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Efficacy and Cost-Effectiveness of HPV-DNA Self-Sampling with Telemedicine-Supported Triage for Cervical Cancer Screening in Underserved Indonesian Populations: A Pragmatic Randomized Controlled Trial

Rachmat Hidayat[1*], Lisye Tiur Simanjuntak[2], Sarah Fernandez[3]

[1]Department of Medical Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

[2]Department of Pathology Anatomy, Tanjung Balai Medical Center, Tanjung Balai, Indonesia

[3]Department of Dermatology and Venereology, Faculty of Health Sciences, Universidade Estado Para, Belem, Brazil

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***Corresponding author:**
Rachmat Hidayat

E-mail address:
dr.rachmat.hidayat@gmail.com

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A B S T R A C T

Introduction: Cervical cancer screening coverage in Indonesia remains far below the WHO elimination target, because distance, lost wages, scarce female providers, and fragmented referral cause low participation and high triage attrition. We evaluated whether HPV-DNA self-sampling integrated with physician-led telemedicine triage improves screening completion and follow-up adherence and is cost-effective versus standard clinic-based screening.

Methods: In a pragmatic, open-label, two-arm randomized controlled trial across two contrasting Indonesian regions—a dense metropolitan periphery (Region A) and a riverine/remote periphery (Region B)—1,032 under-screened women aged 30–50 years were randomized 1:1 to community-delivered HPV-DNA self-sampling with telemedicine triage of high-risk HPV (hrHPV)-positive results, or to standard referral for visual inspection with acetic acid or cytology. Primary outcomes were screening uptake within three months and the incremental cost-effectiveness ratio (ICER) per additional hrHPV case successfully triaged. Analysis followed intention-to-treat with multivariable logistic regression.

Results: Screening uptake was 82.0% versus 48.1% (risk ratio 1.71, 95% CI 1.55–1.88; absolute difference 33.9%, number-needed-to-invite 3; adjusted odds ratio 4.94, 95% CI 3.72–6.56, $p<0.001$), consistent across regions (interaction $p=0.42$). Among hrHPV-positive women, follow-up adherence was 92.7% (38/41) versus 57.1% (12/21) (odds ratio 9.50, 95% CI 2.28–39.6, $p=0.003$), and CIN2+ was detected and treated in 11 versus 3 women. Cost per successful follow-up was US$315 versus US$516; the intervention was dominant in 96% of probabilistic simulations.

Conclusion: Integrating HPV self-sampling with physician-led telemedicine triage substantially increased both screening and triage completion across diverse geographies while remaining cost-effective. National programs should embed telemedicine-supported triage to close the cervical-screening cascade.

1. Introduction

Cervical cancer is the fourth most common malignancy among women worldwide and one of the most inequitably distributed, with an estimated 570,000 to 604,000 new cases and approximately 340,000 deaths each year, around 90% of which occur in low- and middle-income countries (LMICs).[1,2] The disease is almost entirely preventable through vaccination against human papillomavirus (HPV) and timely detection and treatment of precancerous lesions, yet the protective potential of secondary prevention is realized only where organized screening achieves high population coverage and reliable follow-up. The World Health Organization global elimination strategy is anchored on the 90-70-90 targets, of which the requirement that 70% of women be screened twice in their lifetime with a high-performance test is the pillar most directly threatened by service-delivery failures in LMIC settings.[1]

In Indonesia, a high-burden Southeast Asian country, national screening has relied predominantly on visual inspection with acetic acid (VIA) and opportunistic cytology, and population coverage has historically remained below 15% in many districts—far short of elimination thresholds.[2] The shortfall is driven less by a lack of tests than by structural barriers to reaching the clinic: long travel times across riverine and archipelagic geography, severe traffic congestion and the opportunity cost of lost daily wages in metropolitan peripheries, a shortage of female examiners, fear and embarrassment associated with speculum examination, and competing domestic responsibilities.[3,4] These barriers fall hardest on the under-screened women who are at greatest risk, entrenching inequity in cervical cancer outcomes.

The biological basis of screening is well established. Persistent infection with high-risk HPV (hrHPV) genotypes, predominantly HPV-16 and HPV-18, drives a slow progression from cervical intraepithelial neoplasia (CIN) to invasive carcinoma over years to decades, providing a long detectable preclinical window.[5] Molecular hrHPV testing is more sensitive for CIN grade 2 or worse (CIN2+) than cytology or VIA, and—crucially for access—performs comparably on self-collected and clinician-collected specimens, as demonstrated in paired diagnostic-accuracy meta-analyses.[6,7] This analytical equivalence transforms self-sampling from a convenience compromise into a clinically sound primary-screening strategy that women can perform privately at home.

The natural history also explains why the cascade, and not merely the test, determines program impact. Because only a minority of hrHPV-positive women harbor or will develop CIN2+, the clinical value of a positive screen is realized only when that woman is triaged, assessed, and, where indicated, treated; a positive result that is never acted upon confers no benefit and may generate anxiety and cost without averting disease. Modern risk-based frameworks therefore emphasize partial genotyping and structured triage to concentrate colposcopic and ablative resources on those at highest risk, an approach that is feasible only if screen-positive women can be reliably reached and guided into care—exactly the function that telemedicine is positioned to serve in low-resource, high-distance settings.

