

Manuscript Number:

Title: Response to letters of Dr. Sawalha (18-00092) and Dr. Zheng (18-00414) relating to: Arthroscopic subacromial decompression for subacromial shoulder pain: letter to the Editor

Article Type: Invited Correspondence

Keywords: shoulder, arthroscopy, trial, placebo

Corresponding Author: Professor David Beard, MA MSc DPhil

Corresponding Author's Institution: University of Oxford

First Author: David Beard, MA MSc DPhil

Order of Authors: David Beard, MA MSc DPhil; Andrew Carr; Jonathan Cook

Manuscript Region of Origin: UNITED KINGDOM

Letter Sawalha & Waseem

We would like to comment on the CSAW study by Beard and colleagues 1.

We note that 20 hospitals recruited less than ten patients with subacromial impingement over three years. More than a quarter of all patients in the trial (84, 27%) were recruited from one centre that was running the trial. Given the disparity in recruitment, we are concerned that patient selection criteria were not uniform in all participating centres.

It is not specified whether other pathologies commonly associated with impingement, like acromioclavicular joint and long head of biceps degeneration, 2,3 were considered. This could be an important confounding variable.

In the arthroscopy only (AO) group; the protocol specifies that surgery does not involve surgical removal of bursal tissue. The arthroscopy findings gives details of the bursal partial thickness tears found intraoperatively. We would argue that it is not possible to assess the rotator cuff tendons as such without performing significant amount of clearance and resection of the bursal tissue. Bursectomy has been previously shown to result in equivalent outcomes to acromioplasty 4. We are concerned that the AO group did not receive a 'purely' placebo surgery and that there was a therapeutic component from performing bursectomy while assessing the cuff tendons.

The proportion of patients in whom the OSS improved above the minimal clinically-important difference was not presented 5.

We believe that whilst this is an important piece of work, the limitations highlighted above suggest that the study may not readily translate into significant changes in daily practice.

Authors' response to Sawalha & Waseem

Patient selection criteria were applied as universally as possible for a pragmatic surgical trial. Variation in the number recruited by site does not per se indicate there was variation in patient selection with many factors such as available research time and support, surgical list size, site policies and set-up all contributing to the resultant recruitment numbers. Some minor variation in patient selection between surgeons is inevitable but also reflective of clinical practice. Moreover, the trial site was one of the factors controlled in the randomisation algorithm therefore preventing any imbalance between groups relating to site (note the baseline data supports this view).

The inclusion and exclusion criteria were specifically designed to reflect the real world practice of subacromial decompression for subacromial shoulder pain. Patients with isolated acromioclavicular joint osteoarthritis or long head of biceps pathology were excluded, but patients with predominantly subacromial impingement associated with acromioclavicular joint pain and long head of biceps degeneration were included. Six out of the 90 patients in the group allocated to subacromial decompression also had surgery to the acromioclavicular joint or the long head of biceps.

Both in the written protocol, and in our site education programmes for principal investigators, we emphasised the importance of not removing any tissue in the arthroscopy only group. This was validated by noting the absence of resection instruments used during the procedure and the operation record. We recognise that this may result in a possible under recognition of bursal side partial thickness tears. We believe the fidelity to the protocol in the arthroscopy only group was high.

The OSS was not dichotomised as per the statistical analysis plan as this would have been a statistically suboptimal way to analyse the data. A cut off for clinical importance is never an absolute or unquestionable and any results using it needs to be interpreted carefully. To be transparent, the values for the three groups were 59%, 57%, and 48% for ASAD, AO and NT respectively at 6 months, using the value of a 6 points or more within group improvement in the OSS [given existing studies Christiansen et al 2015;and van Kampen 2013(1,2)]. Corresponding values for 12 months were 77%, 74%, and 61% respectively. These values do not indicate any greater benefit for ASAD than the analyses previously presented which we favour for the aforementioned reasons.

References

1. van Kampen DA, Willems WJ, van Beers LWAH, Castelein RM, Scholtes VAB, Terwee CB. Journal of Orthopaedic Surgery and Research 2013, 8:40 <http://www.josr-online.com/content/8/1/40>
2. Christiansen DH, Frost P, Falla D, Haahr JP, Frich LH, Svendsen SW. Responsiveness and Minimal Clinically Important Change: A Comparison Between 2 Shoulder Outcome Measures. J Orthop Sports Phys Ther. 2015 Aug;45(8):620-5

Letter Wang et al.

