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Inefficiencies and high-value improvements in U.S. cervical cancer screening practice: A cost-effectiveness analysis

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Abstract

Background—Studies suggest that cervical cancer screening practice in the United States is inefficient. The cost and health implications of non-compliance in the screening process compared to recommended guidelines are uncertain.

Objective—To estimate the benefits, costs, and cost-effectiveness of current cervical cancer screening practice and assess the value of screening improvements.

Design—Model-based cost-effectiveness analysis.

Data Sources—New Mexico HPV Pap Registry; medical literature.

Target Population—Cohort of women eligible for routine screening.

Time Horizon—Lifetime.

Perspective—Societal.

Interventions—Current cervical cancer screening practice; improved compliance to guidelines-based screening interval, triage testing, diagnostic referrals, and precancer treatment referrals.

Outcome Measures—Reductions in lifetime cervical cancer risk, quality-adjusted life-years (QALYs), lifetime costs, incremental cost-effectiveness ratios (ICERs), incremental net monetary benefits (INMBs)

Results of Base-Case Analysis—Current screening practice was associated with lower health benefit and was not cost-effective relative to guidelines-based strategies. Improvements in the screening process were associated with higher QALYs and small changes in costs. Perfect compliance to a 3-yearly screening interval and to colposcopy/biopsy referrals were associated with the highest INMBs (\$759 and \$741, respectively, at a willingness-to-pay threshold of \$100,000 per QALY gained); together, the INMB increased to \$1,645.

Results of Sensitivity Analysis—Current screening practice was inefficient in 100% of simulations. The rank ordering of screening improvements according to INMBs was stable over a range of screening inputs and willingness-to-pay thresholds.

Limitations—The impact of HPV vaccination was not considered.

Conclusions—The added health benefit of improving compliance to guidelines, especially the 3-yearly interval for cytology screening and diagnostic follow-up, may justify additional investments in interventions to improve U.S. cervical cancer screening practice.

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Introduction

Cytology-based screening has been heralded as a public health success story in the United States, leading to substantial declines in cervical cancer incidence and mortality since its introduction in the 1940s (1). Yet, there is evidence that cervical cancer screening practice is

inefficient. Variable screening rates (2, 3), with some women screened too frequently while others not at all, and sub-optimal management of women with abnormal tests (4), with some women being over-managed while others are lost to follow-up, contribute to the inefficiencies and approximately 12,000 new cases and 4,000 deaths from cervical cancer each year (5). These cases are disproportionately experienced by underserved populations, especially women who belong to racial/ethnic minority groups (6, 7). Furthermore, U.S. cervical cancer screening practice bears a hefty economic burden of roughly \$6 billion each year on screening, diagnosis, and pre-cancer treatment (8).

A better understanding of the natural history of human papillomavirus (HPV), the causal agent of cervical cancer, and the emergence of new technologies for both primary (i.e., HPV vaccination) and secondary (e.g., HPV testing) prevention, have created opportunities for improving cervical cancer prevention while also potentially reducing the health and economic burden of screening. However, these opportunities also pose challenges for policy-making. Given the decades-long natural history of HPV infection to cervical cancer, decisions regarding how to optimally use current and new technologies are being made before cancer outcomes can be observed. Increasingly, mathematical models have been developed to simulate the burden of disease and extrapolate short-term measures of intervention effectiveness to project long-term population-based health outcomes for the purpose of informing policy decisions and guidelines. Such models synthesize data from multiple sources on the epidemiology and biology of disease, clinical efficacy or effectiveness of health interventions, and resource use. While these data are quite robust, model inputs on screening practice patterns in the United States have relied primarily on data from national surveys, such as the National Health Interview Survey (NHIS), that are subject to respondent recall-bias and provide cross-sectional snapshots of screening behavior in the aggregate, usually capturing uptake of the initial screening visit only (3).

The New Mexico HPV Pap Registry (NMHPVPR), a public health surveillance unit at the University of New Mexico, serves as the only existing population-based cervical cancer screening registry in the United States. Through statewide regulation, the NMHPVPR receives data from all institutions providing cervical cancer screening services to residents of New Mexico, enabling linkages of clinical and laboratory records at the individual-level on the full spectrum of cervical cancer preventive care (2, 4, 9, 10) (see Appendix for details). The pairing of individual-level data from the NMHPVPR with disease simulation models provides a unique opportunity to reflect patterns of screening longitudinally, permitting important individual-level associations to be captured, such as loss-to-follow-up for diagnostic and treatment procedures.

