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ORIGINAL ARTICLE

Impact of government-organized screening programs on the economic burden of cervical cancer across five disease courses: a multistage regression and mediation analysis

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ABSTRACT

Objective: To evaluate the impact of government-organized screening on the economic burden among patients with cervical cancer and precancerous lesions, and explore mediating pathways across diagnosis, initial treatment, radiotherapy/chemotherapy, follow-up, and recurrence/progression/metastasis.

Methods: A multicentre, nationwide survey across 5 disease courses was conducted from 26 hospitals in China. Multivariable regression and structural equation modeling were used to assess the effects of government-organized screening on economic burden by comparing government-organized screening with workplace check-up, self-paid check-up, and symptom-based detection.

Results: Workplace check-up, self-paid check-up, and symptom-based detection were associated with progressively higher costs across diagnosis [β: 1.10, 95% confidence interval (CI): 0.54–1.67; β: 1.46, 95% CI: 1.00–1.92; and β: 1.68, 95% CI: 1.25–2.11, respectively], initial treatment (β: 0.36, 95% CI: 0.18–0.55; β: 0.51, 95% CI: 0.35–0.66; and β: 0.56, 95% CI: 0.42–0.70, respectively), and follow-up (β: 0.63, 95% CI: 0.38–0.88; β: 0.83, 95% CI: 0.61–1.04; and β: 0.85, 95% CI: 0.65–1.06, respectively) compared to government-organized screening (all $P < 0.05$). Earlier clinical staging and greater use of lower-level hospitals mediated 44.74%–54.97% of cost differences in diagnosis, 73.27%–85.04% in initial treatment, and 30.38%–54.73% in follow-up. Fifteen percent of the cost differences during initial treatment were related to lower overtreatment for precancerous lesions.

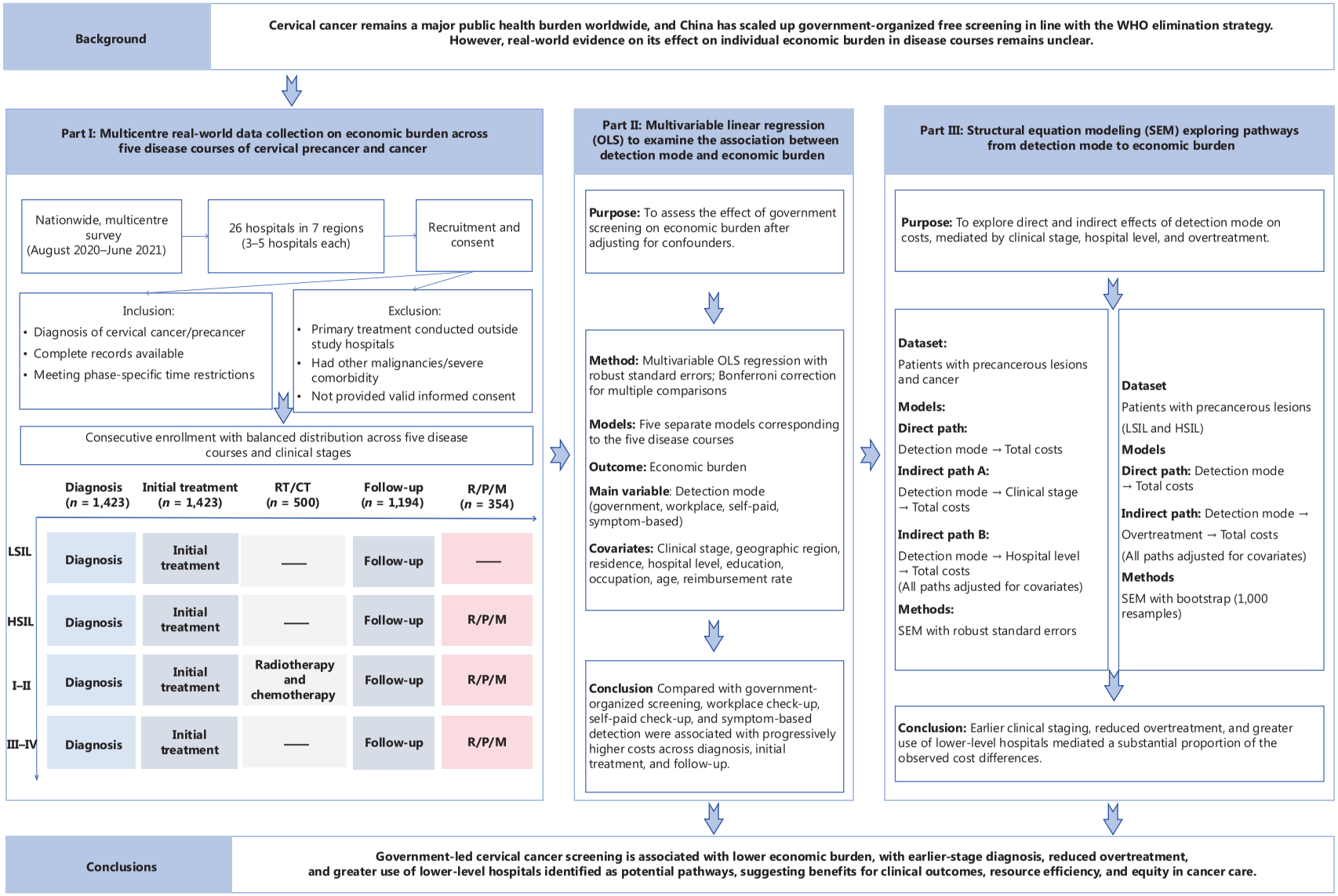
Conclusions: Government-led cervical cancer screening was associated with lower economic burden with pathways involving earlier-stage diagnosis, reduced overtreatment, and decreased reliance on higher-level hospitals, suggesting potential clinical benefits, efficient resource use, and improved equity in cancer care.

KEYWORDS Cervical cancer; government-organized screening; economic burden; early detection

Introduction

An estimated 662,044 new cases and 348,709 deaths from cervical cancer occurred globally in 2022, making cervical cancer the fourth most frequently diagnosed cancer and the fourth leading cause of cancer deaths among women[1]. Approximately Approximately 150,700 new cases and 55,700 deaths were reported in China in 2022[2]. In response, the World Health Organization (WHO) launched a global strategy to eliminate cervical cancer as a public health problem[3]. China has adopted this goal as a national priority with the 2023–2030 action plan targeting 50% screening coverage by 2025 and 70% by 2030[4]. Since 2009 China has offered free cervical and breast cancer screening in rural areas with the programme formally integrated into the National Basic Public Health Service package in 2019[5]. Under this policy, women 35–64 years of age are offered government-organized cervical cancer screening at not cost using cytology every 3 y or high-risk human papillomavirus (HPV) testing every 5 y, depending on local implementation capacity[6]. Great than 280 million screenings were performed from 2009–2023 and by October 2024 the programme had

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Background
Cervical cancer remains a major public health burden worldwide, and China has scaled up government-organized free screening in line with the WHO elimination strategy. However, real-world evidence on its effect on individual economic burden in disease courses remains unclear.
Part I: Multicentre real-world data collection on economic burden across five disease courses of cervical precancer and cancer
Nationwide, multicentre survey (August 2020–June 2021)
26 hospitals in 7 regions (3–5 hospitals each)
Recruitment and consent
Inclusion:
• Diagnosis of cervical cancer/precancer
• Complete records available
• Meeting phase-specific time restrictions
Exclusion:
• Primary treatment conducted outside study hospitals
• Had other malignancies/severe comorbidity
• Not provided valid informed consent
Consecutive enrollment with balanced distribution across five disease courses and clinical stages
Diagnosis (n = 1,423)
Initial treatment (n = 1,423)
RT/CT (n = 500)
Follow-up (n = 1,194)
R/P/M (n = 354)
LSIL
Diagnosis
Initial treatment
——
Follow-up
——
HSIL
Diagnosis
Initial treatment
——
Follow-up
R/P/M
I–II
Diagnosis
Initial treatment
Radiotherapy and chemotherapy
Follow-up
R/P/M
III–IV
Diagnosis
Initial treatment
——
Follow-up
R/P/M
Part II: Multivariable linear regression (OLS) to examine the association between detection mode and economic burden
Purpose: To assess the effect of government screening on economic burden after adjusting for confounders.
Method: Multivariable OLS regression with robust standard errors; Bonferroni correction for multiple comparisons
Models: Five separate models corresponding to the five disease courses
Outcome: Economic burden
Main variable: Detection mode (government, workplace, self-paid, symptom-based)
Covariates: Clinical stage, geographic region, residence, hospital level, education, occupation, age, reimbursement rate
Conclusion Compared with government-organized screening, workplace check-up, self-paid check-up, and symptom-based detection were associated with progressively higher costs across diagnosis, initial treatment, and follow-up.
Part III: Structural equation modeling (SEM) exploring pathways from detection mode to economic burden
Purpose: To explore direct and indirect effects of detection mode on costs, mediated by clinical stage, hospital level, and overtreatment.
Dataset:
Patients with precancerous lesions and cancer
Models:
Direct path:
Detection mode → Total costs
Indirect path A:
Detection mode → Clinical stage → Total costs
Indirect path B:
Detection mode → Hospital level → Total costs
(All paths adjusted for covariates)
Methods:
SEM with robust standard errors
Dataset
Patients with precancerous lesions (LSIL and HSIL)
Models
Direct path: Detection mode → Total costs
Indirect path: Detection mode → Overtreatment → Total costs
(All paths adjusted for covariates)
Methods
SEM with bootstrap (1,000 resamples)
Conclusion: Earlier clinical staging, reduced overtreatment, and greater use of lower-level hospitals mediated a substantial proportion of the observed cost differences.
Conclusions
Government-led cervical cancer screening is associated with lower economic burden, with earlier-stage diagnosis, reduced overtreatment, and greater use of lower-level hospitals identified as potential pathways, suggesting benefits for clinical outcomes, resource efficiency, and equity in cancer care.

