Background

- Investigators at Quest Diagnostics responded via published letter to an article by Cotton et al., who recommended against the use of mRNA-based HPV testing as a first-line screening tool for cervical cancer.
- In the Cotton et al. study, investigators retrospectively examined the results of HPV mRNA tests performed November 2014 through June 2016 among women ≥30 who had at least 1 positive DNA-based HPV test result before November 2014.
- Among 425 women with a positive HPV DNA test and a subsequent mRNA test, 68.6% had negative results on the HPV mRNA test. Of these, 201 (69.6%) would have likely had their test followed up based on the negative mRNA result.
- The investigators concluded that mRNA-based HPV testing is not as sensitive as DNA-based HPV testing for detecting HPV infections.

Response

- In their response letter, Quest investigators pointed out limitations of the Cotton et al. study.
  - A major limitation was that there was no clinical follow-up, meaning that clinical sensitivity and specificity could not be directly assessed.
- The Quest investigators also cited other studies that contradicted Cotton et al.‘s conclusions.
  - Two recent head-to-head comparisons and a review of over 60 studies showed that mRNA- and DNA-based HPV testing methods have comparable sensitivity for detecting high-risk lesions, with mRNA-based testing exhibiting superior specificity.
  - Further, the investigators provided data from their own experience.
    - They analyzed de-identified HPV test results of 34,640 women (30-65 years of age) in the United States who had follow-up colposcopy or biopsy within 6 months; 19,228 had mRNA-based HPV test results and 15,412 had DNA-based HPV test results.
    - Of the 34,640 women, 714 women had high-grade lesions (CIN3+), of whom 73 were determined to have cancer.
    - Sensitivity results: The mRNA- and DNA-based HPV testing methods did not significantly differ in sensitivity for detection of high-grade lesions (P=0.4).
      - mRNA-based HPV testing: 98.5%
      - DNA-based HPV testing: 97.1%
    - Specificity results: mRNA-based HPV testing was significantly more specific than DNA-based HPV testing for detection of high-grade lesions (P<0.001).
      - mRNA-based HPV testing: 19.4%
      - DNA-based HPV testing: 13.4%

Conclusions

- Based on the experience of Quest Diagnostics, as well as evidence from multiple studies, the authors have responded that mRNA-based HPV testing is appropriate for use as a first-line screening tool for cervical cancer.