Appendix 3 – Description of the results of the included studies

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| ***Exercise therapy versus usual care for neck pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** | | **Costs** | | **ICER** |
|  |  | *Exercise therapy* | *Usual care* | *Exercise therapy* | *Usual care* |  |
| Korthals-de Bos et al35 | Exercise therapy (n=59)  Usual care (n=64) | Mean (SD) at 12 months  Global perceived recovery: 0.63 (0.37)  Pain intensity (0-10): 2.6 (2.9)  Disability (0-50): 7.6 (8.0)  QALY (0-1): 0.79 (0.14) | Mean (SD) at 12 months  Global perceived recovery: 0.56 (0.36)  Pain intensity (0-10): 2.2 (2.9)  Disability (0-50): 7.4 (7.4)  QALY (0-1): 0.77 (0.16) | Mean (SD) at 12 months  Societal perspective: £1,652 (4,424) or €1,852 (4,964) | Mean (SD) at 12 months  Societal perspective: £1,759 (3,951) or €1,970 (4,434) | ICER – cost per recovered patient, societal perspective: £-1,610 (€-1,807)  ICER – cost per point deterioration in pain intensity score, societal perspective: £-104 (€-118)  ICER – cost per point deterioration in functional disability score, societal perspective: £-45 (€-51)  ICER – cost per QALY gained for societal perspective: £-3,421 (€-3,840), i.e. cost-effective |
|  |  | Effect difference (95% CI)  Global perceived recovery:  0.06 (-0.11 to 0.24)  Pain intensity (0-10): -1.0 (-2.0 to 0.0)  Functional disability (0-50): -2.2 (-5.0 to 0.5)  QALY (0-1): 0.02 (-0.04 to 0.09) | | Costs difference (95% CI)  Societal perspective: £-103 (-1,353 to 1,840) or €-117 (-1,518 to 2,065) | |
| Rosenfeld et al37 | Exercise therapy <96 hours after the trauma (n=21)  Usual care <96 hours after the trauma (n=22) | Mean (SD) at 6 months  Pain intensity (0-10):  1.3 (2.4)  Sick leave days: 15.1 (42.0)  Mean (SD) at 36 months  Pain intensity (0-10):  3.6 (2.8)  Sick leave days: 11.2 (44.0) | Mean (SD) at 6 months  Pain intensity (0-10):  3.5 (3.0)  Sick leave days: 10.3 (22.0)  Mean (SD) at 36 months  Pain intensity (0-10):  3.2 (2.2)  Sick leave days: 40.2 (71.0) | Mean SD at 6 months  Societal perspective: £560 (906) or €646 (1,044)  Mean SD at 36 months  Societal perspective: £326 (575) or €374 (662) | Mean SD at 6 months  Societal perspective: £1,265 (2,733) or €1,458 (3,150)  Mean SD at 36 months  Societal perspective: £1,148 (2,001) or €1,323 (2,307) | ICER not reported  Exercise therapy was more effective and less costly than usual care at intermediate and long-term (i.e. cost-effective) |
|  | Exercise therapy >2 weeks after the trauma (n=23)  Usual care >2 weeks after the trauma (n=22) | Mean (SD) at 6 months  Pain intensity (0-10):  2.5 (1.9)  Sick leave days: 11.5 (38.0)  Mean (SD) at 36 months  Pain intensity (0-10):  2.4 (2.2)  Sick leave days: 10.0 (42.0) | Mean (SD) at 6 months  Pain intensity (0-10):  6.5 (2.2)  Sick leave days: 28.9 (51.0)  Mean (SD) at 36 months  Pain intensity (0-10):  3.7 (2.7)  Sick leave days: 20.5 (50.0) | Mean (SD) at 6 months  Societal perspective: £641 (919) or €739 (1,059)  Mean SD at 36 months  Societal perspective: £246 (496) or €283 (571) | Mean (SD) at 6 months  Societal perspective: £1,417 (2,248) or €1,632 (2,591)  Mean SD at 36 months  Societal perspective: £525 (1,083) or €606 (1,249) |
