	Once every 10 years		2915273·2	894·1	8,811	6,729
	Once every 5 years		2915307·2	928·1	9,543	7,461
	Once every 3 years		2915305·3	926·2	10,583	8,501

HC-2	Once	Yes	2915183·0	803·9	9,332	7,251
	Twice		2915241·5	862·4	10,227	8,146
	Once every 10 years		2915281·7	902·6	11,383	9,301
	Once every 5 years		2915305·8	926·7	14,342	12,261
	Once every 3 years		2915295·8	916·7	18,354	16,272
Pap+HC-2	Once	Yes	2915150·4	771·3	9,669	7,588
	Twice		2915214·3	835·2	10,774	8,693
	Once every 10 years		2915260·0	880·9	12,184	10,103
	Once every 5 years		2915321·9	942·9	15,725	13,644
	Once every 3 years		2915346·9	967·8	20,505	18,424
LBC+HC-2	Once	Yes	2915155·2	776·1	10,132	8,050
	Twice		2915219·8	840·7	11,582	9,500
	Once every 10 years		2915265·8	886·7	13,419	11,338
	Once every 5 years		2915325·7	946·6	18,026	15,944
	Once every 3 years		2915348·8	969·7	24,227	22,146

[a]QALYs and costs are expressed as the present value in 2019. VIA=visual inspection with acetic acid. Pap=Papanicolaou test. HC-2=Hybrid Capture-2. LBC=liquid-based cytology. QALYs=quality-adjusted-life-years. ICER=incremental cost-effectiveness ratio.

Univariate sensitivity analysis results

Univariate sensitivity analysis was performed for all parameters within their respective ranges. The incremental cost-effectiveness ratio (ICER) was relatively sensitive to the vaccination cost, the utility score of CIN2/3 after cryosurgery or loop electrosurgical excision procedure (LEEP), the compliance in follow-up visits, and the cervical cancer screening coverage. Table S9 demonstrated the cost-effectiveness of intervention strategies compared to the lower-cost non-dominated strategy, when these main sensitive parameters were the upper or lower limits of their respective ranges. Overall, varying these parameters did not substantially vary the ranking of cost-effectiveness of intervention strategies. With the reduction of the vaccination cost or the screening coverage, combined screening and vaccination strategies would become more dominant to their counterparts without vaccination at a willingness-to-pay (WTP) threshold of 3-times per-capita GDP.

Table S9 Cost-effectiveness results of intervention strategies compared with the lower-cost non-dominated strategy when the main sensitive parameters were at the lower and upper limits of their respective ranges

Strategy			Cost of vaccination		Utility score of cryotherapy or LEEP		Compliance of follow-up visits		Screening coverage	
Screening method	Screening frequency	Vaccination	Lower limit (US$74·9)	Upper limit (US$99·8)	Lower limit (0·9)	Upper limit (1·0)	Lower limit (0·5)	Upper limit (0·9)	Lower limit (0·2)	Upper limit (0·8)
VIA	Once	No	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving	Cost saving
	Once every 10 years									
	Once every 5 years				Dominated					
	Once every 3 years				Dominated					
Pap	Once	No	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 3 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
*Care*HPV	Once	No	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated		Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated		Dominated	Dominated			Dominated	
	Once every 3 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
HC-2	Once	No	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 3 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
Pap+HC-2	Once	No	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 3 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
LBC+HC-2	Once	No	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 3 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
		Yes	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
VIA	Once	Yes	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years				Dominated	Dominated				Dominated
	Once every 3 years		Dominated	Dominated	Dominated		Dominated	Dominated	Dominated	Dominated
Pap	Once	Yes	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 3 years		Dominated	Dominated		Dominated	Dominated	Dominated	Dominated	Dominated
*Care*HPV	Once	Yes	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated		Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years				Dominated					
	Once every 3 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
HC-2	Once	Yes	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 3 years		Dominated	Dominated	Dominated		Dominated	Dominated	Dominated	Dominated
Pap+HC-2	Once	Yes	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 10 years		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 5 years		Dominated	Dominated		Dominated	Dominated	Dominated	Dominated	Dominated
	Once every 3 years				Dominated	Dominated	Dominated			
LBC+HC-2	Once	Yes	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
	Twice		Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated

Once every 10 years	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated	Dominated
Once every 5 years	Dominated	Dominated		Dominated	Dominated	Dominated	Dominated	Dominated
Once every 3 years			Dominated	Dominated	Dominated			

The ICER is lower than 1-times per-capita GDP.

