OPEN

Enduring Consensus Guidelines for Cervical Cancer Screening and Management: Introduction to the Scope and Process

Nicolas Wentzensen, MD, PhD,[1] Francisco Garcia, MD,[2] Megan A. Clarke, PhD,[1] L. Stewart Massad, MD,[3] Li C. Cheung, PhD,[1] Didem Egemen, PhD,[1] Richard Guido, MD,[4] Warner Huh, MD,[5] Debbie Saslow, PhD,[6] Robert A. Smith, PhD,[6] Elizabeth R. Unger, PhD,[7] Rebecca B. Perkins, MD,[8] for the Enduring Consensus Cervical Cancer Screening and Management Guidelines Committee

Objectives: The Enduring Consensus Cervical Cancer Screening and Management Guidelines (Enduring Guidelines) effort is a standing committee to continuously evaluate new technologies and approaches to cervical cancer screening, management, and surveillance.

Methods and Results: The Enduring Guidelines process will selectively incorporate new technologies and approaches with adequate supportive data to more effectively improve cancer prevention for high-risk individuals and decrease unnecessary procedures in low-risk individuals. This manuscript describes the structure, process, and methods of the Enduring Guidelines effort. Using systematic literature reviews and primary data sources, risk of precancer will be estimated and recommendations will be made based on risk estimates in the context of established risk-based clinical action thresholds. The Enduring Guidelines process will consider health equity and health disparities by assuring inclusion of diverse populations in the evidence review and risk assessment and by developing recommendations that provide a choice of well-validated strategies that can be adapted to different settings.

Conclusions: The Enduring Guidelines process will allow updating existing cervical cancer screening and management guidelines rapidly when new technologies are approved or new scientific evidence becomes available.

Key Words: cervical cancer, human papillomavirus, screening, triage, management, risk, precancer, recommendations, consensus guidelines

(*J Low Genit Tract Dis* 2024;28: 117–123)

Cervical cancer screening aims at reducing cervical cancer risk by detecting cancer precursors; successfully treating these lesions prevents cervical cancer. For decades, cervical cancer screening was based on cervical cytology. Recently, human papillomavirus (HPV) testing has been integrated into screening and management approaches due to its high sensitivity and the strong, long-term reassurance of a low cancer risk provided by a negative test.[1] Human papillomavirus-based screening has been proven to be superior to cytology screening for detection of cervical

[1]Division of Cancer Epidemiology & Genetics, National Cancer Institute, Rockville, MD; [2]Health and Community Services Administration, Pima County, Tucson, AZ; [3]Department of Obstetrics and Gynecology, Washington University, St. Louis, MO; [4]University of Pittsburgh School of Medicine, Magee-Womens Hospital, Pittsburgh, PA; [5]Department of Obstetrics and Gynecology, University of Alabama at Birmingham, Birmingham, AL; [6]American Cancer Society, Atlanta, GA; [7]Chronic Viral Diseases Program, Centers for Disease Control and Prevention, Atlanta, GA; [8]Department of Obstetrics and Gynecology, Boston University Chobanian and Avedisian School of Medicine/Boston Medical Center, Boston, MA

Reprint requests to: Nicolas Wentzensen, MD, PhD, MS, Division of Cancer Epidemiology and Genetics, National Cancer Institute, 9609 Medical Center Dr, Room 6E-448, Bethesda, MD 20892-9774. E-mail: wentzenn@mail.nih.gov

N.B. has served as a consultant for Dysis. M.E. has served as a consultant for Papivax, Merck, BD, and PDS. R.G. has served as a consultant for Inovio. D.H. has served as a consultant for Roche. W.H. has served as a consultant for Roche, SeeGene, and AstraZeneca. R.N. has participated in an educational meeting supported by Roche. The other authors have declared they have no conflicts of interest.

Disclaimer: The conclusions, findings, and opinions expressed by authors contributing to this journal do not necessarily reflect the official position of the US Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention (CDC), and the National Cancer Institute. Enduring Guidelines are not CDC-led and have not been written by CDC as CDC guidelines.