|  |  | Effect difference (95% CI) not reported  There were significant differences between interventions for pain intensity at 6 and 36 months and sick leave at 36 months (p<0.05) | | Costs difference (95% CI) not reported  There were significant differences for costs at 6 and 36 months (p<0.05) | |
| ***Exercise therapy versus usual care for acute low back pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** | | **Costs** | | **ICER** |
|  |  | *Exercise therapy* | *Usual care* | *Exercise therapy* | *Usual care* |  |
| Aboagye et al39 | Exercise therapy (n=52)  Usual care (n=55) | Mean (SD) at 12 months  QALY (0-1): 0.79 (0.14) | Mean (SD) at 12 months  QALY (0-1): 0.75 (0.23) | Mean (SD) at 12 months  Employer perspective: £251 or €266  Societal perspective: £1,779 or €1,969 | Mean (SD) at 12 months  Employer perspective: £99 or €110  Societal perspective: £3,787 or €4,191 | ICER – cost per QALY gained, employer’s perspective: £4,712 (€5,214), i.e. cost-effective  ICER – cost per QALY gained, societal perspective: cost-effective (<£-10,874 [<€-12,032]), exercise therapy showed lower costs and larger effect than usual care |
|  |  | Effect difference (95% CI)  QALY (0-1): 0.04 (-0.03 to 0.11) | | Employer perspective: £141 or €156  Societal perspective: £-1,062 or €-2,222 | |
| Cherkin et al42 | Exercise therapy (n=133)  Usual care (n=66) | Mean (SD) at 4 weeks  Bothersomeness (0-10): 2.3 (2.6)  Disability (0-24): 4.1 (4.7)  Mean (SD) at 12 weeks  Bothersomeness (0-10): 2.7 (2.9)  Disability (0-24): 4.1 (5.3) | Mean (SD) at 4 weeks  Bothersomeness (0-10): 3.1 (3.1)  Disability (0-24): 4.9 (4.6)  Mean (SD) at 12 weeks  Bothersomeness (0-10): 3.2 (3.3)  Disability (0-24): 4.3 (5.0) | Total mean costs at 24 months  Healthcare perspective: £519 or €582 | Total mean costs at 24 months  Healthcare perspective: £181 or €203 | ICER not reported  Exercise therapy was associated with higher costs than usual care |
|  |  | Effect difference (95% CI) not reported  There were no significant differences between interventions for bothersomeness and disability at 4 and 12 weeks (p>0.05) | | Costs difference (95% CI) not reported | |
| Seferlis et al49 | Exercise therapy (n=60)  Usual care (n=60) | Number of days off work at 12 months: 61 | Number of days off work at 12 months: 70 | Total costs at 12 months  Societal perspective: £5,727 or €6,604 | Total costs at 12 months  Societal perspective: £6,410 or €7,391 | ICER not reported  Exercise therapy had lower costs than usual care |
|  |  | Effect difference (95% CI) not reported | | Costs difference (95% CI) not reported | |
| Wright et al54 | Exercise therapy (n=55)  Usual care (n=56) | Mean at 1 month  McGill – visual analogue scale (0-10): 23.6  McGill – present pain intensity (0-10): 1.1  McGill – sensory (0-10): 4.3  McGill – emotional (0-10): 1.0  Quality of life – physical: 16.0  Quality of life –mental: 22.0  Mean at 2 months  McGill – visual analogue scale: 18.4  McGill – present pain intensity: 1.1  McGill – sensory: 4.4  McGill – emotional: 1.1  Quality of life – physical: 16.4  Quality of life –mental: 22.1 | Mean at 1 month  McGill – visual analogue scale (0-10): 34.9  McGill – present pain intensity (0-10): 1.7  McGill – sensory (0-10): 6.8  McGill – emotional (0-10): 1.5  Quality of life – physical: 13.0  Quality of life –mental: 20.0  Mean at 2 months  McGill – visual analogue scale: 30.9  McGill – present pain intensity: 1.5  McGill – sensory: 6.1  McGill – emotional: 1.4  Quality of life – physical: 14.6  Quality of life –mental: 20.8 | Intervention costs: £1,266 or €1,423 | Intervention costs: £198 or €222 | ICER not reported  Cost saving for exercise therapy was of £369 (€414), and £854 (€959) per patient |
