Authors' reply to the Letter to the Editor of J. Bakhsheshian et al. concerning "Intrawound vancomycin to prevent infections after spine surgery: a systematic review and meta-analysis" by Evaniew N, Khan M, Drew B, Peterson D, Bhandari M, Ghert M (2014) Eur Spine J; DOI 10.1007/s00586-014-3357-0

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Dear Editor,

We thank the authors of this letter for their interest in our article and appreciate their insightful comments. The two ongoing randomized controlled trials (NCT01977989, NCT01566422) were noted in our discussion, and we are pleased to read the additional non-randomized pharmacokinetics study (NCT01764750) that aims to inform a third future trial.

We agree that the clinical heterogeneity of the included studies should indeed be emphasized, as should the identified variation in intrawound vancomycin dosing protocols and the use of local co-interventions. Baseline differences in risks for infection between varying populations under study can produce exaggerated or misleading treatment effects, particularly in observational studies [1, 2]. Future randomized controlled trials of intrawound vancomycin must be rigorously designed and adequately powered to minimize potential bias due to both known and unknown prognostic factors. Local co-interventions should be standardized across participating clinical sites as much as feasible, and should be reported clearly and reproducibly.

The authors of this letter also noted that surgical site infections were neither uniformly nor clearly diagnosed in the studies that were included. Future trials may consider employing blinded centralized adjudication committees (CACs) to minimize potential bias across outcomes assessors [3–5]. CACs typically consist of three or more physicians who are experts in their fields and are experienced in clinical research. CACs operate according to pre-

defined Adjudication Charters, and they assess blinded outcome events according to pre-defined criteria. In multicenter trials, CACs can also minimize the variability associated with having multiple investigators at multiple sites evaluating the primary outcome of the trial.

We again thank the authors of this letter for their interest. They have raised several important points that support further investigation with high-quality randomized controlled trials.

Conflict of interest None of the authors has any potential conflict of interest.

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