Reply to He et al

To the Editor—We thank He and colleagues [1] for their attentive reading and interesting comments on our article, [2] which they recognize as a valuable study. In their comment, the authors questioned the methodology of our meta-analysis. Most questions have their answers in the Supplementary Data provided with the manuscript (available at: http://cid.oxfordjournals.org/content/59/2/256/suppl/DC1), including our comprehensive methodology with our research strategy and bias evaluation following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) recommendations [3]. We would, however, like to take this opportunity to emphasize the importance of clinical vs statistical-driven medical progress based on the authors’ questions.

The authors proposed to choose the model of meta-analysis after a statistical test of heterogeneity ($I^2$ calculation). This common error is a perfect example of the inappropriate statistical-driven approach. Indeed, the selection of the model should be done a priori on the fact that dispersion could be imputed only to sampling error (fixed-effects model) or to real differences in effect size across studies (random-effects model) [4]. Heterogeneity in study design (case reports, case series, cohort studies, clustered randomized controlled trial during an outbreak, record linkage studies), diagnostic techniques, and criteria among clinical studies on Q fever and pregnancy prevents the assumption that all dispersion of observed effects is due to sampling error. Conversely, some of the dispersion is expected to reflect real differences in effect size across studies, so the random-effects model should be selected regardless of the $I^2$.

The authors rightly suggest the use of conventional methods, such as the Newcastle-Ottawa Quality Assessment Scale, to perform a sensitivity analysis as usually recommended in meta-analysis. Once more, such an analysis is impossible here-in because of the substantial heterogeneity of the included studies as mentioned above and the fact that there are no published clinical case-control nor exposed-unexposed cohorts. From there, what decision to take?

As medical experts of such a subtle disease as Q fever [5], we know that clinical expertise is critical and absolutely cannot be replaced by isolated biological criteria nor statistics on inaccurate public health data (as with population-based serological studies). That is why, although studies focusing on biological parameters (serology) with improved methodology (case-control...
studies) were available, we focused our systematic review on published clinical case series. In fact, we first concluded that a meta-analysis of clinical cases was not possible, and no meta-analysis was included in the first submission of our work to Clinical Infectious Diseases because of the heterogeneity of the clinical studies. The reviewers freed us from this by asking us to still achieve a meta-analysis, arguing that the random-effects model would precisely allow us to take into account this heterogeneity.

In conclusion, we thank He et al and the reviewers of Clinical Infectious Diseases for giving us the opportunity to emphasize that statistics are the key instrument of medical progress only when they are in the service of clinical expertise.

Notes

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References