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Cost–benefit analysis of p16^{INK4a} immunocytology and liquid-based cytology triage after primary HPV testing for cervical cancer screening in China

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Abstract

Background HPV testing has become the recommended primary screening method for cervical cancer in China. However, referring all HPV-positive patients for colposcopy is not practical. This study monetized clinical performance metrics to evaluate the relative performance of 10 secondary triage strategies compared to referring all patients for colposcopy.

Methods Using real-world HR-HPV sample data and strictly adhering to the HPV-FRAMEWORK, a Markov model was employed to simulate the missed diagnosis losses and health utility losses associated with referring all patients for colposcopy. These losses were monetized using one-time 2023 per capita GDP in China. Incremental net benefits of secondary triage strategies were calculated to identify the optimal strategy. Extensive sensitivity analyses were conducted to assess parameter and sample uncertainty. Additionally, the technical suitability of strategies was explored in the context of healthcare resource allocation in China.

Results Solely relying on HPV genotyping for secondary triage is not recommended, and necessary secondary triage testing should be implemented. p16 performed better than LBC, particularly in the overall sample and in most age groups. The strategy of HPV16/18+ or (OH-HPV+ and p16+) was the most attractive, with an incremental net benefit of US$492,473.78 compared to referring all patients for colposcopy. Extensive sensitivity analyses confirmed the robustness of these results. Considering healthcare resource allocation in China, p16 demonstrated higher technical suitability.

Conclusion Based on real-world sample data and the monetization of clinical performance metrics, this study recommends p16 as the secondary triage technology. The HPV16/18+ or (OH-HPV+ and p16+) strategy is not only the most attractive but also holds high potential for large-scale implementation in China.

Keywords p16^{INK4a} immunocytology, Liquid-based cytology, Cost–benefit analysis, Machine learning, Cervical cancer

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Introduction

Cervical cancer is a common malignant tumor that poses a significant threat to women's health and has become a major global public health issue. In November 2020, the World Health Organization (WHO) officially launched the "Global Strategy to Accelerate the Elimination of Cervical Cancer", which received strong responses and commitments from 194 countries, including China [1].

Against this backdrop, China has further promoted cervical cancer screening, calling for improvements in the cervical cancer prevention and control service system and enhancing comprehensive prevention capabilities [2–4]. As an integral part of this service system, effective management of screening and rational strategies for triaging abnormal cases are crucial.

Persistent high-risk HPV (HR-HPV) infection is considered a necessary prerequisite for the occurrence and progression of cervical cancer [5, 6]. Substantial clinical and practical evidence supports the use of HPV testing as the primary screening method for cervical cancer, which has been increasingly adopted in several countries, including China [3, 7–10]. However, most HR-HPV infections have high self-clearance rates and slow disease progression, meaning that a positive HPV result cannot be equated with cervical lesions [10, 11]. Consequently, not all HPV-positive patients should undergo colposcopy, as this could lead to unnecessary medical expenditures and health utility losses due to overdiagnosis [12]. Simultaneously, failing to identify patients with lesions, such as cervical intraepithelial neoplasia 2+ (CIN2+), in a timely manner could result in missed diagnoses and associated medical costs. Therefore, there is an urgent need to study how to perform rational secondary triage after HPV-positive results to reduce overdiagnosis while improving lesion detection rates.

Currently, U.S. screening guidelines recommend colposcopy referrals based on liquid-based cytology (LBC) results (Atypical Squamous Cells of Undetermined Significance Plus, ASC-US+) and HPV16/18 positivity (HPV16/18+) [13–15]. However, China's guidelines have yet to clarify secondary triage strategies following primary screening positivity [2, 3]. In addition to LBC, biomarkers such as $p16^{INK4a}$ (p16), with their outstanding clinical performance, have emerged as potential alternatives for secondary triage [16, 17]. However, relying solely on clinical evidence to evaluate the advantages and disadvantages of triage strategies lacks quantitative metrics, making comparisons between different strategies challenging.

This study, guided by the HPV-FRAME framework, monetized all relevant clinical evidence [18]. First, secondary triage strategies were determined based on national guidelines, publicly available literature, and expert opinions. Next, a Markov model was used to simulate the cost savings and utility gains (in Quality-adjusted life years, QALYs) associated with detecting CIN2+ under different triage strategies compared to natural history with opportunistic screening. Overdiagnosis-related utility losses due to colposcopy were obtained from the literature to determine the cost and utility profiles for each strategy. Utility was monetized following the WHO-recommended threshold to determine the net benefit of each strategy. Incremental net benefit was calculated by comparing the net benefit of all secondary triage strategies to the net benefit of referring all patients for colposcopy, thereby identifying the optimal strategy. Probabilistic sensitivity analysis was performed on all model parameters to assess parameter uncertainty, and bootstrap analysis was conducted to evaluate sample uncertainty. Finally, considering China's healthcare resource allocation, the study identified the most feasible strategy for implementation in China. Additionally, age-specific triage strategies were reported. The results of this study will provide critical policy support and practical guidance for improving cervical cancer prevention and screening systems in China.

