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Clarifications on the design and conduct of the PROFHER trial

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Sir

We are pleased to see this editorial continuing the discussion on this key treatment question for these fractures. We write to address the concerns expressed by Ghert and McKee on the design, conduct and reporting of PROFHER in relation to the study population.[1]

Foremost, we wish to correct the misapprehension that surgeons participating in the PROFHER trial were placed in a quandary as to the inclusion of fracture dislocations. As shown in Table I of our article in this journal,[2] these together with clear indications for surgery ("such as severe soft-tissue compromise requiring surgery/emergency treatment (nerve injury/dysfunction)") were explicitly excluded from our study population. In compliance with CONSORT reporting standards, we reported on the numbers who were ineligible and therefore excluded for each category in the participant flow diagram.[1] Given journal word limit, it is inevitable that some information appeared "in the fine print".

As observed in the editorial, the number of four-part fractures identified in the independent classification was low but, as discussed in our article, the numbers of fractures perceived by surgeons to be four-part is likely to have been higher.[2] Our subgroup analyses for fracture severity based on tuberosity involvement and the Neer classification did not suggest any trend of differential treatment response for more complex fractures.[1]

Regarding the representativeness of the population at individual centres, given the relatively low proportions of PROFHER participants recruited in some centres, the impact of any selective local recruitment practices will have been at least partly mitigated by the inclusion of many diverse recruiting sites with a large number of recruiting surgeons. We never expected the number of trial participants recruited to include all cases seen in clinical practice given the trial's exclusion criteria and the patient consent rate. We have described and discussed the representativeness of the whole trial population elsewhere,[1,2] and we believe that the PROFHER participants are representative of those cases for which true uncertainty regarding surgical or non-surgical treatment existed. From an analytical perspective, the relatively small number of patients per surgeon and recruiting site have minimised the influence of such clustering on the trial outcomes, as shown by our sensitivity analysis testing of this aspect.[1] We hope that the above allays the concerns relating to PROFHER raised in the editorial.

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1. **Rangan A, Handoll H, Brealey S, et al.** Surgical vs nonsurgical treatment of adults with displaced fractures of the proximal humerus: the PROFHER randomized clinical trial. *JAMA* 2015;313:1037-1047.
2. **Handoll HH, Brealey SD, Jefferson L, et al.** Defining the fracture population in a pragmatic multicentre randomised controlled trial: PROFHER and the Neer classification of proximal humeral fractures. *Bone Joint Res* 2016;5:481-489.

Conflict of Interest:
None declared.