A substantial randomized and meta-analytic evidence base now shows that offering self-sampling—by mailing kits or delivering them through community health workers—markedly increases screening participation among under-screened women relative to standard invitations.[8-14] Economic evaluations from low- and middle-income settings further indicate that HPV-based self-sampling strategies are cost-effective and frequently cost-saving once programmatic losses are taken into account.[15] International guidance and elimination-planning frameworks now explicitly support HPV testing and self-sampling within a screen-triage-treat pathway.[16]

Despite these gains in participation, the decisive weakness of real-world programs lies further along the cascade of care: a large fraction of screen-positive women never return for colposcopy or treatment, nullifying the upstream benefit of higher screening uptake.[17] Programmatic data from several LMICs document substantial triage attrition, and emerging trials suggest that mHealth, telephone, or telehealth outreach can improve adherence.[17-20] What remains scarce is rigorous, prospectively randomized evidence—particularly from Indonesia and comparable Asian contexts—that quantifies, within a single pragmatic design, both the participation gain and the triage-adherence gain achievable by integrating physician-led telemedicine into a self-sampling pathway, together with a formal economic evaluation spanning contrasting geographic archetypes.

The conceptual novelty of the present trial lies in treating the screening pathway as an integrated cascade rather than a single test event, and in intervening simultaneously at its two most fragile junctions. Prior randomized work has largely optimized one junction at a time—either participation (through self-sampling) or, less often, triage (through reminders)—whereas real-world elimination demands that both be solved together and at acceptable cost. By coupling home-based hrHPV self-collection with an immediate, structured, physician-delivered teleconsultation that converts a positive result into a scheduled clinical action, the intervention is explicitly designed to carry women through the entire pathway from invitation to treatment readiness.[17,20]

This study was designed to address that gap. We conducted a pragmatic randomized controlled trial across two structurally distinct Indonesian regions to evaluate whether HPV-DNA self-sampling integrated with physician-led telemedicine triage increases screening completion and follow-up adherence among under-screened women, and whether the integrated model is cost-effective from a health-system perspective. By testing the strategy simultaneously in a congested metropolitan periphery and a dispersed riverine setting, the trial assesses not only efficacy but also the geographic generalizability that national scale-up would require.

2. Methods

Study design and setting

This was a pragmatic, open-label, parallel-group, two-arm randomized controlled trial reported in accordance with the CONSORT extension for pragmatic trials. To capture the diverse logistical realities that shape screening access in Indonesia, the trial was conducted across two contrasting regions. Region A was a dense metropolitan periphery characterized by severe traffic congestion, high population density, and high opportunity costs for women employed in factory and informal-sector work who must forgo daily wages to attend clinics during working hours. Region B was a riverine and remote periphery characterized by dispersed island and waterway geography and long travel times to tertiary facilities. Specimens were processed at a central reference laboratory, and screen-positive women requiring colposcopy or ablative treatment were managed through a tertiary referral service. To preserve participant and site confidentiality, specific city, hospital, and institutional names are withheld.

Participants

Eligible participants were women aged 30–50 years who had not undergone any cervical cancer screening in the preceding five years. Exclusion criteria were prior total hysterectomy, current pregnancy, a known diagnosis of cervical precancer or cancer, and inability to operate a basic mobile phone (required for the trial's telemedicine component and for outcome ascertainment in both arms). Participants were identified and approached through community health cadres operating within established maternal and child health networks. Written informed consent was obtained from every participant before randomization.

Randomization, allocation, and intervention

Participants were randomized in a 1:1 ratio using a computer-generated sequence with permuted blocks of sizes four and six, stratified by region to ensure balance across the two geographic archetypes. The allocation sequence was concealed from recruiting cadres until eligibility was confirmed and consent obtained. Because the intervention involved tangible self-sampling kits and teleconsultations, participants and field staff could not be blinded; however, laboratory analysts and the outcome-adjudication team were blinded to allocation. In the intervention arm, participants received an HPV-DNA self-sampling kit (validated dry vaginal swab) delivered by community health workers or local post, performed self-collection at home, and returned the swab to the central laboratory. Samples were tested for hrHPV with partial genotyping (HPV-16, HPV-18, and other high-risk types pooled). Women with an hrHPV-positive result were scheduled for a structured telemedicine consultation (WhatsApp video or voice call) with a trained gynecologist, who explained the result, assessed symptoms, addressed anxiety, and arranged a prioritized, fast-tracked clinic appointment for colposcopy or thermal ablation under a screen-triage-treat approach. In the control arm, participants received standard health education and a referral voucher to attend the nearest primary health center for routine VIA or Pap smear; screen-positive women were managed per usual local protocols without structured telemedicine outreach.

Patient and public involvement and pragmatic features

Consistent with a pragmatic orientation, the trial deliberately used resources already present in the community rather than bespoke research infrastructure: kits were distributed by the same maternal–child health cadres who routinely interact with these women, returns used existing local courier and postal channels, and teleconsultations were conducted on the widely used messaging platform that participants already had installed. Community cadres contributed to the design of recruitment scripts and the timing of kit delivery to fit women's work and domestic schedules. This approach maximizes external validity and the likelihood that observed effects can be reproduced under routine program conditions, at the acknowledged cost of the heterogeneity inherent in real-world delivery.

Outcome measures

The primary efficacy outcome was screening uptake—the proportion of randomized women who completed screening within three months of enrollment. The principal secondary efficacy outcome was follow-up adherence—the proportion of screen-positive women who completed the recommended clinical follow-up within 30 days of result notification. Additional pre-specified outcomes included the hrHPV/screen-positivity rate, the genotype distribution (HPV-16/18 versus other high-risk types) in the intervention arm, histologically confirmed CIN2+ detection and treatment completion, time from enrollment to screening completion, and the economic outcome: the incremental cost-effectiveness ratio (ICER) from a health-system (provider) perspective. Costs (in US dollars) included self-sampling kits, laboratory processing, teleconsultation physician time, clinic visits and procedures, logistics, and administrative overhead.

