

## LETTER TO EDITOR

**THE HEALTH OUTCOME AND THE COSTS OF PRIMARY HPV TESTING WITH DUAL-STAIN CYTOLOGY TRIAGE IN CERVICAL CANCER SCREENING**

WIEBREN A.A. TJALMA

Multidisciplinary Breast Clinic, Gynaecological Oncology Unit, Department of Obstetrics and Gynaecology, Antwerp University Hospital – University of Antwerp, Antwerpen, Belgium

Dear Editor,

The article by Celewicz *et al.* describes nicely the clinical efficacy of p16/Ki67 dual-stained cervical cytology in secondary prevention of cervical cancer [1]. In their article they show that the assessment of p16/Ki-67 can lead to an increased efficiency of cervical cancer screening through higher sensitivity and specificity. Additionally they state that the cost/benefit ratio may be higher in comparison to HPV DNA or mRNA detection.

Recently, we published a systematic literature review on the diagnostic performance of dual-staining cytology for cervical cancer screening together with a model that looked at the impact of dual-stain cytology on the health outcome and the health system budget [2, 3].

For cervical cancer screening we recommend primary HPV detection instead of cytology [4]. Primary HPV screening has a higher sensitivity than primary cytology screening but a lower specificity. In other words a normal cytology test has a greater chance of being false negative than a normal HPV test. With primary HPV screening you will detect considerably more abnormalities. The HPV testing will detect all HPV infections: transient and persistent. A downside is of course the detection of these transient HPV infection(s). They can be regarded as “false positive”. Referring all HPV positive women for colposcopy and biopsy would increase not only the sensitivity, but also the morbidity and costs. The latter two points could lead to a decrease in cervical cancer screening attendance. Colposcopy triage of HPV positive women based upon dual stain cytology instead of cytology would increase the sensitivity significantly with no significant impact on specificity [2, 3]. In other words dual stain cytology will reduce the incidence of cervical cancer and save more women’s lives.

At the same time, it will lead to a reduction of unnecessary colposcopy referrals, biopsies and follow-up visits. Primary HPV screening with dual-stain cytology triage in Belgium would reduce the cervical cancer incidence and mortality by respectively 36% and 40% [3]. Dual-stain cytology or diagnostic cytology is additional testing and assumes additional costs. A cost-effectiveness evaluation of diagnostic cytology is therefore essential. A Budget Impact Model (BIM) was created based on a Markov decision-analytic model in order to calculate the budget impact of primary HPV screening with dual-stain cytology triage instead of cytology [3]. In a simulation for Belgium we showed that diagnostic cytology could reduce the screenings budget by 21% a year [3]. In the article of Celewicz *et al.* the value of dual staining is described, and they state that the cost/benefit ratio is probably better than HPV DNA detection [1]. We dare to state that combining HPV screening with dual stain cytology triage is probably better and cheaper.

Dual stain cytology or diagnostic cytology has the potential to reduce morbidity, mortality and costs. The created Budget Impact Model can be customized according to the country’s cervical cancer screening strategy. If decision-makers would use the model than they could estimate the costs and the health outcome of cervical cancer screening strategy in their country.

---

*The author declares no conflict of interest.*

**References**

1. Celewicz A, Celewicz M, Wężowska M, et al. Clinical efficacy of p16/Ki-67 dual-stained cervical cytology in secondary prevention of cervical cancer. *Pol J Pathol* 2018; 69: 42-47.

2. Tjalma WAA. Diagnostic performance of dual-staining cytology for cervical cancer screening: A systematic literature review. *Eur J Obstet Gynecol Reprod Biol* 2017; 210: 275-280.
3. Tjalma WAA, Kim E, Vandeweyer K. The impact on women's health and the cervical cancer screening budget of primary HPV screening with dual-stain cytology triage in Belgium. *Eur J Obstet Gynecol Reprod Biol* 2017; 212: 171-181.
4. Tjalma WA. The ideal cervical cancer screening recommendation for Belgium, an industrialized country in Europe. *Eur J Gynaecol Oncol* 2014; 35: 211-218.

### **Address for correspondence**

**Prof. Dr. W. A. A. Tjalma**  
Multidisciplinary Breast Clinic-Unit Gynecological Oncology  
Antwerp University Hospital  
Wilrijkstraat 10  
2650 Edegem, Belgium  
e-mail: Wiebren.Tjalma@uza.be