Methods

Triage strategies and study design

Based on published literature and recommendations from clinical experts, we identified ten secondary triage strategies: HPV16/18+: Patients positive for HPV16 or HPV18 are recommended for colposcopy [13, 15]. HPV16/18/31/33/35/45/52/58+: Positive for any of these eight high-risk types. p16+: Patients positive for p16 are recommended for colposcopy. HPV16/18+ or (OH-HPV+ and p16+): Positive for HPV16 or HPV18, or for other high-risk types with p16 positivity, are recommended for colposcopy [19–21]. OH-HPV refers to other high-risk HPV types apart from the HR-HPV types mentioned in the text. HPV16/18+ or (HPV31/33/35/45/52/58+ and p16+): Positive for HPV16/18 or for HPV31/33/35/45/52/58 with p16 positivity. 8 types+ or (HPV39/51/56/59/66/68+ and p16+): Positive for the eight types or for HPV39/51/56/59/66/68 with p16 positivity. Additionally, we evaluated individual LBC (ASC-US+), as well as four corresponding strategies combining LBC with different HPV genotyping methods [22].

As shown in Fig. 1, based on the established triage strategies, we assessed the performance of ten secondary triage strategies and universal colposcopy screening across all populations and subgroups by age (<35, 35–50, and 50+). Using a Markov model, we quantified the missed diagnosis losses associated with each strategy compared to universal colposcopy, calculated their

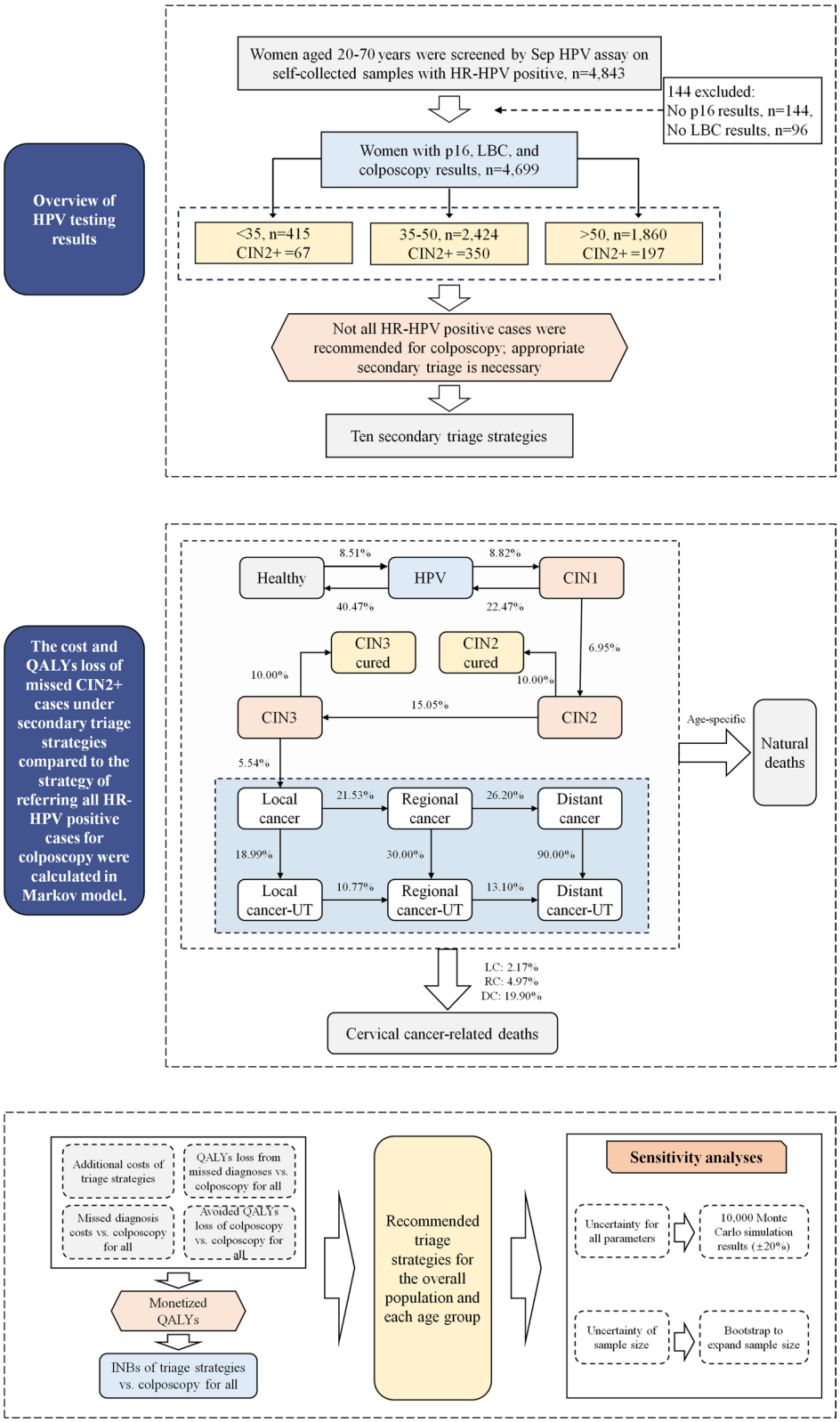

Fig. 1 Study design. *Sep HPV, Self-sampling HPV testing; p16, $p16^{INK4a}$; LBC, Liquid-based cytology; CIN, Cervical intraepithelial neoplasia; QALY, Quality-adjusted life year; UT, Under treatment; LC, Local cancer; RC, Regional cancer; DC, Distant cancer

monetary values, and identified the optimal strategy based on incremental net benefit. Robustness testing was conducted, and additional potential strategies were identified using machine learning and exhaustive search. Furthermore, we evaluated the technological feasibility of all strategies in the Chinese context.