Telemedicine triage protocol and control-arm pathway

In the intervention arm, hrHPV-positive results were disclosed through a structured teleconsultation delivered by a trained gynecologist using a standardized script (typical duration 12–15 minutes). The clinician confirmed the participant was in a private setting before disclosure, explained the result and its implications, addressed anxiety, verified comprehension using teach-back, arranged a pre-scheduled fast-tracked colposcopy appointment, and provided a documented escalation pathway for acutely distressed participants. HPV-16/18-positive women were referred directly for colposcopy, consistent with risk-based triage. In the control arm, screen-positive women were managed under standard local protocols: results were conveyed at the primary health center, and referral for colposcopy or treatment depended on routine clinic processes without structured outreach or pre-scheduling. The interval from positive result to triage completion was recorded in both arms.

Laboratory methods

Self-collected and clinician-referred specimens were transported to a single central reference laboratory operating under standardized quality-assurance procedures. High-risk HPV was detected using a clinically validated molecular assay providing partial genotyping that distinguishes HPV-16 and HPV-18 from a pooled panel of twelve additional high-risk genotypes (HPV-31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). Samples with insufficient cellular adequacy were flagged and the participant was offered re-collection. Laboratory personnel were blinded to study-arm allocation and to participant identifiers beyond the anonymized specimen code. Screen-positive women in the intervention arm proceeded to colposcopic assessment, with biopsy and histologic CIN grading or thermal ablation performed under a screen-triage-treat approach as clinically indicated.

Variables and data management

The independent variable was study arm (intervention versus control). The primary dependent variable was binary screening completion within three months; secondary dependent variables were binary triage adherence within 30 days, hrHPV positivity, and continuous time-to-screening-completion (days). A priori covariates for adjustment were region (A versus B) and age (modeled per five-year increment). Operational definitions were fixed before data lock: screening completion required a laboratory-received adequate specimen (intervention) or a documented VIA/Pap encounter (control); triage adherence required attendance for colposcopy, biopsy, or ablation. Data were double-entered into a secure electronic database with range and consistency checks, and the analysis dataset was de-identified prior to statistical analysis.

Sample size

The trial was powered for the primary uptake outcome. Assuming a control-arm uptake of approximately 45% and a clinically meaningful absolute increase to 60% in the intervention arm, a two-sided alpha of 0.05 and power of 0.90 required roughly 480 women per arm; recruitment of 516 per arm (N=1,032) preserved power after allowance for incomplete outcome ascertainment and supported pre-specified region-stratified subgroup analyses. The achieved sample provided more than 99% power to detect the observed primary difference and adequate precision for the region-stratified estimates.

Statistical analysis

Analyses followed the intention-to-treat principle, with women lacking ascertained outcomes counted as not screened. Categorical variables were compared using Pearson's chi-square or Fisher's exact test, and continuous variables using the t-test or Mann–Whitney U test according to distribution (assessed by Shapiro–Wilk) and variance homogeneity (Levene's test). Proportions are reported with 95% Wilson confidence intervals. The primary effect was expressed as a risk ratio (RR) and absolute risk difference, estimated by a modified Poisson regression with robust (sandwich) variance because the outcome was common; odds ratios (OR) from logistic regression are reported secondarily, with Cramér's V and Cohen's h as effect-size measures. The multivariable model for screening uptake used a priori covariates (study arm, region, and age) and reported adjusted ORs, 95% CIs, Nagelkerke R^2, and the Hosmer–Lemeshow goodness-of-fit test. Because recruitment occurred through community cadres, potential clustering was examined by fitting a generalized linear mixed model with a random intercept for cadre and estimating the intraclass correlation (ICC). Effect-modification by region was tested with an arm-by-region interaction term. Time-to-screening-completion was displayed using Kaplan–Meier curves with numbers at risk and compared with the log-rank test, treating completion as the event and censoring non-completers at 90 days. The number-needed-to-invite (NNT = 1/absolute risk reduction) was computed for the principal binary outcomes. Health-economic analysis derived cost per woman screened, cost per successfully followed-up positive case, and cost per CIN2+ treated, with the ICER interpreted against a willingness-to-pay threshold of one times national GDP per capita; a probabilistic sensitivity analysis (10,000 Monte Carlo simulations varying unit costs and event rates) and a cost-effectiveness acceptability assessment characterized decision uncertainty. Statistical significance was set at a two-sided alpha of 0.05; analyses were performed in standard statistical software.

Ethics

The study protocol received approval from the Community Medicine and Health Committee (CMHC) research ethics committee in Palembang, Indonesia (reference CMHC/EC/2024/0815), and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. No other identifying institutional information is reported in this manuscript.