The ICER is higher than 1-times per-capita GDP but lower than 3-times per-capita GDP.

The ICER is higher than 3-times per-capita GDP.

VIA=visual inspection with acetic acid. Pap=Papanicolaou test. HC-2=Hybrid Capture-2. LBC=liquid-based cytology. GDP=gross domestic product.

Impact of vaccine efficacy

In order to conservatively estimate the vaccine efficacy of the 2-dose schedule, we pessimistically assumed that the vaccine efficacy may be only 80% or even 70%. Figure S8 showed the impact of different vaccine efficacies on the most cost-effective intervention strategy. Reducing the vaccine efficacy to 80% or even to 70% did not affect the conclusion on the most cost-effective intervention strategy.

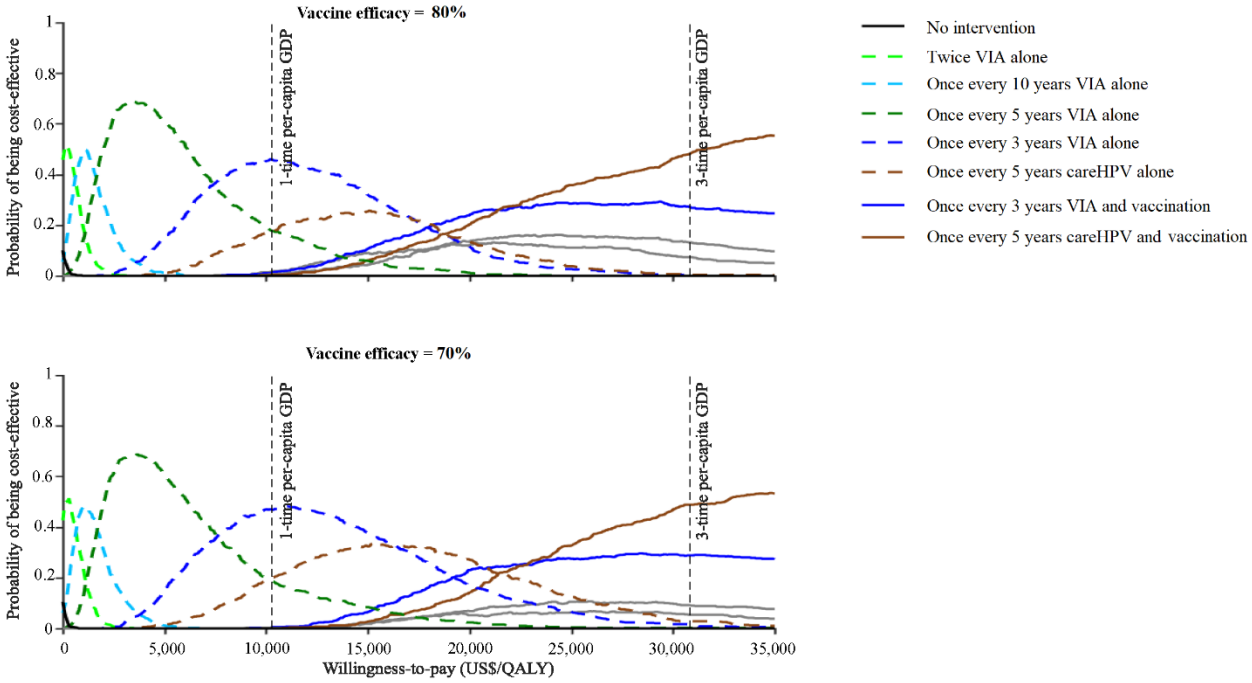


Figure S8 Cost-effectiveness acceptability curves for all strategies at lower vaccine efficacies

Intervention strategies that never have the highest probability of being cost-effective within the willingness-to-pay threshold of 3-times Chinese per-capita GDP are represented in grey. VIA=visual inspection with acetic acid. QALY= quality-adjusted-life-year. GDP=gross domestic product.

