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Inefficiencies and High-Value Improvements in U.S. Cervical Cancer Screening Practice

A Cost-Effectiveness Analysis

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Background: Studies suggest that cervical cancer screening practice in the United States is inefficient. The cost and health implications of nonadherence in the screening process compared with 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.

Intervention: Current cervical cancer screening practice; improved adherence 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, and 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 adherence to screening every 3 years with cytologic testing and adherence 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 $1645.

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.

Limitation: The effect of human papillomavirus vaccination was not considered.

Conclusion: The added health benefit of improving adherence to guidelines, especially the 3-year interval for cytologic screening and diagnostic follow-up, may justify additional investments in interventions to improve U.S. cervical cancer screening practice.

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* For a list of members of the New Mexico HPV Pap Registry Steering Committee, see the **Appendix** (available at www.annals.org).
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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 evidence suggests that cervical cancer screening practice is inefficient. Variable screening rates (2, 3), with some women screened too frequently and others not screened at all, and suboptimal management of women with abnormal test results (4), with some women being overmanaged and others lost to follow-up, contribute to the inefficiencies and approximately 12 000 new cases and 4000 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 precancer 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 (HPV vaccination) and secondary (for example, 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 policymaking. 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 are being used 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

EDITORS' NOTES

Context

Studies indicate variability in cervical cancer screening practices, which may lead to inefficiencies in the diagnosis and management of cervical cancer.

Contribution

Mathematical simulation models were used to compare reductions in lifetime cervical cancer risks, quality-adjusted life-years, and costs for current cervical cancer screening practices with improved adherence to guidelines-based screening intervals (every 3 years), human papillomavirus triage testing, diagnostic referrals, and precancer treatment referrals.

Caution

The model incorporated data from only 1 state-wide, population-based registry on cervical cancer screening.

Implications

Improved adherence to cervical cancer screening guidelines can generate greater health gains with nominal increases in cost.

and biology of disease, clinical efficacy or effectiveness of health interventions, and resource use. Although these data are 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, 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, is the only existing population-based cervical cancer screening registry in the United States. Through statewide regulation, the NMHPVPR receives data from all institutions that provide cervical cancer screening services to residents of New Mexico; it enables 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, available at www.annals.org, 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, such as loss to follow-up for diagnostic and treatment procedures, to be captured.

Using a disease simulation model of the natural history of HPV and cervical cancer (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; we also 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 with 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, and -58), as well as 2 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 development of precancerous lesions. Transition probabilities can also vary by age, history of HPV infection, and prior interventions. We established baseline parameter values for the natural history component of the model by using data from large prospective cohort studies (15–17) and then calibrated the model to epidemiologic data on HPV prevalence and genotype distribution by 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 Adherence)

For guidelines-based screening, we included strategies of 1) cytologic testing alone every 3 years from age 21 to 65 years and 2) cytologic testing alone every 3 years from age 21 to 29 years with a switch to cytologic and HPV "cotesting" every 5 years from age 30 to 65 years (12, 13). We assumed that management of women with equivocal or abnormal test results followed established guidelines with full adherence (12, 14) and that follow-up for both diagnostic and precancer treatment referrals was 100%. For cotesting, women who were HPV-positive and cytologic test–negative were managed by repeated cotesting at 12 months, with referral to colposcopy for any positive re-

sult. We also considered annual cytologic screening to reflect past recommendations. Screening test characteristics and cost inputs were estimated from the published literature (Appendix Table 1, available at www.annals.org) (21–29).

Current Screening Practice

To simulate current screening practice, we incorporated data from the NMHPVPR to estimate several variables along the screening pathway, including screening frequencies, proportions of women undergoing HPV triage testing, proportions receiving diagnostic colposcopy and/or biopsy, and proportions receiving treatment for precancerous lesions with excisional procedures (Table 1) (2, 4, 9). Most cervical excisional procedures were a loop electrosurgical excision procedure (LEEP); other procedures included cone biopsy and cold knife conization. As in a previous analysis, we did not stratify by method of excision (4). Previous calculations of screening intensity, defined as the number of screening tests during a 4-year period (2008–2011) (2), were used to inform the distribution of women who are screened at different frequencies, as well as those who are never screened. For example, women who received 1 test during the 4-year period were assumed to undergo screening every 4 years, whereas women who received 4 or more tests were assumed to undergo screening annually (see Appendix for additional assumptions). We also incorporated data from the NMHPVPR on use of HPV triage testing after abnormal Papanicolaou (Pap) results within 28 days of a screening Pap (Table 1) (9) and the probability of undergoing diagnostic colposcopy and/or biopsy within 1 year of an abnormal screening Pap result, depending on the preceding Pap result (4). Similarly, we incorporated data on the probability of receiving excisional treatment of a precancerous lesion within 1 year of cervical biopsy, depending on the preceding biopsy result (4).

Because of the low use of cytologic and HPV cotesting in New Mexico during the study period (<20% in women aged 30 to 65 years) (9), we restricted our scenario of current screening practice to include cytologic testing alone. We did not consider the effect of HPV vaccination. Under these current screening practice assumptions, we projected estimates of the cumulative risks of CIN2+ and CIN3+ after abnormal Pap results and found that model-predicted outcomes correspond highly with empirical data, demonstrating both internal and external model validity (Appendix Figure 1, available at www.annals.org). Sensitivity analyses, including best-case and worst-case scenarios, evaluated the effect of uncertainty in current screening practice variables (Table 1 and Appendix Table 2, available at www.annals.org).

Improvements in Current Screening

To evaluate the discrepancy between strategies recommended by guidelines and current screening practice, we modified each of the following screening variables, alone and in combination, to reflect perfect adherence to guidelines: 1) routine cytologic screening every 3 years for all eligible women, 2) HPV triage testing only for women with atypical squamous cells of undetermined significance, 3) perfect adherence to referral for colposcopy and/or biopsy, and 4) perfect adherence to referral for precancer excisional treat-

Table 1. Model Parameters and Values for Current Screening Practice From New Mexico HPV Pap Registry

Variable	Base-Case Value (Range), %	Data Source, Year (Reference)
Proportion of women screening at different frequencies*		NMHPVPR, 2008–2011 (2)
1 y	9.3	
2 y	16.2	
3 y	10.6	
4 y	35.2	
5 y	14.4	
None	14.4	
Proportion of women receiving HPV triage testing within 28 d of screening, by preceding cytologic result		NMHPVPR, 2007–2012 (9)
ASCUS	81.7 (80.8–82.6)	
LSIL	24.9 (22.6–27.3)	
ASC-H	42.4 (36.9–48.0)	
HSIL	21.7 (15.9–28.4)	
Proportion of women receiving colposcopy (with biopsy) within 1 y of screening, by preceding cytologic result		NMHPVPR, 2007–2011 (4)
ASCUS	6.8 (6.4–7.2)	
ASCUS, 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)	
Proportion of women receiving excisional treatment within 1 y of cervical biopsy, by preceding biopsy result		NMHPVPR, 2007–2011 (4)
Negative	1.6 (1.2–2.0)	
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 high-grade squamous intraepithelial lesion; ASCUS = atypical squamous cells of undetermined significance; CIN1 = cervical intraepithelial neoplasia, grade 1; CIN2 = cervical intraepithelial neoplasia, grade 2; CIN3 = cervical intraepithelial neoplasia, grade 3 or worse; 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 (available at www.annals.org).