|  |  | Effect difference (95% CI) not reported  There was significant difference between interventions for pain intensity and number of days to return to work at 1 and 2 months (p<0.05) | | Costs difference (95% CI) not reported | |
| ***Exercise therapy versus usual care for subacute and chronic low back pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** | | **Costs** | | **ICER** |
|  |  | *Exercise therapy* | *Usual care* | *Exercise therapy* | *Usual care* |  |
| Chuang et al43 | Exercise therapy (n=156)  Usual care (n=157) | Mean (SD) at 12 months  QALY (0-1): 0.78 (0.14) | Mean (SD) at 12 months  QALY (0-1): 0.72 (0.17) | Mean (SD) at 12 months  Healthcare perspective: £907 (2,043) or €976 (2,198)  Societal perspective: £1,789 (3,038) or €1,925 (3,269) | Mean (SD) at 12 months  Healthcare perspective: £630 (1,106) or €677 (1,193)  Societal perspective: £2,763 (3,798) or €2,972 (4,087) | ICER – cost per QALY gained, healthcare perspective: £16,267 (€17,447); CEAC: 72% at £20,000 or €22,582, i.e. cost-effective  ICER – cost per QALY gained, societal perspective: exercise therapy was dominant; CEAC: 89% at £10,000 (€11,426) and 95% at £20,000 (€22,582), i.e. less costly and more effective |
|  |  | Effect difference (95% CI)  QALY (0-1): 0.04 (-0.01 to 0.07) | | Costs difference (95% CI)  Healthcare perspective: £602 (188 to 1,017) or €648 (202 to 1,094)  Societal perspective: £-253 (-1,224 to 714) or €-272 (-1,318 to 768) | |
| Henchoz et al45 | Exercise therapy (n=56)  Usual care (n=49) | Mean (SD) at 12 months  QALY (0-1): 0.63 (0.09) | Mean (SD) at 12 months  QALY (0-1): 0.62 (0.13) | Mean (SD) at 12 months (estimated by monthly costs)  Societal perspective: £4,174 (10,980) or €4,498 (11,824) | Mean (SD) at 12 months (estimated by monthly costs)  Societal perspective: £3,660 (10,197) or €3,946 (10,939) | ICER – cost per QALY gained, societal perspective: £82,657 (€88,965), i.e. not cost-effective |
|  |  | Effect difference (95% CI) not reported  There was no significant difference between interventions for QALY at 12 months (p>0.05) | | Costs difference (95% CI) not reported  There was no significant difference between interventions for costs at 12 months (p>0.05) | |
| Hlobil et al46 | Exercise therapy (n=67)  Usual care (n=67) | Mean (SD) not reported | Mean (SD) not reported | Mean (SD) at 12 months  Healthcare perspective: £997 (847) or €1,092 (928) | Mean (SD) at 12 months  Healthcare perspective: £891 (1,366) or €977 (1,496) | ICER not reported  Exercise therapy had a mean cost benefit of £1,245 (€1,363) at 12 months and £2,070 (€2,267) over 36 months |
|  |  | Effect difference (95% CI)  Lost productivity days at 12 months: 9.1 (-14.8 to 31.5)  Lost productivity days over 36 months: 12.0 (-50.2 to 64.9) | | Costs difference (95% CI)  Healthcare perspective: £-102 (-581 to 312) or €-113 (-637 to 242)  Employer perspective at 12 months: £-1,245 (-3,884 to 1,337) or €-1,363 (-4,252 to 1,464)  Employer perspective over 36 months: £-2,070 (-8,620 to 5,179) or €-2,267 (-9,437 to 5,671) | |