Group author list:
Abha Goyal, MD, Weill Cornell Medicine-New York Presbyterian Hospital, New York, NY
Ana Reyes, Cervivor, Global Community of Patient Advocates, Upper Marlboro, MD
Anna-Barbara Moscicki, MD, Department of Pediatrics, University of California Los Angeles, Los Angeles, United States
Carol C. Eisenhut, MD, MBA, DCLPatholgy, Indianapolis, IN
David Chhieng, MD, MBA, COLA Inc., Columbia, MD
David Chelmow, MD, Virginia Commonwealth University School of Medicine, Richmond, VA.
Debbie Bamberger, DNP, RN, WHNP-BC, Nurses for Sexual and Reproductive Health and Planned Parenthood Mar Monte, San Jose, CA
Deborah Arrindell, American Sexual Health Association, Washington, DC
Diane D. Davey, MD, University of Central Florida, Orlando, FL
Diane M. Harper, MD, MPH, MS, University of Michigan, Ann Arbor, MI
Eileen Lind, RN, MSN, CPNP, Team Maureen, North Falmouth, MA
Elizabeth W. Patton, MD, MPhil, MSc, Boston University School of Medicine/Boston Medical Center, Boston, MA
Eric C. Huang, MD, PhD, University of Washington School of Medicine/Harborview Medical Center, Seattle, WA
George F. Sawaya, MD, University of California, San Francisco, CA
Jeanne Murphy, PhD, CNM, FACNM, George Washington University School of Nursing, Washington, DC
Jeffrey Quinlan, MD, Department of Family Medicine, Carver College of Medicine, University of Iowa Healthcare
Jennifer Loukissas, MPP, Division of Cancer Epidemiology and Genetics, NCI, Bethesda, MD
June S. Gupta, CRNP, Planned Parenthood Federation of America, New York, NY
Kelly Welch, Team Maureen, North Falmouth, MA
Kim Choma DNP, APN, WHNP-BC, Mountainside, NJ
Mark H. Einstein, MD, MS, Department of OB/GYN & Women's Health, Rutgers New Jersey Medical School, Newark, NJ
Megan Eagen-Torkko, PhD, CNM, ARNP, School of Nursing & Health Studies, University of Washington Bothell, Seattle, WA
Melanie Jacobs, PA-C, Association for Physician Assistants in Obstetrics and Gynecology, Kimberly, WI
Melissa Rodriguez, DMSc, PA-c, Adventhealth Central Florida South, Orlando, FL
Michelle Collins, PhD, RN, American College of Nurse-Midwives, Silver Spring, MD
Morgan Newman, MSW, Cervivor, Global Community of Patient Advocates, Upper Marlboro, MD
Nancy R. Berman, MSN, ANP-BC, MSCP, FAANP, Michigan Healthcare Professionals, Farmington Hills, MI
Randall Ball, MD, Phoenix VA Health Care System/University of Arizona College of Medicine-Phoenix, AZ
Ritu Nayar, MD, Northwestern University Feinberg School of Medicine, Chicago, IL
Robert A. Goulart, MD, Department of Pathology, UMass Chan Medical School, UMass Memorial Medical Center, Worcester, MA
Sana O. Tabbara, MD, Moffitt Cancer Center, Tampa, FL
Teresa M. Darragh, MD, Department of Pathology, University of California, San Francisco, CA
Thomas S. Lorey, MD, Regional Laboratory, Kaiser Permanente Northern California, Oakland, CA.

DOI: 10.1097/LGT.0000000000000804

precancer and the reduction of cancer incidence in large international trials and observational studies.[2] However, to achieve successful cervical cancer prevention, completion of multiple steps including triage, colposcopy, and treatment are necessary.[3] The goal of this multistep process is to provide reassurance to most individuals that the risk of cancer is low while identifying the small proportion of individuals at high risk who need treatment.

In the United States, screening and management recommendations are developed by various organizations (Figure 1). Screening guidelines have been developed independently by the US Preventive Services Task Force (USPSTF) and the American Cancer Society (ACS) and have been widely adopted.[4,5] After a positive screening result, the most current management recommendations are covered by the 2019 ASCCP Risk-Based Management Consensus Guidelines (referred to hereafter as 2019 consensus guidelines)[6] and the ASCCP colposcopy standards.[7] Previously, major guidelines were updated every 7–10 years through a consensus process. However, the field of cervical cancer prevention is changing rapidly, creating a need to quickly integrate new approaches into clinical guidelines. For example, since publication of the 2019 consensus management guidelines, 2 new tests that may have a role in managing positive screening result have received regulatory approval.[8,9] To address this need, the Enduring Consensus Cervical Cancer Screening and Management Guidelines (referred to hereafter as Enduring Guidelines) effort was created as a standing committee to continuously evolve the risk-based process established for the 2019 consensus management guidelines and, after this process, assess new technologies and studies for potential incorporation into the management guidelines.

The risk-based framework uses clinical action thresholds that were defined in the 2019 consensus process. For example, for an immediate risk of cervical intraepithelial neoplasia 3 or worse (CIN3+) of 4% or higher, colposcopy is recommended. Colposcopy or expedited treatment is acceptable for a risk ranging from 25% to 59%, and expedited treatment is preferred for a risk of 60% or higher. Surveillance intervals of 1, 3, and 5 years are based on 5- and 3-year risk-based clinical action thresholds.[6,10] To expand existing recommendations, risk estimates are calculated from studies evaluating new and established technologies, and the placement of these risk estimates in the context of clinical action thresholds guides management.[11,12]

The guiding principles for risk-based guidelines are to balance the benefits of screening and management in terms of detecting and treating CIN3+ to prevent invasive cancer against potential harms, including treatment risks, pain, stress, lost time, and expense associated with colposcopies unlikely to detect CIN3+ and treatment of lesions unlikely to progress to cancer. The Enduring Guidelines effort is responsible for expanding existing guidelines to consider new technologies, new approaches, and new data refining risk assessment following these principles. This approach will allow ongoing incorporation of updates into clinical management recommendations through a standardized process. Here, we describe the rationale and approach for the Enduring Guidelines process. New recommendations will not be covered here but published in subsequent manuscripts.