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 U.S. dollars*	QALY	ICER, *$ 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)	1017 (994–1065)	24.01637 (24.00886–24.01888)	Dominated§
Cytologic testing (every 3 y)‖	80.9 (79.3–81.8)	86.7 (86.0–87.2)	1182 (1153–1230)	24.03849 (24.03597–24.03921)	15 260 (12 040–16 650)
Cytologic testing (every 3 y), cotesting at age ≥30 y (every 5y)‖	91.1 (90.4–91.9)	93.5 (93.0–93.7)	1496 (1425–1609)	24.04377 (24.04303–24.04427)	59 440 (46 960–63 770)
Cytologic testing (every year)	91.4 (90.3–92.2)	93.8 (93.3–94.0)	2860 (2820–2920)	24.04492 (24.04421–24.04517)	1 185 990 (1 040 380–1 535 750)

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-year.
* Values represent the base-case result obtained by using the best-fitting calibrated model; parentheses indicate the minimum and maximum values across 50 calibrated parameter sets. Strategies are listed in order of increasing costs.
† For all strategies, screening begins at age 21 y and ends at age 65 y at intervals indicated in parentheses. For cotesting strategies, switching to cotesting occurs at age 30 y; human papillomavirus (HPV)–positive/cytologic testing–negative women are managed by repeated cotesting at 12 mo, with referral to colposcopy for any positive result (atypical squamous cells of undetermined significance or worse and/or HPV-positive).
‡ Cancer reduction for each strategy reflects percentage reduction in lifetime risk for cervical cancer (incidence or mortality) compared with no screening.
§ Current screening practice has an ICER of $19 530/QALY compared with no screening; this strategy is less costly and less cost-effective (i.e., has a higher ICER) than the guidelines-based strategy of triennial cytologic screening, and therefore is weakly dominated.
‖ These strategies represent currently recommended U.S. guidelines-based strategies (12–14).

ment. For all scenarios, screening was initiated at age 21 years and ended at age 65 years.

Analysis

Main model-projected outcomes included health benefits, in terms of reductions in lifetime risk for 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 of precancerous lesions and invasive cancer (for example, tests, procedures, hospitalizations), based on national-average Medicare reimbursement rates and cost estimates from a previous analysis (Appendix Table 1, available at www.annals.org) (21, 26). Direct nonmedical 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 with 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).

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 subtracts the incremental cost (32). Positive INMB values indicate that the scenario results in a net savings per woman when the QALY benefit is also considered, signaling a favorable cost-effectiveness profile. Because the costs of specific interventions for improving adherence 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 toward interventions in order 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 3, available at www.annals.org.

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RESULTS

Current Screening Practice Versus Guideline Recommendations

Compared with 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 cytologic screening every 3 years resulted in greater cancer benefit (80.9% incidence reduction; 86.7% mortality reduction) and a more attractive (that is, lower) ICER, thereby dominating current screening practice; cytologic screening every 3 years

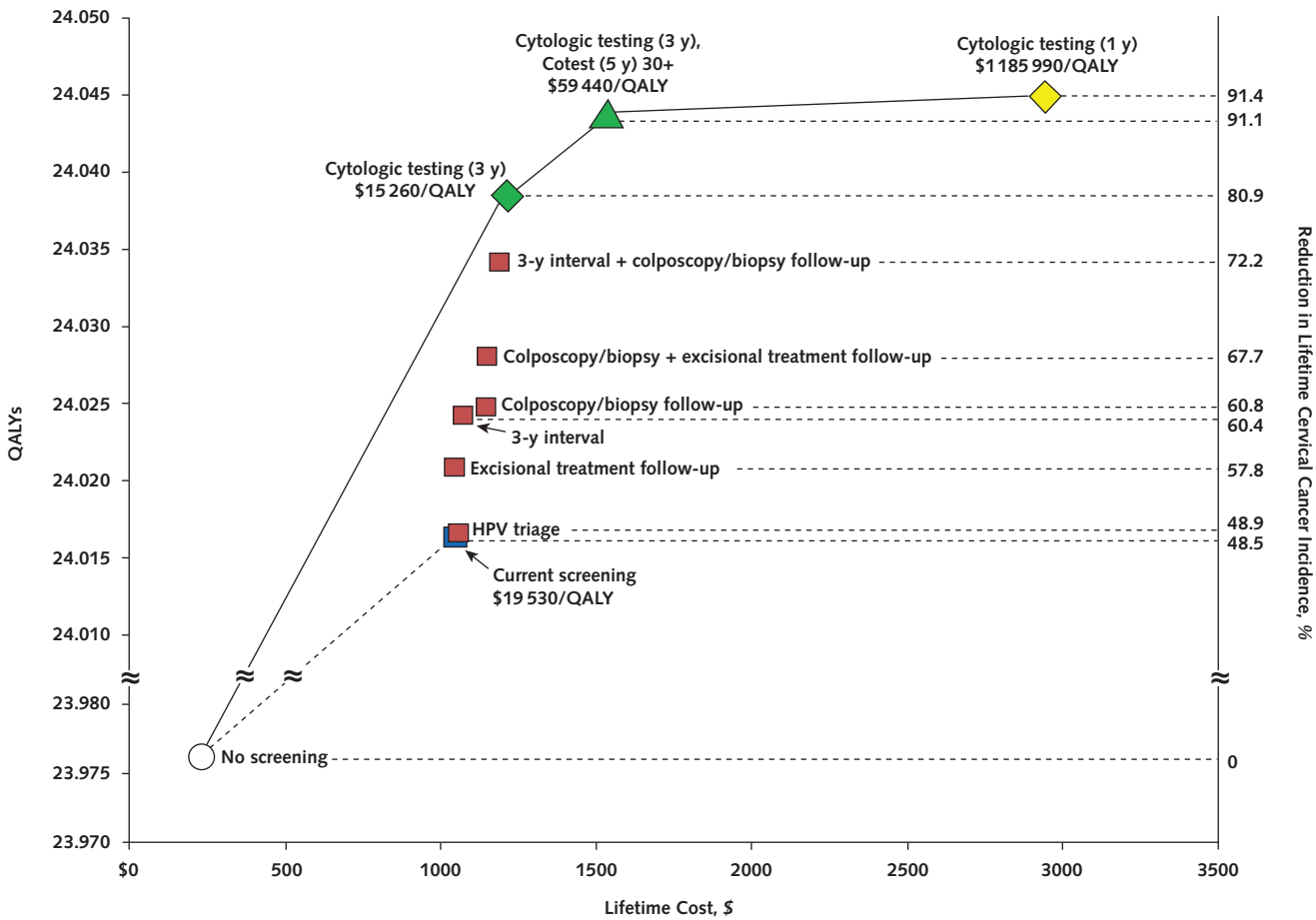
compared with no screening yielded an ICER of $15 260 per QALY gained. Switching from cytologic testing every 3 years to cotesting every 5 years at age 30 years increased cancer benefit (91.1% incidence reduction; 93.5% mortality reduction) but at an increased lifetime cost with an ICER of $59 440 per QALY. Annual cytologic 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 more than $1 million per QALY gained.