References

1 World Health Organization. Comprehensive cervical cancer control: a guide to essential practice. 2nd edition. *Geneva* World Health Organization, 2014:131.

2 Campos NG, Burger EA, Sy S, et al. An updated natural history model of cervical cancer: derivation of model parameters. *Am J Epidemiol* 2014; 180(5):545–55.

3 Kim JJ, Burger EA, Sy S, Campos NG. Optimal cervical cancer screening in women vaccinated against human papillomavirus. *J Natl Cancer Inst* 2017; 109(2):djw216.

4 Campos NG, Maza M, Alfaro K, et al. The cost-effectiveness of implementing HPV testing for cervical cancer screening in El Salvador. *Int J Gynaecol Obstet* 2019; 145(1):40–6.

5 Campos NG, Tsu V, Jeronimo J, et al. Health impact of delayed implementation of cervical cancer screening programs in India: a modeling analysis. *Int J Cancer* 2019; 144(4): 687–96.

6 World Health Organization. WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention. *Geneva* World Health Organization, 2013:9–15.

7 Dong ZW, Qiao YL, Li LD. Chinese cancer screening and early detection and early treated guidelines (trail). *Beijing* Peking University Medical Press, 2005:9–17.

8 Kim JJ, Kuntz KM, Stout NK, et al. Multi-parameter calibration of a natural history model of cervical cancer. *Am J Epidemiol* 2007; 166(2):137–50.

9 Goldhaber-Fiebert JD, Stout NK, Ortendahl J, Kuntz KM, Goldie SJ, Salomon JA. Modeling human papillomavirus and cervical cancer in the United States for analyses of screening and vaccination. *Popul Health Metr* 2007; 5:11.

10 Munoz N, Mendez F, Posso H, et al. Incidence, duration, and determinants of cervical human papillomavirus infection in a cohort of Colombian women with normal cytological results. *J Infect Dis* 2004; 190(12):2077–87.

11 Schmeink CE, Massuger LF, Lenselink CH, et al. Prospective follow-up of 2,065 young unscreened women to study human papillomavirus incidence and clearance. *Int J Cancer* 2013; 133(1):172–81.

12 Li Z, Liu F, Cheng S, et al. Prevalence of HPV infection among 28,457 Chinese women in Yunnan Province, southwest China. *Sci Rep* 2016; 6:21039.

13 Yang L, Lu XJ, Ye YX, et al. Analysis of HPV infection among 8 944 females of health examination in West China Hospital of Sichuan University. *Chin J Evid-based Med* 2017; 17(6):634–9.

14 Xu HH, Wang K, Feng XJ, et al. Prevalence of human papillomavirus genotypes and relative risk of cervical cancer in China: a systematic review and meta-analysis. *Oncotarget* 2018; 9(20):15386–97.

15 Zhang W, Xiao J, Ma C. Clearance of high-risk HPV infection in Chinese women with normal cervical cytology. *Int J Gynaecol Obstet* 2012; 118 (1): 74–5.

16 Guo YL, You K, Qiao J, Zhao YM, Liu CR, Geng L. Natural history of infections with high-risk HPV in Chinese women with abnormal cervical cytology findings at baseline. *Int J Gynaecol Obstet* 2010; 110(2):137–40.

17 Myers ER, McCrory DC, Nanda K, Bastian L, Matchar DB. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. *Am J Epidemiol* 2000; 151(12): 1158–71.

18 Wang J, Xu KK, Shi BG, et al. An analysis of the prognostic factors in 4374 cases with cervical cancer. *China Cancer* 2014; 23(4):281–8.

19 Dong YS, Xu PZ. Effect of different surgical approaches on the prognosis of patients with early cervical cancer. *J Clin Med Pract* 2012; 16(22):30–2.

20 Dai Y. Curative effect of laparoscopic hysterectomy in the treatment of early-stage cervical cancer and its effect on the prognosis of patients with early-stage cervical cancer. *China Modern Med* 2016; 23(25):100–2.

21 Sun L, Sheng X, Jiang J, et al. Surgical morbidity and oncologic results after concurrent chemoradiation therapy for advanced cervical cancer. *Int J Gynaecol Obstet* 2014; 125(2):111–5.

