Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Hopewell S, Keene DJ, Marian IR, et al. Progressive exercise compared with best practice advice, with or without corticosteroid injection, for the treatment of patients with rotator cuff disorders (GRASP): a multicentre, pragmatic, 2×2 factorial, randomised controlled trial. Lancet 2021; published online July 12. http://dx.doi.org/10.1016/S0140-6736(21)00846-1.
APPENDIX: ADDITIONAL TABLES AND FIGURES
CHARACTERISTICS OF PARTICIPATING PHYSIOTHERAPISTS

| Agenda for Change Grade | Band 5 | Band 6 | Band 7 | Band 8a | Other | Total |
|-------------------------|--------|--------|--------|---------|-------|-------|
| Injectors, n (%)        | 0 (0)  | 6 (11) | 13 (23)| 34 (61) | 3 (5) | 56 (100)|
| Best Practice Advice, n (%) | 17 (20) | 38 (46) | 22 (27) | 6 (7) | 0 (0) | 83 (100)|
| Progressive Exercise, n (%) | 16 (15) | 55 (53) | 28 (27) | 5 (5) | 0 (0) | 104 (100)|

a 2 orthopaedic consultants and 1 specialist registrar in orthopaedics
b some physiotherapists provided both injection and exercise interventions; 2 physiotherapists delivered both exercise interventions

CONTENT OF SUB-ACROMIAL CORTICOSTEROID INJECTION

| Content of injection | Injection + Progressive Exercise | Injection + Best Practice Advice | Total |
|----------------------|----------------------------------|---------------------------------|-------|
|                      | N (received injection)=171        | N (received injection)=168      | N (received injection)=339 |
| N (%), median dose/volume (IQR) | N (%), median dose/volume (IQR) | N (%), median dose/volume (IQR) |
| Corticosteroid        |                                  |                                 |       |
| Methylprednisolone, mg| 60 (35%), 40 (32-40)              | 61 (36%), 40 (30-30)            | 121 (36%),40 (30-40) |
| Triamcinolone acetonide, mg | 111 (65%), 40 (20-20)          | 107 (64%), 40 (20-40)           | 218 (64%), 40 (20-40) |
| Local anaesthetic    |                                  |                                 |       |
| 1% lidocaine, mls     | 148 (87%), 4 (2-5)                | 146 (87%), 4 (2-5)              | 294 (87%), 4 (2-5) |
| 0.5% Bupivacaine HCl, mls | 18 (11%), 9 (9-9)              | 15 (9%), 9 (9-10)               | 33 (10%), 9 (9-9) |
| None                 | 5 (3%)                           | 7 (4%)                          | 12 (4%) |
| Shoulder             |                                  |                                 |       |
| Right shoulder       | 91 (53%)                         | 90 (54%)                        | 181 (53%) |
| Left shoulder        | 80 (47%)                         | 78 (46%)                        | 158 (47%) |
| Injection site       |                                  |                                 |       |
| Anterior subacromial | 13 (7%)                          | 14 (8%)                         | 27 (8%) |
| Posterior subacromial| 142 (83%)                        | 136 (81%)                       | 278 (82%) |
| Lateral subacromial  | 15 (9%)                          | 15 (9%)                         | 30 (9%) |
| Glenohumeral joint   | 1 (1%)                           | 3 (2%)                          | 4 (1%) |

a % of participants that received injection
### Content of Best Practice Advice Intervention

| Treatment components, N (%)<sup>a</sup> | Best Practice Advice only N (received BPA)=162 | Injection + Best Practice Advice N (received BPA)=162 | Total N (received BPA)=324 |
|-----------------------------------------|-----------------------------------------------|---------------------------------------------------|---------------------------|
| Exercises prescribed                    | 162 (100)                                     | 162 (100)                                        | 324 (100)                 |
| Advice / information booklet provided   | 161 (99)                                      | 162 (100)                                        | 323 (100)                 |
| Exercise diary issued                   | 162 (100)                                     | 159 (98)                                         | 321 (99)                  |
| Action planner completed                | 160 (99)                                      | 160 (99)                                         | 320 (99)                  |
| Exercise video online / DVD provided    | 160 (99)                                      | 158 (98)                                         | 318 (98)                  |