Our results were stable throughout a probabilistic sensitivity analysis that used a sample of 50 calibrated natural history parameter sets. Most notably, the scenario of current screening practice was inefficient (that is, dominated) in all 50 analyses. Both guidelines-based strategies remained efficient and less than $100 000 per QALY in all 50 simulations, whereas annual cytologic testing consistently exceeded $1 million per QALY.

Improvements in Current Screening Practice

The Figure shows the changes in lifetime costs, QALYs, and cancer incidence reductions with 1 or more improvements in the screening process. Perfect adherence to HPV triage testing had very little effect on outcomes compared with current screening practice; in contrast, scenarios with perfect follow-up for excisional treatment referrals, perfect adherence to screening every 3 years with routine cytologic testing, and perfect follow-up for diagnostic colposcopy/biopsy referrals 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 more than 60% with either tri-

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



Tradeoff of 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. The circle represents no screening; diamonds represent cytologic testing only; and the triangle represents cytologic testing every 3 years from ages 21 to 29 years, switching to cotesting every 5 years from age 30 years. Green symbols indicate current U.S. guidelines–based strategies; the blue square represents current screening practice. Red squares represent scenarios in which screening improvements are assumed (i.e., full adherence to the indicated screening measures); for example, the red square labeled "HPV triage" represents the scenario in which inappropriate HPV triage testing is eliminated from current screening practice. For all scenarios, screening begins at age 21 years and ends at age 65 years. 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 with the next less-costly strategy. Both QALYs and lifetime costs are discounted at 3% per year. HPV = human papillomavirus; QALY = quality-adjusted life-year.

Table 3. Cancer Benefits, Costs, and Incremental Net Monetary Benefits of Improvements in Current Screening Practice*

Scenarios†	Cancer Incidence Reduction, %‡	Cancer Mortality Reduction, %‡	Lifetime Cost, *2012 U.S. dollars*	QALY	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)	1017 (994–1065)	24.01637 (24.00886–24.01888)	–	–
Singular improvements						
HPV triage	48.9 (46.9–49.4)	59.1 (58.0–59.3)	1028 (1012–1073)	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)	1016 (999–1055)	24.02087 (24.01453–24.02237)	226 (210–281)	451 (419–557)
Routine (every 3 y) interval	60.4 (58.7–60.9)	69.0 (68.1–69.2)	1046 (1029–1087)	24.02425 (24.01872–24.02557)	365 (340–458)	759 (709–943)
Colposcopy/biopsy follow-up	60.8 (59.5–61.4)	69.5 (68.4–69.8)	1115 (1096–1158)	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)	1118 (1098–1156)	24.02802 (24.02336–24.02908)	482 (447–621)	1064 (991–1339)
Routine (every 3 y) interval + excisional treatment follow-up	68.3 (67.0–68.9)	76.5 (75.5–77.1)	1044 (1026–1079)	24.02980 (24.02533–24.03077)	645 (603–797)	1316 (1232–1612)
Routine (every 3 y) interval + colposcopy/biopsy follow-up	72.2 (70.9–72.7)	82.0 (81.2–82.5)	1157 (1137–1197)	24.03423 (24.03083–24.03487)	753 (697–954)	1645 (1531–2044)

HPV = human papillomavirus; INMB = incremental net monetary benefit; QALY = quality-adjusted life-year.
* Values represent the outcomes associated with full adherence to each improvement in current screening using the best-fitting calibrated model; values in parentheses indicate the minimum and maximum values across 50 calibrated parameter sets.
† Scenarios are listed in order of increasing health benefit.
‡ Cancer reduction for each strategy reflects percentage reduction in lifetime risk for cervical cancer (incidence or mortality) compared with no screening.
§ The INMB for each scenario is calculated against current screening practice (baseline); see **Appendix Table 3** (available at www.annals.org) 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 4** (available at www.annals.org).

ennial cytologic screening or perfect colposcopy/biopsy follow-up. As expected, assuming more than 1 improvement resulted in greater QALYs and cancer benefits than any single improvement. Notably, when we assumed routine cytologic screening every 3 years for all eligible women simultaneously with perfect colposcopy/biopsy follow-up, an interactive effect yielded more QALYs than the sum of the independent effects and a cancer incidence reduction of 72.2%.

Scenarios with perfect adherence to cytologic screening every 3 years for all eligible women and perfect colposcopy/biopsy follow-up also had the highest INMB values, which were similar at WTP thresholds of $50 000 per QALY ($365 and $321, respectively) and $100 000 per QALY ($759 and $741, respectively) (**Table 3**), indicating that these improvements may be worthy of high investments. By comparison, a scenario of perfect adherence to excisional treatment yielded INMBs of $226 for the $50 000 per QALY threshold and $451 for the $100 000 per QALY threshold. Human papillomavirus triage testing only for women with a result of atypical squamous cells of undetermined significance had the lowest INMBs—$1 for the $50 000 per QALY threshold and $12 for the $100 000 per QALY threshold—indicating that intervention costs to achieve full adherence to appropriate HPV triage testing would have to be low for this improvement to be cost-effective compared with current practice. As with the QALY gains, the INMBs increased when more than 1 improvement was assumed simultaneously; the interaction of universal cytologic screening every 3 years and perfect adherence to colposcopy/biopsy referral led to a greater INMB (for example, $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 4**, available at www.annals.org). Results were sensitive to assumptions regarding the current distribution of women screened at different frequencies (**Appendix Figure 2**, available at www.annals.org). For example, at a WTP threshold of $100 000 per QALY, INMB values ranged from $485 (assuming women are currently screened at a higher frequency than the base case) to $882 (assuming women are screened at a lower frequency). Under the assumption of higher screening frequency, the INMB for improving colposcopy/biopsy follow-up was greater than that for equalizing the routine screening interval; otherwise, the relative ordering of improvement scenarios in terms of INMB values was stable across all analyses. Other screening practice variables were not influential, and variations in best-case/worst-case scenario analyses were driven by the uncertainty in screening frequency.

