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<https://reachmd.com/programs/womens-health-update/cervical-cancer-co-testing-what-is-economic-impact/8201/>

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## Cervical Cancer & Co-testing: What is the Economic Impact?

Narrator:

Welcome to ReachMD. This is a special edition of **Advances in Women's Health**, sponsored by Hologic.

Dr. Russell:

Welcome to a special edition of Advances in Women's Health. I'm your host, Dr. John Russell. I'd like to welcome Dr. Michael Randell to the program. Michael Randell, MD, is a board certified OB/GYN at the Emory St. Joseph's Hospital in Atlanta, Georgia. Dr. Randell joins us to share his insights on cervical cancer testing and whether performing two cervical cancer tests is really more expensive than one from both a clinical and economic standpoint.

Dr. Randell, welcome to the program.

Dr. Randell:

Thank you very much for having me.

Dr. Russell:

So, doctor, a recent clinical economic modeling study by Felix and colleagues shows that Pap plus HPV testing together could provide better clinical and economic outcomes than screening with HPV testing alone. Could you elaborate on that modeling study?

Dr. Randell:

This was a modeling analysis comparing the economic benefits of cotesting versus primary HPV testing for cervical cancer screening. The model projected the cervical screening outcomes of 1 million women from age 30 to 70. The model assessed outcomes based on a 3-year interval for assessment. The outcomes in part include costs, incremental differential costs, invasive cervical cancer cases and deaths, number of colposcopies, quality-adjusted life years, and importantly, provided the basis for one or the other approach being more cost or clinically effective. As I'm sure we'll discuss in greater length later on, the top-line findings for the modeling study demonstrated that cotesting is more cost-effective than primary HPV testing when screening women for cervical cancer over their lifetime, here representing age 30 to 70. In fact, over that time approximately \$4 billion can be saved using cotesting as the preferred approach to cervical cancer screening compared with HPV testing alone.

Dr. Russell:

Doctor, before we get into the full economic discussion with regard to the model, why is the specific technology utilized for the HPV test important here, i.e. MRNA versus DNA, and what is the importance of genotyping with regard to this model?

Dr. Randell:

Well, that's a great question. Messenger RNA-based HPV screening assesses the presence and activity of a high-risk HPV infection, whereas DNA-based HPV screening assesses just the presence of a high-risk HPV infection. This affects sensitivity and specificity. When looking at specific technology, we have to look at sensitivity as well as specificity. Sensitivity is the primary driver of clinical effectiveness. We know that messenger RNA-based screening has the same excellent sensitivity as DNA-based screening. In studies we've seen decreased number of missed cancers and missed CIN 3+ lesions due to HPV-negative results when screening with Pap plus HPV together. Specificity is the primary driver of costs. We know that there is improved specificity with messenger RNA-based testing, 24% reduction in false positives as compared to DNA tests and decrease in colposcopies and follow-up visits.

The importance of genotyping is that reflex genotyping for HPV 16 and 18 when a patient is Pap-negative and HPV-positive is recommended by the major guidelines. In this study that we're talking about here, they compared Pap plus HPV messenger RNA testing, including genotyping for HPV 16

and 18, also known as cotesting, versus DNA-based primary HPV testing with HPV 16 and 18 genotyping, and reflex cytology, also known as HPV primary, for cervical cancer screening. This allowed for more apples-to-apples comparison of screening strategies, which has been missing from prior analysis and publications.

Dr. Russell:

Doctor, can you explain in more detail the findings of the modeling study demonstrating cotesting to be more cost and clinically effective than HPV testing alone?

Dr. Randell:

Well, first, the definition of total cost is screening plus diagnosis plus treatment. This includes, in part, cost of testing, colposcopies, treatment of CIN 2 and CIN 3, first-year costs of treating invasive cervical cancer, and costs of follow-up. The findings from the study included lifetime cumulative costs comparing cotesting to HPV testing alone. What we saw in the study is that over the woman's lifetime, cumulative cost of testing was \$1,129 for HPV testing alone and \$1,319 for cotesting, a cumulative lifetime cost favoring HPV testing alone of \$190. However, when adding in costs for treatment resulting from findings with HPV testing alone or cotesting, costs for HPV testing was \$2,326 compared with \$2,365, essentially identical favoring cotesting by \$39 over the woman's lifetime. So, the bottom line is that over the lifetime of a woman, the total cost for cotesting is not different than the total cost for HPV testing alone, so a larger question becomes: Which approach to screening is clinically more beneficial?

Dr. Russell:

So, following up on your last statement, what is the basis for saying that cotesting is to be preferred over HPV testing alone as you approach the cervical cancer screening in a woman between the ages of 30 and 70?

Dr. Randell:

Data from the modeling study demonstrated that screening with the HPV test alone using a DNA-based test resulted in more referrals to colposcopy and high numbers of false positives when compared to cotesting where fewer patients were referred for colposcopies. Further, use of the HPV test alone, as suggested by my last comment, resulted in a greater number of follow-up visits than did cotesting.