22 Qiao YL, Sellors JW, Eder PS, et al. A new HPV-DNA test for cervical-cancer screening in developing regions: a cross-sectional study of clinical accuracy in rural China. *Lancet Oncol* 2008; 9(10):929–36.
23 Zong LJ, Zhang YZ, Yang XS, et al. Evaluation of several screening approaches for the detection of cervical lesions in rural Shandong, China. *Asian Pac J Cancer Prev* 2015; 16(5):1907–12.
24 Zhao FH, Jeronimo J, Qiao YL, et al. An evaluation of novel, lower-cost molecular screening tests for human papillomavirus in rural China. *Cancer Prev Res* 2013; 6(9):938–48.
25 Fei HL, Cheng YF, Cheng XD, et al. Evaluation of five screening methods for early detection of cervical cancer and its precancerous lesions in Zhejiang province. *Natl Med J Chin* 2011; 91(5):309–12.
26 Hao YF. Comparison of three methods for screening cervical cancer in Southeast Shandong Province. *Chin Tropical Med* 2012; 12(9):1110–2.
27 Tang Q, Xing GH, Chen LR. A comparative study on the application of HPV, LBC and CPS screening methods in early diagnosis of cervical cancer. *J Clin Exp Med* 2015; 14(15):1253–5.
28 Zhang R, Zhao FH, Chen W, et al. The evaluation study of validity and reliability of *care*HPV^{TM} as a screening test for cervical cancer and precancerous lesions. *Oncol Progr* 2012; 10(5):506–10.
29 Dong L, Hu SY, Zhang Q, et al. Risk prediction of cervical cancer and precancers by type-specific human papillomavirus: evidence from a population-based cohort study in China. *Cancer Prev Res (Phila)* 2017; 10(12): 745–51.

Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Checklist

Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section	Item No	Recommendation	Reported on page No/line No
Title and Abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	3−4
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	5−6
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	5
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	5
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	5−6 Table S1
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	5
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	6−7
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type	7

		of analysis performed.	
Measurement of effectiveness	11a	*Single study-based estimates*: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	N/A
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	6 Table S6, Figure S5
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	6
Estimating resources and costs	13a	*Single study-based economic evaluation*: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A
	13b	*Model-based economic evaluation*: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	6
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	6−7
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	5 Figure S1−S2
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	5−6
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	5−7

Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	6−7 Table 1 Table S5
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	8 Figure 1 Table S8
Characterizing uncertainty	20a	*Single study-based economic evaluation*: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	N/A
	20b	*Model-based economic evaluation*: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	8−9 Figure 2−3 Table S9 Figure S8
Characterizing heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	Figure 3 Figure S8
Discussion			
Study findings, limitations, generalizability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	10−11
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	7, 12
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	12

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

The citation for the CHEERS Task Force Report is: Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. *Value Health* 2013; 16:231–50.

HPV-FRAME Reporting Standards Checklist

Table S10 HPV-FRAME core reporting standards

a) Inputs	Reported by age? (Y/N)	Report by sex (F-only, M-only or both)?	Comments
The target population for intervention	Y	F-only	Girls, aged 9–14 years (vaccination) Females, aged 30–59 years (screening)
Sexual behaviour	N	N	The analysis was done with a static model (not a dynamic model).
Cohort examined for evaluation/ time horizon	Y	F-only	Lifetime
Quality of life assumptions	N	F-only	
Calibration	Y	F-only	A Likelihood-based calibration approach to fit the type- and age-specific incidence rates of high-risk HPV infection; using type- and age-specific prevalence rates of high-risk HPV infection in females (China) and the proportional distributions of different infection types in patients with CIN2, CIN3, and cervical cancer (China) as calibration targets
Validation (where possible)	Y	F-only	Age-specific incidence and mortality rates of detected cervical cancer (China); five- and ten-year cumulative risk of CIN2+ by type-specific HPV (16/18/other high-risk HPV) infection
Costs	N	F-only	2019 US dollars; costs of detection and treatment were adjusted to 2019 as the base year according to Chinese consumer price indexes in the category of health; discounted future costs at a discount rate of 3% (0−8%) to account for time preferences
b) Outputs	**Reported by age? (Y/N)**	**Report by sex (F-only, M-only or both)?**	**Report as calibration or validation target? (Y/N)**
Cancer incidence, mortality, life years, QALYs/DALYs (as appropriate)	Y	F-only	Y (validation)
HPV prevalence, pre-intervention	Y	F-only	Y (calibration)
CIN2 detected	Y	F-only	N
Sensitivity analysis of key inputs	Y	Y	N
Incremental cost-effectiveness	Y	Y	

