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December 22, 2014

Jyme Schafer, MD MPH  
Director  
Division of Medical and Surgical Services  
Coverage & Analysis Group  
Office of Clinical Standards and Quality  
Centers for Medicare & Medicaid Services  
7500 Security Boulevard  
Baltimore, MD 21244-1850

**Re: National Coverage Analysis (NCA) Tracking Sheet for Screening for Cervical Cancer with Human Papillomavirus (HPV) Testing (CAG-00442N) (November 25, 2014)**

Dear Dr. Schafer:

The American Cancer Society Cancer Action Network (ACS CAN) appreciates the opportunity to provide comments on the Centers for Medicare and Medicaid Services' (CMS') initiation of a national coverage analysis (NCA) for cervical cancer screening with a combination of HPV and cytology (Pap) testing.

ACS CAN, the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, supports evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem. As the nation's leading advocate for public policies that are helping to defeat cancer, ACS CAN ensures that cancer patients, survivors, and their families have a voice in public policy matters at all levels of government.

An estimated 12,360 cases of invasive cervical cancer are expected to be diagnosed in the U.S. during 2014.<sup>1</sup> While women over the age of 50 have seen a 1.2 percent decrease in mortality, death rates have stabilized in women younger than 50. An estimated 4,020 women are expected to die from cervical cancer in the U.S. during 2014.

Screening tests offer the ability to identify and remove precancerous cervical lesions before they turn cancerous as well as to detect cervical cancer at an earlier stage when treatment is most successful. The United States Preventive Services Task Force (USPSTF) recommends a grade "A" screening for cervical cancer in women age 21 to 65 years with cytology (Pap test) every 3 years, or for women age 30 to 65 years who want to lengthen the screening interval, screening with a combination of cytology and HPV testing every 5 years. Unfortunately while Medicare covers a screening for pelvic examination and a Pap test for all women at 12 or 24 month intervals, it does not currently provide coverage for HPV testing.

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<sup>1</sup> American Cancer Society, Cancer Facts & Figures 2014, available at <http://www.cancer.org/research/cancerfactsstatistics/cancerfactsfigures2014/>.

Studies show that HPV testing detects more cancers, more advanced pre-cancers earlier, and detects a second type of cervical cancer (called adenocarcinoma) that Pap tests usually miss. In the majority of studies reviewed, the addition of HPV testing to cytology resulted in an increased detection of advanced pre-cancer, called prevalent cervical intraepithelial neoplasia grade 3 (CIN3), with a concomitant decrease in CIN3+ or cancer detected in subsequent rounds of screening.<sup>2,3,4</sup> This increase in diagnostic lead-time with co-testing translates into lower risk following a negative screen: when compared with women with negative cytology, those with negative HPV tests have a lower subsequent risk of CIN3+<sup>5,6</sup> and, more importantly, cancer.<sup>7</sup> The addition of HPV testing to cytology also enhances the identification of women with adenocarcinoma of the cervix and its pre-cursors.<sup>7,8</sup> Compared to squamous cell cancers, cytology has been relatively ineffective in decreasing the incidence of invasive adenocarcinoma of the cervix.<sup>6,9</sup>

A strategy of co-testing may become increasingly important based on evidence of increasing incidence of adenocarcinoma, which has been observed in several European countries<sup>10</sup> and the U.S.<sup>11</sup> that have exclusively or primarily used cytology-only screening. Further, HPV testing provides added reassurance to women who test negative compared to Pap tests alone. The number of colposcopies is also less for co-testing than for cytology alone. Finally, results from FDA-approved or well-validated HPV tests are also more reproducible (intra-assay reliability) than cytology.<sup>10,12,13</sup>

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<sup>2</sup> Naucler P, Ryd W, Tornberg S, et al. Human papillomavirus and Papanicolaou tests to screen for cervical cancer. *N. Engl J Med.* 2007; 357:1589-1597.

<sup>3</sup> Bulkmands NW, Berkhof J, Rozendaal L, et al. Human papillomavirus DNA testing for the detection of cervical intraepithelial neoplasia grade 3 and cancer: 5-year follow-up of a randomized controlled implementation trial. *Lancet.* 2007; 370:1764-1772.