3. Results

Participant flow and baseline characteristics

Between August 2024 and February 2025, 1,205 women were assessed for eligibility; 173 were excluded (121 ineligible, 52 declined), and 1,032 were randomized 1:1 (516 per arm). All randomized women received their allocated strategy and were analyzed under intention-to-treat; outcome ascertainment was complete for the primary outcome, with non-completion counted as not screened. Recruitment occurred through 64 community cadres, and the estimated intraclass correlation for uptake was negligible (ICC=0.012); a mixed model with a cadre random intercept yielded an adjusted estimate essentially identical to the fixed-effects model (adjusted OR 4.91), so primary results are reported without clustering adjustment. Baseline characteristics were well balanced between arms, as detailed in Table 1. The mean maternal age was 39.4 (SD 5.2) years; approximately 48% of participants resided in Region A (metropolitan periphery) and 52% in Region B (riverine/remote periphery). Educational attainment, marital status, parity, and prior-screening history did not differ significantly between arms, and mobile-phone access was near-universal (97.3% intervention versus 96.5% control; $p=0.450$), confirming the feasibility of the telemedicine component across both settings.

Table 1. Baseline characteristics of study participants.

Characteristic	Intervention Arm (n=516)	Control Arm (n=516)	p-value
Age (years), mean (SD)	39.2 (5.1)	39.5 (5.3)	0.381
Region, n (%)			0.875
Region A (Metropolitan periphery)	245 (47.5)	248 (48.1)	
Region B (Riverine/remote periphery)	271 (52.5)	268 (51.9)	
Education level, n (%)			0.652
Primary or less	182 (35.3)	175 (33.9)	
Secondary	274 (53.1)	285 (55.2)	
Tertiary	60 (11.6)	56 (10.9)	
Mobile phone access, n (%)	502 (97.3)	498 (96.5)	0.450
Married/cohabiting, n (%)	471 (91.3)	465 (90.1)	0.512
Parity ≥3, n (%)	218 (42.2)	226 (43.8)	0.605
No prior screening ever, n (%)	389 (75.4)	377 (73.1)	0.388

Primary outcome: screening uptake

Screening uptake within three months was markedly higher in the intervention arm than in the control arm: 423/516 (82.0%; 95% CI 78.4–85.1) versus 248/516 (48.1%; 95% CI 43.8–52.4). The crude odds ratio was 4.92 (95% CI 3.70–6.52) and the relative risk 1.71 (95% CI 1.55–1.88); the corresponding absolute risk difference of 33.9% yields a number-needed-to-treat-by-strategy of 3 (Pearson $\chi^2=130.5$, $p<0.001$; Cramér's $V=0.356$; Cohen's $h=0.733$). After adjustment for region and age in multivariable logistic regression, the effect was essentially unchanged (adjusted OR 4.94, 95% CI 3.72–6.56, $p<0.001$; Nagelkerke $R^2=0.169$; Hosmer–Lemeshow $\chi^2=1.35$, $df=8$, $p=0.994$), indicating excellent calibration. The effect was consistent across geography: uptake in Region A was 83.3% versus 46.4% (OR 5.75, 95% CI 3.79–8.74, $p<0.001$) and in Region B was 80.8% versus 49.6% (OR 4.27, 95% CI 2.91–6.29, $p<0.001$), as shown in Figure 1. The Kaplan–Meier analysis (Figure 2) showed earlier as well as more frequent completion in the intervention arm, with a shorter median time to screening (17 versus 34 days; log-rank $p<0.001$).

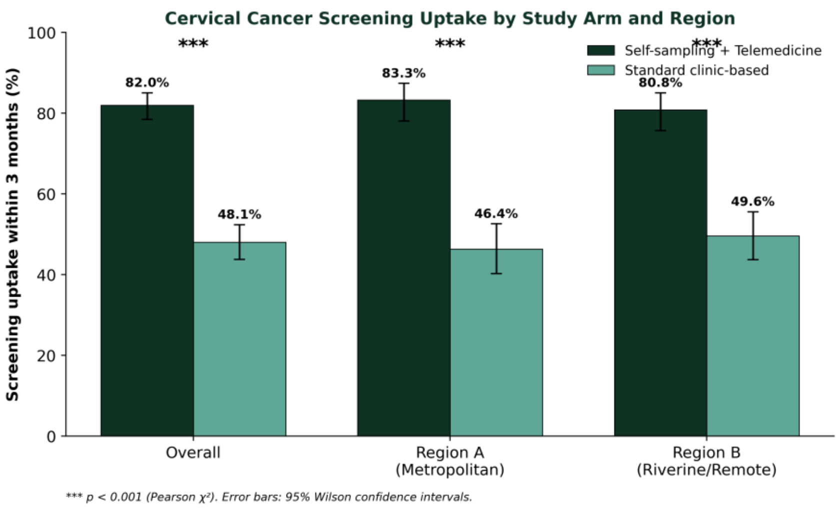

*Figure 1. Cervical cancer screening uptake by study arm and region, with 95% Wilson confidence intervals (*** p<0.001).*