Another finding from the study was that there was an increase in cost in treating cervical cancer likely due to missed cases, and this was coincident with an increase of 37% in the diagnosis of invasive cervical cancer, again, likely due over the women's lifetime to misdiagnosis with HPV testing alone. In

fact, a cumulative assessment within the model suggested that the use of cotesting as opposed to HPV testing alone could result in 150,000 fewer invasive cervical cancers over the study time period. This represents about 19 out of 10,000 women screened. The key point is that this is the framework for why cotesting should be the preferred strategy for screening in women ages 30 to 70, not HPV testing alone. I encourage listeners to read this study for the many valuable pieces of information that may have meaning for your clinical practice.

Dr. Russell:

So, doctor, how is it that the cumulative cost of HPV testing alone and cotesting are essentially identical as screening approaches for cervical cancer over that 30- to 70-year age but that cotesting has superior outcomes with regard to total cumulative cost and clinical benefit?

Dr. Randell:

Well, the authors of the modeling study did an extensive sensitivity and specificity analysis to assess what aspects or aspects contributed the most to both the cost-benefit and clinical outcome benefit of cotesting compared with HPV testing alone. Six variable categories were assessed, and within those 6 variable categories were included 24 subvariables. Further, cost-benefit analyses were offered comparing the two cervical cancer screening strategies as well as presentation of lifetime savings broken to eight age segments. The greatest benefit accrued between ages 35 to 59, and the findings were, that while sensitivity was the greatest driver of effectiveness, specificity of the test strategy was the driver of cost. This suggests the greatest driver for cost with cotesting was reduction in the number of false negatives and the attendant cost associated with treating what could have been a preventable outcome, in addition to the described reduction in women referred for unnecessary follow-up.

Dr. Russell:

So, I notice that a 3-year interval for testing was used in the model. Could you comment on that, and also the pressure to move to a 5-year interval?

Dr. Randell:

Although guidelines currently recommend a 5-year screening interval for Pap plus HPV testing, this continues to be the subject of ongoing debate in the medical community. I personally have concerns about 5-year screening following the data from the US Preventive Service Task Force suggesting that screening intervals longer than 3 years may result in substantial increase in cervical cancer morbidity and mortality.

Walter Kinney's data published last year out of Kaiser demonstrated that a 5-year screening interval

compared with 3 years, there's an additional 1 in 369 cancers diagnosed, and an additional 1 in 1,639 deaths will occur. This translates into approximately 44,000 preventable cancer deaths in the 72 million women 30 to 64 age period by keeping the interval at 3 years. We've seen practice data showing that many clinicians retest with Pap plus HPV at a 3-year interval, and this data certainly supports doing so. This is in line with what our patients want. There's a study that showed that only 7.8% of women would feel comfortable being screened with an HPV test alone. While 68.4% were willing to extend the testing interval to 3 years, only 25.2% would be comfortable with 5 years even if recommended by their physician.

Dr. Russell:

A lot can happen in 5 years.

Dr. Randell:

Well, I honestly believe that the 3-year approach to screening is the right approach. I'm concerned about the possible loss to follow-up when extending to a 5-year interval that could result in an actual interval for patients of 7 to 8 years when they finally remember that they need to be screened.

Dr. Russell:

Dr. Randell, is there other published data to support cotesting compared with HPV testing alone?

Dr. Randell:

Well, results from the largest retrospective study of cervical cancer screening strategies published last year, also known as the Quest study, reinforces screening with Pap plus HPV together as the preferred method for women age 30 to 65. In this study they showed that 1 in 5 women with cervical cancer are missed using HPV testing alone. They also showed that 1 in 16 women with CIN 3 or greater lesions are missed using HPV testing alone. There are many other studies as well that have demonstrated that testing for cervical cancer using Pap plus HPV testing is the preferred strategy for women 30 to 65.

Dr. Russell:

So, doctor, we've covered a lot of material. What would you say is the bottom line for women and the physicians who treat them?

Dr. Randell:

The power of Pap plus HPV together is easy to see. When based on clinical and economic data

modeling, that we discussed earlier, adopting screening with HPV testing alone and eliminating the Pap test from front-line screening could result in a 37% increase in invasive cervical cancer cases for women age 30 to 70. Therefore, the better approach is cotesting; that is performing a Pap and HPV testing together in women 30 years and older. This approach, as shown in the economic modeling data, could over 40 years prevent nearly 150,000 cases of invasive cervical cancer and save approximately \$4 billion in US healthcare costs. Again, I encourage listeners to read the studies I mentioned for the many valuable pieces of information that may have meaning for your clinical practice.

Dr. Russell:

Dr. Randell, thank you so much for sharing your perspectives on this topic with our ReachMD audience.

Dr. Randell:

Thank you.

Narrator:

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