| Hollinghurst et al47 | Exercise therapy (n=72)  Usual care (n=72) | Mean (SD) not reported | Mean (SD) not reported | Mean (SD) at 12 months  Healthcare perspective: £203 (690) or €208 (711) | Mean (SD) at 12 months  Healthcare perspective: £71 (132) or €72 (135) | ICER – cost per point reduction in disability score, healthcare perspective: £80 (€82)  ICER – cost per pain-free day during past four weeks, healthcare perspective: £11 (€11)  ICER – cost per QALY gained, healthcare perspective: £3,760 (€3,874); CEAC: >90% at £1,000 or €1,142, i.e. cost-effective |
|  |  | Effect difference (95% CI)  Disability (0-24): 1.6 (-0.3 to 3.6)  Pain-free days: 11 (1 to 23)  QALY (0-1): 0.04 (0.00 to 0.07) | | Costs difference (95% CI)  Healthcare perspective: £132 (-31 to 295) or €135 (-32 to 189) | |
| UK BEAM51 | Exercise therapy (n=326)  Usual care (n=297) | Mean (SD) at 12 months  QALY (0-1): 0.63 (0.24) | Mean (SD) at 12 months  QALY (0-1): 0.62 (0.23) | Mean (SD) at 12 months  Healthcare perspective: £682 (1,273) or €719 (1,343) | Mean (SD) at 12 months  Healthcare perspective: £485 (844) or €512 (890) | ICER – cost per QALY gained, healthcare perspective: £11,649 (€12,293), i.e. cost-effective |
|  |  | Effect difference (95% CI)  QALY: 0.02 (95% CI: -0.02 to 0.05) | | Costs difference (95% CI)  Healthcare perspective: £196 (4 to 390) or €206 (3 to 410) | |

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| ***Exercise therapy versus manual therapy for neck pain more than 2 weeks*** | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** |
|  |  | *Exercise therapy* | *Manual therapy* | *Exercise therapy* | *Manual therapy* |  |
| Bosmans et al34 | Exercise therapy (n=71)  Manual therapy (n=75) | Mean (SD) at 12 months  Global perceived effect: 0.78 (0.4)  Pain intensity (0-10): 1.1 (2.6)  Disability (0-50): 4.1 (6.7)  QALY (0-1): 0.75 (0.08) | Mean (SD) at 12 months  Global perceived effect: 0.76 (0.4)  Pain intensity (0-10): 1.5 (2.7)  Disability (0-50): 5.1 (6.7)  QALY (0-1): 0.77 (0.09) | Mean (SD) at 12 months  Societal perspective: £1,033 (1,905) or €1,055 (1,945) | Mean (SD) at 12 months  Societal perspective: £724 (1,279) or €740 (1,307) | ICER – cost per recovered patient, societal perspective: £15,481 (€15,812); CEAC: 60% at £21,879 (€25,000)  ICER – cost per point improvement in pain intensity score, societal perspective: £350 (€357); CEAC: 95% at £1,575 (€1,800)  ICER – cost per point improvement in functional disability score, societal perspective: £886 (€906)  ICER – cost per QALY lost, societal perspective: exercise therapy was associated with higher costs and smaller effect (but not statistically significant) than manual therapy, i.e. not cost-effective |
|  |  | Effect difference (95% CI)  Global perceived effect: 0.02 (-0.12 to 0.16)  Pain intensity (0-10): 0.9 (0.0 to 1.7)  Disability (0-50): 2.4 (0.2 to 4.5)  QALY (0-1): -0.02 (-0.06 to 0.02) | | Costs difference (95% CI)  Societal perspective: £306 (-125 to 976) or €314 (-129 to 997) | |