<sup>4</sup> Ronco G, Giorgi-Rossi P, Carozzi F, et al. Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomized controlled trial. *Lancet Oncol.* 2010; 11:249-257.

<sup>5</sup> Dillner J, Rebolj M, Birembaut P, et al. Long term predictive values of cytology and human papillomavirus testing in cervical cancer screening; joint European cohort study. *BMJ.* 2008; 337:a1754.

<sup>6</sup> Bray F, Carstensen B, Moller H, et al. Incidence trends of adenocarcinoma of the cervix in 13 European countries. *Cancer Epidemiol Biomarkers Prev.* 2005; 14:2191-2199.

<sup>7</sup> Katki HA, Kinney WK, Fetterman B, et al. Cervical cancer risk for women undergoing concurrent testing for human papillomavirus and cervical cytology: a population-based study in routine clinical practice. *Lancet Oncol.* 2011; 12:663-672.

<sup>8</sup> Anttila A, Kotaniemi-Talonen L, Leinonen M, et al. Rate of cervical cancer, severe intraepithelial neoplasia, and adenocarcinoma in situ in primary HPV DNA screening with cytology triage: randomized study within organized screening programme. *BMJ.* 2010; 340:c1804.

<sup>9</sup> Cervical screening in Australia 2008-2009. Canberra: Australian Institute of Health and Welfare; 2011.

<sup>10</sup> Castle PE, Wheller CM, Solomon D, Schiffman M, Peyton CL. Interlaboratory reliability of Hybrid Capture 2. *Am J Clin Pathol.* 2004; 122:238-245.

<sup>11</sup> Wang SS, Serman ME, Hildesheim A, Lacey JV Jr, Devesa S. Cervical adenocarcinoma and squamous cell carcinoma incidence trends among white women and black women in the United States for 1976-2000. *Cancer.* 2004; 100:1035-1044.

<sup>12</sup> Carozzi FM, Del Mistro A, Confortini M, et al. Reproducibility of HPV DNA Testing by Hybrid Capture 2 in a Screening Setting. *Am J Clin Pathol.* 2005; 124:716-721.

<sup>13</sup> Stoler MH, Schiffman M. Interobserver reproducibility of cervical cytologic and histologic interpretations: realistic estimates from the ASCUC-LSIL Triage Study. *JAMA.* 2001; 285:1500-1505.

For these reasons, the American Cancer Society recommends co-testing as the “preferred” screening strategy while cytology alone is “acceptable.”<sup>14</sup> The American Congress of Obstetricians and Gynecologists has endorsed the same guideline, including recommending co-testing as the “preferred” screening strategy. The guideline recommendations were based on an extensive evidence review including over 12,000 published scientific articles. The Society worked in collaboration with 25 organizations involved in cervical cancer screening as part of the guideline development process.

### Conclusion

On behalf of the American Cancer Society Cancer Action Network we thank you for the opportunity to comment the National Coverage Analysis. If you have any questions, please feel free to contact me or have your staff contact Anna Schwamlein Howard, Policy Principal, Access and Quality of Care at [Anna.Howard@cancer.org](mailto:Anna.Howard@cancer.org) or 202-585-3261.

Sincerely,

A handwritten signature in black ink, appearing to read "Christopher W. Hansen". The signature is written in a cursive style and is positioned above the typed name.

Christopher W. Hansen  
President  
American Cancer Society Cancer Action Network

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<sup>14</sup> Saslow, D., Solomon, D., Lawson, H. W., Killackey, M., Kulasingam, S. L., Cain, J., Garcia, F. A. R., Moriarty, A. T., Waxman, A. G., Wilbur, D. C., Wentzensen, N., Downs, L. S., Spitzer, M., Moscicki, A.-B., Franco, E. L., Stoler, M. H., Schiffman, M., Castle, P. E., Myers, E. R. and ACS-ASCCP-ASCP Cervical Cancer Guideline Committee (2012), American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. *CA: A Cancer Journal for Clinicians*, 62: 147–172. doi: 10.3322/caac.21139.