Study Flowchat This national multicenter study evaluates the economic impact of government-organized cervical cancer screening in China. **Part I** describes the study design: a nationwide multicentre survey of patients with precancerous lesions and cervical cancer, in which cost data were systematically collected across five disease courses (diagnosis, initial treatment, radiotherapy and chemotherapy, follow-up, and R/P/M). **Part II** applied multivariable linear regression to control for demographic, socioeconomic, and regional confounders, confirming that government-organized screening was associated with significantly lower costs compared with workplace check-up, self-paid check-up, and symptom-based detection. **Part III** applied structural equation modeling to examine potential mediating pathways, indicating that earlier clinical stage, greater use of lower-level hospitals, and reduced overtreatment (for LSIL/HSIL) accounted for a substantial proportion of the observed cost differences. In conclusion, these findings suggest that government-organized screening is associated with lower economic burden of cervical cancer, potentially through earlier detection, more efficient use of healthcare resources, and improved equity in cancer care. R/P/M, recurrence/progression/metastasis; RT/CT, radiotherapy and chemotherapy; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion. Clinical stage I, II, III, and IV refer to the FIGO staging system for invasive cervical cancer.

expanded to cover 97% of counties nationwide[7]. Recent data from 2023–2024 showed that screening coverage among women 35–64 y of age reached 51.5%[8].

Evidence suggests that government-organized screening programmes are more effective than opportunistic screening in reducing the cervical cancer incidence and mortality[9-11]. Although modelling studies have demonstrated the potential long-term economic benefits at the population level[12,13], real-world cost data assessing the impact on individual costs and the mechanisms by which government-organized screening programmes reduce economic burden are limited. Evidence comparing government-led screening with alternative detection modes, such as workplace check-ups, self-paid check-ups, and symptom-based detection, has not been thoroughly explored. In addition, cervical cancer treatment is a prolonged, multi-phase process encompassing diagnosis, initial treatment, follow-up, and disease progression with substantial cost variation across different disease courses[14]. Clarifying the impact of government screening in each disease course could inform more targeted strategies and support more efficient resource allocation across the care continuum.

This study aimed to assess the impact of government-organized screening compared to workplace check-ups, self-paid check-ups, and symptom-based detection on the economic burden among patients with cervical cancer and precancerous lesions and to explore potential mediating pathways across diagnosis, initial treatment, radiotherapy/chemotherapy, follow-up, and recurrence/progression/metastasis (R/P/M). The overall study design and analytic framework are summarized in **Study Flowchat**. The findings are expected to facilitate refinement of cervical cancer screening policies, improve the health and economic outcomes for women affected by cervical cancer and precancerous lesions, and provide policy-relevant evidence to support national efforts toward cervical cancer elimination in China.

Materials and methods

Study design and population

This nationwide, multicentre, cross-sectional hospital survey was conducted between August 2020 and June 2021 across 26 eligible hospitals in 7 administrative regions of China (North China, Northeast China, East China, Central China, South China, Southwest China, and Northwest China) to ensure geographic representation and institutional diversity. A convenience sample of 3–5 hospitals was drawn in each geographic region with explicit criteria requiring the inclusion of 1-to-2 primary-level hospitals and the representation of both urban and rural facilities; 26 hospitals were ultimately included. The number of participants recruited from each hospital was determined by the hospital clinical capacity. Patients were consecutively enrolled if the eligibility criteria were met. The sample size was designed to ensure balanced representation of clinical stages [low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), and cancer stages I–IV] within each disease course. Enrollment across all clinical stages proceeded concurrently and enrollment for a given stage was closed when the target sample size was fulfilled. The following five phases of the disease course were examined to assess the economic burden throughout the continuum of cervical cancer care: diagnosis; initial treatment; radiotherapy/chemotherapy; follow-up; and R/P/M. "Diagnosis" includes the period leading to pathologic confirmation, while "Initial treatment" encompasses surgical or pharmacologic interventions for LSIL, HSIL, and invasive cervical cancer (FIGO stages I–IV). "Radiotherapy/chemotherapy" includes stage I–II patients treated with radiotherapy, chemotherapy, or both, including patients without prior surgery. "Follow-up" applies to all patients from LSIL to stage IV.

"R/P/M" includes patients with HSIL or cervical cancer (stages I–IV). Diagnosis and initial treatment were based on the same patient cohort, while radiotherapy/chemotherapy, follow-up, and R/P/M involved separately sampled populations.

Participants were eligible for inclusion if the following criteria were met: 1) confirmed diagnosis of cervical cancer or cervical precancerous lesions; 2) complete diagnostic and treatment records available at the study hospital, including inpatient or outpatient cases; and 3) treatment had to be completed within the past 30 d for patients in the initial treatment or radiotherapy/chemotherapy. At least 1 y and ≤ 5 y must have elapsed since initiation of follow-up care for patients in the follow-up phase. Main treatment had to be completed within the past 30 d for patients in the R/P/M phase. Patients were excluded for the following reasons: 1) the primary treatment during the relevant disease course was performed outside the study hospital; 2) patients had other primary malignancies or severe co-morbidities, such as coronary artery disease or a history of organ transplantation; and 3) patients were unable to provide valid written informed consent. Patients with common chronic conditions, such as hypertension or diabetes, were not excluded if these co-morbidities were unlikely to substantially affect cervical cancer treatment costs. This study received approval from the Ethics Committees of the National Cancer Center/Cancer Hospital, Chinese Academy of Medical Sciences (NCC/CHCAMS) (Approval No. 19/255-2039).

Data collection and processing

Each patient was assigned to a specific disease-course grouping based on clinical records. Relevant diagnostic and treatment information was extracted from the hospital information system (HIS) and imported into the electronic survey system. These items were pre-filled and therefore omitted during the questionnaire interview if the imported data were complete and accurate. The interviewers collected the necessary information through face-to-face or telephone-based electronic questionnaires for missing or incomplete key data. All interviewers underwent standardized training prior to fieldwork.

Electronic questionnaires were administered using handheld devices equipped with real-time logic checks to ensure data consistency. The data underwent automated validation after initial entry. Records with errors were flagged for correction and verified data were saved and submitted. Extreme cost outliers were identified using the conventional interquartile range (IQR)-based rule (Q1 − 3 × IQR, Q3 + 3 × IQR), which were applied separately for each stratum defined by disease course and clinical stage. The diagnosis and initial treatment phases were assessed jointly because the diagnosis and initial treatment phases involved the same patient group. As a result, 9.8% of records in the diagnosis/initial treatment, 9.7% in the radiotherapy/chemotherapy phase, 15.0% in the follow-up, and 8.6% in the recurrence/progression/metastasis phases were excluded. Missing data were minimal. Three participants (0.09%) had erroneous age values, which were corrected by imputation using the sample median.

Statistical analysis

Key variable definitions

The total costs for each disease course were defined as the sum of direct medical, direct non-medical, and indirect costs. Direct medical costs included expenditures incurred at the study hospital during the relevant disease course, outpatient and inpatient medical expenses at other healthcare facilities prior to reimbursement, and out-of-hospital medication purchases related to the disease. Direct non-medical costs consisted of patient-reported spending on transportation, accommodation for patients and caregivers, hired caregiving services, and nutritional supplements. Indirect costs were defined as productivity losses due to the illness, which were calculated based on the number of workdays missed by patients and caregivers multiplied by the average daily wage for rural or urban residents, depending on the patient's place of residence. Additional self-reported expenses related to the illness but not classified under the above categories were also included in indirect costs. Total costs were estimated by adjusting the reported costs according to the proportion of the scheduled follow-up period that had been completed for patients still in the follow-up at the time of data collection. All costs were initially collected in Chinese yuan (CNY) and converted into United States dollars (USD) using an exchange rate of 1 USD = 7 CNY.

