# Response to: 'Synovial tissue volume and reduction in pain following intra-articular steroid therapy' by Wei *et al*

We thank Wei *et al* for their interest in our work and positive comments about our trial results.[1 2] Wei *et al* highlight a number of issues that we address in turn. Analysis of data from our trial of patients with symptomatic knee osteoarthritis (OA) showed an association between change in the level of knee pain and change in synovial tissue volume (STV) following an intra-articular steroid injection. We agree with Wei *et al* that synovial shrinkage is not the only mechanism by which steroids might result in a reduction in pain; this is underscored, as we highlight in our paper, by the fact that STV accounted for only a small proportion of the variance in change in pain. We think it is unlikely though that our observed findings overestimate the relationship between STV shrinkage and change in pain. As noted by Wei *et al*, only 6.4% of participants had a Kellgren–Lawrence (K/L) radiographic grade 4. In sensitivity analyses in which we removed those, our results were unchanged and remained highly significant. Wei *et al* ask about our approach to analysis of the data, which featured longitudinal data over three study visits. A straightforward linear regression or pairwise correlation (such as Spearman's or Pearson's) would not sufficiently account for the repeated measures on the same patient (and the fact that each patient's observations are therefore correlated), and therefore, the SEs calculated for the model would be unnecessarily large. We also had more than two visits, and so a simple change-versus-change (change in pain vs change in STV) correlation would also mean losing data from the third visit, reducing our sample size unnecessarily. A fixed-effects linear regression allowed us to compare pain and STV using data from all three visits, while removing the effect of change over time in the appropriate manner, accounting for within-patient correlation, and adjusting the SEs in the correct way, which is why we opted for this methodology. More details on the use of these models are given in Gardiner *et al*.[3] In our trial, we included subjects with symptomatic knee OA irrespective of OA compartment subtype and did make any adjustments for this in the analysis. In addition to overall K/L grade, there was no difference in tibiofemoral K/L grade between responders and non-responders. We did not track dosage change of analgesia; generally, however, medication use parallels pain change (ie, pain reduction and rescue medication reduction tend to go together). Lastly, we feel that the term 'within 20%' is preferable to the term 'over 20%' in defining response because it refers to the patient's pain worsening, following an initial response, to a score of 'within' 20% above the baseline value.

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## REFERENCES

1 Wei J, Zeng C, Lei GH. The effect of synovial tissue volume shrinking on pain relief for knee osteoarthritis was overestimated or not?. *Ann Rheum Dis* 2015. Published Online First: 31 Aug 2015. http://dx.doi.org/10.1136/annrheumdis-2015-208223
2 O'Neill TW, Parkes MJ, Maricar N, *et al*. Synovial tissue volume: a treatment target in knee osteoarthritis (OA). *Ann Rheum Dis* 2015. Published Online First: 26 Jun 2015. http://dx.doi.org/10.1136/annrheumdis-2014-206927
3 Gardiner JC, Luo Z, Roman LA. Fixed effects, random effects and GEE: what are the differences? *Stat Med* 2009;28:221–39.