| van Dongen et al38 | Exercise therapy (n=91)  Manual therapy (n=90) | Mean (SD) at 12 months  Global perceived effect: 0.52 (0.5)  Pain intensity (0-10): 2.8 (2.6)  Disability (0-50): 6.6 (6.3)  QALY (0-1): 0.76 (0.12) | Mean (SD) at 12 months  Global perceived effect: 0.62 (0.5)  Pain intensity (0-10): 2.5 (2.6)  Disability (0-50): 5.9 (5.5)  QALY (0-1): 0.77 (0.14) | Mean (SD) at 12 months  Societal perspective: £2,568 (6,576) or €2,811 (7,199) | Mean (SD) at 12 months  Societal perspective: £2,472 (7,281) or €2,706 (7,972) | ICER – cost per recovered patient less, societal perspective: £1,005 (€1,134); CEAC: 12% at £34,131 (€39,000)  ICER – cost per point deterioration in functional disability score, societal perspective: £92 (€101); CEAC: 9% at £3,500 (€4,000)  ICER – cost per QALY lost, societal perspective: £14,740 (€16,138); CEAC: <46% at irrespective of the willingness to pay, i.e. not cost-effective |
|  |  | Effect difference (95% CI)  Global perceived effect: -0.09 (-0.25 to 0.05)  Pain intensity (0-10): -0.3 (-1.1 to 0.5)  Disability (0-50): -1.0 (-2.5 to 0.5)  QALY (0-1): -0.01 (-0.04 to 0.03) | | Costs difference (95% CI),  Societal perspective: £97 (-2,046 to 2,061) or €106 (-2,241 to 2,188) | |
| Korthals-de Bos et al35 | Exercise therapy (n=59)  Manual therapy (n=60) | Mean (SD) at 12 months  Global perceived recovery: 0.63 (0.4)  Pain intensity (0-10): 2.6 (2.9)  Disability (0-50): 7.6 (8.0)  QALY (0-1): 0.79 (0.14) | Mean (SD) at 12 months  Global perceived recovery: 0.72 (0.4)  Pain intensity (0-10): 1.7 (2.4)  Disability (0-50): 6.4 (7.5)  QALY (0-1): 0.82 (0.13) | Mean (SD) at 12 months  Societal perspective: £1,651 (4,424) or €1,852 (4,964) | Mean (SD) at 12 months  Societal perspective: £568 (667) or €635 (750) | ICER – cost per recovered patient less, societal perspective: £12,080 (€13,554)  ICER – cost per point deterioration in pain intensity score, societal perspective: £963 (€1,081); CEAC: 2% at ceiling ratio of zero  ICER – cost per point deterioration in functional disability score, societal perspective: £1,230 (€1,381)  ICER – cost per QALY lost, societal perspective: £39,655 (€44,493), i.e. not cost-effective |
|  |  | Effect difference (95% CI)  Global perceived recovery: -0.09 (-0.06 to 0.08)  Pain intensity (0-10): -1.2 (-2.1 to -0.1)  Disability (0-50): -0.9 (-3.6 to 1.9)  QALY (0-1): -0.03 (-0.09 to 0.04) | | Costs difference (95% CI)  Societal perspective: £1,081 (304 to 2,874) or €1,214 (341 to 3,225) | |
| Leininger et al36 | Exercise therapy: (n=82)  Manual therapy (n=80) | Mean (SD) at 12 months  Pain intensity (0-10): 3.1 (1.9)  Disability (0-50): 17.3 (8.5)  QALY (SF-6D [0-1]): 0.80 (0.21)  QALY (EQ-5D [0-1]): 0.81 (0.09) | Mean (SD) at 12 months  Pain intensity (0-10): 2.9 (2.1)  Disability (0-50): 15.4 (9.9)  QALY (SF-6D [0-1]): 0.81 (0.23)  QALY (EQ-5D [0-1]): 0.82 (0.11) | Mean (SD) at 12 months  Healthcare perspective: £2,578 (508) or €2,670 (526)  Societal perspective:  £4,165 (1,450) or €4,314 (1,501) | Mean (SD) at 12 months  Healthcare perspective: £1,308 (1,807) or €1,355 (1,872)  Societal perspective:  £2,217 (2,058) or €2,296 (2,131) | ICER – cost per point deterioration in pain intensity score, societal perspective: exercise therapy was associated with higher costs and smaller effect  ICER – cost per point deterioration in disability score, societal perspective: exercise therapy was associated with higher costs and smaller effect  ICER – cost per QALY lost (SF-6F and EQ-5D), societal perspective: exercise therapy was associated with higher costs and smaller effect |
