Response to Vaccine-related serious adverse events might have been under-recognized in the pivotal HPV vaccine randomized trial

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To the Editor,

I was dismayed that a recent article from Dr Martinez-Lavin[1] in regards to the 14,000 women study by Joura and colleagues [2] was published due to serious errors the letter contains.

The major focus of Martinez-Lavin is his concern about differences in ‘systematic serious adverse events’ between the 9-valent vaccine and control groups. The first problem is that the author refers to the data examined as ‘systematic serious adverse events’ not as ‘systematic adverse events’ as it is referred to in the original study. The other issue that isn't mentioned by the author is that, out of 233 serious adverse events reported in the 9-valent group, only 25 have an interval of 15 days or less between vaccination and the onset of symptoms.

Martinez-Lavin also presents some ad hoc statistical analysis that presents the differences observed to be statistically significant, a claim not made in the original manuscript. The study by Joura and colleagues covered women from at least three continents with a range of confounders (smoking, chlamydia infections, sexual history and contraception use), and the reported serious adverse events are divided into 25 different categories. Statistical analysis taking these different variables into consideration is the minimal requirement before making broad definitive statements on whether a difference is significant.

Joura and colleagues determined that only 2 subjects in each group were judged to have a vaccine-related serious adverse event. Martinez-Lavin claims that these small numbers represent an ‘incongruity’. However, Table S6 in Joura et al [2] shows that some of the reported serious adverse events that had onset of 15 days or less after 9-valent vaccination include: an ear and labyrinth disorder, two cases of psychiatric disorders, an anaphylactic reaction, and a separate hypersensitivity reaction, to non-study medications, a metabolism and nutrition disorder, and a gastrointestinal disorder. There is no clear biological mechanism for how HPV vaccination could be causational for any of these conditions.

This letter, like other previous work of Martinez-Lavin, has been critical of HPV vaccination. Previous publications have attracted criticism from a range of researchers and organisations. In the current letter Martinez-Lavin cites his previous paper in Clinical Rheumatology, which was a questionnaire-based study. This study has been criticized for flawed methods and analysis by Dr Petousis-Harris [3] in the same journal. Work by Martinez-Lavin was also included in an assessment by the European Medicines Agency (EMA) of HPV vaccination as a possible cause of Complex Regional Pain Syndrome (CRPS)[4]. The EMA concluded that the evidence does not support that HPV vaccines cause CRPS.

Disclosures: None.
1. Martinez-Lavin M (2017) Vaccine-related serious adverse events might have been under-recognized in the pivotal HPV vaccine randomized trial. Clinical rheumatology. doi:10.1007/s10067-017-3575-z

