HPV Testing Among Providers

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[Dr. Saraiya] Welcome to this CDC program on cervical cancer screening. I'm your host, Dr. Mona Saraiya. Joining me today by phone is Dr. Walter Kinney. Dr. Kinney is board-certified in internal medicine, obstetrics and gynecology, and gynecologic oncology. He is a gynecologic oncologist with The Permanente Medical Group in Sacramento, California. He has researched and written about the prevention and treatment of cervical cancer for the past two decades. Thanks, Walter, for being on this show.

[Dr. Kinney] Thanks for the opportunity, Mona.

[Dr. Saraiya] So Walter, what kind of setting do you work in?

[Dr. Kinney] Northern California Kaiser is a prepaid staff model HMO. From the practical standpoint, that means that we have a fixed amount of money to take care of all of the medical needs of our 3.2 million members each year. We are responsible for disease prevention, disease treatment, and for making our insurance as affordable as possible. Our membership is as ethnically and racially diverse as the population of the San Francisco Bay area that we serve, lacking only the extremes of wealth. In that sense we are representative of the diverse U.S. population. The fact that we do not compensate our physicians per procedure or per visit is different than most practice settings in the United States

[Dr. Saraiya] And how long have you been conducting HPV cotesting, that is, doing an HPV test with a Pap test in women 30 years of age and older for routine screening?

[Dr. Kinney] We committed to Pap and HPV cotesting for women 30 and over in late 2002. We introduced this in four pilot facilities in 2003, and rolled it out region-wide in late 2003 and early 2004. Our adoption was motivated but the observation that almost 30 percent of our cancers were preceded by only negative Paps in the three years prior to diagnosis, and by the understanding that most abnormal Paps represent transient HPV infection, the recognition of which adds procedures and visits but does not improve cancer prevention.

[Dr. Saraiya] So, what proportion of women 30 and older are HPV-positive and Pap-negative? And also tell me, what proportion of women are HPV-negative and Pap-negative?

[Dr. Kinney] About 4 percent of our cotested women age 30 and above are Pap-negative HPV-positive, and 91 percent are Pap-negative and HPV-negative. We published the results of the first 800,000 cotests in the March 2009 *Obstetrics and Gynecology*. Phil Castle was the first author.

[Dr. Saraiya] What has been the negative predictive value of women who are negative HPV and normal Pap?

[Dr. Kinney] The negative predictive value for high grade dysplasia and cancer approaches 100 percent for women who are Pap- and HPV-negative. In addition, their risk of developing high grade dysplasia or cancer over the next 10 years is much smaller than women who are Pap-negative but not HPV tested.

[Dr. Saraiya] What about women who are HPV-positive and have a normal Pap test?

[Dr. Kinney] The reported rates for CIN2 and worse in randomized samples in other populations have been 2.4 to 5.1 percent If we assume that our rate is 4 percent and all of those CIN2 and worse lesions were to be detected, it would increase our detection of CIN2 and worse in women age 30 and above by 40 percent That's a smaller number than the increase of 82 percent reported by Mayrand et. al. in the *New England Journal* with the addition of HPV testing to Pap smears. This leads me to suspect that our percentage will be significantly more than 4 percent but we haven't performed a randomized sample to evaluate this.

[Dr. Saraiya] Now have there been any interval cancers?

[Dr. Kinney] Absolutely. There is no testing scheme currently available that eradicates cancer 100 percent, as the recently published experience from the NCI study in Guanacaste indicates. However, it appears that the incidence of cancer in our population (that is, cancers per 100,000 per year) is less in the three years following a negative cotest than it is in the year following a negative Pap.

[Dr. Saraiya] Walter, what is the utility of doing both the HPV and the Pap test every three years?

[Dr. Kinney] The benefit to women who cotest negative is that they have excellent reassurance that they won't be diagnosed with cancer in the next three years. Therefore, they can have screening at three year intervals which means they can avoid having all of the minor abnormalities from transient HPV carriage that would resolve on their own detected, and avoid thereby, unnecessary visits, biopsies, and procedures.

The benefit to women who cotest Pap-negative HPV-positive is that their health care providers can recognize that they are the group at risk for subsequent diagnoses of high-grade dysplasia or cancer, and provide intensified follow-up.

[Dr. Saraiya] So what kind of follow-up takes place among women who are HPV-positive/Pap-negative? Do you wait one year before retesting them?