|  |  | Effect difference (95% CI)  Pain intensity (0-10): -0.4 (-0.8 to -0.0)  Disability (0-50): -1.8 (-3.6 to -0.1)  QALY (SF-6D [0-1]): -0.01 (-0.03 to 0.01)  QALY (EQ-5D [0-1]): -0.01 (-0.03 to 0.00) | | Costs difference (95% CI)  Healthcare perspective: £1,270 (-686 to 1,575) or €1,316 (-711 to 1,631)  Societal perspective: £1,948 (-1,106 to 2,820) or €2,019 (-1,145 to 2,921) | |
| Meta-analysis |  | Meta-analyses were conducted for global perceived effect/recovery,38-40 pain intensity,38, 39, 41 disability38, 39, 41 (Figure 3). The results showed that there were no statistically significant differences in global perceived recovery (mean difference [%]: -0.05; 95% CI: -0.13 to 0.03), pain intensity (mean difference [0-10]: 0.2; 95% CI: -0.2 to 0.7), disability (mean difference [0-50]: 0.5; 95% CI: -0.6 to 1.6). | |  | |  |
| ***Exercise therapy versus manual therapy for acute low back pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** |
|  |  | *Exercise therapy* | *Manual therapy* | *Exercise therapy* | *Manual therapy* |  |
| Cherkin et al42 | Exercise therapy (n=133)  Manual therapy (n=122) | Mean (SD) at 4 weeks  Bothersomeness (0-10): 2.3 (2.6)  Disability (0-24): 4.1 (4.7)  Mean (SD) at 12 weeks  Bothersomeness (0-10): 2.7 (2.9)  Disability (0-24): 4.1 (5.3) | Mean (SD) at 4 weeks  Bothersomeness (0-10): 1.9 (2.0)  Disability (0-24): 3.7 (4.5)  Mean (SD) at 12 weeks  Bothersomeness (0-10): 2.0 (2.2)  Disability (0-24): 3.1 (4.2) | Total mean costs at 24 months  Healthcare perspective: £519 or €582 | Total mean costs at 24 months  Healthcare perspective: £510 or €572 | ICER not reported  Exercise therapy had similar costs and effects compared with manual therapy |
|  |  | Effect difference (95% CI) not reported  There were no significant differences between interventions for bothersomeness and disability at 4 and 12 weeks (p>0.05) | | Costs difference (95% CI) not reported | |
| Seferlis et al49 | Exercise therapy (n=60)  Manual therapy (n=60) | Number of days off work at 12 months: 61 | Number of days off work at 12 months: 55 | Total costs at 12 months  Societal perspective: £5,727 or €6,604 | Total costs at 12 months  Societal perspective: £6,188 or €7,134 | ICER not reported  Exercise therapy had lower costs in comparison with manual therapy |
|  |  | Effect difference (95% CI) not reported | | Costs difference (95% CI) not reported | |
| ***Exercise therapy versus manual therapy for subacute and chronic low back pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** |
| UK BEAM51 | Exercise therapy (n=326)  Manual therapy (n=342) | Mean (SD) at 12 months  QALY (0-1): 0.63 (0.24) | Mean (SD) at 12 months  QALY (0-1): 0.66 (0.24) | Mean (SD) at 12 months  Healthcare perspective: £682 (1,273) or €719 (1,343) | Mean (SD) at 12 months  Healthcare perspective: £759 (1,077) or €801 (1,136) | ICER not reported |
|  |  | Effect difference (95% CI) not reported | | Costs difference (95% CI) not reported | |

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| ***Exercise therapy versus physiotherapy for subacute and chronic low back pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** |
