

## Are the VAERS-included reactions following the human papillomavirus immunization correlated to the number of vaccine doses?

Sir,

Through their recent analysis of VAERS database as regards the individuals who were immunized with human papillomavirus (HPV) vaccine, Neha *et al.* did not identify any new/unexpected safety concern. A large variety of clinically significant adverse events (AEs) following (temporally) the HPV immunization were retrieved by these authors; among those, syncope was the most common AE documented after this vaccination, in terms of cumulative reporting odds ratio (ROR) value. Moreover, several additional “autonomic/neurological” manifestations were reported as well, such as dizziness (following syncope, in terms of cumulative ROR), headache, abasia, paresthesia, anxiety, asthenia/fatigue, (unspecified) general malaise, and arthralgia/myalgia.<sup>[1]</sup> Some of those could be interpreted as somatoform (“pseudo-neurological”) disorders since it is not possible to diagnose any specific or well-defined clinical condition in most cases.<sup>[2]</sup>

Some years ago, we described a case series of female adolescents developing severe somatoform and dysautonomic syndromes temporally related to HPV vaccination; interestingly, only 4 out of 18 patients manifested their complaints after the first dose.<sup>[3]</sup> Therefore, it would be interesting to analyze these AEs with respect to the number of administered doses of HPV vaccine, in order to assess if there is any correlation between the reports number and this specific aspect.

Indeed, recent evidences supported the effectiveness of HPV vaccine despite a reduction of the doses number. Brotherton *et al.* performed a statistical analysis of the quadrivalent HPV vaccine effectiveness, using and linking several national Australian registries, and they correlated the data regarding the number of HPV vaccine doses (0, 1, 2, and 3 doses) with the diagnoses of high-grade cervical intraepithelial neoplasia: they could conclude that “one dose had comparable effectiveness as two or three doses in preventing high-grade disease in a high coverage setting.”<sup>[4]</sup> Very recently, Markowitz *et al.* assessed the prevalence of HPV serotypes in young women (aged 20–29 years), who were screened for cervical cancer, and

considered their immunization status with the quadrivalent HPV vaccine. Among women who received only 1 dose before 18 years of age, the prevalence of the four vaccine serotypes was 0.5%, which was not different from the age-matched women immunized with 2 or 3 doses.<sup>[5]</sup>

Therefore, reducing the dose schedule of HPV immunization seems to be a feasible and reasonable approach: in addition to containing the healthcare-related costs and further promoting the acceptance of this important vaccination, also the number of AEs reports might be reduced in future.

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### Conflicts of interest

There are no conflicts of interest.

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