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The HPV Data Is In — What Do the Newest Updates in Screening Mean For Your Patients?

Announcer Intro:
This is CME on ReachMD! The following activity: *The HPV Data Is In — What Do the Newest Updates in Screening Mean For Your Patients?* is provided in partnership with Omnia Education and supported by an independent educational grant from Roche Diagnostics.

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Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
The cervical cancer screening practice environment is continually changing, but patients remain confused and unsure if these new approaches are better, or even less safe than the cervical cancer cytology that has served them well for so many years. Live from the ReachMD studios in Fort Washington, Pennsylvania, I am your host, Dr. Jennifer Caudle. And joining me today is women's health expert, Dr. Thomas Wright, Jr., from Columbia University. Dr. Wright, welcome to the program.

Dr. Wright:
Thank you for having me here tonight.

Dr. Caudle:
Well, I'm excited that you're here. We have so much to talk about. Why don't we go ahead and jump right in? So, Dr. Wright, what I'd like you to do is to kind of give us a little bit of an overview of the latest cervical cancer screening recommendations from the United States Preventative Services Task Force.

Dr. Wright:
Glad to. These are draft recommendations. I really want to stress that at the beginning of tonight, which is, they have been prepared, they've been put out for public comment, and they are still in draft form. So the Preventative Services Task Force is currently modifying them, so they may change a little, but if history is our guide, they usually remain about the way which they go out in draft form.

Dr. Caudle:
Sure.

Dr. Wright:
So these guidelines have actually changed dramatically the way we are going to screen our patients who are 30 to 65 years of age. Most of you know the previous guidelines, which were from the 2012, both from the American Cancer Society, ACOG, as well as the U.S. Preventive Services Task Force, and they said that for individuals who are 30 to 65 years of age, you could screen in 2 different ways. You could do cytology every 3 years, or you could do cotesting. That is testing with both Pap and an HPV test at a 5-year interval, so you would do it every 5 years. And we had harmonization across all of the groups in 2012 with the same recommendation.

Dr. Caudle:
Right.

Dr. Wright:

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Now, in 2014, the FDA approved 1 HPV test for HPV primary screening, and that approval was specifically written to be for women 25 to 65 years of age, and it had a 3-year interval. After the approval, ACOG, the ASCCP, and the Society of Gynecological Oncologists looked at the data, and they said that this was a reasonable way to screen women 25 to 65 years of age. So I think many of us who thought about what was happening with the U.S. Preventive Services Task Force thought that they might add HPV primary screening—that's HPV screening alone—to women 30 to 65 years of age, but they would probably also keep cotesting as one of the screening methods. Well, it turns out they did a comprehensive review of all of the large clinical trials globally, they did a meta-analysis, and they did a lot of modeling studies looking at the economic and the health outcomes impact of the different screening methods, and they decided, based on the data, that they should not include cotesting as one of the ways to screen individuals who are 30 to 65 years of age. Instead, they said you could either do cytology every 3 years or you could do HPV primary screening—that's HPV alone—at a 5-year interval in this age group, so a big change in the way we're going to screen.

Dr. Caudle:
It is a big change. No, absolutely. And you talked about a number of age groups, primarily 25 to 65, 30 to 65, just that kind of general range.

Dr. Wright:
Right.

Dr. Caudle:
What about other age groups? What are our thoughts about that?

Dr. Wright:
I didn't talk about that because our recommendations actually remain pretty much the same.

Dr. Caudle:
Okay.

Dr. Wright:
There should be no screening at all under the age of 21.

Dr. Caudle:
Okay, right, which is what we've been doing.

Dr. Wright:
Vaccinated or unvaccinated, no screening. Over the age of 65, in individuals who have had a 10-year history of negative screens, then they don't need to ever be screened again. They're out of the screening pool. And the age group 21 to 29, it stays the same. It's a Pap every 3 years.

Dr. Caudle:
Okay, good. And I think it's really good to kind of remind our viewers and our listeners about the things that haven't changed, right¬¬—

Dr. Wright:
Right.