Data cleaning

As illustrated in Fig. 1, the data used in this study were collected from 4,699 high-risk HPV-positive samples in collaboration with Peking University Shenzhen Hospital. These samples were drawn from Henan, Hubei, Guangxi, and Guangdong provinces. The data are cross-sectional and include necessary details about HR-HPV genotypes, LBC, p16, and colposcopy results, along with age information. We stratified the age groups into < 35 years (young population), 35–50 years (high-risk group for cervical cancer), and 50+ years (elderly women) for further analysis.

A total of 4,843 samples were initially retrieved from databases in the four regions. Samples lacking p16 or LBC test results were excluded, leaving 4,699 valid samples. We organized the data to determine the number of CIN2, CIN3, and cervical cancer cases detectable under each triage strategy, as well as the corresponding number of missed cases. The study protocol and informed consent forms were approved by the ethics committee of Peking University Shenzhen Hospital. Details of these procedures have been reported in previous studies [20, 23–25].

Markov model for CIN2+ missed diagnosis losses

As shown in Fig. 1, we constructed a Markov model based on the design of previously published Chinese studies on cervical cancer economic evaluations [26–33]. The study strictly followed the cervical cancer screening section of the HPV framework (Appendix Table 1) [18], with necessary adjustments and assumptions for evaluating missed diagnosis losses compared to universal colposcopy screening, rather than a general economic evaluation of screening strategies.

The health states in the model included: healthy, HPV infection, CIN1–3, CIN2 treatment, CIN3 treatment, CIN2 cured, CIN3 cured, and local, regional, and distant cancers. Transition probabilities were derived from the mean values reported in all published economic evaluations of cervical cancer in China (Appendix Table 2) [26–33]. Natural death could occur in any health state. Age-specific probabilities of natural death were calculated using the GBD 2021 mortality rates, accounting for additional mortality risks associated with disease [34]. Health utilities and costs at each stage were derived from published literature (Appendix Table 3).

Given regional price variations for each triage (Appendix Table 4), we set their costs at the same value (US$20) based on regional price comparisons and clinical expert recommendations. Future health utilities and costs were discounted at a rate of 5%. The model simulated up to 100 years of age, allowing the calculation of costs and health utilities for any starting health state before age 100.

In the context of widespread cervical cancer screening among rural women in China, CIN2+ lesions missed during initial screening may still be detected in future screenings. Over the past decade, approximately 280 million free cervical cancer screenings have been conducted in China, with an annual opportunistic screening and treatment probability of 10% for CIN2 and CIN3 [35]. Cervical cancers, often detected due to symptoms, were modeled based on reported opportunistic screening probabilities [29].

The average age for CIN2 and CIN3 in the sample data was 46 years, while the average age for cervical cancer was 54 years. For instance, we assumed that the difference in cost and health utility between initial CIN2 and CIN2 cured at age 46 represents the loss due to a missed diagnosis. Similarly, losses for CIN3 and cervical cancer were calculated. To simplify calculations, missed diagnosis losses for cervical cancer were defined as the difference between local cancer and local cancer utility states. Accordingly, the missed diagnosis costs for CIN2, CIN3, and cervical cancer were US$591.04, US$1,290.57, and US$−2,633.92, respectively, with corresponding utilities of 0.33 QALYs, 1.41 QALYs, and 0.25 QALYs (Appendix Table 5).

Cost–benefit analysis

As mentioned earlier, compared to universal colposcopy screening, additional costs include triage testing (p16 and LBC), colposcopy, missed CIN2+ diagnosis costs, colposcopy utility losses, and monetary equivalents of missed CIN2+ utility losses. The cost of colposcopy was set at US$16.54 (based on Peking University Shenzhen Hospital). Studies have reported a slight health impact of colposcopy, assumed to be 0.03 QALYs [36]. We reported the cost and utility results and calculated the final net benefit using the above methods. All costs were adjusted to 2024 exchange rates (US$1 = ¥7.25).

