Cost-effectiveness of Human Papillomavirus Self-collection Intervention on Cervical Cancer Screening Uptake among Underscreened U.S. Persons with a Cervix

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ABSTRACT

Background: We evaluate the cost-effectiveness of human papillomavirus (HPV) self-collection (followed by scheduling assistance for those who were HPV+ or inconclusive) compared with scheduling assistance only and usual care among underscreened persons with a cervix (PWAC).

Methods: A decision tree analysis was used to estimate the incremental cost-effectiveness ratios (ICER), or the cost per additional PWAC screened, from the Medicaid/state and clinic perspectives. A hypothetical cohort represented 90,807 low-income, underscreened individuals. Costs and health outcomes were derived from the MyBodyMyTest-3 randomized trial except the usual care health outcomes were derived from literature. We performed probabilistic sensitivity analyses (PSA) to evaluate model uncertainty.

Results: Screening uptake was highest in the self-collection alternative (n = 65,721), followed by the scheduling assistance alternative (n = 34,003) and usual care (n = 18,161). The self-collection alternative costs less and was more effective than the scheduling assistance alternative from the Medicaid/state perspective. Comparing the self-collection alternative with usual care, the ICERs were $284 per additional PWAC screened from the Medicaid/state perspective and $298 per additional PWAC screened from the clinic perspective. PSAs demonstrated that the self-collection alternative was cost-effective compared with usual care at a willingness-to-pay threshold of $300 per additional PWAC screened in 66% of simulations from the Medicaid/state perspective and 58% of simulations from the clinic perspective.

Conclusions: Compared with usual care and scheduling assistance, mailing HPV self-collection kits to underscreened individuals appears to be cost-effective in increasing screening uptake.

Impact: This is the first analysis to demonstrate the cost-effectiveness of mailed self-collection in the United States.

Introduction

Despite prevention and screening efforts which have resulted in lower cervical cancer incidence and mortality in the United States, cervical cancer continues to disproportionately affect racially or ethnically minoritized persons, people living in poverty, and those residing in geographically underserved areas. The hysterectomy-corrected cervical cancer mortality rate in Black persons with a cervix (PWAC) is 10.1 deaths per 100,000, whereas the rate for White PWAC is only 4.7 deaths per 100,000 (1). Cervical cancer incidence is 11%–14% higher in rural counties than in urban counties (2). These racial and geographic disparities have been partly attributed to lower screening uptake (3–10). Over 50% of cervical cancer cases are attributed to not having been screened within the recommended interval (hereafter referred to as "underscreened"; ref. 11). Current screening guidelines recommend Pap testing alone every 3 years for PWAC who are 21 to 29 years of age, and Pap testing alone every 3 years, or Pap testing in combination with human papillomavirus (HPV) testing every 5 years for PWAC who are 30 to 65 years of age (12).

Underscreened individuals may face barriers to screening related to cost, insurance status, transportation, and time constraints (13–16). HPV self-collection is one approach to reducing barriers to screening (17). By allowing individuals to collect their own cervicovaginal sample at home, HPV self-collection eliminates the need for an initial pelvic exam at a clinic visit, decreasing costs for both patients and the health care system. HPV self-collection has been shown to be a cost-effective strategy to increase cervical cancer screening among underscreened PWAC in European countries (18). In the United States, the cost-effectiveness of HPV self-collection has been assessed among Black PWAC living in the Mississippi Delta (19). This study showed that allowing participants to choose between at-home HPV self-collection delivered by a community health worker (CHW) and in-clinic screening was both effective and cost-effective compared with in-clinic screening only. As such, mailing HPV self-collection kits has the potential to further reduce costs by bypassing the need for CHW home visits to provide the initial screening opportunity. In studies conducted in Europe, the effectiveness and cost-effectiveness of mailed HPV self-collection kits has varied across settings and populations (20–22). Consequently, it is essential to assess the cost-effectiveness of mailing HPV self-collection kits to underscreened individuals in the United States who are at highest risk of cervical cancer (11).

We conducted a cost-effectiveness analysis based on data from a randomized controlled trial (RCT) among underscreened PWAC to

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compare (i) mailed at-home HPV self-collection (followed by scheduling assistance for those who were HPV+ or had inconclusive results), (ii) phone-based scheduling assistance to attend in-clinic screening, and (iii) usual care. We compare mailed HPV self-collection with scheduling assistance for in-clinic screening appointments because scheduling assistance is recommended by the Community Preventive Services Task Force (23, 24). This analysis serves to inform clinics, such as Federally Qualified Health Centers (FQHC), and insurance programs, such as Medicaid, as they seek to increase cervical cancer screening rates overall and reduce disparities in screening and health outcomes by race, income, and geography.