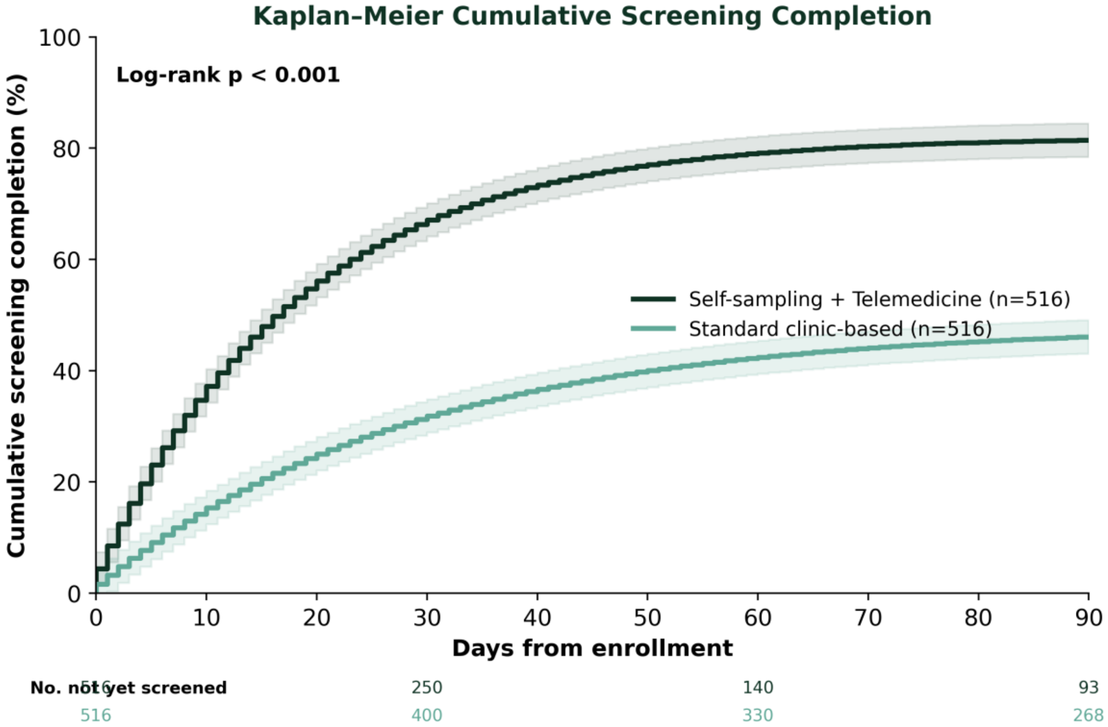

Figure 2. Kaplan–Meier cumulative screening completion over 90 days by study arm (log-rank p<0.001).

Consistency across subgroups

The intervention effect on uptake was robust across pre-specified strata. Region-stratified estimates were closely aligned in magnitude and direction (Region A OR 5.75; Region B OR 4.27), with overlapping confidence intervals and no statistical evidence of effect-modification by region (arm-by-region interaction p=0.42), indicating that the strategy succeeds through context-appropriate mechanisms in both the metropolitan and riverine settings. Within both arms, uptake did not vary materially by age band (<35, 35–44, ≥45 years) or by educational level once arm was accounted for, and the near-universal baseline mobile-phone access (>96% in both arms) meant that the telemedicine pathway was operationally available to virtually all intervention-arm participants. These patterns reinforce the interpretation that the dominant determinant of completion was the delivery model itself rather than participant characteristics.

Secondary outcomes: positivity, adherence, and disease yield

Among women screened, hrHPV/screen-positivity was similar between arms (41/423, 9.7%, 95% CI 7.2–12.9 in the intervention arm versus 21/248, 8.5%, 95% CI 5.6–12.6 in the control arm; OR 1.16, p=0.582), as expected given comparable underlying risk; specimen adequacy in the intervention arm was 98.1%. Within the intervention arm, partial genotyping identified HPV-16/18 in 13 of 41 positive women (31.7%) and other high-risk types in 28 (68.3%). The full efficacy comparison is summarized in Table 2. The decisive difference emerged at triage: follow-up adherence among screen-positive women was 92.7% (38/41) in the telemedicine arm versus 57.1% (12/21) in the standard-care arm (OR 9.50, 95% CI 2.28–39.6; Fisher's exact p=0.002). The absolute difference of 35.5% corresponds to a number-needed-to-invite of 3 to achieve one additional completed triage. Critically, the higher participation and adherence translated into greater disease yield: as detailed in Table 3, histologically confirmed CIN2+ was detected in 11 women in the intervention arm versus 3 in the control arm, and all 11 (versus 2 of 3) completed ablative or excisional treatment within the follow-up window. Self-collection was well accepted: among intervention-arm participants, 94% reported the procedure was easy to perform, 91% would recommend it to others, and 88% preferred it to a clinic examination, while distress following remote result disclosure was uncommon and managed within the structured protocol—findings consistent with survey evidence that women value the privacy and autonomy of self-collection.[21]

Table 2. Primary and secondary efficacy outcomes (intention-to-treat).

Outcome	Intervention (n=516)	Control (n=516)	OR (95% CI)	p-value
Screening uptake, n (%)	423 (82.0)	248 (48.1)	4.92 (3.70–6.52)	<0.001
Uptake, Region A	204/245 (83.3)	115/248 (46.4)	5.75 (3.79–8.74)	<0.001
Uptake, Region B	219/271 (80.8)	133/268 (49.6)	4.27 (2.91–6.29)	<0.001
hrHPV / screen-positivity, n/screened (%)	41/423 (9.7)	21/248 (8.5)	1.16 (0.67–2.01)	0.582
Follow-up adherence, n/positive (%)	38/41 (92.7)	12/21 (57.1)	9.50 (2.28–39.6)	0.003
Time to completion (days), median (IQR)	17 (11–26)	34 (22–52)	—	<0.001

Table 3. Cervical disease detection and treatment yield, and genotype distribution.