The net benefit threshold was derived from WHO recommendations, using the highly cost-effective threshold of one time the 2023 local GDP per capita in China

(US$12,614) as willingness to pay (WTP) [37]. This threshold was used to monetize QALYs and calculate incremental net benefit for all triage strategies compared to universal colposcopy screening. Calculate the incremental net benefits (INBs) of all triage strategies relative to full referral to colposcopy [38, 39].

$$INBs = \left(QALYs\ gained\ compared\ with\ no\ universal\ screening \times WTP\right) - incremental\ cost\ compared\ with\ no\ universal\ screening$$

Uncertainty analyses

Since all parameters in the Markov model and those used for calculating incremental net benefits have inherent uncertainty, we varied all parameters by ± 20% and performed 10,000 Monte Carlo simulations to identify the strategy with the highest incremental net benefit. If incremental net benefits for all strategies were below zero, universal colposcopy was deemed the optimal strategy. we will also consider a more lenient threshold (three-times the per capita GDP). Given the sample size of 4,699 HR-HPV-positive samples, while sufficient to demonstrate results, we used bootstrap sampling to expand the sample size to 100,000 and verify the robustness of conclusions.

Technical suitability of triage strategies

As p16 is an emerging technology, after identifying the optimal strategy, we assessed its technological feasibility in the context of China's healthcare resource allocation.

Results

Overview of triage strategies

Table 1 summarizes the clinical performance and incremental net benefits of each triage strategy compared to universal colposcopy screening for the full sample and different age subgroups. Overall, relying solely on HPV genotyping for colposcopy referral is insufficient. The use of p16 outperforms LBC in both the full sample and the 35+ age group. For the full sample, the optimal strategy is HPV16/18+ or (OH-HPV+ and p16+), with four strategies showing better performance than universal colposcopy screening. For the age subgroups, the optimal strategies are as follows: HPV16/18+ or (OH-HPV+ and ASC-US+) (< 35 years), HPV16/18+ or (OH-HPV+ and p16+) (35–50 years), p16+ (50+ years).

Cost and utilities of triage strategies

As shown in Fig. 2, Examining the costs and utilities of various strategies in the full sample reveals that five strategies (HPV16/18+, HPV16/18/31/33/35/45/52/58+, ASC-US+, 8 types+ or (HPV39/51/56/59/66/68+ and p16+), 8 types+ or (HPV39/51/56/59/66/68+ and ASC-US+)) are completely dominated by universal colposcopy (higher costs and lower health utilities). While the HPV16/18+ or (HPV31/33/35/45/52/58+ and ASC-US+) strategy yields additional utility benefits compared to universal colposcopy, the added costs from missed diagnosis and secondary triage render it a suboptimal choice. As previously described, relying solely on HPV genotyping for secondary triage is insufficient. Incorporating new diagnostic technologies before colposcopy referral is essential. Notably, all p16-based strategies, whether used alone or in combination with HPV genotyping, outperform the corresponding LBC-based strategies.

Cost-benefits analysis of triage strategies

As shown in Fig. 3, the INB of each strategy compared to universal colposcopy in the full sample is primarily influenced by the utility losses from missed CIN2+ diagnoses and the savings from reducing unnecessary colposcopy procedures.

Relying solely on HPV genotyping for triage is insufficient. For example, using HPV16/18+ for colposcopy referral results in significant costs and utility losses due to missed diagnoses. On the other hand, the HPV16/18/31/33/35/45/52/58+ strategy, while reducing missed diagnoses, still leads to an overuse of colposcopy.

Uncertainty analysis

Monte Carlo simulations across all parameter variations show that the results are highly robust. HPV16/18+ or (OH-HPV+ and p16+) consistently emerges as the optimal strategy. Even when the WTP threshold is relaxed to three-times 2023 per capita GDP in China, as recommended by the WHO, the results remain unchanged.

As shown in Fig. 4, p16 consistently outperforms LBC. When the sample size was expanded to 100,000 via bootstrap sampling, the results and conclusions also remained unchanged.

Estimation the technical suitability of triage strategies

Consultations with manufacturers and experts indicate that reading LBC slides requires at least an intermediate professional title and 3 years of experience, while p16 only requires a junior professional title and 1 year of experience. Considering the distribution of healthcare personnel across Chinese provinces, p16 shows high technical suitability nationwide, with a particular focus on regions such as Beijing and