Materials and Methods

RCT

The My Body, My Test Phase 3 (MBMT-3) study was an open-label, two-arm RCT conducted between April 2016 and March 2020 in 22 counties in North Carolina. The protocol for this study has been published (25), and the trial has been registered on ClinicalTrials.gov (NCT02651883). In brief, this RCT evaluated the effectiveness of mailed at-home HPV self-collection (in conjunction with scheduling assistance) compared with scheduling assistance for clinic-based screening alone in terms of the primary study outcome: cervical cancer screening uptake (defined below). MBMT-3 participants included PWAC overdue for cervical cancer screening (i.e., underscreened), defined as not having had a Pap test in the past 4 years or HPV test in the past 6 years. Individuals were eligible for study participation if they were between the ages of 25 and 64, not pregnant, with an intact cervix (no history of hysterectomy), income ≤250% of the U.S. Federal Poverty Level, uninsured or enrolled in Medicaid, and living within the catchment area of a study-associated clinic. The final analytic sample for MBMT-3 included 665 individuals [self-collection arm ($n = 438$), scheduling assistance arm ($n = 227$)]. This study was approved by the University of North Carolina (UNC) Institutional Review Board (IRB).

In the HPV self-collection arm, participants were mailed an HPV self-collection kit. Participants who returned a self-collection kit were informed of their HPV test results by phone. Participants who could not be reached by phone received their results by mail. Participants who tested positive for HPV or who had inconclusive results received scheduling assistance for a free in-clinic screening appointment for Pap/HPV-confirmation co-testing. Participants who did not return a self-collected cervicovaginal sample within 3 weeks also received scheduling assistance for in-clinic screening. While individuals who tested negative for HPV also received scheduling assistance, they were considered as having finished screening after receiving their HPV-negative self-collection result. Consequently, in the current cost-effectiveness analysis, we did not include costs that accumulated once an individual had received a negative HPV self-collection result. Defining screening uptake as in-clinic co-testing or receipt of negative HPV self-collection results aligns with the primary outcome of the MBMT-3 RCT (26).

Participants in the scheduling assistance only arm received the scheduling assistance call 1 week after enrollment, with brief education on cervical cancer and screening and the opportunity to schedule a free in-clinic screening appointment for Pap/HPV co-testing.

Simulation study design

We conducted a population-level decision tree analysis following best practices (27) using Microsoft Excel 2016 (version 16.14.1; Microsoft Corporation; **Fig. 1**). In addition to the HPV self-collection and scheduling assistance only alternatives from the RCT, we also modeled a usual care alternative using estimates from the peer-reviewed published literature (28–32). Specifically, we only included estimates from cervical cancer screening RCTs that were conducted in the United States, had a usual care arm, and included participants who were underscreened and from marginalized populations (see Supplementary Table S1 for brief descriptions of included studies).

Probabilistic chance nodes or branches in the model were based on events that occurred during the MBMT-3 parent study; each set of possible sequences of events through these branches corresponded to mutually exclusive and exhaustive potential pathways in the decision tree. The HPV self-collection, scheduling assistance, and usual care alternatives had 13, four, and two possible pathways, respectively. The terminal node was uptake of in-clinic co-testing or, in the HPV self-collection alternative, receipt of a negative HPV self-collection result.

Analytic perspectives

We conducted our analysis from two perspectives: (i) Medicaid or the state, grouped together because state governments cover a large portion of Medicaid expenses and make decisions about Medicaid administration and public health programmatic offerings for the uninsured; and (ii) the health clinic perspective, which may include county health departments, federally qualified health centers, or primary care providers. Health clinics would be one of the avenues through which at-home HPV self-collection kits would be distributed; this is similar to how fecal immunochemical tests (FIT) have been used to increase colorectal cancer screening (33). We selected a 6-month time horizon because MBMT-3 participants were followed for 6 months after study enrollment.

Population and setting

For each alternative (i.e., usual care, self-collection, and scheduling assistance), we followed a hypothetical cohort of 90,807 individuals. This cohort was created to represent the full scaled-up population of individuals who would have been eligible for the MBMT-3 study based upon estimates from the Kaiser Family Foundation of uninsured and Medicaid-insured PWAC ages 19 to 64 living in poverty in North Carolina and the percentage of PWAC living in poverty up-to-date with cervical cancer screening (34).

Model inputs

The input parameters, including costs and transition probabilities, for the HPV self-collection and scheduling assistance only alternatives, were obtained from the MBMT-3 trial. Costs from the trial were also used to populate the usual care alternative. Transition probabilities (i.e., in-clinic screening uptake) for the usual care alternative were estimated from published cervical cancer screening RCTs with a usual care alternative (28–32). For the HPV self-collection and scheduling assistance only alternatives, beta distributions were estimated for all transition probabilities to inform a range of plausible estimates for probabilistic sensitivity analysis (PSA). For the usual care alternative, previous literature informed a range (i.e., minimum and maximum) of plausible transition probability estimates, and we employed a uniform distribution. Transition probabilities are reported in **Table 1**.