Using a disease simulation model of HPV and cervical cancer natural history (11), we conducted an analysis integrating screening, diagnostic, and treatment utilization data from the NMHPVPR to estimate the associated long-term health and economic outcomes of current cervical cancer screening and management (“current screening practice”) in the United States, and compared its cost-effectiveness against recently-revised U.S. screening guidelines (12–14). To understand the major contributors to inefficiency and to identify high-value improvements, we estimated the change in health benefits, costs, and net

monetary benefits of improving different aspects of the screening process, compared to current practice.

Methods

Model description

We used a recently updated individual-based disease simulation model of the natural history of HPV and cervical cancer (11). The model comprises mutually exclusive health states that represent established stages of cervical disease. Individual girls enter the model at age 9 years with a healthy cervix and transition between health states on a monthly basis until death. As individuals age, they can acquire HPV infections, which can clear or progress to high-grade precancer, classified as cervical intraepithelial neoplasia (CIN), grades 2 or 3. Women with CIN2 or CIN3 can regress or progress to invasive cancer, which can be detected at the local, regional or distant stage; this model focuses on squamous cell carcinoma, the most common histologic subtype of cervical cancer. Death from background mortality can occur from any health state, and excess stage-dependent mortality can occur from the cancer states.

The model stratifies HPV by several high-risk genotypes (HPV-16, -18, -31, -33, -45, -52, -58), as well as two pooled groups of other high-risk types and low-risk types. Transitions to and from health states are governed by HPV genotype and time since HPV acquisition or precancer development. Transition probabilities can also vary by age, history of prior HPV infection, and prior interventions. After establishing baseline parameter values for the natural history component of the model using data from large prospective cohort studies (15–17), we calibrated the model to epidemiologic data on HPV prevalence and genotype distribution using a likelihood-based approach (18, 19). Our model development framework has been previously described (11, 20, 21); further details are included in the Appendix.

Screening scenarios

Guidelines recommended practice (perfect compliance)—For guidelines-based screening, we included strategies of (1) cytology alone every 3 years from ages 21–65, and (2) cytology alone every 3 years from ages 21–29, with a switch to cytology and HPV “co-testing” every 5 years from ages 30–65 (12, 13). We assumed that management of women with equivocal or abnormal tests followed established guidelines with full compliance (12, 14), and that follow-up for both diagnostic and precancer treatment visits was 100%. For co-testing, HPV-positive/cytology-negative women were managed by repeat co-testing at 12 months, with referral to colposcopy for any positive result. We also considered annual cytology screening to reflect past recommendations. Screening test characteristics and cost inputs were estimated from the published literature (Appendix Table 2) (21–29).

Current screening practice—To simulate current screening practice, we incorporated data from the NMHPVPR to estimate several parameters along the screening pathway, including screening frequencies, proportions undergoing HPV triage testing, proportions receiving diagnostic colposcopy/biopsy, and proportions receiving precancer treatment with excisional procedures (Table 1) (2, 4, 9). The majority of cervical excisional procedures

were loop electrosurgical excision procedure (LEEP) but also included treatments designated as cone biopsy and cold knife conization; as in a prior analysis, we did not stratify by method of excision (4). Previous calculations of screening intensity, defined as the number of screening tests over a 4-year period (2008–2011) (2), were used to inform the distribution of women who screen at different frequencies, as well as those who have never been screened. For example, women who received one test over the 4-year period were assumed to screen every four years, whereas women who received four or more tests were assumed to screen annually (see Appendix for additional assumptions). We also incorporated data from the NMHPVPR on utilization of HPV triage testing following abnormal Pap results within 28 days of a screening Pap (Table 1) (9), and the probability of receiving diagnostic colposcopy/biopsy within one year of an abnormal screening Pap, depending on the preceding Pap result (4). Similarly, we incorporated data on the probability of receiving excisional treatment for precancer within one year of cervical biopsy, depending on the preceding biopsy result (4). Because of the low utilization of cytology and HPV co-testing in New Mexico over the study time period (<20% in women ages 30–65) (9), we restricted our scenario of current screening practice to include cytology testing alone. We did not consider the impact of HPV vaccination. Under these current screening practice assumptions, we projected estimates of cumulative risks of CIN2+ and CIN3+ following abnormal cytology results and found that model-predicted outcomes correspond highly with empirical data, demonstrating both internal and external model validity (Appendix Figure 2). Sensitivity analyses, including best- and worst-case scenarios, evaluated the impact of uncertainty in current screening practice parameters (Table 1 and Appendix Table 3).