MISSION AND SCOPE OF ENDURING GUIDELINES

The mission of the Enduring Guidelines effort is:

- To continuously evaluate new technologies and approaches to cervical cancer screening, management, and surveillance.
- To selectively incorporate new technologies and approaches with adequate supportive data to more effectively improve cancer prevention for high-risk individuals and decrease unnecessary procedures in low-risk individuals.
- To consider health equity and health disparities during the consensus guidelines process by assuring inclusion of diverse populations in the evidence review and risk assessment, and by developing recommendations that provide a choice of well-validated strategies that can be adapted to different settings.

Each new technology or question will be evaluated based on the quality of the supportive data and balance of benefits and harms. Recommendations for use are made for technologies and approaches meeting committee approval and are added to existing recommendations. The Enduring Guidelines are primarily focused on management after abnormal screening results. The Enduring Guidelines group may evaluate new technologies or clinical questions related to screening, such as self-sampling, or the impact of factors such as obesity and vaccination on screening. To minimize redundancy between different guideline development activities, the Enduring Guidelines group coordinates efforts with the ACS, which is part of the Enduring Guidelines effort, and other stakeholders involved in developing cervical screening guidelines.

Evaluation of new technologies and approaches follows principles established in the 2019 Consensus Management guidelines process.[6,11,12] The group works to continuously improve and refine its methodology. Major modifications of the 2019 consensus process require approval through a vote of the Enduring

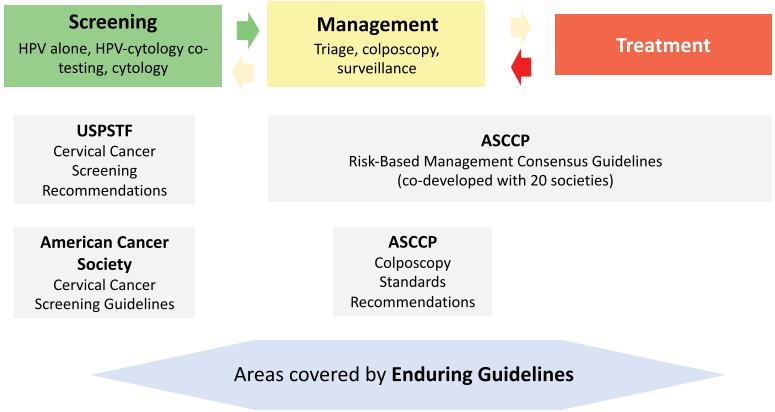

FIGURE 1. Overview of cervical screening and management guidelines in the United States. The figure summarizes the continuum from cervical screening to management and treatment of cervical precancers for prevention of cervical cancer and related US guidelines. The Enduring Guidelines process primarily addresses management of abnormal screening results but may extend to specific questions related to screening and treatment. HPV, human papillomavirus; USPSTF US Preventive Services Task Force.

Guidelines representatives and are documented at https://dceg.cancer.gov/enduring-guidelines. As in previous guidelines, cost and cost-effectiveness are not usually considered because costs of assays and procedures may vary across settings and over time. Screening and management options may be evaluated using a resource usage analysis, a new addition to the guidelines development process that is described subsequently in more detail. Although considerations about implementation of new technologies in laboratories and health systems are important, they are not within the scope of the Enduring Guidelines process, but are addressed by other groups.[13]

ENDURING GUIDELINES AND REGULATORY PROCESSES

Regulatory evaluation of new tests is the purview of regulatory agencies such as the US Food and Drug Administration (FDA). Technologies evaluated in the Enduring Guidelines process have received regulatory approval for clinical use in the United States. Importantly, regulatory approval of new technologies is typically restricted to a limited set of indications because regulatory trials cannot evaluate all possible uses for new technologies in the cervical screening, management, and surveillance context. Recent FDA indications have referred to professional societies for developing guidelines on specific use cases for newly approved assays.[8] Thus, guidelines, in addition to regulatory approval, are an important component for introducing new technologies into clinical practice.[14] Furthermore, it is critical for clinical recommendations to follow regulatory approval with as little delay as possible, highlighting the need for a living guidelines process like Enduring Guidelines. The Enduring Guidelines group assesses new technologies approved by the FDA but does not automatically recommend new technologies that have received regulatory approval. All new technologies will be evaluated according to the principles of risk-based screening and management for various indications as outlined hereafter. Given the limited scope of FDA indications, clinical recommendations developed by the Enduring Guidelines may expand on regulatory indications. This practice has precedents from previous guidelines. For example, new HPV tests that have received regulatory approval for screening indications are also recommended for a wide range of indications in clinical management and surveillance that were not part of regulatory trials.[6]

APPROACH AND GUIDING PRINCIPLES

The Enduring Guidelines are a standing effort that will operate under the guiding principles laid out in this manuscript. More detailed operating procedures are summarized in the Enduring Guidelines manual posted on the Enduring Guidelines home page at https://dceg.cancer.gov/enduring-guidelines; this document will be updated and expanded over time. Given the wide range of guidelines topics and methods for future guidelines development, methodological details for individual recommendations, including description of specific data sources, evidence assessment, and risk assessment, will be included in the respective guideline manuscripts.

STRUCTURE AND ROLES OF THE ENDURING GUIDELINES EFFORT

The authoritative body of the Enduring Guidelines effort includes the membership group of voting representatives from 19 stakeholder organizations that were part of the 2019 guidelines process. The member organizations are listed in Table 1. In addition, nonvoting experts are included in the Enduring Guidelines process to support development of risk estimates and provide expertise on specific assays and topics. The roles and responsibilities of subgroups within the Enduring Guidelines are summarized in Figure 2.