Dr. Caudle:
—in addition to the things that have changed, so that's good reinforcement. So going back to the new recommendations, given the new recommended screening intervals, now let's bring it back to the patient side. We're in the office. We're with our patients in the room. How do we actually communicate these changes, these new guidelines, to our patients?

Dr. Wright:
It's going to be tough, and there are a couple of reasons it's going to be difficult. The first is—and I hear this every day—that we keep changing the guidelines. And this is coming from doctors—

Dr. Caudle:
Yes.

Dr. Wright:
—and from clinicians. They say, "Why do you have to change the guidelines every 3 or 4 years?" And the response to that is, the guidelines are changing in response to data. We have large clinical trials coming out all the time, we're getting better and better data, and the guidelines have changed in response to the data. The data for HPV primary screening right now is incontrovertible. There is just tons of data. And most countries are moving in that direction. When you have your patient in front of you though, that is a harder

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discussion—

Dr. Caudle:
Right.

Dr. Wright:
—because the patients are confused. Older patients grew up being told, “Have a Pap every year.”

Dr. Caudle:
Every year, right.

Dr. Wright:
And so they walk in and you say, “Well, you don’t need a Pap for 3 years,” and they think, “Why are you telling…”

Dr. Caudle:
They think you’re doing something wrong. (Laughter)

Dr. Wright:
Absolutely. And if you tell them, “You don’t need an HPV for 5 years,” they really are going to think.

Dr. Caudle:
Right, right, right.

Dr. Wright:
So this is going to take time for all of this to evolve.

Dr. Caudle:
Right.

Dr. Wright:
When you think back, we first got cotesting approved by the FDA in 2003. And in 2007, it wasn’t being done very much. And it wasn’t really until around 2012, 2013, that we ended up getting a big uptake of cotesting.

Dr. Caudle:
That took a while. It took a while.

Dr. Wright:
And HPV primary will be the same trajectory. It will take a decade, I think, for people to really be comfortable with it.

Dr. Caudle:
That’s interesting. That’s very interesting. Yes, no, I think it’s a really sort of interesting topic, and I’m glad we’re talking about that, too. As a family doctor, these are the questions that we are often faced with, as well as GYNs, etc. So, Dr. Wright, I really want to thank you for that overview. I think it was a really great foundation—

Dr. Wright:
Thank you.

Dr. Caudle:
—to really kind of jump off and really get things started. Now let’s turn to questions from our audience.
Our first question comes from one of our viewers. “Dr. Wright, do you think cotesting should continue to have a role in screening?”

Dr. Wright:
Just by way of disclosure, tomorrow morning at 9:00 I will be reading abnormal Paps. I am a GYN cytopathologist by training.

Dr. Caudle:
Right.

Dr. Wright:
So asking me if I think co-testing has a role…

(Laughter)

Dr. Wright:

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But, in fact, cotesting has had a long role in screening. It is very effective as a screening method. I think many of us were surprised that cotesting did not remain as a possible screening method in the U.S. Preventive Services guidelines, or the draft guidelines.

Dr. Caudle:
Interesting.

Dr. Wright:
Clearly, cytology alone I personally don't think should be used to screen women over the age of 30. It is much less sensitive than HPV-based modalities. So I think every woman who's screened over the age of 30 should have the option of having HPV for screening.

Dr. Caudle:
Yes.

Dr. Wright:
It could be a primary screen, which is very effective, or it could be a cotest. Both of those are highly effective. So cytology, I think, still has a role. We're also using cytology as a way to triage HPV-positive patients. One of the big issues when we go to HPV primary screening is: What do you do with the HPV-positive woman? We've got genotyping. We look for HPV 16 and 18. We're getting new extended genotyping coming out. But we also use cytology to screen those patients who don't have 16 and 18, so it's important in reflex. It's also very important for screening the younger women. The women 21 to 29 or 21 to 25, cytology is a preferred approach. That's because so many of those women are HPV positive. Probably, almost 30% of women between the ages of 21 and 25 will be HPV positive in the United States, so you're not going to use HPV to screen those women.