#### Exercises<sup>b</sup>

| 1 | a) Shoulder abduction supported by table in sitting | 31 (10) | 20 (6) | 51 (8) |
|   | b) Shoulder flexion supported by table in sitting | 22 (7)  | 18 (6) | 40 (6) |
| 2 | a) Isometric shoulder external rotation | 29 (9)  | 30 (9) | 59 (9) |
|   | b) Isometric shoulder abduction | 36 (11) | 35 (11)| 71 (11)|
| 3 | a) Resisted shoulder external rotation - 0°<sup>c</sup> | 89 (28) | 82 (26)| 171 (27)|
|   | b) Shoulder flexion up a wall | 60 (19) | 66 (21)| 126 (20)|
| 4 | a) Resisted shoulder external rotation - 90°<sup>c</sup> | 16 (5)  | 32 (10)| 48 (8) |
|   | b) Shoulder raise using a weight | 26 (8)  | 30 (9) | 56 (9) |
| 5 | a) Resisted shoulder abduction/external rotation<sup>c</sup> | 11 (3)  | 7 (2)  | 18 (3) |
| Total | 320 (100) | 320 (100) | 640 (100) |

<sup>a</sup> % of those who attended best practice advice

<sup>b</sup> Number of times exercise prescribed; number of participants attending = 324 but participants usually received more than one exercise

<sup>c</sup> Using resistance band
## Content of Progressive Exercise Intervention

| Session | Intervention                        | Attended | Exercises prescribed | Advice / information booklet provided | Exercise diary issued / reviewed | Action planner completed / reviewed | Confidence ruler reviewed |
|---------|-------------------------------------|----------|----------------------|---------------------------------------|----------------------------------|-------------------------------------|---------------------------|
| 1       | Progressive Exercise only           | 167 (100)| 167 (100)            | 166 (99)                              | 164 (98)                        | 163 (98)                           | 165 (99)                  |
|         | Injection + Progressive Exercise    | 172 (100)| 172 (100)            | 171 (99)                              | 171 (99)                        | 172 (100)                          | 172 (100)                |
| 2       | Progressive Exercise only           | 161 (100)| 160 (99)             | 30 (19)                               | 153 (95)                        | 91 (57)                            | 150 (93)                  |
|         | Injection + Progressive Exercise    | 160 (100)| 158 (99)             | 28 (18)                               | 147 (92)                        | 99 (62)                            | 144 (90)                  |
| 3       | Progressive Exercise only           | 144 (100)| 138 (96)             | 23 (16)                               | 133 (92)                        | 88 (61)                            | 124 (86)                  |
|         | Injection + Progressive Exercise    | 136 (100)| 132 (97)             | 25 (18)                               | 126 (93)                        | 88 (65)                            | 117 (86)                  |
| 4       | Progressive Exercise only           | 101 (100)| 96 (95)              | 22 (22)                               | 94 (93)                         | 69 (68)                            | 88 (87)                   |
|         | Injection + Progressive Exercise    | 100 (100)| 94 (94)              | 19 (19)                               | 93 (93)                         | 67 (67)                            | 88 (88)                   |
| 5       | Progressive Exercise only           | 72 (100) | 66 (92)              | 16 (22)                               | 66 (92)                         | 52 (72)                            | 62 (86)                   |
|         | Injection + Progressive Exercise    | 69 (100) | 66 (96)              | 11 (16)                               | 64 (93)                         | 49 (71)                            | 62 (90)                   |
| 6       | Progressive Exercise only           | 44 (100) | 42 (95)              | 14 (32)                               | 38 (86)                         | 31 (70)                            | 37 (84)                   |
|         | Injection + Progressive Exercise    | 38 (100) | 36 (95)              | 4 (11)                                | 35 (92)                         | 25 (66)                            | 34 (89)                   |