Improvements in current screening—To evaluate the discrepancy between strategies recommended by guidelines and current screening practice, we modified each of the following screening parameters, alone and in combination, to reflect perfect adherence to guidelines: (1) 3-yearly routine cytology screening for all eligible women, (2) HPV triage testing only for women with atypical squamous cells of undetermined significance (ASC-US), (3) perfect compliance to colposcopy/biopsy referral, and (4) perfect compliance to precancer excisional treatment referral. For all scenarios, screening initiated at age 21 and ended at age 65.

Analysis

Main model-projected outcomes included health benefit, in terms of reductions in lifetime risk of cervical cancer incidence and mortality and gains in quality-adjusted life-years (QALYs), and lifetime costs (in 2012 U.S. dollars). Analyses were conducted from the societal perspective. Costs comprised direct medical costs associated with screening, diagnosis, and treatment for precancer and invasive cancer (e.g., tests, procedures, hospitalizations), based on national-average Medicare reimbursement rates and cost estimates from a previous analysis (Appendix Table 2) (21, 26). Direct non-medical costs, such as patient time and transportation, were also included for all strategies (27, 28).

Cost-effectiveness analysis was conducted to assess the comparative value for money of current screening practice against guidelines-based screening using the incremental cost-effectiveness ratio (ICER), defined as the additional cost divided by the additional health

benefit of a specific strategy compared to the next less-costly strategy. Although no explicit cost-effectiveness threshold exists in the United States, a range of \$50,000 to \$200,000 per QALY gained was used to indicate good value for money (30). Consistent with guidelines for U.S. cost-effectiveness analysis, future life-years and costs were discounted at an annual rate of 3% (31).

In order to compare the relative value of each improvement in the screening process against current practice, we calculated the incremental net monetary benefit (INMB), which translates the incremental benefit (additional QALYs gained) into monetary terms for a given willingness-to-pay (WTP) threshold (by multiplying the QALYs gained by the WTP) and then subtracting the incremental cost (32). Positive INMB values indicate that the scenario results in a net savings per woman when also considering the QALY benefit, signaling a favorable cost-effectiveness profile. Given the cost of specific interventions for improving compliance are not included in the calculations, we can interpret the INMB estimate as the maximum cost that could be additionally incurred per woman before the ICER associated with the scenario exceeds the WTP threshold; in other words, the INMB value provides a measure of how much economic investment can be made towards interventions to achieve the desired improvement in a cost-effective manner. We used the INMB estimates to identify high-value improvements in current screening practice. Equations, definitions, and interpretations of study outcomes are summarized in Appendix Table 4.

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Results

Current screening practice versus guideline recommendations

Compared to no screening, current screening practice reduced lifetime cervical cancer incidence by 48.5% and mortality by 58.4% (Table 2) and had an ICER of \$19,530 per QALY gained. In comparison, guidelines-based cytology screening every 3 years resulted in greater cancer benefit (80.9% incidence reduction; 86.7% mortality reduction) and a more attractive (i.e., lower) ICER, thereby dominating current screening practice; 3-yearly cytology screening compared to no screening yielded an ICER of \$15,260 per QALY gained. Switching from 3-year cytology to 5-year co-testing at the age of 30 increased cancer benefit (91.1% incidence reduction; 93.5% mortality reduction) but at an increased lifetime cost with an ICER of \$59,440 per QALY. Annual cytology screening, historically recommended for routine screening, yielded slightly higher cancer benefit (91.4% incidence reduction; 93.8% mortality reduction), but the added cost far exceeded the gain in health benefit, with a resulting ICER of over \$1 million per QALY gained.