Dr. Caudle:
Okay, that makes a lot of sense, and it's a great answer in terms of being thorough and kind of going through the rationale for these things, too. I think that's really helpful.
So, we have another question, which I think this is a—this is an interesting one. It says, "Dr. Wright, how long do you think it will take for other organizations to adopt the USPSTF guidelines?" It's interesting.

Dr. Wright:
It is interesting.

Dr. Caudle:
Yes, yes.

Dr. Wright:
Prior to 2012, we had a lot of competing guidelines, so the family medicine doctors—

Dr. Wright:
—they tended to follow U.S. Preventive Services, but the OB/GYNs and the women's health clinicians, they tended to follow the American Cancer Society and ACOG recommendations, which were very linked together. What we did in 2012 was a real effort was made to harmonize the guidelines and to get ACOG, ASCCP, all of the groups to combine and have the same recommendations.

Dr. Caudle:
Yes.

Dr. Wright:
I think there is a lot of concern now that since the U.S. Preventive Services did this independently of all the other societies, that we may not have harmonization going forward.

Dr. Caudle:
Interesting.

Dr. Wright:
And it is quite possible that a group like ACOG or the American Cancer Society may look at the same data, but they may end up weighing the data slightly differently, because the differences are actually quite small. It's like cotesting. Is there a real reason not to include cotesting in national screening guidelines? The reason the U.S. Preventive Services Task Force said that cotesting should not be included was that you end up with almost the same level of cancer prevention with primary HPV testing as you do with cotesting, but the difference is you use half as many tests with HPV primary screening per woman's life year saved from cervical cancer, and more importantly, you use a lot more colposcopies and procedures.

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Dr. Caudle:
More procedures, interventions.

Dr. Wright:
And interventions.

Dr. Caudle:
Right.

Dr. Wright:
And so, as part of their health economic modeling, they modeled it for the number of procedures for each of the screening methods, and it was hard to justify cotesting when that was one of your metrics of a potential harm.

Dr. Caudle:
That's interesting.

Dr. Wright:
Yes.

Dr. Caudle:
Risk versus benefits—

Dr. Wright:
Risk versus benefit.

Dr. Caudle:
—and how we weigh data, and that's kind of interesting what you're talking about, how different organizations may look at the data slightly differently or weighing different things a little bit differently to develop their outcomes.

Dr. Wright:
I agree. And they also, remember, have slightly different perspectives.

Dr. Caudle:
Right. That's very true.

Dr. Wright:
U.S. Preventive Services Task Force perspective is for the public health.

Dr. Caudle:
Yes, population.

Dr. Wright:
And screening is a population public health event, whereas American Cancer Society or ACOG, they're much more patient focused. So I think we may end up with different guidelines this time around.

Dr. Caudle:
It'll be interesting to see. That definitely will be interesting to see kind of what comes down the pike. So thank you for that. We do have another question. This viewer says, "After hysterectomy with CIN 2 or 3, what is the followup?"

Dr. Wright:
The followup is that women need to be screened for the next 20 years.

Dr. Caudle:
Ah, okay.

Dr. Wright:
So if she's 55 years old, she needs 20 years of screening with one of the accepted approaches.

Dr. Caudle:
Okay, very good
So this is another question that we're just getting right now is the idea of over-screening, and one of our viewers asked, which I think is a very frank and honest question that we all as clinicians need to be thinking about is, "What's the real harm in over-screening patients who desire a more aggressive approach?" Maybe that woman that's not comfortable with the every 5 years or the 3 years, what's really

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the harm in screening more frequently than maybe is recommended?

Dr. Wright:
At the individual patient perspective, what will happen is she is at increased risk for having detection of an abnormality. She's more likely to be HPV positive, cytology negative, and have a 16 or an 18. You're screening her more frequently, so you will pick up those transient infections—

Dr. Caudle:
Right.

Dr. Wright:
—because people get exposed to HPV all the time. And part of the reason for having an extended interval when you use HPV is to allow transient infections to clear. Fifty percent of new HPV infections clear within 1 year, so if you screen at 3 years, those infections are very likely to disappear, but if you screen yearly, which I see all the time in the Northeast, cotesting on a yearly basis, you're going to pick up those transient infections.

Dr. Caudle:
Right.