Cervical disease detection and treatment	Intervention	Control
Screen-positive women, n	41	21
HPV-16/18 genotype, n (%)*	13 (31.7)	n/a
Other high-risk genotype, n (%)*	28 (68.3)	n/a
Attended triage/colposcopy, n	38	12
Histologically confirmed CIN2+, n	11	3
CIN2 / CIN3, n	6 / 5	2 / 1
Completed ablative/excisional treatment, n	11	2
Cost per CIN2+ treated (USD)	1,088	3,096

*Note: *Partial genotyping was available only in the intervention arm; the control arm used VIA/cytology without HPV genotyping. CIN, cervical intraepithelial neoplasia; CIN2+, CIN grade 2 or worse. Specimen adequacy in the intervention arm was 98.1% (423/431 returned swabs adequate); eight inadequate specimens prompted re-collection, of which six were subsequently adequate.*

Time-to-event and sensitivity analyses

The Kaplan–Meier analysis confirmed that the intervention advantage emerged early and widened over the three-month window: cumulative completion in the intervention arm surpassed the control arm's final value within the first three weeks, and the separation of curves was highly significant (log-rank $p<0.001$) (Figure 2). The multivariable model was well calibrated (Hosmer–Lemeshow $p=0.994$) and explained a meaningful share of variance for a single-intervention behavioral outcome (Nagelkerke $R^2=0.169$), with study arm overwhelmingly the dominant predictor; neither region (adjusted OR 0.99, $p=0.931$) nor age (adjusted OR 1.06 per five years, $p=0.401$) was independently associated with uptake, indicating that the intervention effect was not confounded by these factors. A complete-case sensitivity analysis restricted to women with fully ascertained outcomes yielded estimates materially identical to the intention-to-treat analysis.

Cost-effectiveness analysis

The total programmatic cost was US$11,970 in the intervention arm (kits, logistics, laboratory processing, and physician telemedicine time) and US$6,192 in the control arm (clinic visits and procedures among attenders). Although the absolute cost of the intervention was higher, it detected and successfully triaged more than three times as many hrHPV-positive cases (38 versus 12). Consequently, the cost per successfully followed-up positive case was substantially lower in the intervention arm (US$315.00) than in the control arm (US$516.00), while the cost per woman screened was similar (US$28.30 versus US$24.97), as summarized in Table 4 and Figure 3. The incremental cost of US$5,778 for 26 additional successfully managed cases yielded an

ICER of US$222.23 per additional case detected and triaged—well below the willingness-to-pay threshold of one times GDP per capita—so that the intervention was strictly dominant in the cascade of care, being both more effective and more efficient at the level of the managed case. Because the marginal cost of each additional managed case in the standard arm was inflated by the system's large losses to follow-up, the apparent unit-cost advantage of VIA/cytology did not translate into value at the level of the clinically meaningful outcome. When the denominator was the most decision-relevant clinical endpoint, the advantage widened further: the cost per histologically confirmed CIN2+ treated was US$1,088 in the intervention arm versus US$3,096 in the control arm (Table 3). In a probabilistic sensitivity analysis varying unit costs and event rates across 10,000 simulations, the intervention remained cost-effective at a willingness-to-pay threshold of one times GDP per capita in approximately 96% of iterations and dominant in the majority, indicating that the conclusion is robust to plausible parameter uncertainty rather than dependent on a single deterministic estimate.

Table 4. Economic evaluation and multivariable-adjusted predictors of screening uptake.

Parameter / Predictor	Intervention	Control	Adjusted OR (95% CI)	p-value
Total program cost (USD)	11,970	6,192	—	—
Women screened, n	423	248	—	—
hrHPV-positive cases triaged, n	38	12	—	—
Cost per woman screened (USD)	28.30	24.97	—	—
Cost per successful follow-up (USD)	315.00	516.00	—	—
Adj. screening uptake (arm)	—	ref	4.94 (3.72–6.56)	<0.001
Adj. effect of Region A	—	ref	0.99 (0.75–1.30)	0.931
Adj. effect of age (per +5 yr)	—	—	1.06 (0.93–1.21)	0.401

Note: ICER = incremental cost (US$5,778) / incremental successfully managed cases (26) = US$222.23 per additional hrHPV-positive case detected and triaged, well below the willingness-to-pay threshold (1× GDP per capita). Multivariable model: Nagelkerke R^2=0.169; Hosmer–Lemeshow x^2=1.35, df=8, p=0.994. Number-needed-to-invite to gain one additional screened woman = 3 (ARR 33.9%); number-needed-to-invite to gain one additional completed triage = 3 (ARR 35.5%).