*a % of those who attended session*
# Participant Reported Exercise Adherence

|            | Best Practice Advice | Progressive Exercise | No Injection | Injection | Overall |
|------------|----------------------|-----------------------|--------------|-----------|---------|
|            | n  | %     | n  | %     | n  | %     | n  | %     |
| **8 weeks**|    |       |    |       |    |       |    |       |
| Every day  | 34 | 9.7%  | 40 | 11.2% | 34 | 9.8%  | 40 | 11.1% |
| 6 days per week | 15 | 4.3%  | 15 | 4.2%  | 15 | 4.3%  | 15 | 4.2%  |
| 5 days per week | 152 | 43.2% | 215 | 60.4% | 160 | 46.0% | 207 | 57.5% |
| 4 days per week | 26 | 7.4%  | 19 | 5.3%  | 27 | 7.8%  | 18 | 5.0%  |
| 3 days per week | 15 | 4.3%  | 6  | 1.7%  | 15 | 4.3%  | 6  | 1.7%  |
| 2 days per week | 9  | 2.6%  | 2  | 0.6%  | 6  | 1.7%  | 5  | 1.4%  |
| 1 day per week | 3  | 0.9%  | 0  | 0.0%  | 1  | 0.3%  | 2  | 0.6%  |
| None       | 28 | 8.0%  | 11 | 3.1%  | 18 | 5.2%  | 21 | 5.8%  |
| Missing    | 70 | 19.9% | 48 | 13.5% | 72 | 20.7% | 46 | 12.8% |
| **6 months**|    |       |    |       |    |       |    |       |
| Every day  | 19 | 5.4%  | 14 | 3.9%  | 14 | 4.0%  | 19 | 5.3%  |
| 6 days per week | 5  | 1.4%  | 4  | 1.1%  | 7  | 2.0%  | 2  | 0.6%  |
| 5 days per week | 53 | 15.1% | 66 | 18.5% | 42 | 12.1% | 77 | 21.4% |
| 4 days per week | 24 | 6.8%  | 26 | 7.3%  | 22 | 6.3%  | 28 | 7.8%  |
| 3 days per week | 33 | 9.4%  | 33 | 9.3%  | 34 | 9.8%  | 32 | 8.9%  |
| 2 days per week | 27 | 7.7%  | 19 | 5.3%  | 20 | 5.7%  | 26 | 7.2%  |
| 1 day per week | 13 | 3.7%  | 11 | 3.1%  | 13 | 3.7%  | 11 | 3.1%  |
| None       | 101| 28.7% | 117| 32.9% | 116| 33.3% | 102| 28.3% |
| Missing    | 76 | 21.6% | 65 | 18.3% | 79 | 22.7% | 62 | 17.2% |
| **12 months**|    |       |    |       |    |       |    |       |
| Every day  | 15 | 4.3%  | 16 | 4.5%  | 9  | 2.6%  | 22 | 6.1%  |
| 6 days per week | 3  | 0.9%  | 1  | 0.3%  | 3  | 0.9%  | 1  | 0.3%  |
| 5 days per week | 22 | 6.3%  | 15 | 4.2%  | 13 | 3.7%  | 24 | 6.7%  |
| 4 days per week | 16 | 4.5%  | 12 | 3.4%  | 14 | 4.0%  | 14 | 3.9%  |
| 3 days per week | 24 | 6.8%  | 26 | 7.3%  | 21 | 6.0%  | 29 | 8.1%  |
| 2 days per week | 19 | 5.4%  | 22 | 6.2%  | 17 | 4.9%  | 24 | 6.7%  |
|                  | 1 day per week |     | None         |     | Missing     |     |
|------------------|----------------|-----|--------------|-----|-------------|-----|
|                  |                | 18  | 16           | 21  | 34          |     |
|                  |                | 5.1 | 4.5%         | 6.0 | 4.8%        |     |
|                  |                | 16  | 13           | 176 | 172         |     |
|                  |                | 4.5 | 3.6%         | 50.6| 47.8%       |     |
|                  |                | 21  | 34           |     | 348         |     |
|                  |                |     | 4.8%         |     | 49.2%       |     |
|                  | 165            |     | 183          | 176 | 172         |     |
|                  | 51.4%          |     | 50.6%        | 47.8| 47.8%       |     |
|                  | 46.9%          |     | 50.6%        | 47.8| 47.8%       |     |
|                  | 165            |     | 183          | 176 | 172         |     |
|                  | 51.4%          |     | 50.6%        | 47.8| 47.8%       |     |
|                  | 18             | 16  | 13           | 176 | 172         |     |
|                  | 5.1%           | 4.5%| 3.6%         | 6.0 | 4.8%        |     |
|                  | 51.4%          | 50.6| 47.8%        | 50.6| 47.8%       |     |
|                  | 16             | 13  | 34           |     | 348         |     |
|                  | 5.1%           | 4.5%| 3.6%         | 6.0 | 4.8%        |     |
|                  | 51.4%          | 50.6| 47.8%        | 50.6| 47.8%       |     |
|                  | 69             | 64  | 74           | 59  | 133         |     |
|                  | 19.6%          | 18.0| 21.3%        | 16.4| 18.8%       |     |
|                  | 69             | 64  | 74           | 59  | 133         |     |
|                  | 19.6%          | 18.0| 21.3%        | 16.4| 18.8%       |     |