[Dr. Kinney] We do wait a year; six months is too soon for the virus to resolve on its own. The NCI data suggests that more than 80 percent of women will still be HPV-positive at six months, whereas the number falls to 50 percent by 12 months.

We make an exception to retesting in one year for women that the provider regards as "high-risk." If they had previous treatment for high grade dysplasia or they have a history of poor

compliance with follow-up or an abnormal exam, we leave the options open for the provider to pursue colposcopy in these women after a first Pap-negative HPV-positive screen.

[Dr. Saraiya] Do you use a conventional Pap? And please tell us how hard or easy this is to use and the difference between conventional and a liquid-based cytology?

[Dr. Kinney] We use conventional Pap tests because there's never been convincing evidence that liquid-based cytology was more sensitive, but it is pretty clearly less specific. There are now two meta-analyses and one prospective randomized controlled trial that don't demonstrate increased sensitivity. So we collect a dry slide and a tube for HPV testing. This makes the lab's job easier because they don't have to manually ultracentrifuge and resuspend each liquid-based specimen for HPV testing, and it makes the clinicians' job easier because they don't have to call back the five or six percent of patients because there wasn't enough liquid-based medium left over for HPV testing.

[Dr. Saraiya] How has cotesting been received among providers and your admin staff?

[Dr. Kinney] The administrative staff had to be on board with us 100 percent for us to do it because they had to write a multi-million dollar check to initiate the program the first year. The providers were not opposed to this because we took pains to explain the science and because a major piece of the data underlying this came from Kaiser Northwest. The one stipulation on the part of the doctors was that we were not trying to chase away patients from their annual visit - and we are not. We have to maintain our screening rates and our preventive health care for other conditions. We just don't want to be doing tests that don't benefit the membership, and annual Paps for women who are Pap-negative HPV-negative are not beneficial.

[Dr. Saraiya] Walter, can you share any lessons learned with us?

[Dr. Kinney] We learned several things in the process of starting this. The first thing we learned was that the medical assistants run the clinics; if they don't understand the new testing and want it for themselves, the practice won't be adopted. We learned that the patients are amazingly accepting. If the provider says that this is OK. The doctors thought that all the educational materials and posters were important to patient acceptance. But the patients, and we surveyed 335 of them to find out what mattered, said that the only important factor is the endorsement of the provider. We offer annual Pap smears if you don't want cotesting, but we tell women that we think cotesting is better. Currently, 94 percent of the eligible women over 30 elect cotesting in place of annual Pap smears and they're fine with it as long as it's explained. When there is a problem with adoption, it's been with the doctors.

[Dr. Saraiya] Can you elaborate by what you mean "the problem is with the doctors"?

[Dr. Kinney] Well, the doctors needed several things to be able to accept cotesting. The first thing they needed was reassurance that we weren't trying to prevent annual appointments, regardless of the cotest results, and if they work in the fee-for-service sector, they need to be reassured that their office volume won't go down because of cotesting. Secondly, they need laboratory and Information Technology support, including ordering and reporting of Pap and

HPV results together. And our providers also asked for computerized reporting of results and what they mean directly to the patients, so that they don't have to call each patient and explain what the results mean. The providers need to understand the natural history of and universal exposure to HPV so they know how to explain a positive HPV result to a patient. And finally, they need knowledge of how to manage the Pap-negative HPV-positive women. If these four things aren't in place, then the providers are uncomfortable with the institution of cotesting.

[Dr. Saraiya] Walter, do you have anything else you would like to add about HPV cotesting?

[Dr. Kinney] Yes, I think it is important to understand that better screening is not effective without better colposcopy. Multiple biopsies are essential. We recommend the four quadrant technique of Doctors Pretorius and Belinson where they used 2 mm punches to take at least one biopsy from each quadrant of the cervix, plus an endocervical curettage. The CIN2 and worse detected in Pap-negative HPV-positive women is smaller and harder to see at colposcopy. As a consequence, the president of the ASCCP, Tom Cox, says: "Take more biopsies!" in his recent editorial and I agree. Once they find the first high grady dysplasia in a Pap-negative HPV-positive woman, the previously skeptical physician is an active supporter of cotesting.

[Dr. Saraiya] Walter, thank you so much for sharing your experience at Kaiser Permanente and thank you for joining the show.

[Dr. Kinney] You are most welcome, Mona.

[Announcer] For the most accurate health information, visit www.cdc.gov or call 1-800-CDC-INFO, 24/7.