Table 1 Characteristics of triage strategies

Triage strategies	Positive	CIN2_M	CIN3_M	CC_M	Incremental cost, USD	Incremental QALYs	INBs, USD
HPV16/18+							
All	1538	160	101	4	162,095.35	−101.38	−1,440,902.67
< 35	131	17	16	0	25,999.44	−19.65	−273,864.54
35–50	821	96	61	1	102,612.11	−63.13	−898,933.93
50+	586	47	24	3	33,483.80	−18.60	−268,104.20
HPV16/18/31/33/35/45/52/58+							
All	3269	56	23	1	36,495.23	−8.26	−140,686.87
< 35	275	8	6	0	10,156.14	−6.90	−97,192.74
35–50	1796	31	11	0	18,426.43	−0.18	−20,696.95
50+	1198	17	6	1	7912.66	−1.18	−22,797.18
p16+							
All	1727	58	23	0	108,786.55	37.59	365,373.71
< 35	145	9	9	0	20,768.69	−7.56	−116,130.53
35–50	934	33	12	0	59,601.60	23.61	238,214.94
50+	648	16	2	0	28,416.26	21.54	243,289.30
ASC-US+							
All	1242	131	55	2	179,940.97	−17.57	−401,568.95
< 35	131	16	8	0	23,383.84	−8.04	−124,800.40
35–50	702	75	32	0	106,399.40	−11.49	−251,334.26
50+	409	40	15	2	50,157.73	1.96	−25,434.29
HPV16/18+ or (OH-HPV+ and p16+)							
All	2467	38	6	0	87,265.66	45.96	492,473.78
< 35	218	3	2	0	9395.88	2.10	17,093.52
35–50	1327	25	3	0	49,758.37	27.15	292,711.73
50+	922	10	1	0	28,111.41	16.71	182,668.53
HPV16/18+ or (OH-HPV+ and ASC-US+)							
All	2278	73	6	0	104,826.00	40.08	400,743.12
< 35	218	7	0	0	9178.90	3.60	36,231.50
35–50	1251	41	5	0	60,539.11	21.33	208,517.51
50+	809	25	1	0	35,107.99	15.15	155,994.11
HPV16/18+ or (HPV31/33/35/45/52/58+ and p16+)							
All	2122	77	27	1	129,077.97	13.58	42,220.15
< 35	176	9	6	0	17,409.72	−4.26	−71,145.36
35–50	1128	46	14	0	73,075.02	10.68	61,642.50
50+	818	22	7	1	38,593.23	7.16	51,723.01
HPV16/18+ or (HPV31/33/35/45/52/58+ and ASC-US+)							
All	1926	110	28	1	146,631.02	7.16	−56,314.78
< 35	162	14	6	0	20,133.36	−5.49	−89,384.22
35–50	1049	63	15	0	83,106.61	6.03	−7044.19
50+	715	33	7	1	43,391.05	6.62	40,113.63
8 types+ or (HPV39/51/56/59/66/68+ and p16+)							
All	3526	38	17	1	116,343.87	−1.57	−136,147.85
< 35	298	7	5	0	16,954.95	−5.85	−90,746.85
35–50	1940	24	9	0	67,049.77	0.63	−59,102.95
50+	1288	7	3	1	32,339.15	3.65	13,701.95
8 types+ or (HPV39/51/56/59/66/68+ and ASC-US+)							
All	3450	46	18	1	121,105.72	−3.34	−163,236.48
< 35	293	8	5	0	17,463.29	−6.03	−93,525.71
35–50	1897	27	10	0	69,402.24	−0.48	−75,456.96

Table 1 (continued)

Triage strategies	Positive	CIN2_M	CIN3_M	CC_M	Incremental cost, USD	Incremental QALYs	INBs, USD
50+	1260	11	3	1	34,240.19	3.17	5746.19