Detection modes were classified into four categories based on participants' responses to the question: 'How did you first become aware of your condition?' The response options were as follows: (1) symptoms; (2) government free cervical cancer screening; (3) workplace check-up; (4) self-paid check-up; and (5) incidental findings during diagnosis or treatment for other conditions. Participants who selected option (2) were

categorized as detected through "government screening." Options (3) and (4) were classified as "workplace check-up" and "self-paid check-up," respectively. Options (1) and (5) were merged into the single category, "symptom-based detection."

Overtreatment was defined as the use of interventions not recommended by clinical guidelines, which resulted in potentially unnecessary procedures. This study focused on overtreatment among patients diagnosed with LSIL and HSIL. According to the Chinese Guidelines for Comprehensive Cervical Cancer Prevention and Control[15], patients with pathologically confirmed LSIL should be managed conservatively and further evaluation should be based on cytologic findings to reduce the risk of misdiagnosis. Patients with LSIL who underwent excisional or ablative procedures during the initial treatment were classified as overtreated. These procedures included loop electrosurgical excision procedure (LEEP), laser conization, cold knife conization, thermal coagulation, simple cervical resection, and radical cervical resection. Patients with HSIL who underwent hysterectomy or radiotherapy/chemotherapy were also considered overtreated.

Comparison of baseline characteristics

Baseline demographic and clinical characteristics were compared between the government screening group and the other detection groups. The age and medical reimbursement rate were analysed as continuous variables and summarised using means with standard deviations. Categorical variables, including clinical stage, disease course, geographic region, residential location, hospital level, education, and occupation, are summarised as frequencies and percentages. Histologic differentiation and cell type were analysed only in cancer patients. Overtreatment was assessed in LSIL and HSIL patients during initial treatment. Group comparisons involved four pairwise comparisons between government-organized screening and each of the three other detection modes (workplace check-up, self-paid check-up, and symptom-based detection), as well as an additional comparison between government-organized screening and the combined group of all other detection modes. Standardized mean differences (SMDs) were calculated to assess between-group imbalance with values < 0.1 indicating negligible imbalance.

Multiple linear regression analysis

Five separate multivariable linear regression models were constructed to assess the determinants of total costs across different disease courses of cervical cancer, each corresponding to a specific disease course. Candidate variables were first identified through univariable analyses with those variables showing statistical significance ($P < 0.05$) in any disease course considered for inclusion. Key variable definitions are provided in **Table S1**. Univariable analysis of model variables is shown in **Table S2**. Variables were retained in the final models if the variables were statistically significant in multivariable regression for at least one disease course and were also considered potential confounders of the association between detection mode and cost. The final covariate set comprised detection modes, clinical stage, geographic region, residential location, hospital level, education, occupation, age, and reimbursement rate. The full multivariable linear regression model specifications are presented in **Equations S1–S3**. Log-transformation was applied to improve model fit because cost variable were right-skewed. Residual diagnostic plots (**Figures S1–S5**) were used to assess model assumptions and HC3 heteroscedasticity-consistent standard errors were applied to address potential variance heterogeneity. The Bonferroni correction was applied to control the risk of a type I error because multiple comparisons were performed. The results with a nominal *P*-value and alternative adjusted *P*-values are reported in **Tables S3–S7**.

Mediation mechanism analysis

Structural equation modeling (SEM) was used to quantify the direct and indirect effects of government-organized screening on log-transformed total costs. The direct effect represents the portion of the effect not explained by mediators, whereas the indirect effect quantifies the pathway through mediators, including clinical stage, hospital level, and overtreatment. Total effects were computed as the sum of direct and indirect effects. To better isolate the mediation pathways of government screening, covariates showing baseline differences between detection modes and considered theoretically relevant to the mediators, including age, occupation, education, residential location, and reimbursement rate, were included in the regression models for clinical stage, hospital level, and overtreatment. Clinical stage (LSIL, HSIL, and stages I, II, and III–IV) was modeled as an ordinal categorical variable in the mediation analysis. Robust standard errors were applied in the mediation analysis of clinical stage and hospital level to account for heteroskedasticity. As overtreatment was defined only among patients with LSIL or HSIL undergoing initial treatment, estimation of its mediating role was restricted to this subgroup and 1,000 bootstrap replications were performed to obtain robust confidence intervals. The Benjamini–Hochberg false discovery rate

Table 1 Comparison of patient characteristics between cases detected through government screening and other methods modes

	Total	Government screening	Other detection modes	SMD	Workplace check-up	SMD	Self-paid check-up	SMD	Symptom-based detection	SMD
All patients	*N* = 3,471	*N* = 462	*N* = 3,009		*N* = 267		*N* = 704		*N* = 2,038	
Age (Years)	47.84 (10.83)	48.67 (8.63)	47.71 (11.13)	0.09	42.40 (9.51)	0.70	42.99 (10.42)	0.58	50.03 (10.80)	0.13
Disease course:										
Diagnosis and initial treatment	1,423 (41.00%)	234 (50.65%)	1,189 (39.51%)	0.22	132 (49.44%)	0.02	312 (44.32%)	0.13	745 (36.56%)	0.28
Radiotherapy/chemotherapy	500 (14.41%)	15 (3.25%)	485 (16.12%)	0.44	15 (5.62%)	0.12	36 (5.11%)	0.09	434 (21.30%)	0.55
Follow-up	1,194 (34.40%)	193 (41.77%)	1,001 (33.27%)	0.18	101 (37.83%)	0.08	278 (39.49%)	0.05	622 (30.52%)	0.23
Recurrence/progression/metastasis	354 (10.20%)	20 (4.33%)	334 (11.10%)	0.25	19 (7.12%)	0.12	78 (11.08%)	0.25	237 (11.63%)	0.27
Clinical stage:										
LSIL	549 (15.82%)	153 (33.12%)	396 (13.16%)	0.47	76 (28.46%)	0.10	208 (29.55%)	0.08	112 (5.50%)	0.70
HSIL	803 (23.13%)	198 (42.86%)	605 (20.11%)	0.49	110 (41.20%)	0.03	271 (38.49%)	0.09	224 (10.99%)	0.72
IA	226 (6.51%)	30 (6.49%)	196 (6.51%)	0.00	20 (7.49%)	0.04	56 (7.95%)	0.06	120 (5.89%)	0.03
IB	610 (17.57%)	38 (8.23%)	572 (19.01%)	0.31	27 (10.11%)	0.07	68 (9.66%)	0.05	477 (23.41%)	0.42
IIA	487 (14.03%)	13 (2.81%)	474 (15.75%)	0.45	18 (6.74%)	0.18	46 (6.53%)	0.18	410 (20.12%)	0.54
IIB	282 (8.12%)	11 (2.38%)	271 (9.01%)	0.29	6 (2.25%)	0.01	18 (2.56%)	0.01	247 (12.12%)	0.38
III and IV	514 (14.81%)	19 (4.11%)	495 (16.45%)	0.41	10 (3.75%)	0.02	37 (5.26%)	0.05	448 (21.98%)	0.53
Area**:**										
East	1,284 (36.99%)	172 (37.23%)	1,112 (36.96%)	0.01	111 (41.57%)	0.09	303 (43.04%)	0.12	698 (34.25%)	0.06
Middle	829 (23.88%)	200 (43.29%)	629 (20.90%)	0.48	60 (22.47%)	0.44	143 (20.31%)	0.49	426 (20.90%)	0.48
West	1,358 (39.12%)	90 (19.48%)	1,268 (42.14%)	0.49	96 (35.96%)	0.37	258 (36.65%)	0.38	914 (44.85%)	0.54
Residence**:**										
Urban	1,311 (37.77%)	104 (22.51%)	1,207 (40.11%)	0.38	186 (69.66%)	0.95	362 (51.42%)	0.60	659 (32.34%)	0.22
Rural	2,160 (62.23%)	358 (77.49%)	1,802 (59.89%)	0.38	81 (30.34%)	0.95	342 (48.58%)	0.60	1,379 (67.66%)	0.22
Hospital level:										
Higher-level hospitals	3,075 (88.59%)	301 (65.15%)	2,774 (92.19%)	0.66	247 (92.51%)	0.67	675 (95.88%)	0.78	1,852 (90.87%)	0.62
Lower-level hospitals	396 (11.41%)	161 (34.85%)	235 (7.81%)	0.66	20 (7.49%)	0.67	29 (4.12%)	0.78	186 (9.13%)	0.62