The cost parameters included materials and equipment, personnel costs, clinic/lab reimbursement costs, and community outreach and marketing costs (**Table 2**). Material costs were assigned to both the health clinic perspective and Medicaid/state perspective. These included intervention protocols for the call center, self-collection kits, and reminder letters sent to participants. Personnel costs included time spent on intervention activities performed by call center agents, clinic

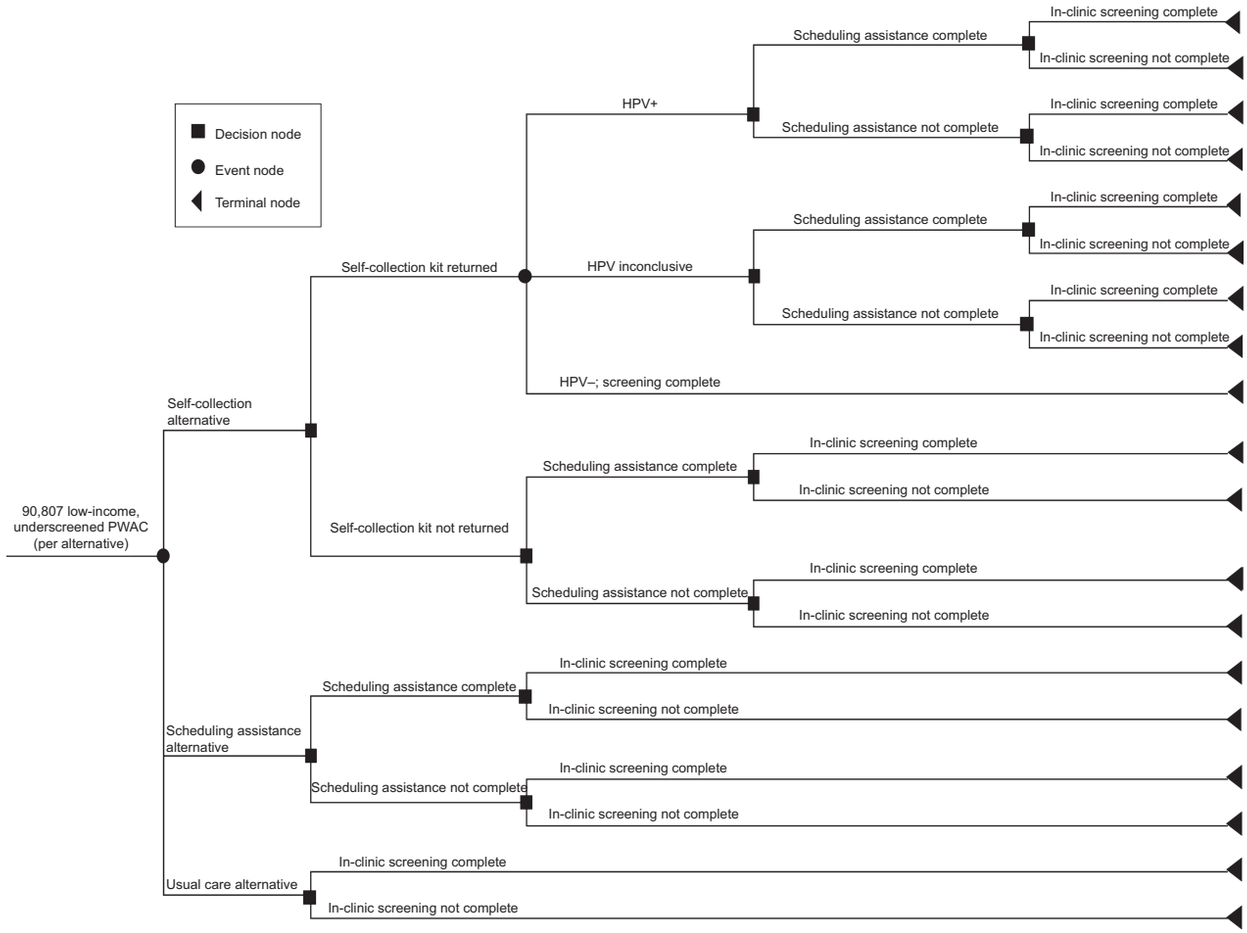

Figure 1.
Decision tree for cervical cancer screening. For each alternative, a hypothetical cohort of 90,807 individuals is followed through the decision tree. The primary outcome is uptake of screening through in-clinic screening or, in the self-collection alternative, receiving an HPV-negative result.

staff, and study staff. Time spent on research-related activities was excluded. Provider and staff costs from time spent on in-clinic activities (i.e., clinic check-in, check-out, and results delivery from in-clinic screening) were not included in the Medicaid/state perspective. In the health clinic perspective, the cost of the clinic exam and screening materials were included for uninsured patients only, as we assumed that these costs were fully reimbursed for patients with Medicaid insurance. Clinics were also not assigned lab costs, because labs typically directly bill patients or insurance payers for their services; in particular, clinics participating in MBMT-3 often did not have on-site laboratory services. The Medicaid/state perspective, we used published North Carolina Medicaid fee to estimate the cost to Medicaid of a clinic exam and Pap/HPV co-testing for patients covered by Medicaid only.

We tracked material and equipment costs throughout the MBMT-3 trial. Clinic costs related to uninsured patients, as well as the proportion of uninsured and Medicaid patients served, were provided from study-affiliated clinics. We estimated personnel costs using micro-costing techniques. Throughout the MBMT-3 trial, the study staff and call center agents tracked their time by type of activity performed. Call center agents' time spent on the phone was tracked in real time, allowing for research activities (e.g., obtaining study consent) to be tracked separately from intervention activities (e.g., providing scheduling assistance). Study staff, including the project manager and research assistants, tracked their hours performing different tasks in an ongoing database; repetitive tasks (i.e., mailing self-collection kits, processing returned kits) were tracked for a total of 6 months. By collecting this data prospectively, we mitigated recall bias that has the potential to taint estimates of labor-related costs (35). For all personnel time-related costs, we assigned hourly wages for equivalent positions in North Carolina from the Bureau of Labor Statistics.