The authors of the CSAW study should be commended for completing a large scale multi-centre randomised controlled surgical trial(1). However, we are concerned that flaws in the study design compromise the value of its results.

The primary outcome was measured at 6 months post-randomisation rather than post-treatment. Substantial gaps (median 90 days) occurred between randomisation and treatment in the decompression and arthroscopy groups, resulting in an average recovery time of only three months before the primary endpoint. There was also wide variation between randomisation and surgical treatment (IQR 58-123 days). This skews the study towards underestimation of the effect of decompression.

Additionally, insufficient patients were recruited to meet the author's stated sample size calculation. The high rate of non-compliance with treatment at 6 months (23% decompression, 42% arthroscopy only, 12% no treatment) reduced the ability of the study to detect differences between treatment groups. The per protocol population was defined as patients who "received the allocated intervention at the specified timepoint" which, theoretically, could mitigate the effect of non-compliance. Only 82% (70/85) and 67% (57/85) of the required number of patients were analysed per protocol for the primary outcome in the decompression and arthroscopy groups.

In summary, use of randomisation rather than treatment date as the study baseline, and noncompliance with treatment have skewed the CSAW study towards under-estimation of the true effect of decompression. Until further studies are conducted, we conclude that arthroscopic decompression should not be discounted as an effective treatment for subacromial pain.

Clinical Professor Allan Wang, President Shoulder Elbow Society of Australia Dr Clair Lee, University of Western Australia Dr Jeff Hughes, President-Elect Shoulder Elbow Society of Australia Ming Hao Zheng, University of Western Australia

1. Beard DJ, Rees JL, Cook JA, Rombach I, Cooper C, Merritt N, et al. Arthroscopic subacromial decompression for subacromial shoulder pain (CSAW): a multicentre, pragmatic, parallel group, placebo-controlled, three-group, randomised surgical trial. *Lancet*. 2017;6736(17):1– 10.

Authors' response to Wang et al

We consider the findings of the CSAW to be reliable and refute the suggestion that the study design is flawed. The issues raised by Wang and colleagues were addressed appropriately in the trial design and statistical analysis. The timing of follow up from post-randomisation or post-treatment in elective surgical trials with waiting lists is not straightforward and this aspect of the CSAW trial was carefully considered. We did not conduct the principal analyses according to timing follow-up from surgery as this would have introduced a bias against the no treatment group in a scenario such as the one observed where the general trend is to improved outcome over time irrespective of the treatment group. The 12 months follow-up results were very similar to the 6 months findings which implies the delay to operation had little impact upon the conclusion. Additionally, sensitivity analyses were carried out to further explore this. The sensitivity analyses for the ASAD versus AO analysis which used 6 months follow-up timed from *surgery* for those who had a substantial delay [as reported in the Appendix(1)] were also consistent with the overall results.

The uncertainty in the statistical analyses is reflected in the confidence intervals (CIs). We note that the 95% CIs for the per-protocol analyses between ASAD and AO does not contain the value of 6 points previous studies have suggested(2,3) reflects a clinically important change in the OSS. While the possibility of a clinically important difference between ASAD and AO existing cannot be fully excluded, we did not find evidence of any difference, let alone a clinically important one. Overall, these considerations along with the full set of sensitivity analyses carried out do not suggest the findings are sensitive to the presence of non-compliance or missing data. We believe CSAW study findings are robust and clinical practice should be considered in light of them.

References

1. Beard DJ, Rees JL, Cook JA, Rombach I, Cooper C, Merritt N, et al. Arthroscopic subacromial decompression for subacromial shoulder pain (CSAW): a multicentre, pragmatic, parallel group, placebo-controlled, three-group, randomised surgical trial. *Lancet*. 2017;6736(17):1– 10.
2. van Kampen DA, Willems WJ, van Beers LWAH, Castelein RM, Scholtes VAB, Terwee CB. *Journal of Orthopaedic Surgery and Research* 2013, 8:40
3. Christiansen DH, Frost P, Falla D, Haahr JP, Frich LH, Svendsen SW. Responsiveness and Minimal Clinically Important Change: A Comparison Between 2 Shoulder Outcome Measures. *J Orthop Sports Phys Ther*. 2015 Aug;45(8):620-5 <http://www.josr-online.com/content/8/1/40>