Table 1 Continued

	Total	Government screening	Other detection modes	SMD	Workplace check-up	SMD	Self-paid check-up	SMD	Symptom-based detection	SMD
Education:										
Elementary school and below	1,027 (29.59%)	172 (37.23%)	855 (28.41%)	0.19	7 (2.62%)	0.87	104 (14.77%)	0.51	744 (36.51%)	0.01
Junior high school	1,094 (31.52%)	200 (43.29%)	894 (29.71%)	0.28	26 (9.74%)	0.76	206 (29.26%)	0.29	662 (32.48%)	0.22
High/technical secondary school	691 (19.91%)	58 (12.55%)	633 (21.04%)	0.23	54 (20.22%)	0.21	178 (25.28%)	0.33	401 (19.68%)	0.19
University/college and above	659 (18.99%)	32 (6.93%)	627 (20.84%)	0.40	180 (67.42%)	1.25	216 (30.68%)	0.61	231 (11.33%)	0.15
Occupation:										
Agricultural worker	941 (27.11%)	218 (47.19%)	723 (24.03%)	0.48	3 (1.12%)	1.08	106 (15.06%)	0.69	614 (30.13%)	0.35
Worker/staff	1,075 (30.97%)	107 (23.16%)	968 (32.17%)	0.20	206 (77.15%)	1.08	258 (36.65%)	0.29	504 (24.73%)	0.04
Self-employed	487 (14.03%)	53 (11.47%)	434 (14.42%)	0.09	18 (6.74%)	0.16	175 (24.86%)	0.35	241 (11.83%)	0.01
Retired	387 (11.15%)	24 (5.19%)	363 (12.06%)	0.24	33 (12.36%)	0.25	60 (8.52%)	0.13	270 (13.25%)	0.28
Student/unemployed/unknown	581 (16.74%)	60 (12.99%)	521 (17.31%)	0.12	7 (2.62%)	0.39	105 (14.91%)	0.06	409 (20.07%)	0.19
Reimbursement rate (%)	0.27 (0.25)	0.21 (0.25)	0.28 (0.25)	0.29	0.22 (0.26)	0.02	0.18 (0.24)	0.13	0.33 (0.24)	0.48
Cancer patients	*N* = 2,119	*N* = 111	*N* = 2,008		*N* = 81		*N* = 225		*N* = 1,702	
Histologic type:										
Squamous cell carcinoma	1,886 (89.00%)	96 (86.49%)	1,790 (89.14%)	0.08	70 (86.42%)	< 0.01	195 (86.67%)	0.01	1,525 (89.60%)	0.10
Non-squamous cell carcinoma	233 (11.00%)	15 (13.51%)	218 (10.86%)	0.08	11 (13.58%)	< 0.01	30 (13.33%)	0.01	177 (10.40%)	0.10
Degree of differentiation:										
Well-differentiated	203 (9.58%)	16 (14.41%)	187 (9.31%)	0.16	13 (16.05%)	0.05	29 (12.89%)	0.04	145 (8.52%)	0.19
Moderately differentiated	889 (41.95%)	54 (48.65%)	835 (41.58%)	0.14	34 (41.98%)	0.13	75 (33.33%)	0.31	726 (42.66%)	0.12
Poorly or undifferentiated	501 (23.64%)	14 (12.61%)	487 (24.25%)	0.30	15 (18.52%)	0.16	32 (14.22%)	0.05	440 (25.85%)	0.34
Unknown	526 (24.82%)	27 (24.32%)	499 (24.85%)	0.01	19 (23.46%)	0.02	89 (39.56%)	0.33	391 (22.97%)	0.03
LSIL patients in initial treatment	*N* = 288	*N* = 82	*N* = 206		*N* = 44		*N* = 103		*N* = 59	
Overtreatment in LSIL stage:										
No	102 (35.4%)	38 (46.3%)	64 (31.1%)	0.17	9 (20.5%)	0.26	36 (35.0%)	0.15	19 (32.2%)	0.14
Yes	186 (64.6%)	44 (53.7%)	142 (68.9%)	0.17	35 (79.5%)	0.26	67 (65.0%)	0.15	40 (67.8%)	0.14

Table 1 Continued

	Total	Government screening	Other detection modes	SMD	Workplace check-up	SMD	Self-paid check-up	SMD	Symptom-based detection	SMD
HSIL patients in initial treatment	*N* = 359	*N* = 106	*N* = 253		*N* = 55		*N* = 121		*N* = 77	
Overtreatment in HSIL stage:										
No	332 (92.48%)	93 (87.74%)	239 (94.47%)	0.18	51 (92.73%)	0.13	117 (96.69%)	0.25	71 (92.21%)	0.11
Yes	27 (7.52%)	13 (12.26%)	14 (5.53%)	0.18	4 (7.27%)	0.13	4 (3.31%)	0.25	6 (7.79%)	0.11

LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion. Clinical stages (IA, IB, IIA, IIB, III, and IV) refer to the International Federation of Gynecology and Obstetrics (FIGO) staging system for cervical cancer, ranging from early localized disease (IA/IB) to advanced/metastatic disease (IV). Standardized mean differences (SMDs) were calculated for workplace check-up, self-paid check-up, symptom-based detection, and their combined category ("other detection"), using government-organized screening as the reference group. The SMD quantifies the magnitude of between-group differences in baseline characteristics, with values < 0.1 generally regarded as negligible.

(FDR) adjustment was applied to account for multiple testing for mediation analyses. The mediation mechanism was specified with full specifications, as shown in **Equations S4–S5**.

Results

Baseline and clinical characteristics based on mode of detection

A total of 3,471 women diagnosed with cervical lesions or cervical cancer were included in the current study. As shown in **Table 1**, 462 (13.31%) women were identified through government-organized screening, 267 (7.69%) through workplace check-ups, 704 (20.28%) through self-paid check-ups, and 2,038 (58.71%) by symptom-based detection. Government-organized screening yielded the largest proportions of LSIL and HSIL cases (33.12% and 42.86%, respectively). In contrast, symptom-based detection was associated with a markedly higher prevalence of advanced-stage disease with 21.98% in stage III–IV (SMD = 0.53) and 12.12% in stage IIB (SMD = 0.38). The proportions of LSIL and HSIL in the workplace and self-paid check-up groups were comparable to the government screening group with LSIL at 28.46% (SMD = 0.10) and HSIL at 41.20% (SMD = 0.03) in the workplace check-up group and LSIL at 29.55% (SMD = 0.08) and HSIL at 38.49% (SMD = 0.09) in the self-paid check-up group. The distribution of disease courses also varied by mode of detection. The symptom-based group had substantially more patients in radiotherapy/chemotherapy with 21.30% *vs.* 3.25% (SMD = 0.55) and in R/P/M with 11.63% *vs.* 4.33% (SMD = 0.27) compared to the government screening group.

The mean age was higher in the government screening group (48.67 ± 8.63 y) than the workplace check-up (42.40 ± 9.51 y; SMD = 0.70) and self-paid check-up groups (42.99 ± 10.42 y; SMD = 0.58). Patients from the western region were more frequently represented in the symptom-based detection group compared to the government screening group (44.85% *vs.* 19.48%; SMD = 0.54). Patients in the government screening group were more often treated in lower-level hospitals (34.85%) compared to the workplace check-up (7.49%; SMD = 0.67), self-paid check-up (4.12%; SMD = 0.78), and symptom-based detection groups (9.13%; SMD = 0.62). Educational attainment was substantially lower in the government screening group with only 6.93% having a college or university education compared to 67.42% in the

Table 2 Comparison of economic burden across disease courses by detection mode

Disease course	Government screening	Other detection modes	*P*	Workplace check-up	*P*	Self-paid check-up	*P*	Symptom-based detection	*P*
Diagnosis	77.14 (1.39–269.01)	348.25 (178.61–816.12)	< 0.001	276.61 (115.28–561.57)	< 0.001	337.44 (154.29–615.77)	< 0.001	385.28 (204.37–1,014.29)	< 0.001
Initial treatment	1,058.54 (403.93–2,023.42)	4,741.45 (1,136.94–9,231.51)	< 0.001	911.88 (566.54–2,721.23)	0.242	1,252.84 (714.29–3,785.70)	< 0.001	6,845.15 (3,615.10–12,767.45)	< 0.001
Radiotherapy/chemotherapy	14,283.56 (11,273.94–16,415.80)	12,887.69 (9,455.31–17,483.74)	0.805	12,857.14 (10,754.83–17,693.07)	0.775	13,516.94 (8,888.76–16,653.54)	0.519	12,886.70 (9,468.38–17,518.50)	0.821
Follow-up	577.43 (171.43–1,441.49)	1,733.70 (829.14–4,596.21)	< 0.001	1,095.51 (521.50–2,164.31)	< 0.001	1,047.63 (618.10–2,205.00)	< 0.001	2,441.09 (1,127.86–6,036.43)	< 0.001
Recurrence/progression/metastasis	3,224.50 (1,694.32–3,863.83)	4,638.14 (1,979.05–14,662.38)	0.069	1,664.68 (615.18–3,209.04)	0.113	1,310.05 (710.61–3,547.57)	0.085	9,012.29 (2,948.66–20,225.75)	< 0.001

Costs are presented in United States dollars (USD) as median (first quartile, Q1 – third quartile, Q3). Results are reported as median values with interquartile ranges for cost variables. Nominal *P*-values for the workplace check-up, self-paid check-up, symptom-based detection, and the combined group of these three modes ("other detection") were calculated relative to the government screening group.

workplace check-up group (SMD = 1.25), 30.68% in the self-paid check-up group (SMD = 0.61), and 11.33% in the symptom-based detection group (SMD = 0.15). The proportion of agricultural workers was highest in the government screening group (47.19% *vs.* 1.12% in the workplace check-up group, 15.06% in the self-paid check-up group, and 30.13% in the symptom-based detection group; SMDs = 1.08, 0.69, and 0.35, respectively). The self-paid check-up group had the lowest mean reimbursement rate (0.18 ± 0.24), which was comparable to the government screening group (0.21 ± 0.25; SMD = 0.13).

