Meta-analysis of penile cancer: conceptual interpretations

The systematic review and meta-analysis presented by Tina Olesen and colleagues,[1] regarding the prevalence of human papillomavirus (HPV) DNA and $p16^{INK4a}$ in penile cancer and penile intraepithelial neoplasms, is of substantial interest and relevance to the field of oncology. The study is of great clinical value, because it highlights the importance and benefits of anti-HPV vaccination in men and boys as a possible counteraction to the development of penile cancer. However, a few aspects of the study warrant further discussion.

The authors have done a meta-analysis without indicating or assessing the weight of each included study upon the pooled results, wherein the parameter of study weight refers to the magnitude of influence each individual study's results have upon the final pooled results. The authors state that they used meta-regression and stratified the analysis to explore the source of heterogeneity between the studies. Meta-regression models often use multiple study-level covariates, and this is also true for the study by Olesen and colleagues.[2] Since multiple covariates exist, it is difficult to observe the contribution of each study to the final pooled values of prevalence. Without a proper analysis of the weight of each study, it might be falsely assumed that each study has an equal effect on the parameter of interest. Hence, to avoid misinterpretation of the analysis and the subsequent results, a thorough analysis of study weight is imperative.

The authors make no mention of possible biases in their study. Meta-analyses are inherently plagued by multiple types of unavoidable biases, because they are based on pre-published literature.[3] Selection bias and retrieval bias are controlled by the use of Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, and individual study bias is controlled by quality assessment. However, publication bias cannot be eliminated from meta-analytical studies. Results of studies influence their likelihood of publication as part of peer-reviewed literature, thereby making publication bias inevitable. This ubiquity of publication bias makes it imperative that all meta-analyses address and assess it. Without assessment of publication bias, the clinical applicability of the presented results can be called into question.[4]

The authors could also have presented the Tau^2 value, representing absolute heterogeneity, to complement the assessment of heterogeneity provided by I^2 and Cochran's Q.[5] Finally, additional analysis of Tau^2 might help enrich the study. However, the study weight and publication bias need to be investigated if the study by Olesen and colleagues is to have clinical relevance.

We declare no competing interests.

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3 Felson DT. Bias in meta-analytic research. *J Clin Epidemiol* 1992; **45:** 885–92.

4 Murad MH, Chu H, Lin L, Wang Z. The effect of publication bias magnitude and direction on the certainty in evidence. *BMJ Evid Based Med* 2018; **23:** 84.

5 Jayaraj R, Kumarasamy C, Madhav MR, et al. Comment on "Systematic review and meta-analysis of diagnostic accuracy of miRNAs in patients with pancreatic cancer". *Dis Markers* 2018; **2018:** 6904569.