|  |  | *Exercise therapy* | *Physiotherapy* | *Exercise therapy* | *Physiotherapy* |  |
| Carr et al41 | Exercise therapy (n=118)  Physiotherapy (n=119) | Mean at 12 months  Disability (0-100):  35.3 (19.6)  SF-12 (physical):  39.5 (6.7)  Sf-12 (mental):  44.3 (11.6)  Pain self-efficacy:  36.0 (11.8)  QALY (0-1):  0.62 (0.20) | Mean at 12 months  Disability (0-100):  36.0 (17.9)  SF-12 (physical):  38.9 (5.9)  Sf-12 (mental):  41.6 (18.8)  Pain self-efficacy:  33.6 (10.0)  QALY (0-1):  0.60 (0.10) | Mean (SD) at 12 months  Healthcare perspective: £273 (397) or €298 (434) | Mean (SD) at 12 months  Healthcare perspective: £480 (1,718) or €525 (1,881) | ICER not reported  Exercise therapy had similar costs and effects in comparison with physiotherapy |
|  |  | Effect difference (95% CI)  Disability (0-100): 0.6 (-1.7 to 1.7)  SF-12 (physical): 1.2 (-1.7 to 4.1)  Sf-12 (mental): 2.2 (-1.3 to 5.7)  Pain self-efficacy: -1.1 (-4.7 to 2.4)  QALY (0-1): 0.03 (-0.06 to 0.12) | | Costs difference (95% CI)  Total healthcare costs: £-205 (-592 to 180) or €-223 (-648 to 197) | |
| Critchley et al44 | Exercise therapy (n=72)  Physiotherapy (n=71) | Mean (SD) at 18 months  Disability (0-100):  28.3 (33.3)  Pain intensity: 3.2 (3.4)  QALY (0-1): 0.90 (0.37) | Mean (SD) at 18 months  Disability: 28.7 (27.9)  Pain intensity: 3.9 (3.2)  QALY (0-1): 0.99 (0.27) | Mean (SD) at 18 months  Healthcare perspective: £512 (1,406) or €523 (1,435) | Mean (SD) at 18 months  Healthcare perspective: £640 (1,135) or €643 (1,159) | ICER – cost per QALY lost, healthcare perspective: £-1,416 (€-1,456); CEAC, healthcare perspective: 35% at £30,000 (€34,278), i.e. less costly and less effective |
|  |  | Effect difference (95% CI) not reported  There were no significant differences between interventions for disability, pain intensity and QALY at 18 months (p>0.05) | | Costs difference (95% CI) not reported  There were no significant differences between interventions for costs at 18 months (p>0.05) | |
| Hurley et al48 | Exercise therapy (n=83)  Walking (n=82)  Physiotherapy (n=81) | Mean (SD) at 12 months  *Exercise therapy*  Disability (0-100): 26.9 (17.8)  Pain intensity (0-10): 5.1 (3.0)  QALY (0-1): 0.62 (0.30)  *Walking*  Disability (0-100): 26.7 (18.4)  Pain intensity (0-10): 4.2 (3.1)  QALY (0-1): 0.63 (0.31) | Mean (SD) at 12 months  Disability (0-100): 27.1 (17.7)  Pain intensity (0-10): 4.1 (3.0)  QALY (0-1): 0.62 (0.30) | Mean total costs at 12 months  *Exercise therapy*  Healthcare perspective: £1,875 or €2,053  *Walking*  Healthcare perspective: £1,090 or €1,194 | Mean total costs at 12 months  Healthcare perspective: £1,426 or €1,561 | ICER for comparison between interventions was not reported |
|  |  | Effect difference (95% CI)  *Walking versus physiotherapy*  Disability (0-100): 1.6 (-4.7 to 7.9)  Pain intensity (0-10): -0.1 (-1.1 to 1.0)  QALY (0-1): 0.02 (-0.10 to 0.13)  *Exercise therapy versus physiotherapy*  Disability (0-100): 3.1 (-3.2 to 9.4)  Pain intensity (0-10): -0.5 (-1.5 to 0.5)  QALY (0-1): 0.03 (95% CI: -0.08 to 0.15) | | Costs difference (95% CI) not reported | |