No meaningful differences were observed in the histologic type across groups among cancer patients (all SMDs < 0.20). A higher proportion of well-differentiated tumours was observed in the government screening group compared to the symptom-based detection group (14.41% *vs.* 8.52%; SMD = 0.19). Differences in overtreatment were modest. Overtreatment during the initial treatment was less frequent in the government screening group compared to the other mode of detection among patients with LSIL (53.7% *vs.* 68.9%; SMD = 0.17). Overtreatment was more common in the government screening group in patients with HSIL (12.26% *vs.* 5.53%; SMD = 0.18).

Median cost comparisons

Table 2 shows that government-organized screening was associated with substantially lower median costs compared to other detection modes during diagnosis (median \$77.14, IQR: 1.39–269.01 *vs.* \$348.25, IQR: 178.61–816.12, $P < 0.001$), initial treatment (\$1,058.54, IQR: 403.93–2,023.42 *vs.* \$4,741.45, IQR: 1,136.94–9,231.51, $P < 0.001$), and follow-up (\$577.43, IQR: 171.43–1,441.49 *vs.* \$1,733.70, IQR: 829.14–4,596.21, $P < 0.001$). Stratified analyses further revealed consistently higher costs in the workplace check-up group during diagnosis (\$276.61, IQR: 115.28–561.57, $P < 0.001$) and follow-up (\$1,095.51, IQR: 521.50–2,164.31, $P < 0.001$), in the self-paid check-up group during diagnosis (\$337.44, IQR: 154.29–615.77, $P < 0.001$), initial treatment (\$1,252.84, IQR: 714.29–3,785.70, $P < 0.001$), and follow-up (\$1,047.63, IQR: 618.10–2,205.00, $P < 0.001$), and in the symptom-based detection group across four disease courses, diagnosis (\$385.28, IQR: 204.37–1,014.29, $P < 0.001$), initial treatment (\$6,845.15, IQR: 3,615.10–12,767.45, $P < 0.001$), follow-up (\$2,441.09, IQR: 1,127.86–6,036.43, $P < 0.001$), and R/P/M (\$9,012.29, IQR: 2,948.66–20,225.75, $P < 0.001$).

Table 3 Multivariate linear regression analysis of factors influencing economic burden

Factors	Diagnosis		Initial treatment		Radiotherapy/chemotherapy		Follow-up		Recurrence/progression/metastasis	
	β (95% CI)	*P*	*β* (95% CI)	*P*	*β* (95% CI)	*P*	*β* (95% CI)	*P*	*β* (95% CI)	*P*
Age	−0.00 (−0.01, 0.01)	1.000	0.00 (−0.00, 0.00)	1.000	−0.01 (−0.01, −0.00)	0.041	−0.01 (−0.01, 0.00)	0.876	−0.01 (−0.01, 0.00)	1.000
Detection modes (ref = Government screening)										
Workplace check-up	1.10 (0.54, 1.67)	0.002	0.36 (0.18, 0.55)	0.002	0.43 (−0.06, 0.91)	1.000	0.63 (0.38, 0.88)	< 0.001	−0.12 (−0.61, 0.37)	1.000
Self-paid check-up	1.46 (1.00, 1.92)	< 0.001	0.51 (0.35, 0.66)	< 0.001	0.10 (−0.32, 0.51)	1.000	0.83 (0.61, 1.04)	< 0.001	−0.22 (−0.54, 0.10)	1.000
Symptom-based detection	1.68 (1.25, 2.11)	< 0.001	0.56 (0.42, 0.70)	< 0.001	0.13 (−0.25, 0.51)	1.000	0.85 (0.65, 1.06)	< 0.001	0.10 (−0.22, 0.42)	1.000
Clinical stage	(reference: LSIL)		(reference: LSIL)		(reference: Stage I)		(reference: LSIL)		(reference: HSIL)	
HSIL	0.71 (0.34, 1.07)	0.002	0.68 (0.55, 0.81)	< 0.001			0.34 (0.16, 0.51)	0.002		
I	0.93 (0.57, 1.30)	< 0.001	2.07 (1.93, 2.21)	< 0.001			1.31 (1.14, 1.48)	< 0.001	1.01 (0.76, 1.26)	< 0.001
II	0.90 (0.53, 1.27)	< 0.001	2.23 (2.07, 2.39)	< 0.001	0.23 (0.13, 0.34)	< 0.001	1.48 (1.30, 1.66)	< 0.001	1.42 (1.17, 1.67)	< 0.001
III and IV	1.11 (0.71, 1.51)	< 0.001	2.94 (2.80, 3.09)	< 0.001			1.73 (1.52, 1.93)	< 0.001	1.55 (1.32, 1.79)	< 0.001
Rural resident	−0.10 (−0.34, 0.13)	1.000	0.08 (0.01, 0.16)	0.414	−0.03 (−0.16, 0.10)	1.000	0.08 (−0.04, 0.20)	1.000	−0.10 (−0.29, 0.09)	1.000
Area (reference: East)										
Middle	0.45 (0.17, 0.73)	0.027	0.36 (0.27, 0.45)	< 0.001	0.52 (0.42, 0.62)	< 0.001	0.71 (0.57, 0.86)	< 0.001	0.59 (0.34, 0.84)	< 0.001
West	0.44 (0.20, 0.68)	0.005	0.11 (0.02, 0.20)	0.244	−0.11 (−0.26, 0.04)	1.000	0.27 (0.15, 0.40)	< 0.001	−0.46 (−0.64, −0.28)	< 0.001
Lower-level hospitals	−1.83 (−2.23, −1.44)	< 0.001	0.01 (−0.12, 0.14)	1.000	0.46 (0.30, 0.62)	< 0.001	−0.18 (−0.38, 0.02)	1.000	0.43 (0.10, 0.76)	0.163
With high school education or above	−0.24 (−0.50, 0.01)	0.901	−0.11 (−0.20, −0.03)	0.132	−0.17 (−0.30, −0.04)	0.157	0.03 (−0.10, 0.16)	1.000	−0.24 (−0.46, −0.01)	0.568
Agricultural worker	−0.38 (−0.64, −0.11)	0.079	−0.14 (−0.22, −0.05)	0.036	−0.08 (−0.19, 0.03)	1.000	−0.06 (−0.19, 0.08)	1.000	0.08 (−0.12, 0.28)	1.000
Reimbursement rate	2.48 (1.96, 3.01)	< 0.001	0.86 (0.68, 1.04)	< 0.001	0.29 (0.01, 0.56)	0.498	1.62 (1.33, 1.92)	< 0.001	1.57 (1.13, 2.02)	< 0.001
R-squared	0.31		0.78		0.22		0.54		0.71	
Adjusted R-squared	0.30		0.78		0.20		0.53		0.70	

CI, confidence interval; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion. Clinical stage I, II, III, and IV refer to the FIGO staging system for invasive cervical cancer. The *β* coefficients represent estimates obtained with HC3 robust standard errors, and the corresponding *P*-values were Bonferroni-adjusted for multiple testing. All *P*-values for the three detection modes (workplace check-up, self-paid check-up, and symptom-based detection) are calculated relative to government-organized screening. Clinical stage was treated as a categorical variable with LSIL used as the reference category for diagnosis and initial treatment, stage I for radiotherapy/chemotherapy, and HSIL for recurrence/progression/metastasis. Geographic region was referenced to the eastern region; residence to urban areas; hospital level to higher-level hospitals; occupation to non-agricultural workers; age and medical reimbursement rate were treated as continuous variables.