TABLE 1. Member Organizations of the Enduring Guidelines for Cervical Cancer Screening and Management

Organization	Type
American Academy of Family Physicians	Medical professional society
American Cancer Society	Medical professional society, patient advocacy organization
American College of Nurse-Midwives	Medical professional society
American College of Obstetricians and Gynecologists	Medical professional society
American Sexual Health Association	Patient advocacy organization
American Society for Clinical Pathology	Medical professional society
American Society of Cytopathology	Medical professional society
ASCCP	Medical professional society
Association for Physician Assistants in Obstetrics and Gynecology	Medical professional society
Cervivor	Patient advocacy organization
College of American Pathologists	Medical professional society
National Cancer Institute	Federal agency
Nurse Practitioners in Women's Health	Medical professional society
Nurses for Sexual and Reproductive Health	Medical professional society
Papanicolaou Society of Cytopathology	Medical professional society
Planned Parenthood Federation of America	Patient advocacy organization, patient advocacy organization
Society of Gynecologic Oncology	Medical professional society
Team Maureen	Patient advocacy organization
Women Veterans Health Strategic Healthcare Group	Medical professional society

Technology and Risk Assessment Group

The technology and risk assessment group based at the National Cancer Institute (NCI) is responsible for evidence aggregation and evaluation, literature review, and risk assessment based on published and primary data.[11,15] Primary data analyses are critical to generating risk estimates for new technologies, for new approaches to screening and management, and to update existing recommendations when more data become available. Evidence summaries and risk estimates generated by this group are shared with the Enduring Guidelines Working Groups.

Working Groups

Working Groups are established by the Steering Committee as needed to address specific topics. Depending on the number of topics evaluated at a specific time, there may be one or more Working Groups operating at the same time. Working Groups are led by 1 or 2 chairs and members are drawn from the entire Enduring Guidelines group membership, supplemented with additional subject matter experts who may be invited to serve depending on the topic area of a particular Working Group. The charge for a Working Group is to evaluate evidence summaries and risk estimates generated by the Risk Assessment Group in the context of clinical action thresholds and clinical management. The Working Group gives feedback to the Risk Assessment Group and may request additional analyses. If supporting evidence is sufficiently robust, the Working Group develops draft recommendations for discussion with

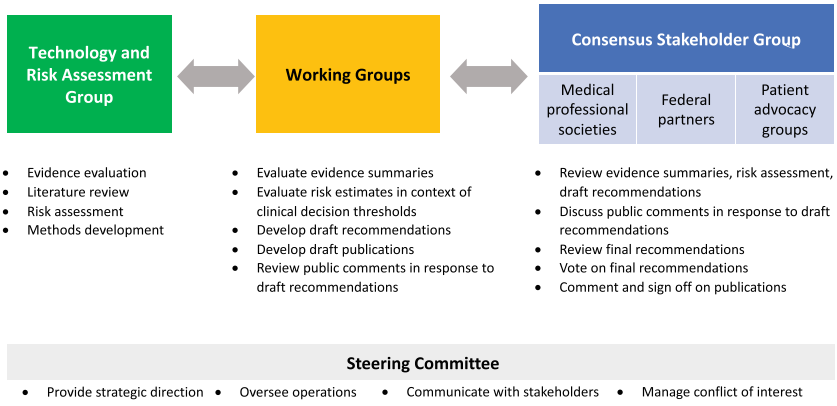

FIGURE 2. Roles and responsibilities in the Enduring Guidelines process. The development of recommendations in the Enduring Guidelines process involves several groups. The Technology and Risk Assessment Group conducts evidence evaluation through literature review and primary data analysis with risk assessment, as well as methods development when necessary. Working Groups include clinical, epidemiological, and statistical experts as well as patient representatives to evaluate evidence provided by the Technology and Risk Assessment Group and to develop draft recommendations. The Consensus Stakeholder Group includes voting members from all participating societies, agencies, and patient advocacy groups. The Stakeholder Group evaluates draft recommendations with supporting evidence and votes on final recommendations. The Steering Committee oversees the operations of the Enduring Guidelines process, communicates with stakeholders, and manages conflicts of interest, where necessary.

the full Enduring Guidelines membership and is also responsible for drafting manuscripts summarizing new recommendations that have been ratified through the Enduring Guidelines process.

Enduring Guidelines Consensus Stakeholder Group

The full Enduring Guidelines stakeholder group is the authoritative body with representatives from 19 organizations as well as additional experts and leadership from previous guidelines processes. Each participating organization may be represented by up to 2 voting members to participate in the Enduring Guidelines process. The group discusses draft recommendations and underlying evidence presented by the Working Groups. Based on internal and public feedback, final recommendations are developed by the Working Groups and presented for a vote by electronic ballot. An additional responsibility of Enduring Guidelines members is to disseminate new recommendations to member societies and educate their members about guidelines updates.