## Progressive Exercise versus Best Practice Advice and Injection versus Best Practice Advice: Inside-the-Table Analysis of SPADI Overall

### SPADI over 12 months

|                      | Progressive Exercise vs Best Practice Advice | Injection + Best Practice Advice vs Best Practice Advice |
|----------------------|---------------------------------------------|----------------------------------------------------------|
|                      | N=174                                       | N=174                                                    |
| Unadjusted mean (SD) | 27.36 (23.49), 166                         | 32.21 (25.39), 164                                      |
|                      | 28.55 (23.11), 175                         | 32.21 (25.39), 164                                      |
| Adjusted mean (SE)   | 28.79 (1.39), 154                         | 30.55, (1.43), 146                                      |
|                      | 28.32, (1.41), 151                         | 30.55, (1.43), 146                                      |
| Unadjusted difference, (99%CI) | -4.64 (-10.20, 0.91)               | -3.50 (-8.99, 1.99)                                      |
| Adjusted difference, (99%CI), p-value | -1.76 (-6.91, 3.39), 0.380 | -2.23 (-7.03, 2.57), 0.230                             |

*a*SPADI unadjusted analysis using a mixed effects model with random effects within participant with time-by-treatment interaction, 1,870 participant data points contribute to the unadjusted model

*b*SPADI adjusted analysis using a mixed effects model with fixed effects for age, sex, baseline SPADI and random effects for observations within participant, physiotherapist and centre, with time-by-treatment interaction, 1,869 participant data points contribute to the adjusted model

SD - Standard Deviation; SE - Standard Error; CI - Confidence Interval

### SPADI at each time point

| SPADI at each time point | Progressive Exercise vs Best Practice Advice | Injection vs Best Practice Advice |
|--------------------------|---------------------------------------------|---------------------------------|
|                          | Adjusted mean (SE, N)                      | Adjusted mean (SE, N)          |
|                          | Adjusted difference (99%CI)               | Adjusted difference (99%CI)    |
|                          | p-value                                    | p-value                        |
| 8 weeks                  | 41.22 (1.78), 156                         | 29.89 (1.75), 163             |
|                          | -13.1 (-6.52, 6.27)                       | -14.7 (-6.52, 6.27)           |
|                          | 0.959                                      | 0.959                          |
| 6 months                 | 26.99 (1.81), 151                         | 24.75 (1.76), 158             |
|                          | -2.6 (-7.45, 2.20)                        | -2.6 (-7.45, 2.20)            |
|                          | 0.611                                      | 0.611                          |
| 12 months                | 23-12(1.81), 153                         | 21-90(1.71), 143              |
|                          | -3.93 (-10.40, 2.55)                      | -1.05 (-5.15, 7.26)           |
|                          | 0.118                                      | 0.663                          |

*a*SPADI adjusted analysis using a mixed effects model with fixed effects for age, sex, baseline SPADI and random effects for observations within participant, physiotherapist and centre, with time-by-treatment interaction, 1,869 participant data points contribute to the adjusted model

SE - Standard Error; CI - Confidence Interval
Box and whisker plots for raw SPADI scores for Progressive Exercise vs Best Practice Advice from baseline to 12 months. SPADI range is from 0 to 100, higher scores are indicative of more disability.