Table 4 Mediation analysis of government screening program reducing economic burden through earlier clinical staging and lower hospital level

Model	Outcome	Factors	Diagnosis		Initial treatment		Follow-up	
			β (95% CI)	*P*	β (95% CI)	*P*	β (95% CI)	*P*
Direct effect model with mediation	Total cost	Detected by workplace check-up	0.55 (0.15, 0.95)	0.012	0.08 (−0.11, 0.26)	0.479	0.33 (0.11, 0.56)	0.005
		Detected by self-paid check-up	0.91 (0.58, 1.25)	< 0.001	0.19 (0.05, 0.34)	0.012	0.57 (0.37, 0.76)	< 0.001
		Detected by symptoms	0.99 (0.67, 1.31)	< 0.001	0.33 (0.20, 0.47)	< 0.001	0.62 (0.43, 0.82)	< 0.001
		Clinical stage	0.43 (0.34, 0.53)	< 0.001	0.73 (0.70, 0.77)	< 0.001	0.48 (0.43, 0.53)	< 0.001
		Received care at lower-level hospital	−2.05 (−2.30, −1.79)	< 0.001	−0.62 (−0.80, −0.43)	< 0.001	−0.48 (−0.72, −0.25)	< 0.001
		Age	−0.01 (−0.02, 0.00)	0.095	−0.00 (−0.00, 0.00)	0.909	−0.01 (−0.01, −0.00)	0.030
		Rural resident	−0.19 (−0.46, 0.07)	0.189	0.09 (0.01, 0.17)	0.045	0.09 (−0.03, 0.22)	0.158
		Middle area	0.02 (−0.25, 0.30)	0.885	0.31 (0.21, 0.41)	< 0.001	0.63 (0.48, 0.78)	< 0.001
		West area	0.08 (−0.19, 0.36)	0.654	0.12 (0.03, 0.21)	0.016	0.28 (0.16, 0.41)	< 0.001
		High school education or above	−0.23 (−0.50, 0.05)	0.139	−0.14 (−0.24, −0.05)	0.004	0.04 (−0.09, 0.18)	0.524
		Agricultural worker	−0.49 (−0.75, −0.23)	< 0.001	−0.19 (−0.29, −0.09)	< 0.001	−0.11 (−0.25, 0.03)	0.134
		Reimbursement rate	2.59 (1.97, 3.21)	< 0.001	1.15 (0.95, 1.35)	< 0.001	1.71 (1.41, 2.02)	< 0.001
Indirect effect mediation model Path A	Clinical stage	Detected by workplace check-up	0.33 (0.09, 0.58)	0.013	0.41 (0.20, 0.62)	< 0.001	0.42 (0.15, 0.68)	0.003
		Detected by self-paid check-up	0.36 (0.18, 0.53)	< 0.001	0.50 (0.33, 0.67)	< 0.001	0.29 (0.10, 0.47)	0.005
		Detected by symptoms	1.55 (1.40, 1.71)	< 0.001	1.63 (1.49, 1.77)	< 0.001	1.37 (1.20, 1.55)	< 0.001
		Age	0.02 (0.02, 0.03)	< 0.001	0.02 (0.01, 0.03)	< 0.001	0.03 (0.02, 0.03)	< 0.001
		Rural resident	0.16 (0.03, 0.30)	0.026	0.16 (0.04, 0.28)	0.014	0.20 (0.07, 0.34)	0.005
		Middle area	−0.11 (−0.26, 0.04)	0.188	−0.03 (−0.17, 0.10)	0.686	−0.10 (−0.25, 0.05)	0.191
		West area	−0.12 (−0.25, 0.01)	0.106	−0.13 (−0.25, −0.01)	0.052	−0.21 (−0.36, −0.07)	0.004
		High school education or above	−0.06 (−0.21, 0.08)	0.465	−0.09 (−0.22, 0.04)	0.232	−0.05 (−0.20, 0.11)	0.569
		Agricultural worker	0.21 (0.06, 0.35)	0.009	0.18 (0.05, 0.31)	0.010	0.12 (−0.03, 0.27)	0.155
		Reimbursement rate	0.42 (0.06, 0.78)	0.034	1.40 (1.18, 1.62)	< 0.001	1.39 (1.09, 1.69)	< 0.001

Table 4 Continued

Model	Outcome	Factors	Diagnosis		Initial treatment		Follow-up	
			β (95% CI)	*P*	*β* (95% CI)	*P*	*β* (95% CI)	*P*
Indirect effect mediation model Path B	Received care at lower-level hospital	Detected by workplace check-up	−0.23 (−0.30, −0.15)	< 0.001	−0.22 (−0.29, −0.15)	< 0.001	−0.22 (−0.29, −0.14)	< 0.001
		Detected by self-paid check-up	−0.29 (−0.35, −0.22)	< 0.001	−0.27 (−0.32, −0.22)	< 0.001	−0.23 (−0.29, −0.17)	< 0.001
		Detected by symptoms	−0.26 (−0.31, −0.21)	< 0.001	−0.27 (−0.32, −0.22)	< 0.001	−0.21 (−0.26, −0.15)	< 0.001
		Age	0.00 (−0.00, 0.00)	0.885	−0.00 (−0.00, 0.00)	0.620	−0.00 (−0.00, −0.00)	0.006
		Rural resident	0.00 (−0.04, 0.04)	0.885	0.00 (−0.03, 0.04)	0.932	0.03 (−0.01, 0.06)	0.191
		High school education or above	0.00 (−0.04, 0.05)	0.885	−0.00 (−0.04, 0.04)	0.983	−0.02 (−0.06, 0.02)	0.340
		Agricultural worker	0.01 (−0.03, 0.06)	0.657	0.01 (−0.03, 0.05)	0.687	0.03 (−0.01, 0.07)	0.116
		Reimbursement rate	−0.02 (−0.10, 0.06)	0.669	0.19 (0.12, 0.26)	< 0.001	0.06 (−0.02, 0.15)	0.158
Total effect of detection modes		Detected by workplace check-up	1.16 (0.73, 1.58)	< 0.001	0.52 (0.28, 0.76)	< 0.001	0.64 (0.37, 0.90)	< 0.001
		Detected by self-paid check-up	1.65 (1.31, 1.99)	< 0.001	0.73 (0.53, 0.92)	< 0.001	0.81 (0.60, 1.03)	< 0.001
		Detected by symptoms	2.19 (1.91, 2.48)	< 0.001	1.69 (1.53, 1.86)	< 0.001	1.38 (1.17, 1.59)	< 0.001
Proportion mediated (Path A, Path B, Path A + B)		Detected by workplace check-up	12.43%, 40.10%, 52.53%		58.70%, 26.34%, 85.04%		31.18%, 16.43%, 47.61%	
		Detected by self-paid check-up	9.38%, 35.36%, 44.74%		50.42%, 22.85%, 73.27%		16.71%, 13.67%, 30.38%	
		Detected by symptoms	30.59%, 24.38%, 54.97%		70.61%, 9.78%, 80.39%		47.46%, 7.27%, 54.73%	

CI, confidence interval. Geographic region was referenced to the East; residence to urban areas; hospital level to higher-level hospitals; occupation to non-agricultural worker. Age and reimbursement rate were modelled as continuous variables. *β* (95% CI) represents unstandardised coefficients with 95% confidence intervals based on robust standard errors. *P*-values were adjusted for multiple testing using the Benjamini–Hochberg false discovery rate (FDR) method. Coefficients shown as −0.00 denote small negative values (< 0.00) that are rounded to two decimal places.

Multiple linear regression results

Cost differentials across detection modes remained evident after adjusting for sociodemographic and clinical covariates, as shown in **Table 3**. Patients diagnosed through workplace check-up incurred significantly higher costs during diagnosis [β: 1.10; 95% confidence interval (CI): 0.54–1.67; $P = 0.002$], initial treatment (β: 0.36; 95% CI: 0.18–0.55; $P = 0.002$), and follow-up (β: 0.63; 95% CI: 0.38–0.88; $P < 0.001$) compared to the government screening group. The self-paid check-up group also showed elevated costs in diagnosis (β: 1.46; 95% CI: 1.00–1.92; $P < 0.001$), initial treatment (β: 0.51; 95% CI: 0.35–0.66; $P < 0.001$), and follow-up (β: 0.83; 95% CI: 0.61–1.04; $P < 0.001$). Patients diagnosed *via* symptoms incurred the greatest cost burden in diagnosis (β: 1.68; 95% CI: 1.25–2.11; $P < 0.001$), initial treatment (β: 0.56; 95% CI: 0.42–0.70; $P < 0.001$), and follow-up (β: 0.85; 95% CI: 0.65–1.06; $P < 0.001$). No significant cost differences were observed between the modes of detection in the radiotherapy/chemotherapy and R/P/M for any group ($P > 0.05$). Detailed results from additional multiplicity corrections are provided in **Tables S3–S7** and the associations with the mode of detection mode remained consistently robust.

Higher clinical stage was consistently associated with greater costs. Expenditures were significantly higher for more advanced stages compared to the earliest stage (LSIL for diagnosis, initial treatment, and follow-up; stage I for radiotherapy/chemotherapy, and HSIL for recurrence/progression/metastasis; all $P < 0.05$) across all disease courses. Age was slightly negatively associated with costs only during radiotherapy/chemotherapy (β: −0.01; 95% CI: −0.01 to −0.00; $P = 0.041$). Patients from the middle region had significantly higher costs across all disease courses compared to patients from the eastern region (all $P < 0.05$). Patients from the western region incurred higher costs during diagnosis (β: 0.44; 95% CI: 0.20–0.68; $P = 0.005$) and follow-up (β: 0.27; 95% CI: 0.15–0.40; $P < 0.001$) but lower costs during R/P/M (β: −0.46; 95% CI: −0.64 to −0.28; $P < 0.001$). Receiving care at lower-level hospitals was associated with lower costs during diagnosis (β: −1.83; 95% CI: −2.23 to −1.44; $P < 0.001$), no significant difference during initial treatment, and higher costs during radiotherapy/chemotherapy (β: 0.46; 95% CI: 0.30–0.62; $P < 0.001$). Occupation as an agricultural worker was associated with significantly lower costs during initial treatment (β: −0.14; 95% CI: −0.22 to −0.05; $P = 0.036$) with no significant associations in other disease courses.