We found that our results were quite stable over probabilistic sensitivity analysis using a sample of 50 calibrated natural history parameter sets. Most notably, the scenario of current screening practice was inefficient (i.e., dominated) in all 50 analyses. Both guidelines-based strategies remained efficient and below \$100,000 per QALY in all 50 simulations, while annual cytology testing consistently exceeded \$1 million per QALY.

Improvements in current screening practice

Figure 1 shows the changes in lifetime costs, QALYs, and cancer incidence reductions with one or more improvements in the screening process. We found that perfect compliance to HPV triage testing had very little impact on outcomes compared to current screening practice; in contrast, scenarios with perfect follow-up for excisional treatment, perfect adherence to 3-yearly routine cytology screening, and perfect follow-up for diagnostic colposcopy/biopsy were associated with increasingly higher QALYs with only small changes in costs. Reduction in lifetime cervical cancer incidence was 57.8% with perfect excisional treatment follow-up and over 60% with 3-year cytology screening and perfect colposcopy/biopsy follow-up. As expected, assuming more than one improvement resulted in greater QALYs and cancer benefits than any single improvement. Notably, when we assumed 3-year routine cytology screening for all eligible women simultaneously with perfect colposcopy/biopsy follow-up, there was an interactive effect that yielded greater QALYs than the sum of the independent effects and a cancer incidence reduction of 72.2%.

Scenarios with perfect compliance to 3-year cytology screening for all eligible women and perfect colposcopy/biopsy follow-up also had the highest INMB values, similar at WTP thresholds of \$50,000 per QALY (\$365 and \$321, respectively) and \$100,000 per QALY (\$759 and \$741, respectively) (**Table 4**), indicating that these improvements may be worthy of high investments. By comparison, a scenario of perfect compliance to excisional treatment yielded INMBs of \$226 for the \$50,000 per QALY and \$451 for the \$100,000 per QALY thresholds. Utilizing HPV triage testing only for women with ASC-US results had the lowest INMBs, \$1 for the \$50,000 per QALY and \$12 for the \$100,000 per QALY thresholds, indicating that intervention costs to achieve full compliance to appropriate HPV triage testing would have to be quite low in order for this improvement to be cost-effective compared to current practice. As with the QALY gains, the INMBs increased when more than one improvement was assumed simultaneously, with the interaction of 3-year cytology screening and perfect compliance to colposcopy/biopsy referral leading to a greater INMB (e.g., \$753 at a WTP of \$50,000 per QALY) than the sum of the individual INMBs. We observed the same trends but with higher INMB values as the WTP threshold increased to \$200,000 per QALY (Appendix Table 5). Results were sensitive to assumptions regarding the current distribution of women screening at different frequencies (Appendix Figure 3). For example, at a WTP threshold of \$100,000 per QALY, INMB values ranged from \$485 (assuming women are currently screening at a higher frequency than the base case) to \$882 (assuming women are screening at a lower frequency). At the higher screening frequency, the INMB for improving colposcopy/biopsy follow-up was greater than that of equalizing the routine screening interval; otherwise, the relative ordering of improvement scenarios in terms of INMB values was quite stable across all analyses. Other screening practice

parameters were not influential, and variations in best-/worst-case scenario analyses were driven by the uncertainty in screening frequency.

Conclusions

Using population-based data on screening utilization from the only U.S. cervical cancer screening registry, we found that screening as currently practiced is inefficient with respect to health benefits and costs when accounting for variable screening frequency, inappropriate HPV triage testing, and imperfect compliance to diagnostic and treatment referrals. In terms of cost-effectiveness, current screening practice remained inefficient in all simulations conducted, implying that although guidelines-based strategies were more costly, the gains in health were also relatively greater.

Our analysis indicates that improvements in current screening practice can generate greater health gains with nominal changes in costs. It is important to note that even without taking into consideration any implementation costs of improving adherence, scenarios with higher screening compliance were generally more costly than current screening (Figure 1); however, the added costs were quite low. The INMB of each improvement scenario (versus current screening practice) represents the maximum cost that could be incurred on average per woman over her lifetime to achieve the improvement without exceeding the willingness-to-pay threshold. Based on our findings, we can conclude that economic investments towards interventions that improve adherence to cervical cancer screening guidelines can be quite substantial.