All costs are reported per MBMT-3 participant; for example, to determine the cost per participant sent an HPV self-collection kit, we divided the cost of the total number of self-collection kits sent by the number of participants in the self-collection kit alternative. We report all costs in 2021 dollars, using the Consumer Price Index medical care component inflation factor. In PSAs, we varied all costs by ±20% and employed a triangular distribution.

Outcomes and analyses

We estimated the cost-effectiveness of each alternative with respect to the number of individuals who finished screening for cervical cancer. Screening uptake was defined as testing negative for HPV through self-collected samples (in the HPV self-collection alternative)

Table 1. Transition probabilities for decision analytic tree.

	Base-case probability value	Distribution (Parameters)
Self-collection alternative		**Beta (α,β)**
Self-collection kit returned	0.78	(341, 97)
HPV+	0.15	(52, 289)
Scheduling assistance complete	0.96	(50, 2)
In-clinic screening uptake	0.44	(22, 28)
No in-clinic screening uptake	0.56	(28, 22)
Scheduling assistance not complete	0.04	(2, 50)
In-clinic screening uptake	0.00	(0, 2)
No in-clinic screening uptake	1.00	(2, 0)
HPV inconclusive	0.04	(12, 329)
Scheduling assistance complete	0.92	(11, 1)
In-clinic screening uptake	0.45	(5, 6)
No in-clinic screening uptake	0.55	(6, 5)
Scheduling assistance not complete	0.08	(1, 11)
In-clinic screening uptake	0.00	(0, 1)
No in-clinic screening uptake	1.00	(1, 0)
HPV−	0.81	(277, 64)
Self-collection kit not returned	0.22	(97, 341)
Scheduling assistance complete	0.36	(35, 62)
In-clinic screening uptake	0.29	(10, 25)
No in-clinic screening uptake	0.71	(25, 10)
Scheduling assistance not complete	0.64	(62, 35)
In-clinic screening uptake	0.05	(3, 59)
No in-clinic screening uptake	0.95	(59, 3)
Scheduling assistance alternative		**Beta (α,β)**
Scheduling assistance complete	0.81	(185, 42)
In-clinic screening uptake	0.44	(81, 104)
No in-clinic screening uptake	0.56	(104, 81)
Scheduling assistance not complete	0.19	(42, 185)
In-clinic screening uptake	0.10	(4, 38)
No in-clinic screening uptake	0.90	(38, 4)
Usual care alternative		**Uniform (min, max)**
In-clinic screening uptake	0.20	(0.15, 0.40)
No in-clinic screening uptake	0.80	(0.60, 0.85)

Note: Transition probabilities and the values informing the beta distributions for the self-collection and scheduling assistance alternatives were directly from the MBMT-3 randomized controlled trial. Transition probabilities for the usual care alternative were based on the published literature (28–32) using estimates from cervical cancer screening randomized controlled trials with a usual care alternative. Beta distributions have 2 parameters, α (defined as number of successful outcomes in a trial) and β (defined as number of unsuccessful outcomes in a trial).

or attending in-clinic screening (all alternatives). For the primary base case analysis, we estimated the incremental cost-effectiveness ratio (ICER) for each perspective by dividing the difference in costs by the difference in number of PWAC who finished screening. Following best practices, ICERs were calculated sequentially in order from least effective (i.e., low screening uptake) to most effective (i.e., high screening uptake), with dominated or extended dominated strategies eliminated (36). We also conducted two scenario analyses. In the first analysis, we removed material and personnel community-based outreach costs. These removed costs represent the expense of identifying and/or recruiting patients for the HPV self-collection intervention (e.g., creating a patient registry, conducting a media and outreach campaign, performing medical record abstraction). Second, we evaluated our assumption that Medicaid would fully reimburse clinics for the cost of the clinic exam. Specifically, we assumed that the cost of screening Medicaid patients would be the cost of the clinic exam for uninsured patients minus the reimbursement of the clinic exam for Medicaid patients.

Finally, we conducted a PSA to examine uncertain input parameters. Specifically, using Crystal Ball (Oracle; 2018), we ran a simulation of 1,000 trials to compare self-collection with usual care. In these simulations, both costs and transition probabilities were varied according to their expected probabilistic distributions. We then created an ICER plane to evaluate how estimates of our outcome of interest, cost per PWAC screened, varied across simulations. Second, because there is no commonly accepted willingness-to-pay (WTP) threshold for screening, we graphed a cost-effectiveness acceptability curve (CEAC). CEACs demonstrate the effectiveness of one intervention over another based on varying WTP thresholds.

The IRB at the UNC approved the trial (Study #14–3042). Informed consent was obtained from all study participants.

Data availability

Investigators interested in using these samples or accessing the final dataset for future research may do so under the following conditions: (i) IRB approval has been obtained from the institution covering the investigator, (ii) data security procedures ensuring patient privacy have been demonstrated by the investigator, and (iii) a data use agreement is completed by UNC and the outside investigator. Final datasets for analysis will not include any identifying information.