Box and whisker plots for raw SPADI scores for Injection vs No Injection from baseline to 12 months. SPADI range is from 0 to 100, higher scores are indicative of more disability.
|                | Best Practice Advice | Progressive Exercise | No Injection | Injection |
|----------------|----------------------|-----------------------|--------------|-----------|
|                | N | Unadjusted mean (SD) | N | Unadjusted mean (SD) | N | Unadjusted mean (SD) | N | Unadjusted mean (SD) |
| **SPADI Pain** |   |                       |   |                       |   |                       |   |                       |
| Baseline       | 352 | 65.1 (18) | 354 | 62.7 (17.4) | 346 | 63.3 (17.6) | 360 | 64.4 (17.9) |
| 8 weeks        | 314 | 46.0 (24.5) | 326 | 46.7 (24.5) | 306 | 50.2 (23.4) | 334 | 42.7 (24.9) |
| 6 months       | 301 | 34.4 (26.4) | 314 | 30.9 (25.7) | 294 | 31.7 (25.6) | 321 | 33.5 (26.5) |
| 12 months      | 304 | 28.7 (27.1) | 314 | 24.6 (25.5) | 296 | 25.5 (25.9) | 322 | 27.7 (26.8) |
| Over 12 months | 339 | 36.6 (27.0) | 343 | 34.2 (26.9) | 339 | 35.9 (27.1) | 343 | 34.7 (26.8) |
| **SPADI Function** |   |                       |   |                       |   |                       |   |                       |
| Baseline       | 352 | 47.2 (22.6) | 354 | 41.5 (21.3) | 346 | 44.2 (22.4) | 360 | 44.5 (21.9) |
| 8 weeks        | 313 | 31.3 (23.6) | 326 | 30.8 (23.5) | 307 | 33.3 (23.5) | 332 | 29.0 (23.3) |
| 6 months       | 301 | 22.0 (22.6) | 314 | 19.9 (22.1) | 294 | 20.7 (22.6) | 321 | 21.2 (22.2) |
| 12 months      | 303 | 19.4 (22.6) | 314 | 15.1 (21) | 296 | 16.3 (21.8) | 321 | 18.0 (22.1) |
| Over 12 months | 339 | 24.3 (23.5) | 343 | 22.0 (23.2) | 339 | 23.6 (23.7) | 343 | 22.8 (23.0) |
| **EuroQol EQ-5D-5L** |   |                       |   |                       |   |                       |   |                       |
| Baseline       | 352 | 0.64 (0.20) | 353 | 0.66 (0.20) | 346 | 0.67 (0.18) | 359 | 0.64 (0.18) |
| 8 weeks        | 283 | 0.71 (0.18) | 311 | 0.70 (0.17) | 279 | 0.69 (0.17) | 315 | 0.71 (0.18) |
| 6 months       | 285 | 0.75 (0.18) | 298 | 0.75 (0.20) | 277 | 0.76 (0.18) | 306 | 0.74 (0.20) |
|                | Baseline | 8 weeks | 6 months | 12 months | Over 12 months |
|----------------|----------|---------|----------|-----------|----------------|
| **12 months**  | 349      | 279     | 276      | 280       | 324            |
| **Fear Avoidance**  | 354      | 307     | 287      | 291       | 332            |
| **Belief Questionnaire**  | 14.5 (5.4) | 11.9 (6.0) | 9.4 (6.4) | 8.1 (6.8) | 9.8 (6.6) |
| **Physical Activity**  | 344      | 276     | 265      | 271       | 316            |
| **Baseline**     | 359      | 310     | 298      | 300       | 340            |
| **10.0 (5.7)**  | 15.2 (5.3) | 11.8 (6.1) | 9.8 (6.3) | 9.1 (6.5) | 10.2 (6.4) |
| **Over 12 months** | 360      | 310     | 298      | 300       | 340            |
| **Pain Self-efficacy**  | 346      | 276     | 266      | 271       | 317            |
| **Questionnaire** | 360      | 310     | 298      | 300       | 340            |
| **Baseline**     | 9.6 (2.3) | 10.2 (2.3) | 10.5 (2.1) | 10.9 (1.8) | 10.5 (2.3) |
| **8 weeks**      | 9.8 (2.3) | 10.3 (2.2) | 10.4 (2.2) | 10.8 (2.2) | 10.5 (2.3) |
| **6 months**     | 9.7 (2.3) | 10.2 (2.3) | 10.5 (2.1) | 10.9 (1.8) | 10.5 (2.3) |
| **12 months**    | 9.6 (2.3) | 10.3 (2.2) | 10.4 (2.2) | 10.8 (2.2) | 10.5 (2.3) |
| **Over 12 months** | 9.6 (2.3) | 10.3 (2.2) | 10.4 (2.2) | 10.8 (2.2) | 10.5 (2.3) |
| **Insomnia Severity**  | 343      | 274     | 267      | 272       | 301            |
| **Index**       | 356      | 306     | 298      | 301       | 301            |
| **Baseline**     | 10.7 (6.1) | 8.0 (6.1) | 6.2 (6.1) | 5.2 (5.7) | 5.6 (6.0) |
| **8 weeks**      | 10.2 (6.3) | 8.7 (6.3) | 7.0 (6.0) | 5.9 (5.9) | 6.2 (6.0) |
| **6 months**     | 10.2 (6.3) | 8.7 (6.3) | 7.0 (6.0) | 5.9 (5.9) | 6.2 (6.0) |
| **12 months**    | 10.7 (6.3) | 8.7 (6.3) | 7.0 (6.0) | 5.9 (5.9) | 6.2 (6.0) |
|                  | Over 12 months | Baseline | 8 weeks | 6 months | 12 months | Over 12 months |
|------------------|----------------|----------|---------|-----------|-----------|----------------|
| **Return to Desired Activities** | 323 6.5 (6.1) | 352 8.1 (2.6) | 278 6.2 (2.5) | 276 5.4 (2.4) | 281 4.8 (2.3) | 325 5.5 (2.5) |
| Baseline         | 329 6.5 (6.1) | 354 7.7 (2.6) | 303 6.2 (2.5) | 290 5.0 (2.3) | 292 4.6 (2.3) | 332 5.3 (2.5) |
| 8 weeks          | 314 6.7 (6.2) | 346 7.8 (2.7) | 274 6.5 (2.6) | 268 5.1 (2.4) | 273 4.6 (2.4) | 317 5.4 (2.6) |
| 6 months         | 338 6.3 (6.0) | 360 7.9 (2.5) | 307 5.9 (2.4) | 298 5.2 (2.3) | 300 4.8 (2.3) | 340 5.3 (2.4) |
| 12 months        | 317 5.4 (2.6) | 340 5.3 (2.4) | 317 5.4 (2.6) | 340 5.3 (2.4) | 317 5.4 (2.6) | 340 5.3 (2.4) |
| Over 12 months   | 325 5.5 (2.5) | 332 5.3 (2.5) | 314 6.7 (6.2) | 338 6.3 (6.0) | 326 8.2 (2.2) | 347 8.5 (2.1) |