Steering Committee

The Enduring Guidelines effort is accountable to a Steering Committee made up of the principals of the 3 organizations that have historically led previous cervical screening and management guidelines: the ACS, ASCCP, and the NCI. The Steering Committee meets at least quarterly to provide strategic direction for the Enduring Guidelines effort, interacts with member societies and other stakeholders, and evaluates and manages possible conflicts of interest of Enduring Guidelines members.

CONFLICT OF INTEREST

Given that the Enduring Guidelines group evaluates new technologies that are brought into the market by individual commercial entities, it is important for the Enduring Guidelines process to be transparent, consistent, and rigorous. This is achieved through a formal scientific process of risk assessment with evaluation of benefits and harms, evaluation by a core group with expertise in evidence assessment, and inclusion of many stakeholders representing diverse interests and perspectives. To avoid improper influence on the guidelines process based on other interests and to address the appearance of improper influence, it is important to annually evaluate conflict of interest (COI) of all members of the guidelines process.[16] The COI procedures for Enduring Guidelines are similar to those used by the ACS for guidelines development.[4] To limit risk of bias and to safeguard the trustworthiness of the process, all participants in the guideline development process (members of the risk assessment group and members of the stakeholder group) are required to disclose all financial (commercial and noncommercial) and intellectual or clinical practice relationships and circumstances that may have or seem to have a bearing on the guideline topic. Enduring Guidelines leadership evaluates disclosures for potential COIs and may recommend that individual participants recuse themselves from participating in specific activities if these raise a concern about actual or perceived COI, or may recommend exclusion from the entire process if there is concern about improper influence.

ENDURING GUIDELINES PROCESS TO DEVELOP NEW RECOMMENDATIONS

The process through which the Enduring Guidelines effort develops new recommendations is summarized in Figure 3 and described in detail subsequently.

TOPIC AREAS FOR ENDURING GUIDELINES RECOMMENDATIONS

Enduring Guidelines activities are needed in at least 4 different areas (Figure 3): 1) When new technologies for cervical screening or management receive regulatory approval, it is necessary to assess their potential, and if appropriate, develop clinical recommendations for their use. 2) When new risk data become available, recommendations may need updating to reflect improved evidence, particularly when previous recommendations were based on expert opinion. 3) When population prevalence of HPV infections or precancers substantially change, for example, when the proportion of HPV-vaccinated cohorts increases in the screening population, recommendations may need to be modified to reflect the lower population risk. 4) When new discoveries are made with relevance for cervical screening and management that have not been considered previously, new clinical recommendations may need to be developed or existing recommendations modified. Topics for consideration through the Enduring Guidelines process can be proposed by all members of the Enduring Guidelines committee, including the representatives of the stakeholder organizations. The general public may

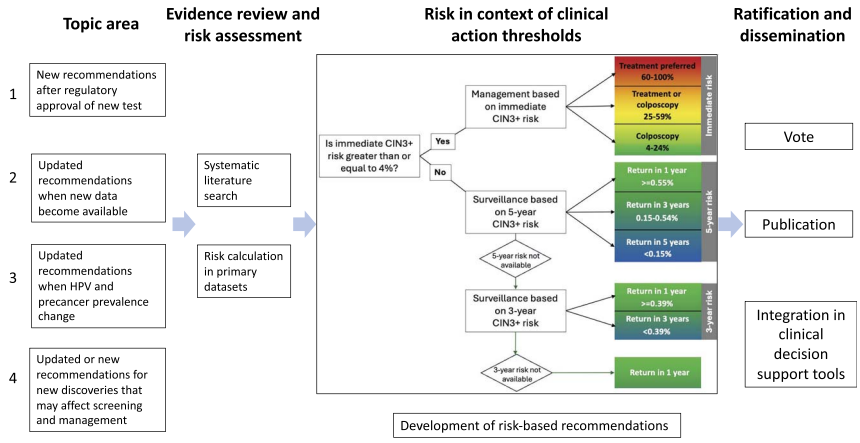

FIGURE 3. Enduring Guidelines process to develop new recommendations. The Enduring Guidelines process goes through several steps for development of new recommendations in 1 of 4 topic areas. Following evidence review and risk assessment, risk estimates are evaluated in the context of clinical action thresholds that form the bases of draft recommendations. Recommendations are discussed and revised as necessary before voting occurs. Ratified recommendations are published in peer-reviewed journals and integrated into clinical decision support tools.

approach member organizations to propose topics for consideration. The topics under consideration by the Enduring Guidelines committee are listed at https://www.asccp.org/management-guidelines.

EVIDENCE REVIEW AND RISK ASSESSMENT FROM PRIMARY DATA SOURCES

The 2019 guidelines process was largely based on risk estimates from a dataset including more than 1.5 million individuals undergoing HPV and cytology cotesting at Kaiser Permanente Northern California (KPNC).[12] Because HPV and cytology testing were performed at all screening and management visits, this dataset allowed for the generation of highly precise risk estimates for population strata based on HPV, cytology, and clinical history. To evaluate portability of risk estimates across diverse populations, baseline risk data for HPV and cytology were analyzed in the National Breast and Cervical Cancer Early Detection Program, with similar results.[11,17] Because the Enduring Guidelines process evaluates new technologies and approaches that are currently not the clinical standard, it relies on data from research studies, including clinical trials, regulatory studies, and other observational studies, as well as clinical implementation studies and occasionally, clinical data from international settings. As new technologies are gradually adopted into clinical practice, real-life clinical data from the United States will complement those from research studies and may lead to updated recommendations.

