

# Letters to the Editor

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This series is coordinated by Kenny Lin, MD, MPH, Associate Deputy Editor for *AFP* Online.

## Additional Protection from 9-Valent HPV Vaccine if Administered Before HPV Exposure

**Original Article:** 9-Valent HPV Vaccine Offers Only Small Advantage Over Quadrivalent Vaccine [POEMs]

**Issue Date:** July 1, 2015

**See additional reader comments at:** <http://www.aafp.org/afp/2015/0701/p54.html>

TO THE EDITOR: Dr. Ebell's review of the study by Joura and colleagues<sup>1</sup> asserts that the 9-valent human papillomavirus (HPV) vaccine offers only a small advantage over the quadrivalent vaccine. He bases this on his assessment of data presented for the modified intention-to-treat population that includes persons who were already infected before vaccination.

HPV vaccines are prophylactic (i.e., they prevent HPV infection in persons who have not been exposed to the virus). They have no impact on HPV infections acquired before vaccination. Thus, an intention-to-treat analysis, which includes persons infected with HPV before vaccination, is not a suitable evaluation of prophylactic efficacy.<sup>2</sup> Prophylactic efficacy is assessed in the per-protocol population, which approximates a susceptible population of HPV-naïve individuals.

The per-protocol analysis showed that vaccine effectiveness against disease caused by the additional HPV types in the 9-valent vaccine was 96.7% (95% confidence interval, 80.9 to 99.8).<sup>1</sup> Based on these results, the Advisory Committee on Immunization Practices (ACIP) has included the 9-valent HPV vaccine in its recommended routine HPV vaccinations for girls and boys 11 and 12 years of age, and catch-up vaccination of girls and women 13 to 26 years of age and boys and men 13 to 21 years of age who have not been vaccinated previously.<sup>3</sup> The introduction of 9-valent HPV vaccination in both males and females was cost-saving

compared with the quadrivalent HPV vaccine in cost-effectiveness analyses.<sup>3</sup>

From these results, we can conclude that the 9-valent HPV vaccine represents a meaningful advantage over existing HPV vaccines. This added protection against infection and disease caused by HPV types 31, 33, 45, 52, and 58 offers the potential to prevent an additional 30% to 35% more high-grade cervical lesions<sup>4</sup> and to increase cervical cancer prevention from approximately 70% to 90%.<sup>4,5</sup> Early vaccination before HPV exposure is key to derive the optimal benefit. Health care professionals should vaccinate all eligible 11- to 12-year-old patients using every appropriate opportunity, because these preadolescents are much less likely to have been exposed to HPV than are older adolescents. In addition, clinicians should vaccinate older patients who have not been previously vaccinated according to the ACIP recommendations for these catch-up cohorts.

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IN REPLY: I do not dispute the results of the per-protocol analysis. I acknowledged in my review that among uninfected women, there is a statistically significant reduction in the likelihood of HPV infection, but that this is relatively small (number needed to treat = 160 for three years to prevent one high-grade lesion). The per-protocol analysis that is emphasized by Dr. Joura provides the most optimistic estimate of benefit and does not reflect what would happen in primary care practice, where physicians do not typically check for evidence of previous HPV exposure before beginning a series of immunizations. As I stated, the 9-valent HPV vaccine provides an overall benefit, but it is modest. Fortunately, the cost of these two immunizations is fairly similar. It is also important to note that the ACIP recommends a ceiling age of 21 years for men and 26 years for women for catch-up immunization.<sup>1</sup>

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## Diagnostic Tool for Gout Without Need for Joint Fluid Aspiration

**Original Article:** Differential Diagnosis of Polyarticular Arthritis

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TO THE EDITOR: We appreciate this comprehensive and engaging article. We agree that joint

fluid analysis is the preferred method for the diagnosis of gout, and that uric acid measurements are not beneficial when interpreted in isolation. However, as mentioned in an earlier article on gout published in *American Family Physician*,<sup>1</sup> a diagnostic tool was developed in 2010 to aid primary care physicians in diagnosing the condition without the need for joint aspiration.<sup>2</sup> This tool uses seven independent criteria, including serum uric acid level, to determine the likelihood that a patient is experiencing a gouty flare (*Table 1*).<sup>3</sup> It was validated in a 2015 study, in which scores of 4 or less demonstrated a negative predictive value of 0.95, whereas scores of 8 or more had a positive predictive value of 0.87.<sup>3</sup> Although scores between 4 and 8 may warrant joint aspiration and fluid analysis, this diagnostic tool may prove clinically useful when a gouty cause is suspected in patients with arthritic symptoms and the capability of joint aspiration does not exist or is impractical.

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Army, Department of the Air Force, Department of Defense, or the U.S. government.

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IN REPLY: Thank you for bringing these articles to our attention. The decision tool may perform well when the typical and classic features of gout are present and may be especially valuable in resource-poor settings.<sup>1-2</sup> However, its use is limited to straightforward cases. Synovial fluid testing remains indicated in patients with a mixed crystal arthritis, comprising both gout and pseudogout; when ►

**Table 1. Diagnostic Tool for the Evaluation of Suspected Gouty Arthritis**

Criteria	Points
Male	2
Previous self-reported arthritis attack	2
Onset within 1 day	0.5
Joint redness	1
Involvement of first metatarsophalangeal joint	2.5
Hypertension or at least one of the following conditions: angina pectoris, cerebrovascular accident, heart failure, myocardial infarction, peripheral vascular disease, transient ischemic attack	1.5
Serum uric acid level > 5.88 mg per dL (350 $\mu$ mol per L)	3.5
Total	____ (out of 13 possible points)

NOTE: Gout is unlikely with a score  $\leq 4$  (negative predictive value = 0.95); gout is likely with a score  $\geq 8$  (positive predictive value = 0.87). The probability of gout is uncertain with scores between 4 and 8, warranting further diagnostic testing or joint fluid aspiration.

Adapted with permission from Kienhorst LB, Janssens HJ, Fransen J, Janssen M. The validation of a diagnostic rule for gout without joint fluid analysis: a prospective study. *Rheumatology* (Oxford). 2015;54(4):612.

empiric gout treatment fails; or if there is a need for better informed decisions regarding newer generation uric acid-lowering agents, which are expensive and have considerable risks of other organ toxicity.<sup>3-4</sup>

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