Mediation analysis of clinical stage and hospital level

Table 4 shows the mediating roles of clinical stage and hospital level in the association between modes of detection and total costs across three disease courses. Detection *via* workplace check-up was associated with later clinical stage at diagnosis (β: 0.33; 95% CI: 0.09–0.58; $P = 0.013$), initial treatment (β: 0.41; 95% CI: 0.20–0.62; $P < 0.001$), and follow-up (β: 0.42; 95% CI: 0.15–0.68; $P = 0.003$) compared to government-organized screening. Self-paid check-up was also associated with later stage at diagnosis (β: 0.36; 95% CI: 0.18–0.53; $P < 0.001$), initial treatment (β: 0.50; 95% CI: 0.33–0.67; $P < 0.001$), and follow-up (β: 0.29; 95% CI: 0.10–0.47; $P = 0.005$). Symptom-based detection had the strongest association with advanced stage at diagnosis (β: 1.55; 95% CI: 1.40–1.71; $P < 0.001$), initial treatment (β: 1.63; 95% CI: 1.49–1.77; $P < 0.001$), and follow-up (β: 1.37; 95% CI: 1.20–1.55; $P < 0.001$). Older age, rural residence, agricultural occupation, and higher reimbursement rate were also associated with a later stage at presentation.

Workplace check-up was associated with lower likelihood of receiving care at a lower-level hospital during diagnosis (β: −0.23; 95% CI: −0.30 to −0.15; $P < 0.001$), initial treatment (β: −0.22; 95% CI: −0.29 to −0.15; $P < 0.001$), and follow-up (β: −0.22; 95% CI: −0.29 to −0.14; $P < 0.001$) compared with government screening. The same pattern was observed for self-paid check-up (β range: −0.29 to −0.23) and symptom-based detection (β range: −0.27 to −0.21; all, $P < 0.001$). Clinical stage and hospital level jointly explained a substantial share of the cost differences across modes of detection. The proportion of the total effect mediated was 52.53% (diagnosis), 85.04% (initial treatment), and 47.61% (follow-up) for workplace check-up, 44.74%, 73.27%, and 30.38% for self-paid check-up, and 54.97%, 80.39%, and 54.73% for symptom-based detection, respectively. The path diagrams illustrating the mediation effects of clinical stage and hospital level during diagnosis, initial treatment, and follow-up are presented in **Figures S6–S8**.

Mediation analysis of overtreatment in patients with precancerous lesions

Mediation analysis (**Table 5**) showed that government-organized screening was significantly associated with lower total costs during the initial treatment for patients with cervical precancerous lesions with the association mediated by lower overtreatment

Table 5 Mediation analysis of government screening program reducing economic burden through reducing overtreatment in patients with cervical precancerous lesions

Model	Outcome	Factors	β (95% CI)	*P*
Direct effect model with mediation	Total cost	Detected by other detection modes (reference: government screening)	0.51 (0.28, 0.74)	< 0.001
		Overtreatment	0.65 (0.42, 0.88)	< 0.001
		LSIL (reference: HSIL)	−1.02 (−1.25, −0.79)	< 0.001
		Age	0.00 (−0.01, 0.00)	0.394
		Rural resident	0.04 (−0.14, 0.23)	0.677
		Middle Area (reference: East)	0.43 (0.19, 0.66)	< 0.001
		West Area (reference: East)	0.29 (0.09, 0.50)	0.010
		Received care at lower-level hospital	−0.24 (−0.49, 0.01)	0.088
		High school education or above	−0.25 (−0.46, −0.04)	0.038
		Agricultural worker	−0.26 (−0.5, −0.02)	0.059
		Reimbursement rate	1.15 (0.79, 1.50)	< 0.001
Indirect effect mediation model	Overtreatment	Detected by other detection modes (reference: government screening)	0.14 (0.04, 0.25)	0.015
		LSIL (reference: HSIL)	0.62 (0.54, 0.71)	< 0.001
		Age	0.00 (0.00, 0.01)	0.534
		Rural resident	0.05 (−0.04, 0.13)	0.394
		Received care at lower-level hospital	0.04 (−0.06, 0.14)	0.563
		High school education or above	0.01 (−0.09, 0.10)	0.896
		Agricultural worker	0.03 (−0.08, 0.14)	0.658
		Reimbursement rate	0.36 (0.20, 0.51)	< 0.001
		Household income	−0.01 (−0.06, 0.03)	0.568
ACME			0.09 (0.02, 0.17)	0.029
Total effect			0.60 (0.36, 0.84)	< 0.001
Proportion mediated			15.00%	

ACME, average causal mediation effect; CI, confidence interval; LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion. β (95% CI) represents the regression coefficient with 95% confidence intervals obtained from bootstrap resampling. Geographic region was referenced to the East; residence to urban areas; hospital level to higher-level hospitals; occupation to non-agricultural worker. Age, reimbursement rate and household income were modelled as continuous variables.

(β: 0.14; 95% CI: 0.04–0.25; P = 0.015). LSIL diagnosis *vs.* HSIL was associated with a higher likelihood of overtreatment (β: 0.62; 95% CI: 0.54–0.71; P < 0.001), and higher insurance reimbursement rates were also linked to more overtreatment (β: 0.36; 95% CI: 0.20–0.51; P < 0.001). Other detection modes were associated with significantly higher total costs (total effect: 0.60; 95% CI: 0.36–0.84; P < 0.001), of which 15.00% was mediated through overtreatment [average causal mediation effect (ACME) = 0.09; 95% CI: 0.02–0.17; P = 0.029] compared to government screening; the remaining effect was a direct effect [average direct effect (ADE) = 0.51; 95% CI: 0.28–0.74; P < 0.001]. **Figure S9** presents the path diagram of overtreatment as a mediator during initial treatment for patients with cervical precancerous lesions. A higher number of bootstrap replications (1,000–10,000) yielded consistent results for indirect and total effects, supporting the robustness of the mediation findings (**Table S8**).

Discussion

This nationwide, multicentre survey suggested that government-organized cervical cancer screening reached a greater proportion of socioeconomically disadvantaged women than other detection modes. Medical costs were lowest among women detected through government-led screening, higher among those detected through workplace and self-paid check-ups, and highest among those detected by symptoms across the diagnosis, initial treatment, and follow-up. Mediation analysis showed that earlier clinical staging and greater use of lower-level hospitals together accounted for greater than one-half of the cost differences. Lower overtreatment explained approximately one-sixth of the cost-saving effect during initial among patients with precancerous lesions.

Government-organized screening contributes more effectively to improving women's health. In the current study, the government-organized screening group had the highest proportion of LSIL and HSIL cases and the lowest proportion of advanced-stage cancers, followed by the workplace check-up, self-paid check-up, and symptom-based groups. The proportion of LSIL and HSIL was nearly five times higher, while stage III–IV cancers were one-fifth as common compared to symptom-based detection. This finding could be explained by the structured design of government screening, which targets asymptomatic women using validated testing methods. In contrast, screening in the workplace or self-paid check-up may vary in test quality and follow-up mechanisms, potentially resulting in lower detection rates of precancerous lesions. Symptom-based detection reflects diagnosis prompted by overt clinical manifestations, often at a more advanced stage. A higher proportion of well- or moderately-differentiated tumours were also identified in the government screening group, supporting the role in facilitating diagnosis at less aggressive stages. Women identified through government screening accounted for a smaller proportion of those receiving radiotherapy/chemotherapy (3.25% *vs*. 16.12%) and women experiencing disease recurrence/progression/metastasis (4.33% *vs*. 11.10%), which is consistent with these findings and compared to other modes of detection. This finding suggests that the increased detection of early-stage lesions through government-organized screening may contribute to lowering the risk of radiotherapy/chemotherapy and disease recurrence/progression/metastasis among women. The findings herein are consistent with the international experience. Transitions from opportunistic to organized screening were associated with improved outcomes in Italy and Brazil. Italy reported declines in incidence and earlier-stage diagnoses after launching a national programme[16], while a Brazilian city implemented a DNA-HPV-based screening model that detected more early-stage cancers (83% at stage I) at younger ages compared to the prior system[17]. Modelling studies from Hong Kong and Spain further demonstrated that organized programmes are more efficient and cost-effective than opportunistic screening, requiring fewer tests per case prevented and achieving greater coverage at a lower cost per person under equivalent resource conditions[18,19]. Our multivariable linear analysis further indicated that government-organized screening was associated with the lowest costs across diagnosis, initial treatment, and follow-up with a stepwise increase observed in workplace check-up, self-paid check-up, and symptom-based detection. The mode of detection exhibited one of the strongest associations with economic burden among all examined factors, exceeding the influence of most sociodemographic variables. These findings underscore the institutional advantage of government-organized screening in reducing individual economic burden and improving the efficiency of cervical cancer control.