Evidence Review

When new technologies and approaches are evaluated in the Enduring Guidelines process, the risk assessment group conducts systematic literature reviews to identify studies evaluating these new approaches, particularly focusing on US-based data. Absolute risk estimates from these studies may be evaluated in the context of clinical decision thresholds to inform guidelines development. For some recommendations, the systematic literature review will be the only source of evidence.

Primary Data Sources

Where available, primary data are used to calculate risk estimates to develop risk-based recommendations in the context of clinical action thresholds. Inclusion of studies from diverse populations is critical to ensure generalizability of recommendations. The benefit of primary data analyses is that risk estimates can be tailored to specific requirements for guideline development, for example, by allowing derivation of subsets of the population for specific indications (e.g., triage, surveillance) or by allowing estimation of risk for time intervals that are relevant for clinical action thresholds (e.g., immediate, 1-year, 3-year risk) using comparable risk models.[11] Enduring Guidelines recommendations are primarily developed for US clinicians and patients. Therefore, primary data analyses will focus on diverse, US-based studies that are representative of the population for which the recommendations are developed, assess screening and management approaches specific to the United States that may differ from international settings, and evaluate the assays and specific assay configurations that have received regulatory approval in the United States. Specific data requirements vary dependent on the topic under review. As a general principle, data supporting new recommendations need to come from sufficiently powered studies to ensure risk estimates are precise. For each guideline area, different sets of studies are used, depending on the availability of relevant data. Two NCI-funded studies will provide primary data for several Enduring Guidelines areas: the first is the Improving Risk-Informed HPV Screening (IRIS) cohort (racial/ethnic distribution: 44% White, 20% Hispanic, 20% Asian, 10% African American) nested in the Guidelines Cohort,[18,19] which was designed to evaluate new technologies for cervical screening and management and is conducted in collaboration with Kaiser Permanente Northern California, a major source of the risk data underlying the 2019 Consensus Management guidelines. Another study with a similar design is the STudying Risk to Improve DisparitiES in Cervical Cancer in Mississippi (STRIDES) cohort study (racial/ethnic distribution: 66% African American, 30% White) that is conducted among individuals undergoing screening at publicly funded clinics run by the Mississippi State Department of Health as well as at clinics affiliated with the University of Mississippi.[20,21] Together, these studies represent a wide range of US racial/ethnic, socioeconomic, and geographic diversity. Other studies with relevant and accessible primary data may be included in the guideline development process, with specific criteria for inclusion depending on the guidelines questions that are addressed.

Risk Assessment in Context of Clinical Action Thresholds

The Enduring Guidelines apply the risk-based management approach established for the 2019 consensus guidelines. This approach is based on calculation of risk of precancer and cancer at baseline and during follow-up using prevalence-incidence mixture

models as previously described.[10–12] The primary end point for risk estimates is CIN3, adenocarcinoma in situ, or cancer (CIN3+). Risk of cancer may be evaluated as a secondary endpoint when there is concern that precancers may be missed and risk of cancer may be increased, for example, in individuals with HPV18 infections and negative cytology who have a disproportionally increased risk of cancer compared with CIN3. Important indications evaluated in the Enduring Guidelines process include triage of HPV-positive test results, or triage of positive cotesting results. Other indications may focus on surveillance in a postcolposcopy or posttreatment population. The indications and populations evaluated may differ by technologies or approaches and data availability.

First, baseline risk is calculated and compared with established clinical action thresholds (Figure 3). When baseline risk is lower than 4%, 5-year risk estimates are evaluated to decide on repeat intervals (1 year vs 3 years vs 5 years). When 5-year data are not available, 3-year risk estimates can be used to decide on repeat intervals (1 year vs 3 years).[10] When the baseline risk of CIN3+ is 4% or higher, an immediate management decision is required: colposcopy referral (risk between 4% and <25%), either colposcopy referral or immediate treatment (risk between 25% and <60%), or immediate treatment (risk ≥60%). When only baseline data are available, the default repeat interval is 1 year until follow-up data become available. A management confidence probability can be calculated for individual strata with a risk-based recommendation as previously described.[11] The confidence probability indicates the likelihood that a different sample from the same population would have the same clinical recommendation for that stratum. When primary data are available from multiple populations, risk will be estimated separately to assess portability of risk estimates and clinical decisions across populations.

Resource Utilization Analysis

Although every test is evaluated on its own merits, the Enduring Guidelines process will provide some context about the implications of adopting a new technology. To that end, basic resource Utilization metrics will be calculated for specific recommendations and compared with existing practice. Given the complexity of management approaches and their variability across different tests, simple clinical performance metrics cannot fully capture the impact of a new technology on the entire screening program. For example, 1 triage test may refer fewer screen-positives to immediate colposcopy but may have a similar referral number as the current standard over an entire screening and management cycle. Therefore, resource Utilization estimates are calculated for a fixed population and a complete screening and management cycle (Egemen in preparation). Key metrics include the number of tests required, the number of visits required, the number of colposcopies required, and number of years between detection of a CIN3+ outcome for a specific strategy compared with when it would be detected if all individuals were immediately followed up for precancer outcomes. The capacity and cost to run tests and to perform colposcopy and surveillance visits may differ substantially between settings. Resource Utilization metrics can support decision-making processes about which technology to implement, and whether to implement, in different steps of the screening and management continuum.

