

# Authors' reply re: Reflex cytology for triage of high-risk human papillomavirus positive self-sampled material in cervical cancer screening: a prospective cohort study. (Response to BJOG-20-1479)

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Dear editor/Sir,

We thank Song et al. for their insightful comments (1) on our article (2) and commend them for their study about human papillomavirus (HPV)-genotyping on self-samples and their analysis on different triage strategies for detecting cervical intraepithelial neoplasia grade 2 or worse (CIN2+) (3). They report that cytology on physician-sampled material has a sensitivity of 74.8% for detecting CIN2+, while HPV-genotyping for 16/18 has a sensitivity of 52.6% for detecting CIN2+. This means that HPV-genotyping in their hands, is still inferior to cytology testing and cannot fully replace this triage strategy. However, adding HPV-genotyping to cytology testing could increase the sensitivity, as has been described by others as well. While our study shows that reflex cytology on self-samples cannot replace triage with regular cytology for HPV-positive women, because of the low sensitivity of 29.4% for detecting CIN2+, it is valuable as an additional method for triage (2). With a positive predictive value (PPV) of 68.1% for detecting CIN2+ it is effective to refer HPV-positive women with abnormal cytology on self-sampling directly for colposcopic evaluation without the requirement of an extra visit to the general practitioner. A PPV of 21.2% for HPV-genotyping for 16/18 on self-samples for detecting CIN2+ is not enough to refer these women directly for colposcopy. We agree that cost-effectiveness is important. It is not sure if 15% of direct referral will completely cover the costs for 85% of double cytology testing. As the collection in PreservCyt (Cytoc Corporation, Boxborough, MA, USA) has already been performed for HPV-testing on the self-samples, extra costs will include the use of ThinPrep slides (Hologic Inc, Marlborough, MA, USA) and cytotechnicians' time for analysing the slides. On the other hand, there will be a reduction in costs for consulting the general practitioner and for regular cytology testing, including material costs (Cervex brush (Rovers® Medical Devices B.V., Oss, the Netherlands), PreservCyt jar, ThinPrep slide), transportation costs, and cytotechnicians' time for analysing the slides. However, besides cost-effectiveness, patient comfort is at least as important, as well as reduction in loss-to-follow-up and diagnostic delay, in which the latter also positively influences the costs. It remains a challenge to find a triage method on HPV-positive self-samples which could fully replace regular cytology. Molecular tests, such as methylation markers and microRNA detection, are promising future triage methods (4, 5). They are more objective than cytology testing and highly reproducible, however not ready yet for full implementation in cervical cancer screening. Further research on self-samples is warranted to find an optimal triage strategy. Until then, reflex cytology on self-samples could be easily implemented in the current screening programme and improve cervical cancer prevention.

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**Disclosure of interest:** the authors report no conflicts of interest