**Global Impression of Treatment**

|                  | Baseline | 8 weeks | 6 months | 12 months | Over 12 months |
|------------------|----------|---------|----------|-----------|----------------|
| Baseline         | .. 8.1 .. 7.8 (1.8) | 304 8.7 (2.1) | 291 8.5 (2.2) | 293 9.1 (2.2) | 332 8.5 (2.1) |
| 8 weeks          | 274 7.3 (2.0) | 307 8.1 (1.8) | 269 8.5 (2.2) | 298 8.5 (2.2) | 317 8.2 (2.2) |
| 6 months         | 274 7.3 (2.0) | 307 8.1 (1.8) | 269 8.5 (2.2) | 298 8.5 (2.2) | 317 8.2 (2.2) |
| 12 months        | 274 8.9 (2.1) | 302 8.8 (2.4) | 274 8.9 (2.1) | 302 8.8 (2.4) | 317 8.2 (2.2) |
| Over 12 months   | 326 8.2 (2.2) | 332 8.5 (2.1) | 314 6.7 (6.2) | 338 6.3 (6.0) | 317 8.2 (2.2) |
### Subgroup Adjusted SPADI Analysis for Progressive Exercise versus Best Practice Advice at 8 Weeks

| Subgroup                          | Numbers       | ES (99% CI)            |
|-----------------------------------|---------------|------------------------|
| **Age (years)**                   |               |                        |
| 64 years old or less              | 251 vs. 261   | 2.54 (-2.95, 8.02)     |
| Over 64 years old                 | 101 vs. 95    | 2.54 (-2.95, 8.02)     |
| **Sex**                           |               |                        |
| Male                              | 176 vs. 183   | 1.68 (-4.63, 7.99)     |
| Female                            | 176 vs. 173   | 3.55 (-2.87, 9.98)     |
| **Smoking**                       |               |                        |
| Never smoked                      | 185 vs. 200   | 2.04 (-4.08, 8.17)     |
| Former or current smoker          | 167 vs. 154   | 3.23 (-3.48, 9.95)     |
| **Baseline SPADI**                |               |                        |
| Baseline SPADI less disability (less than 50) | 134 vs. 160 | -0.37 (-7.19, 6.45)   |
| Baseline SPADI higher disability (50 or more) | 218 vs. 196 | 5.25 (-0.77, 11.26)    |
| **Baseline Pain Self-Efficacy Questionnaire** |       |                        |
| Higher PSEQ at baseline (8 or more) | 296 vs. 306 | 2.03 (-2.94, 7.01)     |
| Lower PSEQ at baseline (less than 8) | 56 vs. 50    | 5.65 (-5.87, 17.17)    |
| **SPADI at 8 weeks**              | 297 vs. 316   | 2.54 (-2.16, 7.23)     |