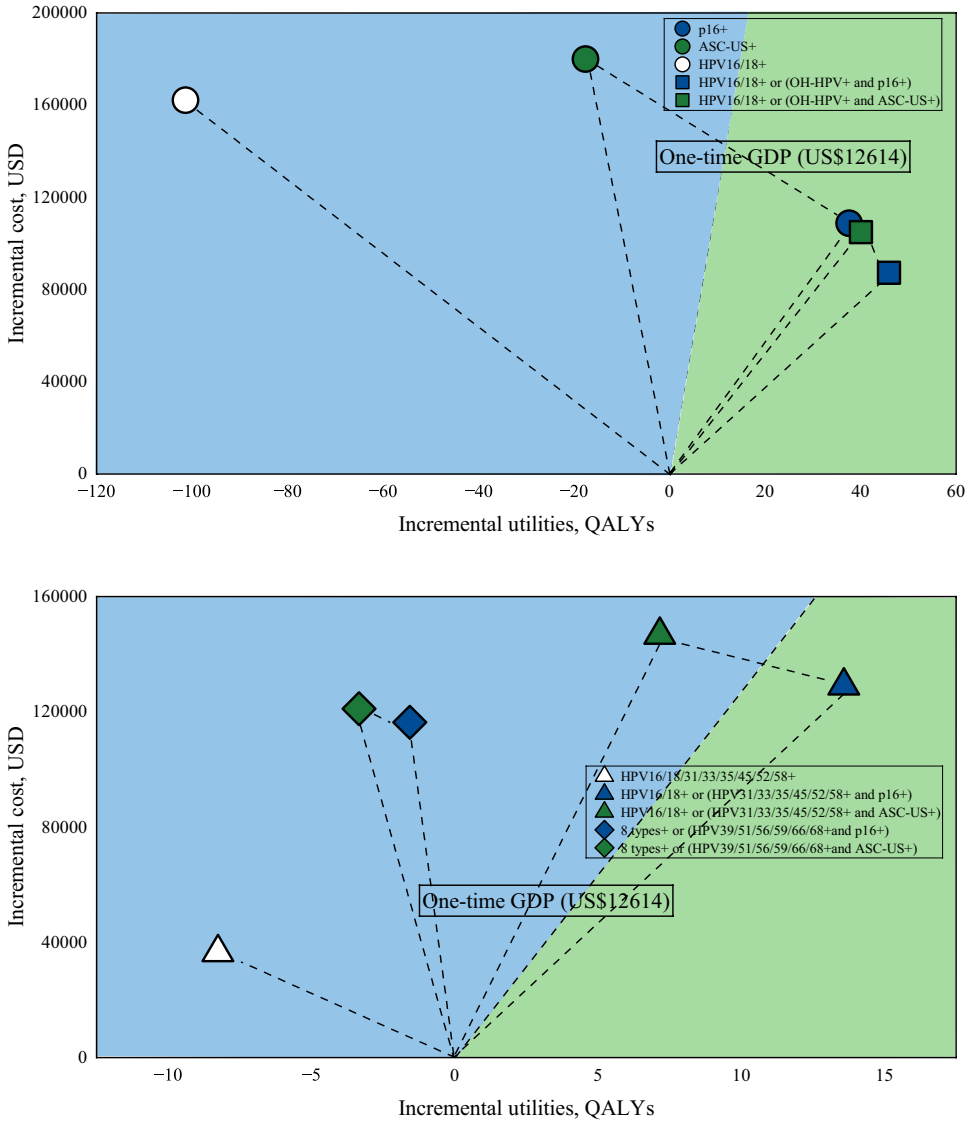

Fig. 2 Cost and utilities of triage strategies. *The points of strategies falling in the blue region indicate they are dominated by universal colposcopy when using one-time 2023 per capita GDP in China as the willingness-to-pay (WTP) threshold. Points in the green region indicate a cost-effective advantage

Guangdong [40]. In contrast, the suitability of LBC is significantly lower, suggesting that the HPV16/18+ or (HPV31/33/35/45/52/58+ and p16+) strategy is highly suitable for large-scale implementation in China.

Discussion

Our findings indicate that relying solely on HPV genotyping results from initial screening for secondary triage is insufficient. Strategies with a narrow genotyping scope result in substantial missed diagnoses, while those with

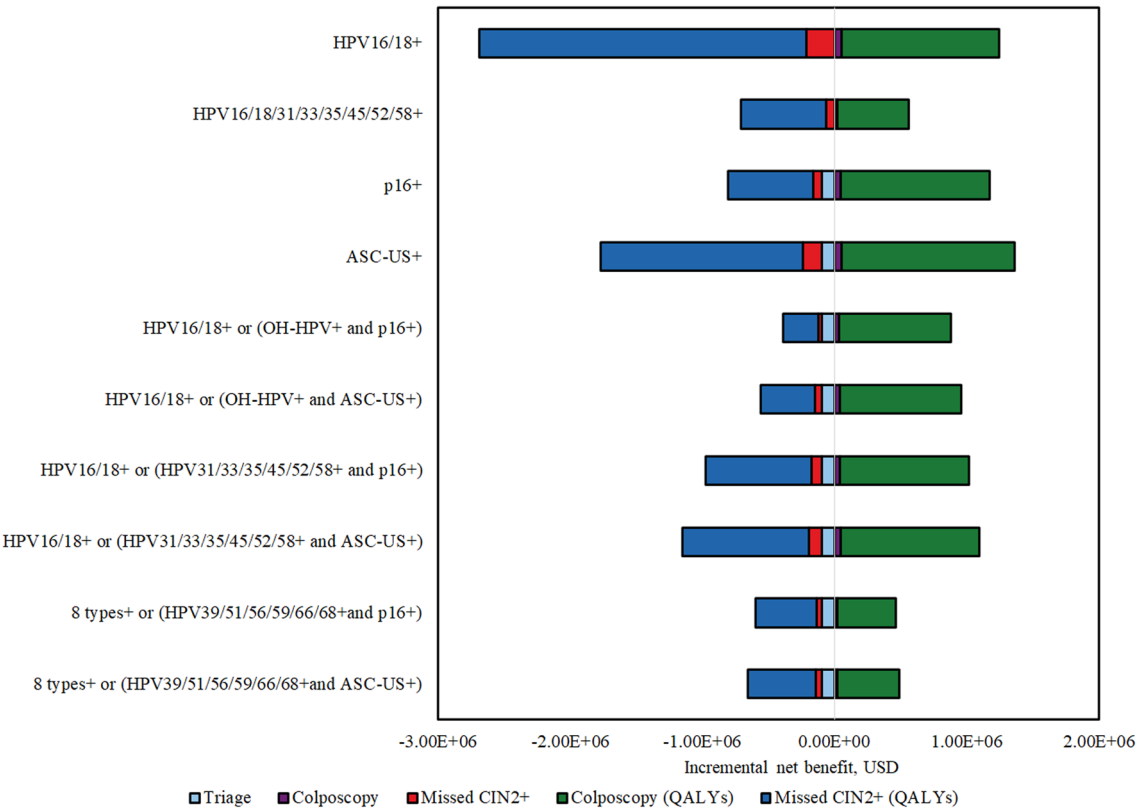

Fig. 3 Cost–benefit analysis of triage strategies

a broader genotyping scope, though capable of reducing missed cases to some extent, do not substantially reduce the gap in overdiagnosis when compared to universal colposcopy screening. Thus, introducing necessary secondary diagnostic tests and triage for colposcopy referral is of practical significance. Optimized secondary triage strategies are crucial for managing high-risk HPV-positive patients effectively. Our study highlights the importance of incorporating emerging technologies into triage strategies. The results demonstrate that both the standalone use of p16 and its combination with initial HPV genotyping outperform the LBC-based strategies recommended by the current U.S. guidelines [13, 15]. The HPV16/18+ or (OH-HPV+ and p16+) strategy achieved the highest incremental net benefit and is one of the most promising strategies for widespread implementation.