Table 2. Per-person cost inputs for decision analytic model.

	Health clinic			Medicaid/State perspective		
Item/Unit	**Self-collection alternative**	**Scheduling assistance alternative**	**Usual care**	**Self-collection alternative**	**Scheduling assistance alternative**	**Usual care**
Materials and equipment						
Call center materials	$0.14	$0.14	—	$0.14	$0.14	—
Self-collection kits, printed materials and postage[a]	$18.32	—	—	$18.32	—	—
Self-collection results, printed materials and postage[b]	$0.09	—	—	$0.09	—	—
Personnel costs						
Training call center agents	$3.46	$3.46	—	$3.46	$3.46	—
Scheduling assistance	—	$1.13	—	—	$1.13	—
Mailing self-collection kits[a]	$3.26	—	—	$3.26	—	—
Processing returned self-collection kits	$3.68	—	—	$3.68	—	—
Self-collection HPV− results delivery	$0.71	—	—	$0.71	—	—
Self-collection HPV+ results delivery	$0.79	—	—	$0.79	—	—
Self-collection HPV inconclusive results delivery	$0.63	—	—	$0.63	—	—
Follow-up scheduling assistance among participants with HPV+ self-collection result	$1.58	—	—	$1.58	—	—
Follow-up scheduling assistance among participants with inconclusive self-collection result	$1.23	—	—	$1.23	—	—
Follow-up scheduling assistance among participants with no returned self-collection kit	$1.11	—	—	$1.11	—	—
Clinic check-in[c]	$9.22	$9.22	$9.22	—	—	—
Clinic check-out	$0.77	$0.77	$0.77	—	—	—
Clinic HPV− results delivery	$3.07	$3.07	$3.07	—	—	—
Clinic HPV + or inconclusive results delivery	$6.13	$6.13	$6.13	—	—	—
Clinic/Lab reimbursement costs[d]						
Clinic exam, Medicaid-insured patient	—	—	—	$84.90	$84.90	$84.90
HPV test (in-clinic or self-collection), Medicaid-insured patient	—	—	—	$32.74	$32.74	$32.74
Pap test, Medicaid patient	—	—	—	$34.00	$34.00	$34.00
Clinic exam, uninsured patient[e]	$199.76	$199.76	$199.76	—	—	—
Community outreach and marketing costs						
Community-based outreach, materials	$60.66	$60.66	—	$60.66	$60.66	—
Community-based outreach, personnel costs	$75.32	$75.32	—	$75.32	$75.32	—

Note: All costs were from MBMT-3, which included 665 participants [self-collection ($n = 438$), scheduling assistance ($n = 227$)].
[a]These costs include both the self-collection kits ($N = 531$) and the mailed reminders to return the self-collection kits ($N = 245$). The costs of a single self-collection kit (without postage, packaging, or instructions) is $0.45.
[b]Most individuals were initially called to be given their self-collection results. However, those who could not be reached by phone were sent letters to remind them to call for their results ($N = 36$). Participants who never called for their self-collection results were mailed results ($N = 4$).
[c]Costs include conducting appointment reminder phone calls, processing and completing paperwork for new patients, and checking patients in for their appointment.
[d]Lab costs to analyze the results from in-clinic co-testing (Pap test and HPV test) were not included from the clinic's perspective since the lab bills the patient directly.
[e]For uninsured patients, the clinic does not get reimbursed, so the clinic exam is therefore a cost to the clinic.

Results

Within the modeled cohort ($N = 90,807$ individuals per arm), the number of cervical cancer screenings was highest among those in the self-collection alternative [$n = 65,721$ (72%)], followed by the scheduling assistance only alternative [$n = 34,003$ (37%)] and usual care alternative [$n = 18,161$ (20%)]. Total screening costs were lowest in the usual care alternative from both the Medicaid/state ($2.8 million) and clinic perspective ($1.5 million). The scheduling assistance alternative had the highest total costs from the Medicaid/state perspective ($17.9 million), and the self-collection alternative had the highest total costs from the clinic perspective ($15.7 million).

From the Medicaid/state perspective, the scheduling assistance alone alternative cost more and was less effective than the self-collection alternative and therefore was dominated. Similarly, from the clinic perspective, the self-collection alternative exhibited extended dominance over the scheduling assistance only alternative. Subsequently, in comparing the self-collection alternative with usual care, the ICERs were $284 per additional PWAC screened from the Medicaid/state perspective and $298 per additional PWAC screened from the clinic perspective (**Table 3**).

Scenario analyses

In a scenario analysis where community-based outreach costs were excluded from the scheduling assistance and self-collection alternatives, the scheduling assistance alternative continued to be dominated by the self-collection alternative from the Medicaid/state perspective and extended dominated from the clinic perspective. In comparing the

Table 3. Cost-effectiveness results of HPV self-collection alternative compared with scheduling assistance alternative and usual care alternative.