ES - Effect Size, CI - Confidence Interval
SUBGROUP ADJUSTED SPADI ANALYSIS FOR PROGRESSIVE EXERCISE VERSUS BEST PRACTICE ADVICE AT 6 MONTHS
### Subgroup Adjusted SPADI Analysis for Progressive Exercise versus Best Practice Advice at 12 Months

| Subgroup                                      | Numbers       | ES (99% CI)     |
|-----------------------------------------------|---------------|-----------------|
| **Age (years)**                               |               |                 |
| 64 years old or less                          | 251 vs. 281   | -3.17 (-8.75, 2.41) |
| Over 64 years old                             | 101 vs. 95    | -3.38 (-11.57, 4.82) |
| **Sex**                                       |               |                 |
| Male                                          | 176 vs. 183   | -4.70 (-11.04, 1.65)  |
| Female                                        | 176 vs. 173   | -1.49 (-8.03, 5.06)  |
| **Smoking**                                   |               |                 |
| Never smoked                                  | 185 vs. 200   | -3.66 (-9.76, 2.44)  |
| Former or current smoker                      | 167 vs. 154   | -2.47 (-9.39, 4.44)  |
| **Baseline SPADI**                            |               |                 |
| Baseline SPADI less disability (less than 50) | 134 vs. 160   | -5.31 (-12.13, 1.51) |
| Baseline SPADI higher disability (50 or more)  | 218 vs. 196   | -1.56 (-7.69, 4.57)  |
| **Baseline Pain Self-Efficacy Questionnaire** |               |                 |
| Higher PSEQ at baseline (8 or more)           | 296 vs. 306   | -3.82 (-8.84, 1.19)  |
| Lower PSEQ at baseline (less than 8)          | 56 vs. 50     | 1.25 (-10.59, 13.09) |
| SPADI at 12 months                            | 288 vs. 307   | -3.10 (-7.85, 1.64)  |

**ES** - Effect Size, **CI** - Confidence Interval

Subgroup adjusted SPADI analysis for progressive exercise versus best practice advice at 12 months.
### Subgroup Adjusted SPADI Analysis for Injection versus No Injection at 8 Weeks

| Subgroup                              | Numbers  | ES (99% CI)   |
|---------------------------------------|----------|---------------|
| **Age (years)**                       |          |               |
| 64 years old or less                  | 250 vs. 262 | -7.14 (-12.23, -2.05) |
| Over 64 years old                     | 98 vs. 98  | -1.81 (-9.77, 6.16)   |
| **Sex**                               |          |               |
| Male                                  | 177 vs. 182 | -4.41 (10.43, 1.61)   |
| Female                                | 171 vs. 178 | -7.03 (-13.14, -0.92) |
| **Smoking**                           |          |               |
| Never smoked                          | 184 vs. 201 | -5.50 (-11.28, 0.29)   |
| Former or current smoker              | 162 vs. 159 | -5.73 (-12.16, 0.70)   |
| **Baseline SPADI**                    |          |               |
| Baseline SPADI less disability (less than 50) | 144 vs. 150 | -0.36 (-6.87, 6.16)   |
| Baseline SPADI higher disability (50 or more) | 204 vs. 210 | -9.67 (-15.37, -3.97) |
| **Baseline Pain Self-Efficacy Questionnaire** |          |               |
| Higher PSEQ at baseline (0 or more)   | 297 vs. 305 | -5.42 (-10.05, -0.79)   |
| Lower PSEQ at baseline (less than 8)  | 51 vs. 55  | -7.32 (-18.64, 4.01)   |
| SPADI at 8 weeks                      | 300 vs. 313 | -5.64 (9.93, -1.35)    |

**ES** - Effect Size, **CI** - Confidence Interval

**Subgroup adjusted SPADI analysis for injection versus no injection at 8 weeks**
SUBGROUP ADJUSTED SPADI ANALYSIS FOR INJECTION VERSUS NO INJECTION AT 6 MONTHS
**Subgroup Adjusted SPADI Analysis for Injection versus No Injection at 12 Months**