DEVELOPMENT AND RATIFICATION OF RECOMMENDATIONS

If the working group determines that there is sufficient evidence and a favorable benefit-harms trade-off for a new test or approach, draft clinical recommendations are developed by the working group using a standardized procedure. When risk estimates are available, recommendations are usually based where the calculated risk estimates fall with respect to the clinical action thresholds. This approach is referred to as "management according to risk." There may be exceptions to the risk-based approach, such as the example of HPV18-positive negative for intraepithelial lesion or malignancy, for which colposcopy referral is recommended not based on the CIN3+ risk—which is below the colposcopy threshold—but because of a disproportionally high risk of cancer attributed to HPV18. When data are insufficient for risk-based recommendations, recommendations may be made based on expert opinion. Recommendations use the terminology previously established for the 2019 guidelines process:

A new approach or technology may be:

- **Recommended:** When there are good data to support use and no other option is acceptable
- **Preferred:** When the option is the best (or one of the best) among multiple options
- **Acceptable:** When it is one of multiple options when data do not clearly favor any single option or when there are data indicating that another approach is superior
- **Not recommended:** When there is weak evidence against use and marginal risk for adverse consequences.
- **Unacceptable:** When there is good evidence against use.

The evidence supporting all recommendations is rated considering the strength of the recommendation (A through E) and the quality of evidence (I–III) as previously described.[6]

Draft recommendations are presented to all stakeholders in the full Enduring Guidelines group for input and revision. Subsequently, draft recommendations are presented to participating organizations members, and to the general public using a Web-based survey to solicit feedback. The public comment period is announced on the ASCCP home page (www.asccp.org) where comments are collected for several weeks. Feedback from the public is reviewed by members of the working group and may lead to further revisions to address substantive comments. Recommendations are finalized and put to an anonymous electronic vote of the Enduring Guidelines group. A two-thirds majority of all voting members is required to pass a recommendation. If a recommendation fails to achieve the two-thirds majority, modifications can be made by the working group or the stakeholder group, and the new recommendation can be voted again; this process can be repeated until the recommendation is passed or abandoned.

DISSEMINATION AND IMPLEMENTATION OF NEW RECOMMENDATIONS

The dissemination and implementation efforts of the Enduring Guidelines process revolve around making recommendations and supporting evidence widely available and facilitating integration of new recommendations in clinical decision tools, recognizing the increasing complexity of cervical screening and management guidelines. After recommendations have been finalized and approved by the Enduring Guidelines stakeholder group, a manuscript will be drafted, usually by members of the respective Working Group, edited, approved by the Enduring Guidelines group, and submitted for publication. After completion of the peer-review process and acceptance of the manuscript, and as soon as the accepted publication is publicly accessible, either as online advance publication or in a print issue, the recommendations are considered official. This is particularly important for the integration of new recommendations into clinical decision tools,[22,23] which require a published recommendation and data source. To ensure that clinical recommendations for new technologies and approaches are disseminated and reach target audiences, particularly practitioners, successfully, the Enduring Guidelines group will make several important efforts: 1) Guidelines manuscripts will be made available as open access publications to ensure widespread and immediate

access to recommendations and supporting evidence. 2) New recommendations and supporting risk data will be published on the Enduring Guidelines Web pages (https://dceg.cancer.gov/enduring-guidelines and https://www.asccp.org/management-guidelines), allowing easy access to risk data and recommendations. 3) The Enduring Guidelines group will work closely with developers of clinical decision tools to support integration of new recommendations, which is critical to facilitate adoption of new recommendations. 4) The Enduring Guidelines group will coordinate with member organizations to announce and promote new recommendations, and 5) encourage Enduring Guidelines representatives to inform their sponsoring participating organizations, peers and other constituent interest groups about new recommendations.

SUMMARY AND FUTURE DIRECTIONS

The Enduring Guidelines process is a new type of "living guidelines" in an effort to keep cervical screening and management guidelines up-to-date. It is founded on the risk-based screening and management approach that was developed over the last 2 rounds of consensus management guidelines updates[6,24] and resulted in a framework that separates the risk assessment for individual tests and approaches from the clinical management decision threshold, which facilitates updating recommendations more easily and more frequently. The current framework can be updated if the need arises. Examples of topics that are in development or under consideration by the Enduring Guidelines process are the use of dual stain and/or extended genotyping in management of abnormal screening results (topic area 1: new technology), the role of self-sampling in cervical screening and management (topic area 1: new technology), the impact of obesity on screening and management practice (topic area 4: discovery relevant to screening and management), as well as updates of existing guidelines when new risk data become available (topic area 2: additional evidence for existing guidelines). In the future, the Enduring Guidelines process will also evaluate the impact that an increasing proportion of vaccinated individuals in the screening population has on risk of specific tests and clinical decision thresholds (topic area 3: changes in population risk). All these topics address the stated goals of the Enduring Guidelines process to improve the benefits of screening and management, while reducing the harms, and to extend the availability of well-validated tests. The profound health inequities and disparities that underlie cervical cancer are multifactorial. Successfully addressing these factors requires concerted multidisciplinary efforts from public health authorities, clinical providers, insurance providers, population scientists, and many others. To the extent possible, the Enduring Guidelines process will consider health inequities in the area of cervical screening and management by assuring inclusion of diverse populations in the evidence review and risk assessment, and by developing recommendations that provide a choice of well-validated strategies that can be adapted to different settings.