	Total cervical cancer screening (CCS) costs	Total CCS uptake	Δ in CCS costs	Δ in CCS uptake	Incremental cost per additional PWAC screened
Medicaid/State perspective					
Usual care alternative	$2,753,995	18,161	—	—	—
Scheduling assistance alternative	$17,913,821	34,003	$15,159,826	15,841	*Dominated*
Self-collection alternative	$16,238,440	65,721	$13,484,445	47,560	$284
Clinic Perspective					
Usual care alternative	$1,471,651	18,161	—	—	—
Scheduling assistance alternative	$15,512,958	34,003	$14,041,307	15,841	*Extended Dominated*
Self-collection alternative	$15,652,895	65,721	$14,181,244	47,560	$298

Note: Scheduling assistance was dominated by self-collection from the Medicaid/state perspective and extended dominated from the clinic perspective. Therefore, consistent with best practice (36), the incremental cost per additional PWAC screened for self-collection was calculated in comparison with usual care (not to scheduling assistance).
Abbreviation: CCS, cervical cancer screening.

self-collection alternative with usual care, the ICERs decreased to $24 per additional PWAC screened from the Medicaid/state perspective and to $39 per additional PWAC screened from the clinic perspective (Supplementary Table S2).

In the second scenario analysis, we assumed that the reimbursement provided by Medicaid would not fully cover the exam costs from the clinic perspective. The scheduling assistance alone alternative was found to cost more and be less effective than the self-collection alternative and therefore was dominated. In comparing the self-collection alternative with usual care, the ICER was $282 per additional PWAC screened from the clinic perspective (Supplementary Table S2).

ICER planes for the self-collection alternative versus usual care are presented in **Fig. 2A** from the Medicaid/state perspective and in **Fig. 2B** from the health clinic perspective. From both the Medicaid/state perspective and the clinic perspective, the self-collection alternative was both more effective but also more costly compared with usual care in all trials. From the Medicaid/state perspective, among the 1,000 simulations comparing the self-collection alternative with usual care, the ICERs ranged from $282 per additional PWAC screened to $373 per additional PWAC screened. Similarly, from the clinic perspective, the ICERs ranged from $219 per additional PWAC screened to $414 per additional PWAC screened, when comparing the self-collection alternative with usual care.

CEACs illustrate the probability that self-collection would be cost-effective, compared with usual care, at different WTP thresholds (**Fig. 3**). From the Medicaid/state perspective, the self-collection alternative was expected to be cost-effective compared with usual care in 66% of simulations at a WTP of $300 per additional PWAC screened and 97% of simulations at a WTP of $350 per additional PWAC screened. From the clinic perspective, the self-collection alternative was cost-effective compared with usual care in 58% of simulations at a WTP of $300 per additional PWAC screened and 91% of simulations at a WTP of $350 per additional PWAC screened.

Discussion

Our findings show that employing HPV self-collection was both affordable and effective in increasing cervical cancer screening uptake among underscreened, Medicaid-insured or uninsured individuals. Specifically, self-collection (followed by scheduling assistance for those who were HPV+ or had inconclusive results) was likely cost-effective compared with usual care from both the Medicaid/state and clinic perspectives. Furthermore, sensitivity analyses demonstrated that, at a WTP thresholds of $300 per person screened, self-collection was consistently cost-effective compared with usual care.

The results from this economic evaluation are similar to those from other interventions to increase cancer screening uptake in the United States among underscreened individuals. Recently, a systematic review examined the cost-effectiveness of breast, cervical, and colorectal cancer screening interventions implemented in the United States among historically marginalized populations. Among the 30 studies included, 15 reported the incremental cost per additional person screened. On the basis of 17 estimates from these 15 studies, the median ICER was $250 per additional person screened (interquartile range: $45–$609 per additional person screened; ref. 37). In particular, cervical cancer screening interventions among individuals overdue for screening had a median ICER of $315 per additional PWAC screened (37).

It is difficult to compare our results with other screening interventions that involve at-home screening tests. In North Carolina, a colorectal cancer screening intervention among underscreened Medicaid enrollees found that reminders and mailed FIT kits were cost-effective 90% of the time at a WTP of $20 per additional person screened from the Medicaid/state perspective, and 75% of the time at a WTP of $100 per additional person screened from the health clinic perspective (33). One explanation for these substantially lower WTP thresholds is that this study did not include community-based outreach costs. In addition, no U.S.-based studies examining HPV self-collection have calculated the incremental cost per additional PWAC screened. One study among Black PWAC conducted in Mississippi found that offering individuals the choice to be screened through self-collection (compared with usual care) reduced the lifetime risk of cervical cancer by 14.8% at a cost of approximately $62,720 per life year saved (19).