DISCUSSION

Using population-based data on screening 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 account-

ing for variable screening frequency, inappropriate HPV triage testing, and imperfect adherence 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 are more costly, the gains in health are also relatively greater.

Our analysis indicates that improvements in current screening practice can generate greater health gains with nominal changes in costs. Even without considering any implementation costs of improving adherence, scenarios with higher screening adherence were generally more costly than current screening (**Figure**); however, the added costs were low (**Table 3**). The INMB of each improvement scenario (vs. 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 WTP threshold. On the basis of our findings, we can conclude that economic investments toward interventions that improve adherence to cervical cancer screening guidelines can be substantial.

In deconstructing the individual effects of the different breakdowns in current screening practice, we found that achieving universal screening every 3 years with cytologic testing for all eligible women and perfect adherence to colposcopy/biopsy referrals yielded the greatest gains in health compared with current practice, indicating that these improvements may be high priorities to consider. Across a range of WTP thresholds, adherence to the triennial cytologic testing interval and adherence to colposcopy/biopsy referrals were also associated with the highest INMBs, especially when they occurred simultaneously. This finding indicates that these improvements in screening may be worthy of high investment. The relatively lower added benefit of improving only excisional treatment adherence signals that important (that is, high-risk) women are not being screened and are lost in the transition between screening and diagnosis; as expected, the effect of these improvements was heightened when adherence to excisional treatment referral was simultaneously improved. In all scenarios (alone and in combination with other improvements), eliminating inappropriate HPV triage testing yielded only a slight increase in health and the lowest INMB values.

To our knowledge, 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 laboratory reports on all women screened in New Mexico from 2007 to 2011 or 2012 (depending on the specific measure) and therefore provide an empirical assessment of screening practice based on individual-level data on coverage and follow-up. A previous analysis relied on self-reported data from the National Health Interview Survey (3), which is subject to recall bias and reports much greater screening intensity than does the NMHPVPR, resulting in higher cost and QALY estimates (33). The previous 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.

Our analysis had several limitations. As noted in previous reports (2, 4, 9, 10), although we are confident that NMHPVPR reporting is very thorough, data from the NMHPVPR rely 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, although our screening measures 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; therefore, we made simplified assumptions regarding screening utilization over a longer period. Although the population in New Mexico is largely similar to the overall U.S. population in terms of demographic and social characteristics (**Appendix Table 5**), important differences in the composition of race/ethnicity (for example, a higher proportion of Hispanic and Latina women in New Mexico) and the largely rural nature of the state 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 (**Appendix Figure 3**), 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, the INMB estimates are generated under assumptions of perfect adherence and represent, in principle, the maximum economic cost that society would be willing to expend to attain perfect adherence; however, perfect adherence 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 improve adherence 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 with 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 complete diagnostic follow-up and that we can make sizable investments toward these

improvements. These model-projected outcomes can inform strategic investments in interventions designed to improve the screening process, as well as examine the effect of new HPV-related technologies.

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Appendix

New Mexico HPV Pap Registry

Steering Committee Members

Members of the New Mexico HPV Pap Registry (NMHPVPR) Steering Committee reviewed and gave input to the manuscript as contributors and supported the concept and directions of the NMHPVPR, including the evaluations presented in this manuscript. The NMHPVPR Steering members participating are as follows: Nancy E. Joste, MD, University of New Mexico Health Sciences Center and Tricore Reference Laboratories; Walter Kinney, MD, Kaiser Permanente Northern California; Cosette M. Wheeler, PhD, University of New Mexico Health Sciences Center; William C. Hunt, MS, University of New Mexico Health Sciences Center; Scott Norville, MD, New Mexico Department of Health; Alan Waxman, MD, MPH, University of New Mexico Health Sciences Center; David Espey, MD, Centers for Disease Control and Prevention; Steven Jenison, MD, Community Member; Mark Schiffman, MD, MPH, National Cancer Institute; Philip Castle, PhD, MPH, Albert Einstein College of Medicine; Vicki Benard, PhD, Centers for Disease Control and Prevention; Debbie Saslow, PhD, American Cancer Society; Jane J. Kim, PhD, Harvard T.H. Chan School of Public Health; Mark H. Stoler, MD, University of Virginia; Jack Cuzick, PhD, Wolfson Institute of Preventive Medicine; Giovanna Rossi Pressley, MSc, Collective Action Strategies and RWJF Center for Health Policy at University of New Mexico; and Kevin English, RPh, MPH, Albuquerque Area Southwest Tribal Epidemiology Center. No compensation was received for contributions to this manuscript by any named authors or by the NMHPVPR Steering Committee members.

Overview

The NMHPVPR was established in collaboration with the New Mexico Department of Health to monitor the state's cervical cancer screening and prevention programs and to determine the public health significance and cost-effectiveness of longitudinal changes affecting HPV-related cervical disease incidence. Currently, New Mexico is the only state with the capacity to fully monitor cervical screening and prevention with population-based, woman-based information systems. In anticipation of the critical need for U.S. population-based surveillance of cervical cancer screening programs, the New Mexico Notifiable Diseases and Conditions incorporated mandatory state-wide reporting via NMAC 7.4.3. This regulation specifies that laboratories must report all Pap cytologic, cervical pathologic, and HPV tests performed on individuals residing in New Mexico to the NMHPVPR.

Laboratory reporting to the NMHPVPR began in 2006. Standard file formats and secure encrypted data delivery systems have been implemented at laboratories throughout New Mexico. Laboratories representing more than 95% of the state's data have provided reports to the NMHPVPR and are reporting once or twice each month. In addition, data are received from multiple national corporations (such as Quest, LabCorp, AmeriPath, BioReference, Tenet Healthcare, and ARUP). All reporting entities have provided retrospective data beginning January 2006, and many have provided retrospective data before 2006. Analysis of NMHPVPR data for provider facility and ZIP code demonstrates that few New Mexico residents receive Pap tests, cervical biopsies, or HPV tests in neighboring states; rather, laboratories outside of New Mexico are contracted by a small number of New Mexico providers. We estimate that we capture reporting for 97% to 99% of the targeted state-wide events.

Generalizability

The NMHPVPR represents a one-of-a-kind public health resource documenting the delivery of cervical

cancer prevention efforts across the screening continuum and transcending the state, organization, facility, provider, and patient levels. Although a state-wide registry, the NMHPVPR is intended as a national and international sentinel surveillance program. We provide comparisons that provide reassurance about the overall comparability of the New Mexico population with the broader U.S. population: 1) demographic, social, and economic characteristics from the American Community Survey, 2009-2013, conducted by the U.S. Census Bureau (Appendix Table 5) (34); 2) cancer incidence and mortality data from the Surveillance, Epidemiology, and End Results program (Appendix Figure 3) (1); and 3) screening outcomes in terms of 3-year cumulative risk for high-grade cervical disease from Kaiser Permanente Northern California (35) and NMHPVPR (10) (also used for model validation in Appendix Figure 1).

