Reply to Qingpeng Xie and Dianqiu Shen s Letter to the Editor re: Bhavan P. Rai, Jos Luis Dominguez Escrig, Lu s Vale, et al. Systematic Review of the Incidence of and Risk Factors for Urothelial Cancers and Renal Cell Carcinoma Among Patients with Haematuria. Eur Urol 2022;82:182 92

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We read with interest the suggestions and comments by Xie and Shen [1] on our systematic review (SR). The SR strictly adhered to the guidelines recommended by the Cochrane Collaboration [2 4] and the protocol was scrutinized and ratified by the European Association of Urology (EAU) Guidelines Office Methods Committee. The review protocol was registered with PROSPERO (CRD42020214108) and includes a PICO (Population, Intervention, Comparator, Outcome) statement.

For our SR we applied the Mantel-Haenszel model for analysis of dichotomous data and the inverse variance (IV) method for analysis of continuous data using random-effect models. According to the Cochrane guidelines, the differences in estimate confidence intervals (CIs) and heterogeneity between these methods for dichotomous data are relatively trivial [3]. However, Xie and Shen [1] report that using an IV heterogeneity model they achieved a notable effect size for the risk ratio of 1.61 (95% CI 1.38 1.88) with an I^2 value of 44%, stating that this yields a higher effect size than our random-effect model when analysing gender. Our analysis for the same outcome resulted in a risk ratio of 1.54 (95% CI 1.34 1.78) with an I^2 value of 45%. This difference in effect size between the two statistical models is regarded as trivial from a Cochrane Collaboration perspective [2,3]. Furthermore, this supposed statistical difference almost certainly has no clinical relevance. We exercised significant caution in presenting pooled analyses in our SR, limiting them to studies with low risk of bias for individual outcomes. The interpretation of these pooled analyses was coupled with assessment of the certainty of evidence according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [5]. The GRADE process includes heterogeneity for outcomes along with other factors when assessing the certainty of evidence for individual pooled analysis [5].

In addition, we would like to highlight that our search strategy and quality assessment were in accordance with the Cochrane guidelines. There is currently no mandate for formal assessment of interobserver agreement using Cohen s values. However, it is noteworthy that interobserver agreement in the SR exceeded 90% for all assessments.

The inclusion criteria for the study types included in the SR were studies with a population of at least 50 patients; prospective, retrospective, and cross-sectional studies; publications in the English language; and journal articles as the publication type. Geographical location was not a restrictive criterion for inclusion. As a result, our SR encompasses studies from diverse regions, including Pakistan, Nigeria, South Korea, Malaysia, South Africa, Turkey, Australia, the USA, and various European countries.

We would like to emphasize the importance of analysis of individual patient data (IPD), which was outside the scope of our SR. Meta-analysis of IPD could be used to explore the heterogeneity of characteristics at the individual patient level. We recognize that performing IPD analysis can be challenging owing to lack of engagement from the authors of primary studies, is time-consuming, and has resource implications. However, heterogeneity in patient characteristics can only be reliably accounted for by exploring data at the individual patient level.

References:

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[4] Higgins JPT, Green S, editors. Cochrane handbook for systematic reviews of interventions, version 5.1.0 (updated March 2011). The Cochrane Collaboration; 2011. www.handbook.cochrane.org.
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