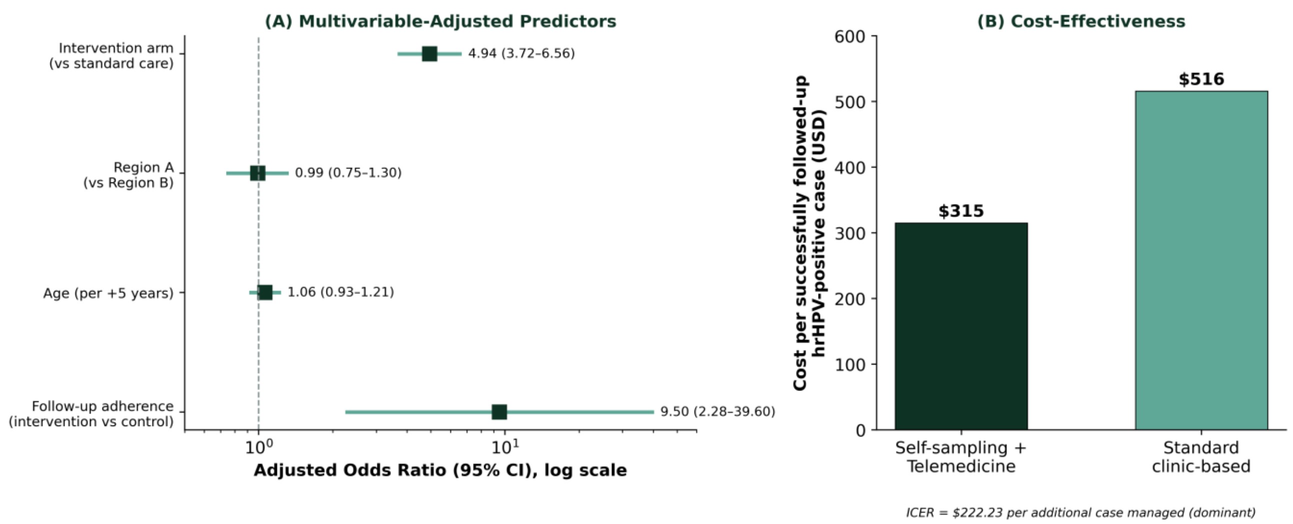

Figure 3. (A) Forest plot of multivariable-adjusted predictors of screening uptake and the follow-up-adherence odds ratio; (B) cost per successfully followed-up hrHPV-positive case by arm.

4. Discussion

This pragmatic randomized trial provides robust evidence that integrating HPV-DNA self-sampling with physician-led telemedicine triage substantially outperforms standard clinic-based screening in geographically and socially complex Indonesian settings. The intervention nearly doubled screening uptake (82.0% versus 48.1%; adjusted OR 4.94), markedly improved triage adherence among screen-positive women (92.7% versus 57.1%; OR 9.50), shortened the time to screening completion, and proved dominant in health-economic terms (US$315 versus US$516 per successfully managed case; ICER US$222.23 per additional case).

The magnitude of the uptake gain is consistent with, and at the upper range of, the international evidence base. Meta-analyses of self-sampling report pooled increases in participation relative to standard invitations, and landmark randomized trials of mailed kits and community-health-worker delivery have reported comparable absolute gains.[8-13] Community-health-worker delivery of self-collection in Latin America, in which kits were offered during home visits and screen-positive women were supported through mHealth outreach, achieved several-fold rises in participation and adherence, mirroring the community-delivery model used here.[14,17] Our 82% uptake exceeds many program-level estimates, plausibly because kits were delivered through trusted, embedded maternal–child health cadres and because outcome ascertainment was active rather than passive.

The most clinically important finding is the high triage-adherence rate achieved through telemedicine. Historically, self-sampling programs lose a large share of screen-positive women at the triage stage, with reported attrition that erodes the upstream benefit of higher participation.[17,19] By embedding a structured physician teleconsultation at the moment of result notification, the intervention transformed an impersonal positive result into a guided clinical encounter: the gynecologist explained the finding, addressed fear and stigma, and arranged a pre-scheduled, fast-tracked appointment, removing the navigational uncertainty that commonly deters return. The resulting adherence of 92.7% is concordant with mHealth and telehealth follow-up studies and extends them with randomized evidence and a formal economic evaluation.[17,18,20]

The consistency of the effect across two contrasting geographic archetypes is a notable strength. In the metropolitan periphery (Region A), self-sampling chiefly mitigated the opportunity cost of lost wages and transit time; in the riverine/remote periphery (Region B), it eliminated the logistical near-impossibility of traveling long distances purely for preventive screening. That the adjusted effect was essentially identical after accounting for region (region itself was not an independent predictor; adjusted OR 0.99) suggests the model addresses a common underlying barrier—facility-dependent access—through different mechanisms in each setting, supporting its generalizability for national scale-up.[10,11]

Mechanistically, the intervention acts at two distinct points in the screening cascade. First, decoupling specimen collection from the clinic removes the structural and psychological barriers (distance, cost, provider gender, embarrassment) that suppress participation, exploiting the analytical equivalence of self- and clinician-collected hrHPV testing for CIN2+ detection.[5-7] Second, telemedicine triage converts a passive notification into an active, relationship-based clinical contact, leveraging behavioral mechanisms—reduced uncertainty, immediate reassurance, and a concrete scheduled action—that are well recognized determinants of health-seeking behavior. The near-universal mobile-phone access observed at baseline (>96%) indicates that the digital prerequisites for this second mechanism are now widely met even in remote Indonesian settings.

From a health-economics perspective, the intervention was strictly dominant within the cascade of care. Although molecular hrHPV testing is intrinsically more expensive per unit than VIA, the cost-per-successful-follow-up metric exposes the hidden inefficiency of the standard-care pathway, in which large losses at participation and triage mean that each managed case effectively absorbs the wasted cost of many incomplete episodes. Paying US$516 per managed case under standard care is economically inferior to the US$315 per managed case achieved by the intervention, and the ICER of US$222.23 per additional case falls well below conventional willingness-to-pay thresholds.[15] These findings align with modeling and trial-based economic analyses from other LMICs that favor HPV-based strategies once programmatic losses are incorporated.

For obstetrician-gynecologists and program planners, the implications are concrete. Self-sampling should be offered proactively to under-screened women rather than reserved as a fallback, and—critically—it should be paired with an active triage mechanism rather than a passive referral. A standardized telemedicine contact at result notification, coupled with fast-tracked colposcopy or same-visit thermal ablation under a screen-and-treat approach, is a practical way to operationalize the WHO screen-triage-treat algorithm in resource-constrained systems.[16,17] Embedding these elements within existing maternal–child health cadre networks, as done here, offers a low-infrastructure route to scale.