Screening Data

Previous calculations of screening intensity, defined as the number of screening tests during a 4-year period (2008–2011) (2), were used to inform the distribution of women who underwent screening at different frequencies, as well as those who never undergo screening (Appendix Table 2). In the base case, we assumed all women who received 4 or more tests during the 4-year period undergo screening annually; for those with 3 tests, 50% undergo screening annually and 50% screen biennially; for those with 2 tests, 50% undergo screening biennially and 50% undergo screening triennially; all who received 1 test undergo screening every 4 years; for those with 0 tests, 50% undergo screening every 5 years and 50% never undergo screening.

In sensitivity analysis, we evaluated scenarios of "low" and "high" screening coverage assuming different distributions of screening frequencies based on the NMHPVPR data. In the "low"-frequency scenario, all women who received 4 or more tests during the 4-year period were assumed to undergo screening annually; all women who received 2 or 3 tests undergo screening biennially; for those who received 1 test, 50% undergo screening triennially and 50% undergo screening every 4 years; for those with 0 tests, 25% undergo screening every 5 years and 75% never undergo screening. In the "high"-frequency scenario, all women who received 3 or more tests during the 4-year period were assumed to undergo screening annually; all who received 2 tests undergo screening biennially; for those with 1 test, 25% undergo screening triennially and 75% undergo screening every 4 years; for those with 0 tests, 75% undergo screening every 5 years and 25% never undergo screening.

Additional sensitivity analyses evaluated the effect of data uncertainty in the proportions receiving HPV triage testing, colposcopy/biopsy, and excisional treatment (input ranges are displayed in Table 1). We analyzed best- and worst-case scenarios to explore the extreme ranges of these screening practice data simultaneously. The optimistic (best-case) scenario of current screening practice reflects high screening frequency, high adherence to HPV triage testing, and high adherence to colposcopy/biopsy and excisional treatment referrals. The pessimistic (worst-case) scenario reflects low screening frequency, low adherence to HPV triage testing, and low adherence to colposcopy/biopsy and excisional treatment referrals.

Other model inputs associated with the screening process that did not originate from the NMHPVPR, such as screening test performance and costs, were estimated from the published literature (Appendix Table 1) (21–29).

First-Order Monte Carlo Simulation Model

Model Structure

The individual-based model of the natural history of HPV and cervical cancer comprises mutually exclusive health states that represent established stages of cervical disease (11). Individual girls enter the model at an early age (age 9 years) with a healthy cervix and transition between health states on a monthly basis until death. HPV infection is stratified by several individual high-risk genotypes (HPV-16, -18, -31, -33, -45, -52, -58); other high-risk types and low-risk types are pooled into separate health states. Invasive cancer can be detected through symptoms or screening at the local, regional, or distant stage. Death from background mortality can occur from any health state, and excess stage-dependent mortality can occur from the cancer states. Transitions to and from health states are governed by HPV genotype and time since HPV acquisition or lesion development. Transition probabilities can also vary by age; history of HPV infection; and previous interventions, such as treatment of precancerous lesions. The model can closely adhere to complex screening algorithms dependent on prior events (for example, screening result or biopsy result) and keeps track of each individual woman's health status and resource use over time, which are then aggregated at the population level.

Model Parameterization and Calibration

Details of the model development process, including initial parameterization and calibration, have been previously published (11). Derivation of model parameter values requires an iterative process involving comprehensive literature reviews, data synthesis and analysis, consultations with experts, and explorations of the influence of uncertain parameters and assumptions in

the model. HPV incidence rates, as a function of genotype and age, were derived from published data from a prospective cohort of sexually active women age 15 to 85 years in Bogota, Colombia, because of the availability of genotype incidence by age (17). Because HPV incidence is known to vary by population as a function of sexual behaviors, age-specific HPV incidence and natural immunity following initial infection were considered important candidates for calibration. For transitions occurring from the HPV state, we leveraged primary longitudinal data from the control arm of the Costa Rica Vaccine Trial and a natural history study of HPV in Guanacaste, Costa Rica, which enabled derivation of time-dependent rates of clearance and progression by genotype (16, 36). Type-specific data on CIN2 and CIN3 regression and progression are limited (37), but we experimented with values similar in magnitude to those of published studies. Because of the computational intensity of microsimulation models, we selected the parameters for which we had a range of plausible values but also good information on calibration targets (for example, HPV prevalence to calibrate HPV incidence).

To calibrate the model, we set plausible search ranges around baseline input values and performed repeated model simulations in the absence of any preventive intervention. For each simulation, we randomly selected a single value for each of the uncertain parameters from the identified plausible range, creating a unique vector of parameter values (that is, a parameter "set"). After more than 1 000 000 repeated samplings, we identified the parameter sets with the highest correspondence to the empirical calibration target data by calculating and aggregating the log-likelihood of model-projected outcomes. We used the parameter set with the highest likelihood score (that is, the best overall fit to the empirical data) for all primary analyses and a sample of 50 top-scoring sets in order to capture uncertainty in the model parameters as a form of probabilistic sensitivity analysis.

Model Validation

After calibration, we assessed validation of the model by comparing model-projected outcomes against observed data not used in model development. We projected estimates of cumulative risks for CIN2 or worse and CIN3 or worse after abnormal cytologic results and found that the model outcomes corresponded highly with those observed in the NMHPVPR data (10), demonstrating internal validity, as well as in a large health delivery organization whose data were not used to inform model parameters or calibration (Kaiser Permanente Northern California) (35), demonstrating external validity (Appendix Figure 1).

Model Outcomes

The equations, definitions, and interpretations of main model outcomes are summarized in Appendix Table 3.

Additional Results

Effect of Current Screening Parameters

In one-way and multiway (best-case/worst-case) sensitivity analysis, INMB results were most sensitive to assumptions regarding the screening frequency distribution for current screening practice (Appendix Figure 2). When we assumed lower overall screening frequency (for example, higher proportion of women never screened) than the base case (Appendix Table 2), the INMB associated with equalizing the screening interval to triennial cytologic testing for all screen-eligible women increased by 16% (from $759 to $882); in contrast, when we assumed higher overall screening (for example, higher proportion of women screening annually), the INMB decreased by 36% (to $485). Not surprisingly, these findings indicate that the value of equalizing the screening interval in the whole population is greater when the baseline current screening is less frequent (and vice versa). In contrast, the INMBs for improving colposcopy/biopsy follow-up and excisional treatment follow-up increased when we assumed that current screening is more frequent than in the base case, although the changes were not as pronounced; for example, the INMB associated with perfect colposcopy/biopsy adherence increased by 3% (from $741 to $762) and the INMB associated with perfect excisional treatment adherence increased by 7% (from $451 to $483). When we considered improvements in both screening interval and colposcopy/biopsy follow-up simultaneously under assumptions of more frequent current screening, the downward effect of improving screening interval outweighed the upward effect of colposcopy/biopsy adherence, and the INMB decreased by 17% (from $1645 to $1372); this trend was similar when improvements in screening interval and excisional treatment adherence were considered simultaneously.

