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## Reply to the editor

*Dear Editor,*

We thank Jayaraj and Kumarasamy for their response to our systematic review and meta-analysis of the prevalence of cervical human papilloma virus (HPV) infection in women with systemic lupus erythematosus (SLE) [1], whose main objective was to evaluate the prevalence of cervical HPV in SLE pacientes compared with healthy controls and, secondarily, to determine whether risk factors were more frequent in SLE patients with cervical HPV infection. In almost all the original studies included also had the main objective of comparing cervical HPV infection prevalences between SLE patients and controls and some also analyzed possible associated risk factors, both traditional and SLE-related factors (particularly immunosuppresive therapy). It is established that the major risk factors for HPV infection are behaviors related to sexual activity [2], but factors unrelated to sexual behavior have been identified such as the first sexual intercourse at an early age, long-term oral contraceptive use [3], ethnicity [4], etc. Although, we placed no restriction on risk factors the lack of evidence in original studies, or a low level of evaluation of some traditional risk factors and differing definitions limited the inclusion of risk factors such as early age at the first sexual intercourse or contraceptive use, etc. Despite these shortcommings, we extracted data from four studies [5–8] that analyzed multiple sexual partners as a classical risk factor for genital HPV, without finding it was significant.a

We understand the importance of cervical HPV genotypes. However, we found only three studies [5,9,10], including 333 SLE patients and 4879 controls, which compared the prevalence of HR-HPV genotypes between SLE patients and healthy controls. Data from these studies was pooled in a new analysis, which showed that SLE patients had a greater frequency of cervical HR-HPV than controls (18.3% vs. 7.8%; OR: 3.94 [95%CI: 2.76–5.72], $I^2$: 0%), showing the further studies longitudinally evaluating the persistance of HR-HPV infection are required.

Jayaraj and Kumarasamy refer to measures to assess publication bias and between-study heterogeneity using Orwin's Fail-safe N test and Duval and Tweedie's Trim and Fill calculations, and the $Tau^2$ parameter, respectively. Those measures apply for random effects meta-analysis models, not for multilevel linear (mixed-effects) models in the short meta-regression models that were used in our analysis. Likewise, these tests cannot ameliorate or adjust for publication bias, but are correctly used to measure the magnitude of the aforementioned bias under very specific assumptions.

The Tau parameter is one variance component which appears in random effects models. In our multilevel models we determined, using statistical parsimony (AIC and deviance criteria), that only one variance component was needed, and thus it is reported as $Sigma^2$. This may be interpreted as variability due to measures from different studies (i.e. this is the variance at the study level). Assessment of publication bias in meta-regression models is not as straight forward as is the case for fixed or random effects models. We encourage the authors to review the documentation of the R package metafor [11] and its home web page http://www.metafor-project.org, which has many examples and references about the models we used.

Last but not least, we recognize the importance of registering the protocols of systematic reviews (SR) in repositories such as PROSPERO [12] and other registries such as Systematic Review Data Repository (SRDR) [13] and research registry® [14]. SR registration is not yet required by most journals (nor is it an International Committee of Medical Journal Editors-ICMJE-journal requirement); therefore, the motivation of systematic reviewers to register their SR is likely due to other factors [15]. We followed the PRISMA guidelines [16], which states that depositing a review in a public repository is not mandatory. Tsujimoto et al. [17] analyzed whether or not registration of SR protocols reduced outcome reporting bias in high-impact journals and found that of all protocols analyzed only 21% were registered, that protocol registration was not associated with outcome reporting bias, and that the association between PRISMA adherence and protocol registration was not statistically significant.

However, according to Jayaraj and Kumarasamy's suggestion, we have uploaded the completed dataset to the Mendeley Data for Journals Repository, as encouraged by an Elsevier editorial, and we do not now use PROSPERO.

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Availability of data and materials

Not applicable.

### Conflict of interest

The authors declare no conflicts of interest.

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## References


[1] Garcia-Carrasco M, Mendoza-Pinto C, Rojas-Villarraga A, Molano-Gonzalez N, Vallejo-Ruiz V, Munguia-Realpozo P, et al. Prevalence of cervical HPV infection in women with systemic lupus erythematosus: a systematic review and meta-analysis. Autoimmun. Rev. 2019;18:184–91.

[2] Chelimo C, Wouldes TA, Cameron LD, Elwood JM. Risk factors for and prevention of human papillomaviruses (HPV), genital warts and cervical cancer. J. Infect. 2013 Mar;66(3):207–17.