| Subgroup                               | Numbers       | ES (99% CI)          |
|----------------------------------------|---------------|----------------------|
| **Age (years)**                        |               |                      |
| 64 years old or less                   | 250 vs. 262  | 1.49 (-3.69, 6.66)   |
| Over 64 years old                      | 98 vs. 98    | 3.33 (-4.62, 11.28)  |
| **Sex**                                |               |                      |
| Male                                   | 177 vs. 182  | 2.95 (-3.09, 8.99)   |
| Female                                 | 171 vs. 178  | 0.66 (-5.37, 7.09)   |
| **Smoking**                            |               |                      |
| Never smoked                           | 184 vs. 201  | -0.28 (-6.63, 5.48)  |
| Former or current smoker               | 162 vs. 159  | 4.87 (1.77, 11.51)   |
| **Baseline SPADI**                     |               |                      |
| Baseline SPADI less disability (less than 50) | 144 vs. 150 | 4.23 (-2.29, 10.75) |
| Baseline SPADI higher disability (50 or more) | 204 vs. 210 | 0.14 (-5.68, 5.95) |
| **Baseline Pain Self-Efficacy Questionnaire** |           |                      |
| Higher PSEQ at baseline (8 or more)    | 297 vs. 300  | 1.14 (3.63, 5.81)    |
| Lower PSEQ at baseline (less than 8)   | 51 vs. 55    | 6.80 (-4.84, 18.44)  |
| **SPADI at 12 months**                 | 296 vs. 321  | 1.93 (-2.41, 6.27)   |

ES - Effect Size, CI - Confidence Interval
Regression analysis with an interaction term, including imputation of missing values and adjustment for baseline utility, sex and age (base case analysis)

|                      | Total costs mean (SE) | QALYs mean (SE) | NMB‡ mean (SE) |
|----------------------|-----------------------|-----------------|---------------|
| Best Practice Advice (B) | £195 (£54)           | 0.737 (0.013)   | £14,538 (£290) |
| Injection + Best Practice Advice (IB) | £205 (£20)          | 0.757 (0.011)   | £14,939 (£227) |
| Progressive Exercise (P)  | £247 (£23)           | 0.756 (0.012)   | £14,865 (£255) |
| Injection + Progressive Exercise (IP) | £307 (£30)      | 0.742 (0.012)   | £14,524 (£263) |
| Injection simple effect (IB-B) | £10 (£44)           | 0.021 (0.015)   | £402 (£322)   |
| (p=0.747)             | (p=0.184)            |                 | (p=0.212)     |
| Progressive Exercise simple effect (P-B) | £52 (£44)          | 0.019 (0.016)   | £327 (£323)   |
| (p=0.247)             | (p=0.220)            |                 | (p=0.309)     |
| Interaction (B-IB-P+IP) | Progressive Exercise by injection | £50 (£57)       | -0.035 (0.022) |
|                       |                       | (p=0.397)       | (p=0.106)     |

Values represent the mean (standard error) for each group for males of age 55.46 years and a baseline utility of 0.653; since there was assumed to be no interaction between baseline variables and treatments, the simple effects for each treatment and the interaction between treatments are assumed to be the same for all participant subgroups, although the absolute costs and absolute QALYs may be higher or lower depending on participants’ sex, age and baseline utility.

† Net monetary benefit calculated at a ceiling ratio of £20,000 per quality-adjusted life-year (QALY).
COST-EFFECTIVENESS ACCEPTABILITY CURVE FOR THE COMPARISON BETWEEN TREATMENT GROUPS (BASE CASE ANALYSIS)

*BPA= Best Practice Advice; ** The Frontier indicated which treatment is economically preferred at different threshold values for cost-effectiveness
MEDLINE SEARCH STRATEGY

Database: Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present
Search Strategy:

1  Shoulder Pain/ (4378)
2  Shoulder Impingement Syndrome/ (1655)
3  Rotator Cuff/ and Tendinopathy/ (477)
4  Shoulder/ and (Bursitis/ or Tendinopathy/) (438)
5  ((shoulder* or rotator cuff or subacromial or sub-acromial) adj5 (bursitis or impinge* or tendinitis or tendonitis or tendinopathy or pain*)).ti,ab. (12483)
6  1 or 2 or 3 or 4 or 5 (14765)
7  (Cortisone/ or Glucocorticoids/) and Injections/ (1354)
8  ((subacromial or sub-acromial or corticosteroid* or cortisone or glucocorticoid*) adj5 inject*).ti,ab. (5093)
9  CSI.ti,ab. (3029)
10 7 or 8 or 9 (9227)
11 6 and 10 (480)
12 randomized controlled trial.pt. (477274)
13 controlled clinical trial.pt. (92948)
14 (randomized or randomised).ab. (522076)
15 placebo.ab. (195900)
16 drug therapy.fs. (2088506)
17 randomly.ab. (306731)
18 trial.ab. (455979)
19 groups.ab. (1887811)
20 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 (4404372)
21 exp animals/ not humans.sh. (4554611)
22 20 not 21 (3810278)
23 11 and 22 (320)