Effect of WTP Threshold

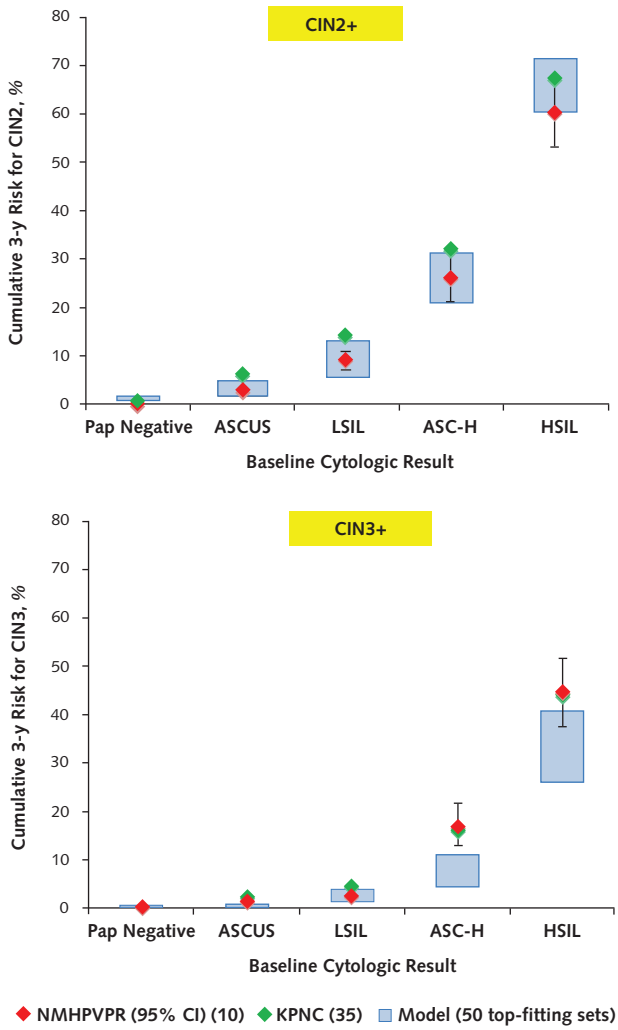
Because there is no consensus on the WTP for a QALY gained in the United States, we explored a threshold range of $50 000 to $200 000 per QALY gained (30) (Appendix Table 4).

Appendix Table 1. Screening Test Characteristics and Cost Inputs

Model Parameter	Input Values
Test characteristics (%)	
Cytology (22–24)*	
Sensitivity	70
Specificity	95
HPV DNA test (24, 25)†	
Sensitivity	91
Specificity	93
Costs (2012 U.S. dollars)‡	
Screening test (21, 26–28)	
Cytology	37
HPV DNA test	49
Office visit	28
Patient time and transport	27
Diagnostic follow-up (21, 26–28)	
Colposcopy	395
Biopsy	65
Office visit	65
Patient time and transport	56
Treatment for CIN2,3 (21)§	3610
Treatment for cervical cancer (21)§	
Local invasive cancer	28 360
Regional invasive cancer	30 350
Distant invasive cancer	48 620

CIN2 = cervical intraepithelial neoplasia, grade 2; CIN3 = cervical intraepithelial neoplasia, grade 3; HPV, human papillomavirus.
* Cytology sensitivity (specificity) values represent probabilities of ASC-US or worse (<ASC-US) given presence (absence) of CIN2 or worse health status.
† HPV DNA testing is assumed to be 100% sensitive (specific) in detecting the presence (absence) of high-risk HPV types (pooled or by genotype). Under this assumption, the model generates an implied clinical sensitivity for detecting CIN2 or worse of 91.0% and specificity of 93.0%.
‡ Costs were inflation-adjusted to constant 2012 U.S dollars using the medical component of the Consumer Price Index (29).
§ Treatment costs were inclusive of cost of procedures, office visit, and woman's time.

Appendix Figure 1. Validation of model-predicted 3-y cumulative risk for CIN2+ (*top*) and CIN3+ (*bottom*), by baseline cytologic result in women aged 30 y or older against empirical data (10, 35).



ASC-H = atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; ASCUS = atypical squamous cells of undetermined significance; CIN2+ = cervical intraepithelial neoplasia, grade 2 or worse; CIN3+ = cervical intraepithelial neoplasia, grade 3 or worse; HSIL = high-grade squamous intraepithelial lesion; LSIL = low-grade squamous intraepithelial lesion; NMHPVPR = New Mexico HPV Pap Registry; Pap = Papanicolaou.

Appendix Table 2. Proportion of Population Screening at Different Frequencies: Alternative Scenarios Used in Sensitivity Analysis*

Frequency	Base Case	Low	High
1-year	9.3	3.6	14.9
2-year	16.2	32.5	21.1
3-year	10.6	17.6	8.8
4-year	35.2	17.6	26.4
5-year	14.4	7.2	21.5
None	14.4	21.5	7.2

* Estimates based on screening intensity reported in Cuzick et al (2). See section above for details.