Economic evaluations of cancer screening interventions vary in terms of whether they include community-based outreach costs. In some instances, outreach costs are considered part of the trial recruitment process and are therefore excluded as research-related study costs (38, 39). On the other hand, costs related to community outreach may alternatively be viewed as part of the intervention implementation process (29, 40, 41). Ultimately, the significance and relevance of community-based outreach costs would depend on how a Medicaid

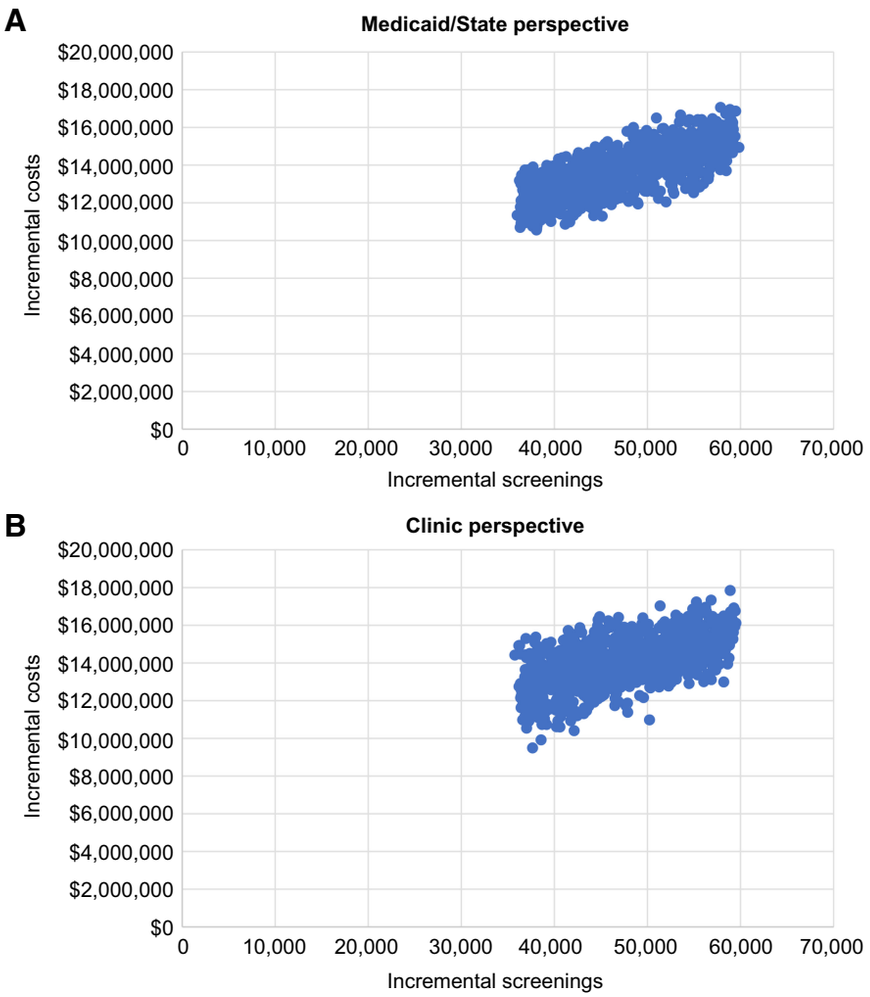

Figure 2.

ICERs for self-collection alternative versus usual care from the Medicaid/state perspective (**A**) and clinic perspective (**B**). The ICER plane presents PSA results in terms of incremental costs and incremental effectiveness (additional PWAC screened). From both the Medicaid/state perspective and the clinic perspective, the self-collection alternative is both more effective and more costly compared with usual care in all trials.

program or individual clinic decided to identify and reach the target screening population. For example, community-based outreach costs could potentially reflect the costs of building a patient registry using electronic health records (EHR) to identify individuals to target for screening if screening was not already consistently documented in the EHR. It could also reflect costs of publicizing and promoting HPV self-collection within communities, as was done in the MBMT-3 trial. Because of this variability in relevance and interpretation, we present results with and without outreach costs. While the inclusion of outreach costs increased the ICERs to $284 per additional PWAC screened from the Medicaid/state perspective and $298 per additional PWAC screened from the clinic perspective, these ICERs nevertheless remain comparable with prior cervical cancer screening interventions among underscreened individuals, where the median was $315 per additional PWAC screened (37).

Limitations of our cost-effectiveness analysis should be noted. First, we employed a relatively short time horizon of 6 months to match the length of the MBMT-3 trial. However, previous cost-effectiveness analyses focused on screening uptake have used similar time horizons; shorter time horizons are particularly important from the Medicaid/state perspective, as state-level decision-makers often make choices about which Medicaid programs to invest resources in based on short-term (i.e., annual) budgets (33). Second, our analysis did not include estimates or costs of the detection and treatment of cervical intraepithelial neoplasia and cancer, and our sole outcome of interest was screening uptake. Screening is the first step in the care process, and increased screening does not automatically lead to increased treatment and follow-up; in particular, self-collection may be less likely than in-clinic screening to result in follow-up for HPV-positive individuals (19). To fully evaluate the cost-effectiveness of self-collection, future analyses should include outcomes such as the cost per precancer treated or cost per life-year saved. Future interventions may also consider pairing HPV self-collection with patient navigation to increase linkage to management and treatment. Third, while transition probabilities for the self-collection and scheduling assistance only alternatives were from the MBMT-3 trial, the usual care alternative's transition probabilities were estimated from the published literature. However, even when usual care alternative estimates were varied across a range of plausible parameters from the literature, our conclusions remained the same. Finally, the generalizability of our findings may be limited as MBMT-3 was conducted in a single state, North Carolina. However, North Carolina is one of the most populous states in the United States with a highly diverse population in regard to race, ethnicity, and rurality. Consequently, our results still provide valuable insights to policy-makers and decision-makers aiming to design cost-effective programs that will increase cervical cancer