Dr. Wright:
You're going to do more colposcopies, and the data is quite clear that you don't give better protection against invasive cancer.

Dr. Caudle:
The outcomes.

Dr. Wright:
The outcomes are very good at 3 years.

Dr. Caudle:
Right, right. And I think that's also… Like I'm sort of thinking about this as you're talking about it. I think that's a really good reminder about how long on average it may take for HPV to clear. You mentioned 1 year, which may be contributing to why we say 3 years and 5 years, etc. I think as clinicians it's important for us to remember that there is rationale and there is data and science behind why these recommendations and guidelines exist the way they do.

Dr. Wright:
Right. The other important point for women 30 to 65 years of age is that once you have had a negative HPV or a negative cotest—you come back in and you're found to have positive HPV, either as a cotest or as primary screening—your risk of high-grade disease is much less than if you're found HPV positive the first time.

Dr. Caudle:
Oh, okay.

Dr. Wright:
So in well-screened women who come in and are HPV positive, risk drops considerably if they have a history of being HPV negative, so that's why you really don't want to screen frequently with HPV.

Dr. Caudle:
Yes, point well taken. We have another question. "Does clinical trial data on cervical cancer screening reflect outcomes in medical practice?"—speaking of outcomes.

Dr. Wright:
Yes, this is difficult, because most of the data that we have comes from large, either randomized clinical trials, all of which have been done in Europe, or from large non-randomized observational trials in the United States and North America. There are 2 from Canada. We've got the large ATHENA trial from the United States. And those are very different settings than your practice or our listeners' practices, because patients are incentivized to come in, clinicians are incentivized to make sure the patients get followed up, and everything is done correctly. Probably, the best data that we have on what really is happening in the real world comes from Kaiser Northern California. In 2007, Kaiser Northern California made a policy throughout the entire healthcare system that they would cotest every woman 30 years and older, and they would do it at 3-year interval. So they have now over 10 years of data looking at outcomes after cotesting. It's over a million women have years of follow up. A million women have been published in this, so it's a huge database.

Dr. Caudle:

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Wow, it's huge.

Dr. Wright:
And what they find is very clear, and it's been consistent now for a number of years. In 2014, they published what was a woman's risk with a negative screening test of having CIN 3 or invasive cancer diagnosed over the ensuing 5 years. If you have an annual Pap, your risk of having CIN 3 or cancer being detected is approximately 7 per 10,000, so it's quite small at a 1-year interval for cytology. And that's kind of the baseline. That's what the American Cancer Society and ACOG told people for years, "Come in yearly." So that's kind of the best scenario and what we've told women to expect. Now, if you do HPV primary screening, HPV alone, but you do a 3-year interval, you have exactly the same risk.

Dr. Caudle:
That's interesting.

Dr. Wright:
There are 7 cases per 10,000 women.

Dr. Caudle:
Wow.

Dr. Wright:
So HPV at a 3-year interval is equivalent to yearly cytology. But now the U.S. Preventive Services isn't calling for yearly cytology anymore. What it's saying is let's do 3-yearly cytology. Risk goes from 7 with yearly cytology to 19 with 3-yearly cytology, so you get almost a tripling of risk by going from yearly to every 3 years. Now, if we look at HPV and we extend the interval out—we go from 3 years to 5 years, which is what the current U.S. Preventive Services Task Force is calling for—your risk now goes up to 14, so you have 14 cases. It's not a huge jump, but it's more than 7.

Dr. Caudle:
Sure.

Dr. Wright:
It's double. If you look at cotesting done at a 5-year interval, which is what the old guidelines called for, the risk was 11 cases per 10,000, so it's a little lower than what we get now. Actually, now we're increasing risk with the new guidelines compared to the old guidelines., not dramatically but a little bit.

Dr. Caudle:
That's interesting. And it looks like we have 1 more question—it's kind of a 2-parter—by one of our viewers. First part is, "What will be the impact of the HPV vaccine on disease, and how will this then impact cervical cancer screening in the United States and internationally?" So let's start with part 1.