REFERENCES

1. Wentzensen N, Arbyn M, Berkhof J, et al. Eurogin 2016 roadmap: how HPV knowledge is changing screening practice. *Int J Cancer* 2017;140: 2192–200.
2. Bouvard V, Wentzensen N, Mackie A, et al. The IARC perspective on cervical cancer screening. *N Engl J Med* 2021;385:1908–18.
3. Wentzensen N, Schiffman M, Palmer T, et al. Triage of HPV positive women in cervical cancer screening. *J Clin Virol* 2016;76:S49–55.
4. Fontham ETH, Wolf AMD, Church TR, et al. Cervical cancer screening for individuals at average risk: 2020 guideline update from the American Cancer Society. *CA Cancer J Clin* 2020;70:321–46.
5. US Preventive Services Task Force, Curry SJ, Krist AH, Owens DK, et al. Screening for cervical cancer: US Preventive Services Task Force recommendation statement. *JAMA* 2018;320:674–86.
6. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP Risk-Based Management Consensus Guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 2020;24:102–31.
7. Wentzensen N, Massad LS, Mayeaux EJ Jr., et al. Evidence-based consensus recommendations for colposcopy practice for cervical cancer prevention in the United States. *J Low Genit Tract Dis* 2017;21:216–22.
8. Food and Drugs Administration. CINtec PLUS cytology 2020 Available from: https://www.accessdata.fda.gov/cdrh_docs/pdf19/P190024B.pdf.
9. Food and Drugs Administration. BD Onclarity HPV assay 2020 Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P160037S004. Accessed February 20,2024.
10. Egemen D, Perkins RB, Clarke MA, et al. Risk-based cervical consensus guidelines: methods to determine management if less than 5 years of data are available. *J Low Genit Tract Dis* 2022;26:195–201.
11. Cheung LC, Egemen D, Chen X, et al. 2019 ASCCP Risk-Based Management Consensus Guidelines: methods for risk estimation, recommended management, and validation. *J Low Genit Tract Dis* 2020; 24:90–101.
12. Egemen D, Cheung LC, Chen X, et al. Risk estimates supporting the 2019 ASCCP Risk-Based Management Consensus Guidelines. *J Low Genit Tract Dis* 2020;24:132–43.
13. Downs LS Jr., Nayar R, Gerndt J, et al. American Cancer Society primary HPVSISC. Implementation in action: collaborating on the transition to primary HPV screening for cervical cancer in the United States. *CA Cancer J Clin* 2023;73:458–60.
14. Wentzensen N, Silver MI. Biomarkers for cervical cancer prevention programs: the long and winding road from discovery to clinical use. *J Low Genit Tract Dis* 2016;20:191–4.
15. Clarke MA, Darragh TM, Nelson E, et al. Reporting and assessing the quality of diagnostic accuracy studies for cervical cancer screening and management. *J Low Genit Tract Dis* 2020;24:157–66.
16. Schunemann HJ, Al-Ansary LA, Forland F, et al. Guidelines International Network: principles for disclosure of interests and management of conflicts in guidelines. *Ann Intern Med* 2015;163:548–53.
17. Saraiya M, Cheung LC, Soman A, et al. Risk of cervical precancer and cancer among uninsured and underserved women from 2009 to 2017. *Am J Obstet Gynecol* 2021;224:366 e1–e32.
18. Gage JC, Raine-Bennett T, Schiffman M, et al. The Improving Risk Informed HPV Screening (IRIS) study: design and baseline characteristics. *Cancer Epidemiol Biomarkers Prev* 2022;31:486–92.
19. Raine-Bennett T, Gage JC, Poitras N, et al. Development of a large biorepository of cervical specimens for the Improving Risk Informed HPV Screening study (IRIS). *J Clin Virol* 2021;145:105014.
20. Clarke MA, Risley C, Stewart MW, et al. Age-specific prevalence of human papillomavirus and abnormal cytology at baseline in a diverse statewide prospective cohort of individuals undergoing cervical cancer screening in Mississippi. *Cancer Med* 2021;10:8641–50.
21. Risley C, Stewart MW, Geisinger KR, et al. STRIDES - STudying Risk to Improve DisparitiES in cervical cancer in Mississippi—design and baseline results of a statewide cohort study. *Prev Med* 2021;153:106740.
22. ASCCP. ASCCP management guidelines App Available from: https://www.asccp.org/mobile-app. Accessed February 20, 2024.
23. Saraiya M, Colbert J, Bhat GL, et al. Computable guidelines and clinical decision support for cervical cancer screening and management to improve outcomes and health equity. *J Womens Health (Larchmt)* 2022;31:462–8.
24. Massad LS, Einstein MH, Huh WK, et al. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis* 2013;17:S1–27.