Mediation analysis indicated that that the lower costs associated with government-led screening were partly explained by earlier-stage diagnosis and greater use of lower-level rather than higher-level hospitals. Between 9.38% and 30.59% of the cost-reducing effect of government screening in the diagnosis phase compared to other modes of detection could be explained by earlier clinical staging. Government screening primarily identifies precancerous lesions (LSIL and HSIL), which require biopsy for confirmation, whereas invasive cancers often necessitate additional imaging for staging, thereby increasing diagnostic costs. In addition, Chinese government-organized screening programmes deliver free cervical pathology services, which often include fast-track referral and diagnostic support through local public health facilities. This service supports timely care and helps reduce diagnostic costs for patients by reducing delays in diagnosis and treatment initiation[20]. In the initial treatment, differences in clinical stage accounted for 50.42%–70.61% of the observed cost difference. Studies have shown that treatment costs increase significantly with advancing disease stage[21,22]. Early-stage lesions are typically treated with LEEP, loop excision, or simple hysterectomy, which involve shorter treatment durations and lower costs[23]. In contrast, advanced-stage cancer often requires radical

hysterectomy, radiotherapy, or concurrent chemoradiotherapy, which are more costly and accompanied by additional direct non-medical costs, such as transportation and accommodation, as well as indirect costs, including lost productivity[24]. In the follow-up, between 16.71% and 47.46% of the cost reduction from government-led screening was mediated by earlier clinical stage, as longer and more complex follow-up procedures are typically required for late-stage patients[21]. In addition, government-organized screening programmes include standardised follow-up protocols, which are accompanied by early detection of recurrent disease and reduce unnecessary repeat testing, thereby lowering follow-up costs[25]. Our meditation analysis showed that the mode of detection indirectly affected total costs *via* hospital level, reflecting differences in care-seeking preferences. Individuals identified through workplace check-up were typically employed with greater health awareness and insurance coverage and tended to seek care at higher-level hospitals. Self-paid check-up participants often have higher socioeconomic status comparable to preferred higher-level facilities. Symptom-detected patients, due to urgency or severity, were more likely to present directly to large general hospitals. In contrast, government-organized screening was delivered through primary care facilities, where participants with asymptomatic abnormalities were more likely to continue care due to established referral pathways and perceived lower urgency, potentially resulting in reduced costs. Our meditation analysis also showed that older age, rural residence, and agricultural occupation were also associated with more advanced disease. Government-organized screening was more likely to reach these groups and detect disease earlier, reinforcing its role in reducing severity and financial burden among underserved populations.

After adjusting for hospital level and sociodemographic characteristics, approximately 15% of the cost reduction in the initial treatment of cervical precancerous lesions associated with government-organized screening could be explained by reduced overtreatment. The mechanisms by which government-led screening reduces overtreatment remain insufficiently studied. Government-led screening is likely to be more effective in reducing overtreatment compared to other modes of detection because government-led screening is guided by standardised national protocols. These recommend routine follow-up rather than immediate treatment for LSIL and tailored management for HSIL based on excisional pathology, discouraging routine hysterectomy and supporting referral of specimens to higher-level hospitals when needed[25]. Women participating in government-organized screening programmes might place greater trust in the clinical recommendations received, especially in rural areas where health literacy is limited and government-endorsed services are viewed as more authoritative. This trust could promote adherence to medical advice and reduce unnecessary interventions. Previous studies have also linked overtreatment to limited trust in healthcare providers, underscoring the value of credible public screening programmes in supporting informed and appropriate decision-making[26]. Furthermore, local facilities for implementing government-led screening receive regular centralised training, supervision, and performance feedback, which strengthen adherence to clinical guidelines and promote more consistent clinical decision-making[6]. Through these mechanisms, government-led screening programmes could help reduce overtreatment and improve the quality of cervical cancer care.

Beyond the mode of detection, economic burden varied significantly according to clinical stage, insurance coverage, and patient characteristics. Earlier clinical stage and lower insurance reimbursement rate were associated with lower total costs across most phases of the disease course. Higher insurance reimbursement was linked to elevated spending across all stages because enhanced financial coverage may shift patient preferences toward more comprehensive care and extended diagnostic services[27]. Agricultural workers incurred lower costs in initial treatment, possibly reflecting more cost-conscious health-seeking behaviors and a tendency to avoid higher-priced services[28]. These findings highlight wide cost variation shaped by both individual and structural factors, underscoring the need to improve government-led screening programmes and coordinating financing and referral policies across regions could help contain avoidable costs and improve equity.

The current study showed that government-led cervical cancer screening in China primarily serves socioeconomically disadvantaged populations with a higher disease burden. Women identified *via* the national screening programme were more likely to live in rural areas, have lower educational attainment, engage in agricultural work, and receive care at lower-level health facilities compared to women diagnosed through workplace check-up, self-paid check-up, or symptom-based detection. These populations are also the most vulnerable to the economic burden of cervical cancer and precancerous lesions. Previous research demonstrated that rural patients face nearly twice the risk of catastrophic health expenditure compared to urban counterparts across all

disease stages[14]. In addition, studies have shown that women with lower educational attainment are less aware of the importance of cervical cancer screening and are more likely to develop the disease[29,30]. Agricultural workers often face high physical workloads, limited access to health care, and low screening coverage[31]. To address such disparities, China has actively expanded screening accessibility among vulnerable groups. The current national screening strategy explicitly prioritises rural women and urban women receiving minimum living allowances[6]. Many local facilities implementing government-organized screening have adopted outreach-based approaches, including community mobilisation and on-site screening conducted by mobile medical teams. These efforts have effectively increased participation among rural, low-income, and farming populations, thereby advancing health equity. We also observed substantial regional variation in the proportion of cervical cancer and precancerous cases detected through government screening in the current study, as follows: 13.4% in eastern provinces; 24.0% in central provinces; and only 6.6% in western provinces. These disparities may reflect regional differences in policy implementation and service delivery capacity[32-34]. Available data indicate that screening coverage in western China remains substantially lower than in central and eastern regions (24.8% *vs.* 28.1% and 33.4%, respectively) among women 20–64 y of age between 2018 and 2019[35]. To achieve nationwide cervical cancer prevention, further expansion of government-led screening in underserved areas and tailored interventions for women diagnosed outside government-organized screening programmes are both essential.

This study had several key strengths. This is the first multicentre study using real-world cost data in China to suggest that government-organized cervical cancer screening is associated with lower economic burden of the disease. This study uniquely compared government-organized screening with multiple alternative detection modes, including workplace check-up, self-paid check-up, and symptom-based detection, across different disease courses. The first empirical evidence was provided through mediation analysis indicating that earlier clinical staging, greater use of lower-level health facilities, and reduced overtreatment are factors linked to the cost-reducing effects of government-organized screening.

The current study had several limitations. The cross-sectional design could preclude causal inference. The small subgroup sizes limited the interpretation of results for the radiotherapy/chemotherapy and (R/P/M). The absence of statistically significant differences may also reflect the intrinsic characteristics of these phases, in which treatment is relatively standardized in radiotherapy/chemotherapy and costs related to recurrence, progression, or metastasis are largely determined by clinical and biological factors rather than detection mode. Future studies with larger cohorts will be needed to clarify whether detection mode influences costs in these settings. Additionally, the mediation analysis did not capture individual- or provider-level factors that may influence treatment decisions, such as patient health anxiety or clinician practice styles. These factors may differ across detection modes but the net direction of potential bias remains uncertain.

Conclusions

In conclusion, government-led cervical cancer screening programmes offer broader coverage among underserved populations and are associated with lower economic burdens across diagnosis, initial treatment, and follow-up compared to all other modes of detection. Associations with earlier detection, greater use of lower-level hospitals, and reduced overtreatment indicate that government-organized screening may support more timely intervention, enhance standardization of clinical pathways, and promote efficiency and equity in healthcare resource allocation. These findings provide evidence to optimise screening strategies in China and to strengthen national cervical cancer control efforts. As coverage expands and digital technologies are integrated, government-organized screening programmes will remain pivotal in advancing health equity, enhancing service delivery, and accelerating the progress towards cervical cancer elimination in China.

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Conflict of interest statement

No potential conflicts of interest are disclosed.

Author contributions

Conceived and designed the analysis: Fanghui Zhao, Xuelian Zhao.
Collected the data: Fanghui Zhao, Xuelian Zhao.
Contributed data or analysis tools: Mingjie Dong.
Performed the analysis: Mingjie Dong.
Wrote the paper: Mingjie Dong, Jiaxin Xie.

Data availability statement

The data generated in this study are available upon reasonable request from the corresponding author.

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