Dr. Wright:
Yes. What the impact is going to be really depends on how effective we've been at vaccination. If you go to Australia... And we've got good data now coming out of Denmark and Australia and the United Kingdom where they have been able to vaccinate 70 to 80% of young women because they have school-based vaccination programs. What they have shown is dramatic drops in high-grade disease and in condylomas after vaccination. The United States, we don't have a school-based screening program, vaccination program. We wish we did, but we don't, so we have less across-the-board vaccination, so the impact is less, although we have measurable impacts now in the United States. So, if you are in Australia, what are you going to do? You are going to begin screening at an older age. They've just changed their screening program to not screen until age 25.

Dr. Caudle:
Because of how high their vaccination rate is.

Dr. Wright:
Because of how high the vaccination rate is.

Dr. Caudle:
Right.

Dr. Wright:
There's so little high-grade disease. They are going to screen at a 5-year interval with HPV, which in a low-prevalent setting of high-grade disease makes a lot of sense. In addition, most countries which have looked at cytology versus HPV testing in vaccinated

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populations really believe that cytology is going to start to perform poorly in a low-prevalent setting of high-grade disease. And when you think about it, cytology really is very subjective. Technicians sit down; they look at the slides; they try to decide whether or not a cell is abnormal or not abnormal. If you drop the prevalence of high-grade disease, they're going to be looking at lots of normal slides.

Dr. Caudle:
That's true.

Dr. Wright:
More than they are now.

Dr. Caudle:
That's true.

Dr. Wright:
And therefore, the performance of the test is going to get worse.

Dr. Caudle:
Interesting.

Dr. Wright:
So most epidemiologists who've looked at potential screening methods in vaccinated versus unvaccinated, they say cytology probably should go away in a heavily vaccinated population, and HPV should become the test of choice.

Dr. Caudle:
Interesting.

Dr. Wright:
But we aren't there in the United States.

Dr. Caudle:
Sure, sure.

Dr. Wright:
So how are our vaccination programs going to impact screening in the United States? Well, the new recommendations don't talk about a vaccinated population versus a non-vaccinated because we don't a vaccine registry. So you have a woman come in for screening; you do not know if she really was vaccinated against HPV, how many doses she got, and at what age she was vaccinated.

Dr. Caudle:
Right.

Dr. Wright:
So we're not going to be able to change how we screen over the next few years until we get a very high prevalence of vaccination or coverage of vaccination in the United States. Once we get that, I think we will also start screening at 25 and older and we'll continue to screen at 5-year intervals.

Dr. Caudle:
Very interesting. Thank you so much for that. We've gotten a lot of great questions from you guys, and we've covered a lot of wonderful information, and I can't thank you enough for that. And before we close out, I just wonder, Dr. Wright, based on some of the questions that we've gotten, do you have a final take-home message for our viewers tonight?

Dr. Wright:
I think there are 2 points that really came home from these questions and that come home when I speak to clinicians. The first is, this is going to be a slow process. People are still wary of HPV primary screening. Patients are a little wary of it. And it's going to take a few more years before people get really comfortable with it. The second is, things are really complex, and it's going to take lots of education of providers to make them comfortable with the changing guidelines, and it's going to take even more discussion with your patients to get your patients comfortable with the changing guidelines.

Dr. Caudle:
I think those are good reminders and kind of a good forecast, perhaps, for what's to come.

Dr. Wright:
Right. It's going to take even more time to counsel women when you tell them, "Well, we're not going to do a Pap. We have this better

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test, HPV. It's recommended. And if you're negative, I don't need to see you for another 5 years."

Dr. Caudle:
Very interesting. Well, with that, I'd really like to thank you, Dr. Wright, for joining us tonight. Thank you so much for being here.

Dr. Wright:
Thank you. Thank you for having me.

Dr. Caudle:
And this has been a wonderful discussion reviewing the latest cervical cancer screening guidelines as well as answering your questions. And I'd also like to thank you all, our audience, for your participation in this program. We certainly couldn't do it without you. Live from the ReachMD studios in Fort Washington, Pennsylvania, I am Dr. Jennifer Caudle for ReachMD, encouraging you to Be Part of the Knowledge.

Announcer Close:
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