Compared to international studies, our research deepens the exploration of triage strategies for HPV-positive patients [7, 15, 19, 21, 22, 41–43]. Current U.S. ACS/ASCCP guidelines recommend triage for patients with HPV16/18 genotyping positivity or abnormal LBC results (e.g., ASC-US or higher) [15]. However, some studies highlight the significant limitations of relying solely on LBC for triage, such as subjectivity of results, inconsistent interpretation standards, and dependence on the examiner's experience, especially in regions with limited resources or challenges in maintaining quality control for screening [7, 41–43].

In contrast, our study, conducted within the Chinese context, is the first to comprehensively evaluate the performance of various triage strategies using economic analyses. The proposed HPV16/18+ or (OH-HPV+ and p16+) strategy offers lower missed diagnosis rates and significant economic feasibility advantages. This not only provides theoretical support for cervical cancer screening in China but also serves as a reference for optimizing screening strategies in other low- and middle-income countries.

Our research complements and contrasts with existing literature on secondary screening technologies. In recent years, studies have explored the application of biomarkers such as p16 and Ki-67, focusing primarily on diagnostic performance, with limited attention to economic evaluations [20, 23, 24]. A notable advantage of our study is its comprehensive analysis of these technologies in terms of missed diagnoses, overdiagnosis, and referral efficiency, as well as the monetization of economic feasibility indicators. This enables more