In deconstructing the individual effects of the different breakdowns in current screening practice, we found that achieving universal 3-year cytology screening for all screen-eligible women and perfect compliance to colposcopy/biopsy referrals yielded the greatest gains in health compared to current practice, indicating that these improvements may be high priorities to consider. Across a range of willingness-to-pay thresholds, compliance to the 3-yearly cytology interval and to colposcopy/biopsy referrals were also associated with the highest INMBs, especially when occurring simultaneously, indicating that these improvements in screening may be worthy of high investment. The relatively lower added benefit of improving only excisional treatment compliance signals that important (i.e., high-risk) women are not being screened and are lost in the transition between screening and diagnosis; as a result, the effect of these improvements was heightened when compliance to excisional treatment referral was simultaneously improved. In all scenarios (alone and in combination with other improvements), eliminating inappropriate HPV triage test utilization yielded only a slight increase in health and the lowest INMB values.

This analysis is the first to leverage longitudinal, population-based screening utilization data to inform model assumptions regarding recent cervical screening practice in the United States. The data from the NMHPVPR are based on lab reports on all women screened in New Mexico from 2007 to 2011 or 2012 (depending on the specific measure) and therefore is an empirical assessment of screening practice that provides individual-level data on coverage and follow-up. A previous analysis relied on self-reported data from the NHIS (3), which is subject to recall bias and reports much greater screening intensity than the

NMHPVPR, resulting in higher cost and QALY estimates (33). The prior study also did not include loss to follow-up in screen-positive women, but nonetheless yielded the same qualitative finding that current screening practice is inefficient.

There are several limitations to our analysis. As noted in previous reports (2, 4, 9, 10), though we are confident that NMHPVPR reporting is highly complete, data from the NMHPVPR are reliant on our ability not only to ascertain all cervical screening, diagnosis and treatment reports but also to perform linkages between these events, which are not perfect. Furthermore, while our screening parameters based on data from the NMHPVPR are the most comprehensive longitudinal measures of screening utilization that have been used to date in a U.S. model-based analysis, the data are from a limited period and therefore, we made simplified assumptions regarding screening utilization over a longer time period. Although the population in New Mexico is largely comparable to the overall U.S. population in terms of demographics and social characteristics, there are important differences in the composition of race/ethnicity (e.g., higher proportion of Hispanic and Latina women in New Mexico) and the largely rural nature of the state that may challenge the generalizability of findings. Screening practice in New Mexico may also not be generalizable to the United States as a whole; however, the burden of cervical cancer incidence and mortality in New Mexico largely mimics that of the broader U.S. population (see Appendix Figure 1), suggesting that screening practice patterns in New Mexico may be representative. We also did not incorporate future likely changes to guidelines with the recent U.S. Food and Drug Administration approval of HPV primary testing and the uptake of HPV vaccination. As data continue to become available from the NMHPVPR and as practice changes with new technologies and revised guidelines, we can revisit the definition of current screening practice and update analyses as needed. Finally, it is important to note that the INMB estimates are generated under assumptions of perfect compliance and represent, in principle, the maximum economic cost that society would be willing to expend to attain perfect compliance; however, perfect compliance is not realistic and different interventions may have different effectiveness in improving the screening process, leading to potentially lower return on investments. Costs of programs and additional resources to achieve improved compliance to screening, including additional human resources, technology, and infrastructure, need to be carefully assessed to determine the feasibility of these improvements and the actual return on investments.

Despite these limitations, our findings robustly support the notion that there is room for improvement in the current practice of cervical cancer screening. Multiple breakdowns along the screening pathway contribute to the relatively low health benefit and inefficiency, compared to currently recommended strategies. Our analysis indicates that we stand to gain the most health benefit by equalizing the screening rate for all eligible women and ensuring timely and complete diagnostic follow-up and that we can make sizable investments towards these improvements. These model-projected outcomes can inform strategic investments in interventions designed to improve the screening process, as well as examine the impact of new HPV-related technologies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ASC-H	atypical squamous cells, cannot exclude HSIL
ASC-US	atypical squamous cells of undetermined significance
CIN	cervical intraepithelial neoplasia
HPV	human papillomavirus
HSIL	high-grade squamous intraepithelial lesion
LSIL	low-grade squamous intraepithelial lesion
NMHPVPR	New Mexico HPV Pap Registry