Appendix Table 3. Definition and Interpretation of Study Outcomes

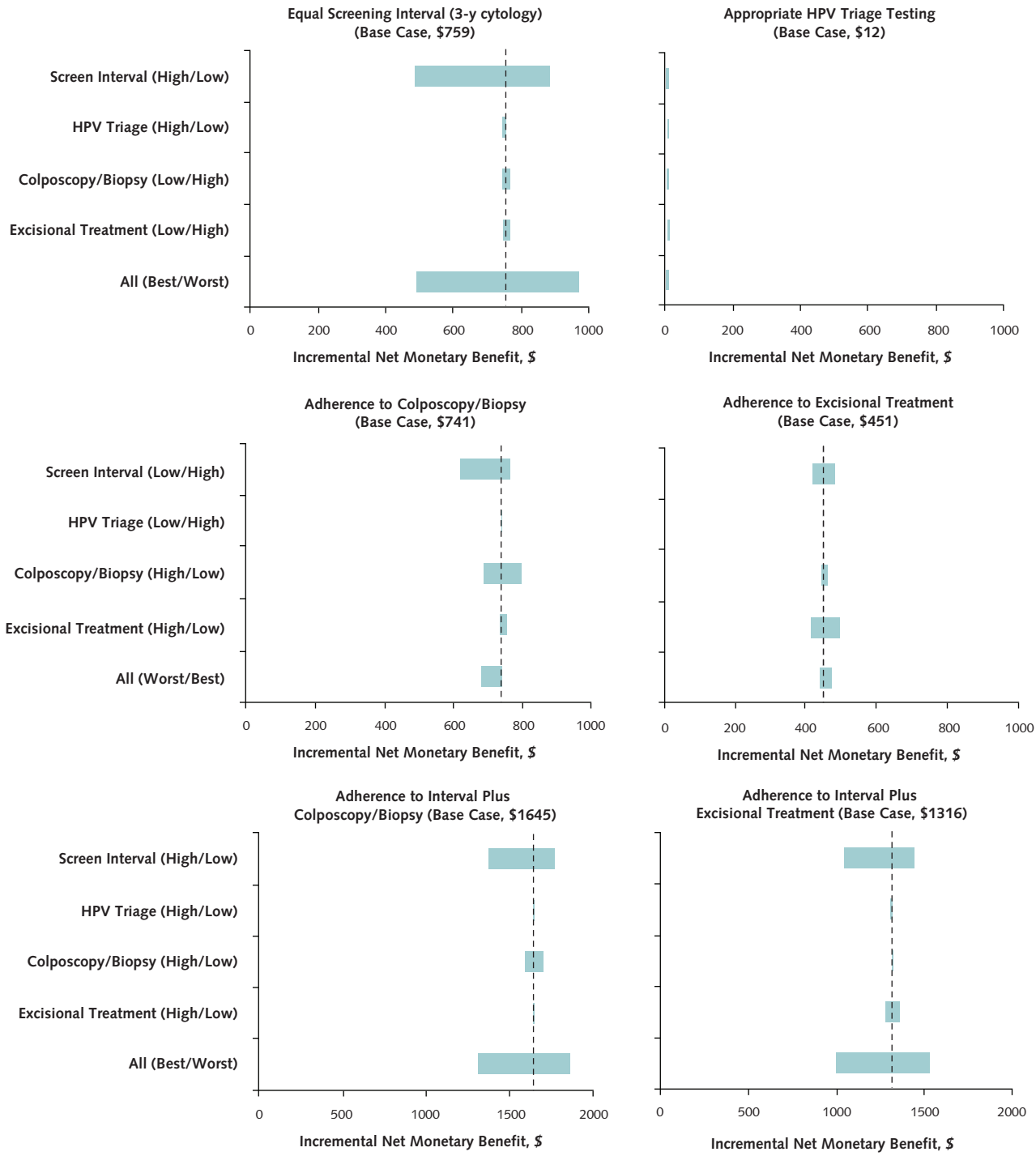
Outcome	Equation	Definition/Interpretation
Cancer reduction (incidence or mortality)	$\frac{\text{CC risk}_{no\ screen} - \text{CC risk}_{screen}}{\text{CC risk}_{no\ screen}} \times 100$	Percent reduction in lifetime cervical cancer risk (incidence or mortality) associated with screening, compared to no screening.
Incremental cost-effectiveness ratio (ICER)	$\frac{\text{Cost}_{strategy\ 2} - \text{Cost}_{strategy\ 1}}{\text{QALY}_{strategy\ 2} - \text{QALY}_{strategy\ 1}}$	Net gain in total cost divided by net gain in health effect of one strategy (strategy 2) compared to the next less costly strategy (strategy 1). In this analysis, the ICER is expressed as a "cost per quality-adjusted life year (QALY) gained." The ICER is an indicator of an intervention's efficiency or "value for money"; when an intervention has an ICER that is less than the willingness to pay (WTP) for a health unit (e.g., QALY) gained, it may be considered "good value for money." In the United States, a range of $50,000 to $100,000 per QALY has been used; recently, a WTP of up to $200,000 per QALY has been suggested (30).
Incremental net monetary benefit (INMB)	$\underbrace{\Delta\text{QALY} \times WTP}_{\text{"expected" cost}} - \underbrace{\Delta\text{Cost}}_{\text{"actual" cost}}$ where $\Delta\text{QALY} = (\text{QALY}_{improved} - \text{QALY}_{current})$ $\Delta\text{Cost} = (\text{Cost}_{improved} - \text{Cost}_{current})$, and WTP = willingness-to-pay threshold	A derivative of the ICER, the INMB indicates efficiency for a *pre-specified* willingness-to-pay (WTP) threshold. In this analysis, the INMB of each improvement scenario is compared against current screening practice to provide a measure of how much economic investment could be made per woman to achieve the improvement without exceeding the WTP. The difference in the *expected* cost (given a specific WTP threshold and the predicted health gain from the improvement(s)) and *actual* (model-predicted) cost of the scenario represents the dollar amount that can be increased to achieve the improvement while keeping screening cost-effective (i.e., such that the ICER of improved screening will equal the WTP threshold). In the vast majority of scenarios evaluated, the INMB had a positive value, which indicates that additional costs can be incurred to achieve the desired improvement.

Appendix Table 4. Incremental Net Monetary Benefits of Improved Screening Practice*

Improvement in Current Screening Practice	Willingness to Pay *($ per QALY)*			
	50 000	100 000	150 000	200 000
Singular improvements				
Routine (3-y) interval	365	759	1152	1,546
HPV triage testing	1	12	24	37
Colposcopy/biopsy follow-up	321	741	1161	1581
Excisional treatment follow-up	226	451	676	901
Multiple improvements				
Colposcopy/biopsy + excisional treatment follow-up	482	1064	1647	2229
3-year interval + excisional treatment follow-up	645	1316	1987	2659
3-year interval + colposcopy/biopsy follow-up	753	1645	2538	3431
Full adherence to guidelines				
Cytology (3-y interval)†	940	2046	3152	4258
Cytology (3-y interval); cotest (5-y interval) 30+†	891	2261	3630	5000

HPV = human papillomavirus; QALY = quality-adjusted life-year.
* Values represent the incremental net monetary benefit (in 2012 U.S. dollars) associated with full adherence to each improvement in screening according to U.S. recommended guidelines (12-14), compared to current screening practice.
† These scenarios reflect current recommended guidelines with perfect adherence throughout the screening process; for cotesting strategy, 3-y cytology begins at age 21 years and switch to cotesting occurs at age 30 years; HPV-positive/cytology test–negative women are managed by repeated cotesting at 12 mo, with referral to colposcopy for any positive result (ASCUS or worse and/or HPV-positive).

Appendix Figure 2. Effect of screening parameter uncertainty on incremental net monetary benefits at a willingness-to-pay threshold of $100 000 per quality-adjusted life-year.