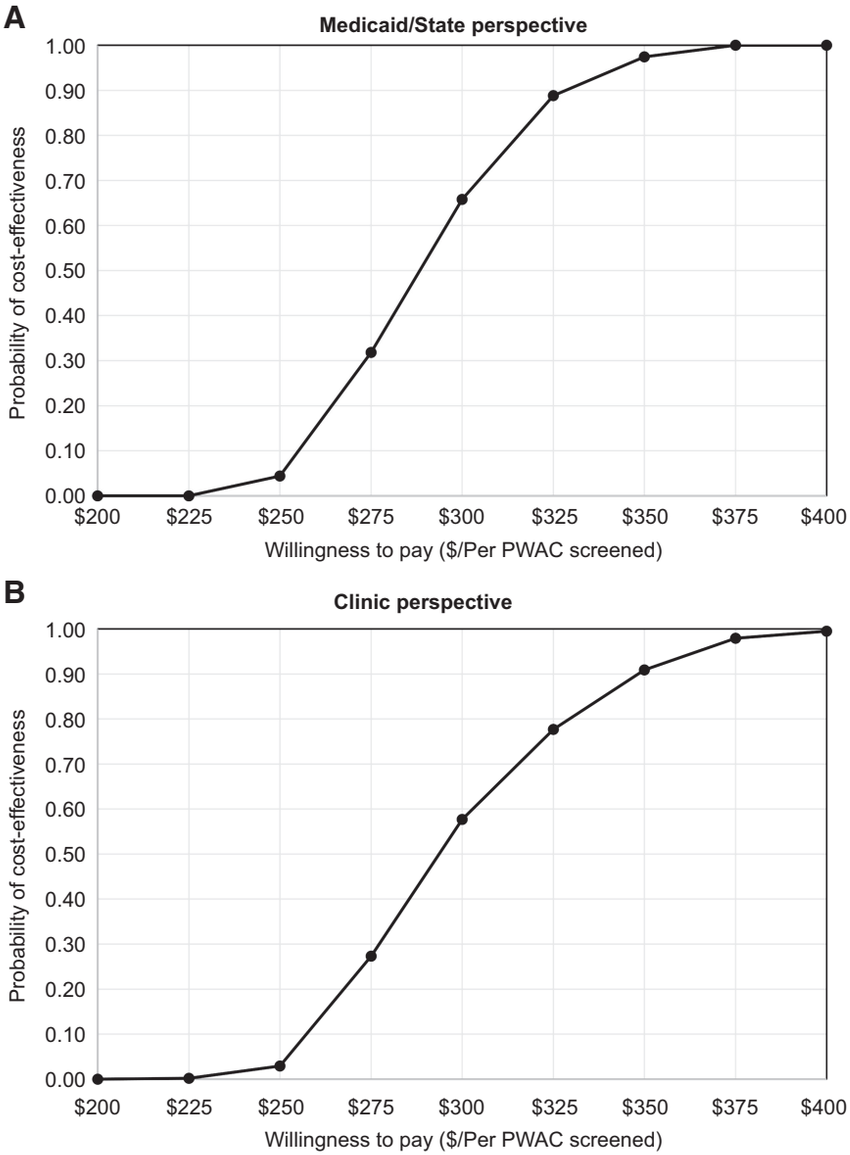

Figure 3.
Cost-effectiveness acceptability curves (CEACs) for self-collection alternative versus usual care from the Medicaid/state perspective (**A**) and clinic perspective (**B**). These figures present the probability that the self-collection alternative will be cost-effective compared with usual care at various WTP thresholds.

screening among underscreened individuals. Implementing HPV self-collection through Medicaid programs and FQHCs in other states should be explored in future studies.

While the FDA approved the first HPV test for use in primary cervical cancer screening in 2016, at-home HPV tests are currently not FDA approved. This analysis supports the use of at-home HPV self-collection to increase cervical cancer screening uptake among underscreened individuals. It is the first analysis to demonstrate the cost-effectiveness of mailed self-collection in the United States. Only one other U.S.-based study has evaluated the cost-effectiveness of self-collection delivered by CHWs. While both studies found self-collection to be cost-effective, further studies should explore how different implementation factors can affect both effectiveness and cost, including mode of delivery (i.e., self-collection via mail or CHW), mode of HPV results notification (i.e., phone calls, mail, patient EHR portals), approaches for patient identification and outreach, and staffing and workflow factors.

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Authors' Contributions

L.P. Spees: Conceptualization, data curation, formal analysis, validation, investigation, visualization, methodology, writing–original draft. **C.B. Biddell:** Data curation, formal analysis, visualization, writing–review and editing. **J.S. Smith:** Data curation, supervision, funding acquisition, investigation, writing–review and editing. **A.C. Des Marais:** Resources, data curation, project administration, writing–review and editing. **M.G. Hudgens:** Supervision, methodology, writing–review and editing.

B. Sanusi: Data curation, project administration, writing–review and editing. **S. Jackson:** Resources, data curation, project administration, writing–review and editing. **N.T. Brewer:** Methodology, writing–review and editing. **S.B. Wheeler:** Conceptualization, supervision, visualization, methodology, writing–review and editing.

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Note

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