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Figure 1. Health benefits and costs of current and improved cervical cancer screening

The figure displays the tradeoff of quality-adjusted life years (QALYs, left y-axis) and reductions in lifetime cervical cancer incidence (right y-axis) against lifetime costs (x-axis) for each of the screening scenarios. Circle represents no screening; diamonds represent cytology (cyto) only; triangle represents 3-year cytology-only from ages 21–29, switching to 5-year co-testing from age 30 (cotest); green symbols indicate current U.S. guidelines-based strategies; blue square represents current screening practice; red squares represent scenarios in which screening improvements are assumed (i.e., full adherence to the indicated screening parameter(s)); for example, the red square labeled “HPV triage” represents the scenario in which inappropriate human papillomavirus (HPV) triage testing is eliminated from current screening practice. For all scenarios, screening begins at age 21 and ends at age 65. The curve indicates the strategies that are efficient; the incremental cost-effectiveness ratios of strategies on the curve represent the increase in lifetime cost divided by the increase in QALYs compared to the next less-costly strategy. Both QALYs and lifetime costs are discounted at 3% per year.

Table 1

Model parameters and values for current screening practice from NMHPVPR *

Variable	Base-Case Value (Range)	Source
% screening at different frequencies [†]		
1-year	9.3	NMHPVPR, 2008–2011 (2)
2-year	16.2	
3-year	10.6	
4-year	35.2	
5-year	14.4	
None	14.4	
% receiving HPV triage testing within 28 days of screening, by preceding cytology result		
ASC-US	81.7 (80.8–82.6)	NMHPVPR, 2007–2012 (9)
LSIL	24.9 (22.6–27.3)	
ASC-H	42.4 (36.9–48.0)	
HSIL	21.7 (15.9–28.4)	
% receiving colposcopy (with biopsy) within 1 year of screening, by preceding cytology result		
ASC-US	6.8 (6.4–7.2)	NMHPVPR, 2007–2011 (4)
ASC-US, HPV+	49.4 (48.4–50.4)	
LSIL	50.7 (49.8–51.6)	
ASC-H	62.3 (60.0–64.6)	
HSIL	76.0 (73.8–78.1)	
% receiving excisional treatment within 1 year of cervical biopsy, by biopsy result		
Negative	1.6 (1.2–2.0)	NMHPVPR, 2007–2011 (4)
CIN1	4.1 (3.6–4.6)	
CIN2	47.3 (45.0–49.5)	
CIN3+	63.0 (60.2–65.6)	

* ASC-H, atypical squamous cells cannot exclude HSIL; ASC-US, atypical squamous cells of undetermined significance; CIN1, cervical intraepithelial neoplasia, grade 1; CIN2, cervical intraepithelial neoplasia, grade 2; CIN3, cervical intraepithelial neoplasia, grade 3; HPV, human papillomavirus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; NMHPVPR, New Mexico HPV Pap Registry.

† Assumptions for base case analysis and alternative distributions of screening frequencies used in sensitivity analysis are provided in the Appendix.

Table 2

Cancer benefits, costs, and cost-effectiveness of current screening practice and guidelines-based strategies^{*}

Strategy [†]	Cancer incidence reduction (%) [‡]	Cancer mortality reduction (%) [‡]	Lifetime cost (2012 USD)	QALY (years)	(\$ per QALY)
No screening	--	--	231 (210–286)	23.97611 (23.95955–23.98260)	--
Current screening practice	48.5 (46.6–48.8)	58.4 (57.5–58.9)	1,017 (994–1,065)	24.01637 (24.00886–24.01888)	dominated [§]
Cytology (3-year) ^{//}	80.9 (79.3–81.8)	86.7 (86.0–87.2)	1,182 (1,153–1,230)	24.03849 (24.03597–24.03921)	15,260 (12,040–16,650)
Cytology (3-year), Co-test 30+ (5-year) ^{//}	91.1 (90.4–91.9)	93.5 (93.0–93.7)	1,496 (1,425–1,609)	24.04377 (24.04303–24.04427)	59,440 (46,960–63,770)
Cytology (1-year)	91.4 (90.3–92.2)	93.8 (93.3–94.0)	2,860 (2,820–2,920)	24.04492 (24.04421–24.04517)	1,185,990 (1,040,380–1,535,750)

^{*} Values represent the base case result using the best-fitting calibrated model; parentheses indicate the minimum and maximum values across 50 calibrated parameter sets. Strategies listed in order of increasing costs. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; USD, United States dollar.