ratios and costs saved

CIN: cervical intraepithelial neoplasia; F: female; M: male.

Table S11 HPV-FRAME reporting standards for models of vaccination in adolescent individuals

a) Inputs	Reported? (Y/N)	Reported by age? (Y/N)	Report by sex? (Y/N)	Comments
Vaccine uptake	Y	Y	Y (F-only)	0·7 (0·5–0·95)
Vaccine efficacy	Y	Y	Y (F-only)	0·94 (0·8–0·94); In order to conservatively estimate the vaccine efficacy of the 2-dose schedule, the vaccine efficacy was pessimistically assumed at 0·8 or even 0·7 in sensitivity analyses
Vaccine cross-protection	N	N	N	
Duration vaccine protection and waning	Y	Y	Y (F-only)	lifetime protection
Vaccine and delivery costs	Y	N	Y (F-only)	The vaccine price; the cost of staff services in vaccination (including disposable syringe); the cost of advocacy for vaccination
Pre-vaccination disease burden (including population attributable fractions for HPV)	Y	Y	Y (F-only)	Age-specific prevalence rates of high-risk HPV infection; age-specific incidence and mortality rates of detected cervical cancer
Duration of natural immunity	e	N	N	
b) Outputs	**Reported? (Y/N)**	**Report by age? (Y/N)**	**Report by sex? (B, F, or M)**	**Report as calibration or validation target? (Y/N)**
Absolute reductions in HPV infections, and/ or warts, post-vaccination	N	N	N	
Absolute reductions in CIN2+ post-vaccination	N	N	N	
Absolute reductions in invasive cancer (cervical and other HPV cancers, as relevant) post-vaccination	e	N	N	

CIN: cervical intraepithelial neoplasia; B: both sexes; F: female; M: male.

Table S12 Additional HPV-FRAME reporting standards for models of HPV prevention in low- and middle-income countries

Inputs	Reported? (Y/N)	Report by Age? (Y/N)	Report by sex? (Y/N)	Comment
HIV prevalence rates, if	N	N	N	

endemic in country				
Description of any opportunistic or pilot/demonstration screening projects ongoing	Y	Y	F-only	National Cervical Cancer Screening Programme in Rural Areas (NCCSPRA)
Costs	Y	N	F-only	2019 US dollars; costs of detection and treatment were adjusted to 2019 as the base year according to Chinese consumer price indexes in the category of health; discounted future costs at a discount rate of 3% (0−8%) to account for time preferences

Table S13 Additional HPV-FRAME reporting standards for integrated models of cervical screening and vaccination

Inputs	Reported? (Y/N)	Reported by age? (Y/N)	Report by sex? (B, F, or M)	Comments
HPV type incidence, clearance and progression rates	Y	Y	F	HPV incidence, clearance and progression rates were considered to be related to type (16/18/other high-risk HPV) and the duration of infection
Herd effect	N	N	N	The analysis was done with a static model
Association between vaccination and screening uptake	N	N	N	
Screening test(s) and colposcopy accuracies	Y	N	F	Sensitivity and specificity
Fixed – variable costs	Y	N	F	The costs of vaccination included the vaccine price, the cost of staff services in vaccination, and the cost of advocacy for vaccination; the costs of the screening programme included the costs of screening, diagnosis, and treatment, as well as the administration cost

B: both sexes; F: female; M: male.

The citation for the HPV-FRAME reporting standards is: Canfell K, Kim JJ, Kulasingam S, et al. HPV-FRAME: A consensus statement and quality framework for modelled evaluations of HPV-related cancer control. *Papillomavirus Res* 2019; 8:100184.