[3] Ley C, Bauer HM, Reingold A, Schiffman MH, Chambers JC, Tashiro CJ, et al. Determinants of genital human papillomavirus infection in young women. J. Natl. Cancer Inst. 1991 Jul;83(14):997–1003.

[4] Burk RD, Ho GY, Beardsley L, Lempa M, Peters M, Bierman R. Sexual behavior and partner characteristics are the predominant risk factors for genital human papillomavirus infection in young women. J. Infect. Dis. 1996 Oct;174(4):679–89.

[5] Klumb EM, Pinto AC, Jesus GR, Araujo MJ, Jascone L, Gayer CR, et al. Are women with lupus at higher risk of HPV infection? Lupus 2010;19(13):1485–91. [Internet]. Available from:. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med6&NEWS=N&AN=20605875.

[6] Yu SL, Chan PKS, Wong CK, Szeto CC, Ho SC, So K, et al. Antagonist-mediated down-regulation of Toll-like receptors increases the prevalence of human papillomavirus infection in systemic lupus erythematosus. Arthritis Res. Ther. 2012;14(2):R80.

[7] Mendoza-Pinto C, Garcia-Carrasco M, Vallejo-Ruiz V, Taboada-Cole A, Munoz-Guarneros M, Solis-Poblano JC, et al. The impact of glucocorticoids and anti-cd20 therapy on cervical human papillomavirus infection risk in women with systemic lupus erythematosus. Clinics (Sao Paulo) 2013;68(12):1475–80. [Internet]. Available from:. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=24473503.

[8] Amaral JL, Araújo MV, Dias GA, Ledebur EI, Quaresma JA, Fuzii HT. Clinical and epidemiological study of human papillomavirus infection in women with systemic lupus erythematosus in eastern brazilian amazon. Acta Reumatol. Port. 2016:47–54. [Internet]. Available from:. http://www.ncbi.nlm.nih.gov/pubmed/27750272.

[9] Lee YH, Choe JY, Park SH, Park YW, Lee SS, Kang YM, et al. Prevalence of human papilloma virus infections and cervical cytological abnormalities among Korean women with systemic lupus erythematosus. J. Korean Med. Sci. 2010 Oct;25(10):1431–7.

[10] Nath R, Mant C, Luxton J, Hughes G, Raju KS, Shepherd P, et al. High risk of human papillomavirus type 16 infections and of development of cervical squamous intraepithelial lesions in systemic lupus erythematosus patients. Arthritis Rheum. 2007;57(4):619–25. [Internet]. Available from:. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=med5&NEWS=N&AN=17471531.

[11] Viechtbauer M. Conducting meta-analyses in R with the metafor package. J. Stat. Softw. 2010;36:1–48.

[12] Booth A, Clarke M, Dooley G, Ghersi D, Moher D, Petticrew M, et al. The nuts and bolts of PROSPERO: An international prospective register of systematic reviews. Syst. Rev. 2012;1(1).

[13] Lau J, Hadar N, Iovin R, Ip S, Balk EM. Proposed governance and data management policy for the systematic review data repository. Agency Healthc. Res. Qual. U. S. 2012 [Cited 2019 Jan 10]. Available from. http://www.ncbi.nlm.nih.gov/pubmed/23101051.

[14] Fowler AJ, Dowlut N, Limb R, Baldacchino MV, Sonagara V, George N, et al. Analysis of the first 2645 registrations at the research registry®: a global repository for all study types involving human participants. Int. J. Surg. 2018 Dec;60:231–5. [Internet]. [cited 2019 Jan 10]. Available from:. https://linkinghub.elsevier.com/retrieve/pii/S1743919118316820.

[15] Page MJ, Shamseer L, Tricco AC. Registration of systematic reviews in PROSPERO: 30,000 records and counting. Syst. Rev. 2018;7(1):1–9.

[16] Moher D, Liberati A, Tetzlaff J, Altman DG, Mulrow C, Gotzsche PC, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 2009 Jul 21;339:b2700.

[17] Tsujimoto Y, Tsujimoto H, Kataoka Y, Kimachi M, Shimizu S, Ikenoue T, et al. Majority of systematic reviews published in high-impact journals neglected to register the protocols: a meta-epidemiological study. J. Clin. Epidemiol. 2017;84(2017):54–60. https://doi.org/10.1016/j.jclinepi.2017.02.008. [Internet].



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