[†] For all strategies, screening begins at age 21 and ends at age 65 at intervals indicated in parentheses. For co-testing strategy, switch to co-test occurs at age 30; HPV-positive/cytology-negative women are managed by repeat co-testing at 12 months, with referral to colposcopy for any positive result (ASC-US or worse and/or HPV-positive).

[‡] Cancer reduction for each strategy reflects % reduction in lifetime risk of cervical cancer (incidence or mortality) compared to no screening.

[§] Current screening practice has an ICER of \$19,530/QALY compared to No screening; this strategy is less costly and less cost-effective (i.e., has a higher ICER) than the guidelines-based strategy of 3-year cytology screening, and therefore is weakly dominated.

^{//} These strategies represent currently recommended U.S. guidelines-based strategies (12–14).

Table 3

Cancer benefits, costs, and incremental net monetary benefits of improvements in current screening practice*

Scenarios [†]	Cancer incidence reduction (%) [‡]	Cancer mortality reduction (%) [‡]	Cost (2012 USD)	QALY (years)	INMB (\$50,000 per QALY threshold) \$	INMB (\$100,000 per QALY threshold) \$
Current screening practice	48.5 (46.6–48.8)	58.4 (57.5–58.9)	1,017 (994–1,065)	24.01637 (24.00886–24.01888)	--	--
Singular improvements						
HPV triage	48.9 (46.9–49.4)	59.1 (58.0–59.3)	1,028 (1,012–1,073)	24.01662 (24.00933–24.01842)	1 (–4–4)	12 (5–21)
Excisional treatment follow-up	57.8 (56.6–58.6)	64.1 (63.5–64.7)	1,016 (999–1,055)	24.02087 (24.01453–24.02237)	226 (210–281)	451 (419–557)
Routine (3-year) interval	60.4 (58.7–60.9)	69.0 (68.1–69.2)	1,046 (1,029–1,087)	24.02425 (24.01872–24.02557)	365 (340–458)	759 (709–943)
Colposcopy/biopsy follow-up	60.8 (59.5–61.4)	69.5 (68.4–69.0)	1,115 (1,096–1,158)	24.02477 (24.01931–24.02601)	321 (295–417)	741 (686–932)
Multiple improvements						
Colposcopy/biopsy + excisional treatment follow-up	67.7 (66.9–68.2)	72.6 (72.0–72.9)	1,118 (1,098–1,156)	24.02802 (24.02336–24.02908)	482 (447–621)	1,064 (991–1,339)
Routine (3-year) interval + excisional treatment follow-up	68.3 (67.0–68.9)	76.5 (75.5–77.1)	1,044 (1,026–1,079)	24.02980 (24.02533–24.03077)	645 (603–797)	1,316 (1,232–1,612)
Routine (3-year) interval + colposcopy/biopsy follow-up	72.2 (70.9–72.7)	82.0 (81.2–82.5)	1,157 (1,137–1,197)	24.03423 (24.03083–24.03487)	753 (697–954)	1,645 (1,531–2,044)

* Values represent the outcomes associated with full compliance to each improvement in current screening using the best-fitting calibrated model; parentheses indicate the minimum and maximum values across 50 calibrated parameter sets. HPV, human papillomavirus; INMB, incremental net monetary benefit; QALY, quality-adjusted life-year; USD, United States dollar.

[†] Scenarios are listed in order of increasing health benefit.

[‡] Cancer reduction for each strategy reflects % reduction in lifetime risk of cervical cancer (incidence or mortality) compared to no screening.

[§] The INMB for each scenario is calculated against current screening practice (baseline); see Appendix Table 4 for formal definition and interpretation of INMBs. Because of the lack of consensus on society's willingness to pay for a QALY gained in the United States, we used a range of \$50,000 to \$100,000 per QALY, but provide additional results in Appendix Table 5.