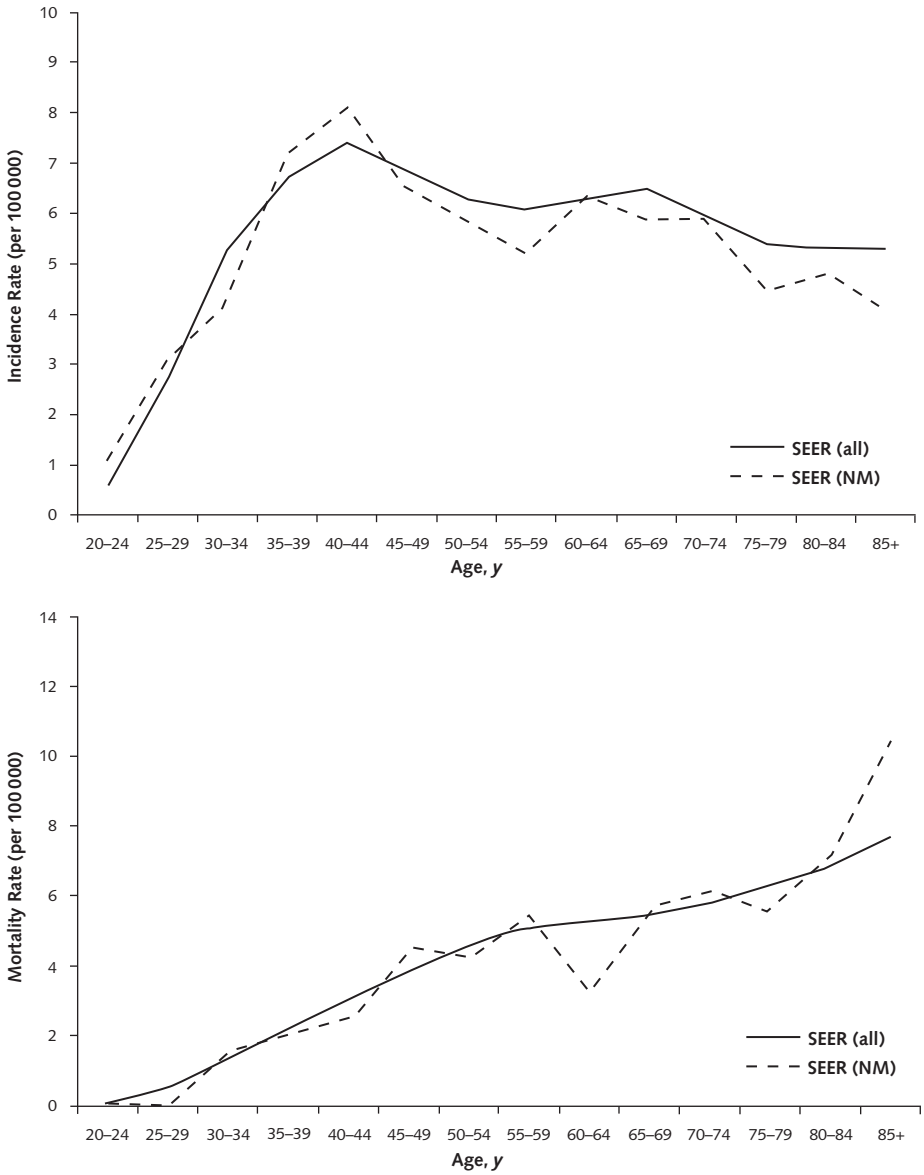
HPV = human papillomavirus.

Appendix Table 5. Comparison of Demographic, Social, and Economic Characteristics Between the United States and New Mexico Populations From the American Community Survey, 2009–2013*

Variable	United States	New Mexico
Demographic characteristics		
Sex		
Male	49.20%	49.50%
Female	50.80%	50.50%
Age		
Under 5 y	6.40%	6.80%
5–9 y	6.60%	6.90%
10–14 y	6.60%	6.90%
15–19 y	7.00%	7.10%
20–24 y	7.10%	7.20%
25–34 y	13.40%	13.10%
35–44 y	13.10%	11.90%
45–54 y	14.30%	13.60%
55–59 y	6.50%	6.60%
60–64 y	5.60%	6.00%
65–74 y	7.40%	7.90%
75–84 y	4.20%	4.30%
≥85 y	1.80%	1.60%
Race and ethnicity		
White	76.40%	75.60%
Black or African American	13.60%	2.70%
American Indian and Alaska Native	1.70%	10.40%
Asian	5.70%	1.90%
Native Hawaiian and Other Pacific Islander	0.40%	0.20%
Other race	5.30%	12.40%
Hispanic or Latino (of any race)	16.60%	46.70%
Social characteristics		
Marital status (females aged ≥15 y)		
Never married	29.10%	29.80%
Now married, except separated	47.00%	44.80%
Separated	2.50%	2.30%
Widowed	9.20%	8.80%
Divorced	12.10%	14.30%
Educational attainment		
Less than 9th grade	5.90%	7.30%
9th to 12th grade, no diploma	8.00%	9.00%
High school graduate (includes equivalency)	28.10%	26.40%
Some college, no degree	21.20%	23.90%
Associate's degree	7.80%	7.50%
Bachelor's degree	18.00%	14.70%
Graduate or professional degree	10.80%	11.10%
Economic characteristics		
Employment status (females aged ≥16 y)		
Civilian labor force	59.00%	55.90%
Employed	53.60%	50.90%
Income and benefits (2013 inflation-adjusted dollars)		
<$10 000	7.20%	9.40%
$10 000–$14 999	5.40%	6.40%
$15 000–$24 999	10.80%	12.90%
$25 000–$34 999	10.30%	11.40%
$35 000–$49 999	13.60%	14.40%
$50 000–$74 999	17.90%	17.20%
$75 000–$99 999	12.20%	11.30%
$100 000–$149 999	12.90%	10.60%
$150 000–$199 999	4.90%	3.60%
≥$200 000	4.80%	2.90%
Health insurance coverage		
With health insurance coverage	85.10%	80.80%
With private health insurance	66.00%	55.10%
With public coverage	30.20%	37.00%
No health insurance coverage	14.90%	19.20%
Percentage of families and people whose income in the past 12 mo is below the poverty level		
All families	11.30%	15.60%
All people	15.40%	20.40%
Under 18 y	21.60%	28.90%
18–64 y	14.30%	18.80%
≥65 y	9.40%	12.10%

* From reference 34.

Appendix Figure 3. Comparison of age-specific cervical cancer incidence (*top*) and mortality (*bottom*) rates between United States and New Mexico from the Surveillance, Epidemiology, and End Results Program, 2000–2012 (1).



NM = New Mexico; SEER = Surveillance, Epidemiology, and End Results Program.