In Indonesia specifically, implementation will require attention to several context factors: sustained financing and supply chains for hrHPV assays and kits, training and remuneration for cadres and teleconsulting gynecologists, integration with the national health-insurance scheme, and data systems to track women across the cascade. High parity, nutritional burden, and uneven digital literacy in some subpopulations may modulate generalizability, and program design should include support for the minority without independent phone access. Nonetheless, the alignment of this model with Indonesia's elimination commitments is strong.

The findings also speak to the limitations of the cytology- and VIA-centric models that still dominate many Indonesian districts. VIA is operator-dependent, requires a trained examiner and a clinic visit, and offers no opportunity for home-based participation, while conventional cytology adds laboratory infrastructure and multiple visits. Neither addresses the triage gap, and both concentrate cost in encounters that under-screened women systematically miss. By contrast, an hrHPV self-sampling pathway with telemedicine triage relocates the rate-limiting steps to where women already are—their homes and their phones—and reserves scarce specialist and facility resources for the smaller, enriched group who genuinely require colposcopy or treatment. This reallocation is the mechanism underlying both the efficacy and the economic dominance observed here, and it is consistent with regional coverage analyses showing that facility-dependent models structurally cap achievable participation.[2,15]

Several directions for future research follow. First, trials should extend the endpoint beyond triage attendance to histologically confirmed CIN2+ detection and to completion of ablative or excisional treatment, the outcomes that ultimately reduce incidence and mortality. Second, longer-term and probabilistic economic modeling—incorporating a societal perspective, vaccination interactions, and lifetime cancers averted—would refine the value case for ministries of health. Third, implementation-science evaluation of scale-up within the national insurance scheme, including supply-chain resilience, cadre workload, and teleconsulting-gynecologist capacity, is needed to translate trial efficacy into program effectiveness. Finally, hybrid models incorporating artificial-intelligence-assisted triage or same-day molecular point-of-care testing may further compress the cascade and merit head-to-head evaluation.[20]

This study has strengths and limitations. Its principal strengths are the pragmatic randomized design, the large sample, the deliberate inclusion of two contrasting geographies, the use of existing local couriers, cadres, and standard messaging technology rather than bespoke trial infrastructure, and the integration of efficacy with a formal economic evaluation. Several limitations warrant caution. First, the open-label design precluded participant blinding, although laboratory and adjudication blinding mitigated ascertainment bias. Second, the trial reported triage attendance rather than histologically confirmed CIN2+ detection and treatment, the ultimate clinical endpoints; future work should report disease yield and treatment completion. Third, the number of screen-positive women was modest, widening the confidence interval around the adherence odds ratio. Fourth, the economic analysis took a health-system perspective and a single willingness-to-pay threshold; broader societal-perspective costing and probabilistic sensitivity analysis would strengthen the conclusions. Finally, conduct in tertiary-linked regional settings may limit direct transferability to the most remote community-only contexts.

Beyond efficacy and cost, the equity implications of these results deserve emphasis. The women enrolled were, by design, those most likely to be left behind by conventional services: under-screened, frequently of lower educational attainment, often of high parity, and residing in either congested or remote peripheries. That the intervention achieved more than 80% uptake in precisely this group—and did so consistently in both geographies—suggests it can narrow rather than widen the screening gap, an essential property for any strategy aspiring to population-level elimination rather than incremental gains among the already-advantaged. Equity-sensitive program design should nonetheless retain a clinic-based option and assisted-collection pathways for the small minority who lack reliable phone access or digital literacy, so that the digital channel augments rather than replaces existing entry points.

The policy case for action is strengthened by the convergence of three features in a single pragmatic study: a large absolute gain in participation, a decisive improvement in triage completion, and economic dominance at the level of the managed case. For a health system pursuing the WHO 70% screening target under resource constraints, these properties are precisely those required for scalable impact. Embedding hrHPV self-sampling with telemedicine triage into national guidelines—supported by reimbursement codes for teleconsultation, integration with cadre networks, and cascade-tracking information systems—would operationalize the screen-triage-treat algorithm in a form suited to Indonesian geography. The model is also synergistic with HPV vaccination scale-up: as vaccinated cohorts age into screening eligibility, an efficient, low-attrition screening pathway will be needed to manage a lower-prevalence but still substantial residual burden.

5. Conclusion

HPV-DNA self-sampling combined with physician-led telemedicine triage was highly efficacious and cost-effective for cervical cancer screening across both a dense metropolitan periphery and a remote riverine setting in Indonesia. The strategy nearly doubled screening uptake (adjusted OR 4.94) and raised triage adherence among screen-positive women to 92.7% (OR 9.50), while remaining dominant in economic terms (ICER US$222.23 per additional case managed). By closing the two principal gaps in the screening cascade—participation and triage—this model offers a scalable, equity-oriented route toward elimination. Health ministries should consider embedding telemedicine-supported triage within national HPV self-sampling guidelines, and future multicenter trials should confirm CIN2+ detection and treatment yield and evaluate long-term cost-effectiveness through national registries.

Declarations

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Author contributions

Conceptualization, methodology, and writing — original draft: RH. Data curation and formal analysis: LTS. Investigation and project administration: SF. Supervision, writing — review and editing: RH, LTS. All authors reviewed and approved the final manuscript.

Conflict of interest

The authors declare no conflict of interest.

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Ethics and consent

The study was approved by the Community Medicine and Health Committee (CMHC) research ethics committee in Palembang, Indonesia (Ref: CMHC/EC/2024/0815), and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. The manuscript contains no identifiable patient material.

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