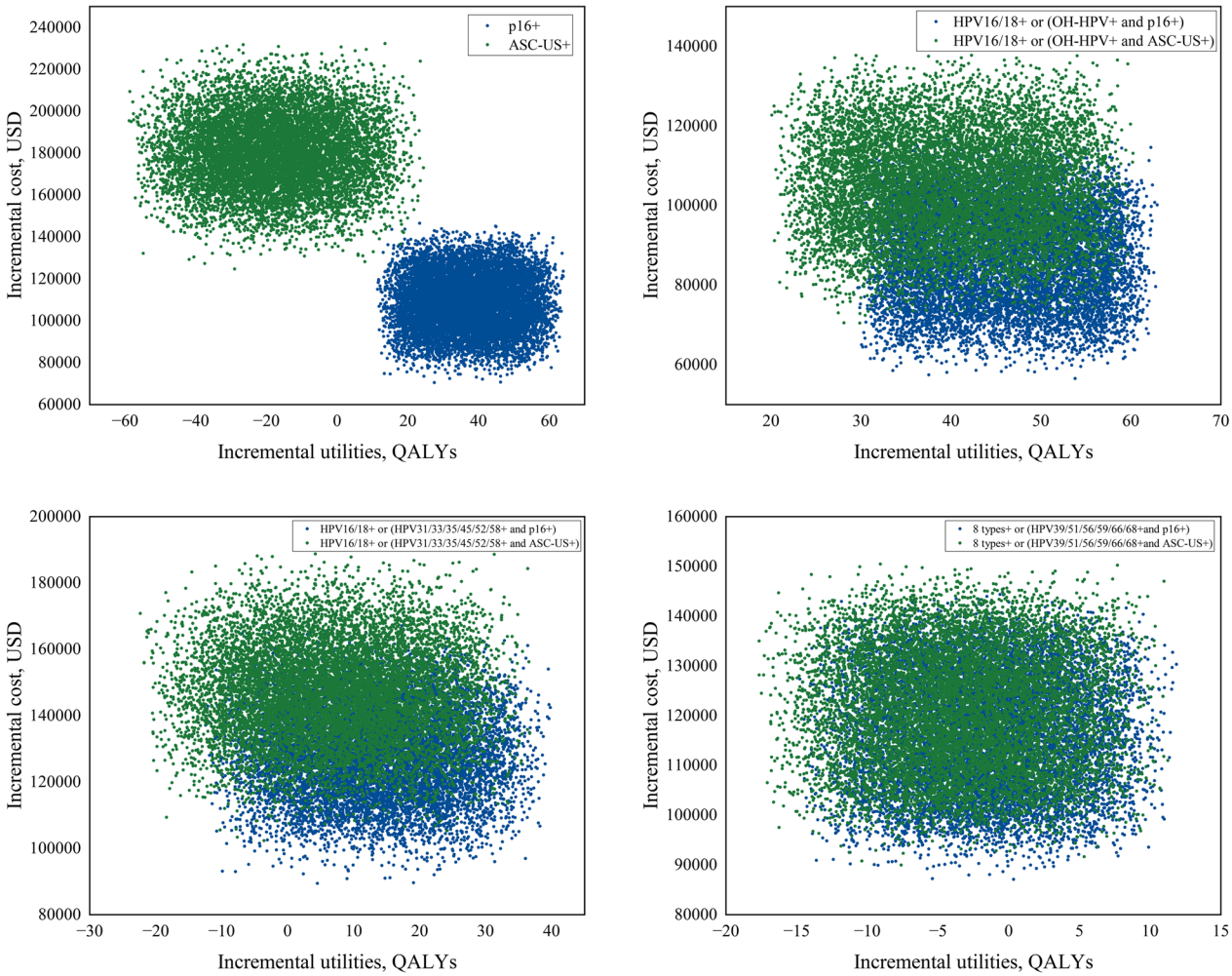

Fig. 4 Sensitivity analysis-Monte Carlo simulation results

intuitive and concrete comparisons among different strategies.

An effective secondary triage strategy should reduce missed CIN2+ cases while minimizing resource wastage and health utility losses due to overdiagnosis. In our study, missed diagnosis utility loss and colposcopy utility loss accounted for the majority of net benefit, indicating that the success of a triage strategy depends on balancing these two factors. From the perspective of incremental net benefit, the HPV16/18+ or (OH-HPV+ and p16+) strategy accurately identified the majority of CIN2+ cases while significantly reducing colposcopy usage through p16-based triage, achieving the best balance between missed diagnoses and overdiagnosis utility losses. The results of our study further validate the role of p16 as a cost-effective diagnostic technology with excellent diagnostic performance in optimizing secondary triage strategies.

In the context of cervical cancer screening in China, addressing the challenges in rural and low-income regions is a priority. Since the initiation of the "Double Cancer Screening" program in 2009, rural and low-income urban women have been prioritized [44, 45]. However, existing triage strategies face economic and technical barriers to implementation in these regions. Our study shows that p16 technology, due to its lower diagnostic equipment and expertise requirements and its ability to significantly improve CIN2+ detection accuracy, is particularly suitable for resource-limited areas. Considering that women in rural and low-income areas are the primary target population for cervical cancer screening in China, the widespread adoption of this technology could enhance screening coverage and reduce overdiagnosis. Age-stratified subgroup analyses further support this conclusion, demonstrating that p16 is an especially attractive triage test for women aged 35 and

older, who are the primary target group for cervical cancer screening.

From a policy perspective, our study has significant implications for optimizing cervical cancer screening strategies in China. Current Chinese guidelines do not specify detailed triage strategies following HR-HPV positivity. By providing comprehensive economic and clinical evaluations, our study fills this gap and offers a reliable basis for developing evidence-based screening management policies. In the context of uneven distribution of economic and technical resources, our findings offer guidance on maximizing resource utilization in resource-limited regions. Additionally, the results highlight the ease of operation and low cost of p16 technology, which can be further promoted in the "Double Cancer Screening" program. This would improve screening coverage, reduce regional disparities, and support the goal of early diagnosis and treatment for cervical cancer.

While our study provides valuable insights, several limitations should be acknowledged: Firstly, our study's findings are based on a dataset of 4,699 HR-HPV-positive samples from four regions, and while we performed bootstrap uncertainty analyses, the reliance on this dataset may limit the generalizability of the results. Secondly, some parameters used in the Markov model to estimate CIN2+ missed diagnosis losses were derived from published literature, such as the probability of opportunistic screening, which directly influences missed diagnosis outcomes. Despite extensive uncertainty analyses, the possibility of errors cannot be completely excluded. Thirdly, while we attempted to monetize all metrics, our approach did not incorporate broad expert consultation or complex weighted metrics for multi-dimensional decision-making, leaving some challenging-to-quantify factors, such as generalizability, to be addressed qualitatively in the results and discussion sections. Lastly, although we utilized machine learning to identify the most sensitive indicators for CIN2+ detection and conducted exhaustive searches to determine optimal strategies, the feasibility of implementing these strategies and their acceptance among experts remain uncertain, thus serving as a reference point for future exploration.

Conclusion

Based on real-world sample data, our study monetized all clinical indicators and identified p16 as a recommended technology for secondary triage. The HPV16/18+ or (OH-HPV+ and p16+) strategy is the most attractive option with significant potential for large-scale implementation in China.

Abbreviations

HPV	Human papillomavirus
LBC	Liquid-based cytology
p16	$p16^{INK4a}$
CIN	Cervical intraepithelial neoplasia
QALY	Quality-adjusted life year
GDP	Gross domestic product
OH-HPV	Other high-risk human papillomavirus
AS-CUS	Atypical squamous cells of undetermined significance
LC	Local cancer
RC	Regional cancer
DC	Distant cancer
Ca/CC	Cervical cancer

Supplementary Information

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Additional file 1.

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Not applicable.

Author contributions

DZ analyzed and interpreted the data, and was a major contributor in drafting and revising the manuscript. JH coordinated across multiple institutions and contributed to the study's conception and critical manuscript revisions. JX contributed to data acquisition, visualization, and manuscript drafting. YL contributed to data acquisition, visualization, and manuscript revision. RW, WT, and XQ provided financial support, contributed to the study's conception, and critically revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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