| van der Roer et al53 | Exercise therapy (n=60)  Physiotherapy (n=54) | Mean (SD) not reported | Mean (SD) not reported | Mean (SD) at 12 months  Societal perspective: £4,603 (8,295) or €4,702 (8,473) | Mean (SD) at 12 months  Societal perspective: £4,328 (7,063) or €4,421 (7,215) | ICER – cost per point reduction in disability score, societal perspective: £19,345 (€19,760)  ICER – cost per point deterioration in pain intensity score, societal perspective: £206 (€211)  ICER – cost per point improvement on the global perceived recovery, societal perspective: £2,034 (€2,078)  ICER – cost per QALY gained, societal perspective: £6,759 (€6,213), i.e. cost-effective |
|  |  | Effect difference (95% CI)  Disability (0-24): 0.1 (-2.2 to 2.3)  Pain intensity (0-10): -1.0 (-2.1 to 0.1)  Global perceived recovery: 1.7 (0.7 to 4.4)  QALY (0-1): 0.03 (-0.06 to 0.12) | | Costs difference (95% CI)  Societal perspective: £274 (-2,585 to 3,270) or €281 (-2,902 to 3,340) | |
| Torstensen et al52 | Exercise therapy (n=71)  Physiotherapy (n=67)  Walking (n=70) | Mean (SD) at 12 months  *Exercise therapy*  Pain intensity (0-10): 4.0 (2.4)  Disability (0-100): 44.1 (13.8)  *Walking*  Pain intensity (0-10): 5.0 (2.8)  Disability (0-100): 50.6 (16.6) | Mean (SD) at 12 months  Pain intensity (0-10): 4.3 (2.9)  Disability (0-100): 43.0 (12.9) | Total direct costs at 15 months  *Exercise therapy*  Societal perspective: £840,511 or €943,025  *Walking*  Societal perspective:  £945,696 or €1,061,039 | Total direct costs at 15 months  Societal perspective: £727,310 or €816,017 | Physiotherapy was £218,383 (€245,021) less than walking at 15 months or £2,654 (€2,978) per patient  Exercise therapy was £113,200 (€127,006) more expensive than physiotherapy or £1,326 (€1,488) per patient  ICER not reported |
|  |  | Effect difference (95% CI) not reported  There were significant differences for disability at 12 months (p<0.05) in favour of physiotherapy and exercise therapy in comparison with walking  There were no differences for pain intensity at 12 months between interventions  There were no significant differences between exercise therapy and physiotherapy for pain intensity and disability at 12 months (p>0.05) | | Costs difference (95% CI) not reported | |
| Meta-analysis |  | We combined three studies for pain intensity,45, 55, 57 and four studies for disability45, 52, 55, 57 (Figure 4). Results showed that exercise therapy had similar improvements as physiotherapy (pain intensity [0-10]: 0.0, 95% CI: -1.0 to 1.0; disability [0-100]: 0.1, 95% CI: -2.6 to 2.8). | |  | |  |

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| ***Exercise therapy versus cognitive behavioural approach for back and neck pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** |
|  |  | *Exercise therapy* | *CBA* | *Exercise therapy* | *CBA* |  |
| Manca et al55 | Exercise therapy (n=161)  Cognitive behavioural approach (n=154) | Mean at 12 months  QALY (0-1): 0.70 | Mean at 12 months  QALY (0-1): 0.68 | Mean (SD) at 12 months  Healthcare perspective: £174 (169) or €177 (171)  Societal perspective: £1,092 (2,679) or €1,115 (2,736) | Mean (SD) at 12 months  Healthcare perspective: £141 (135) or €143 (137)  Societal perspective: £812 (2,294) or €825 (2,343) | ICER – cost per QALY gained, healthcare perspective: £1,649 (€1,683); CEAC: 80% at £1,000 (€1,142), i.e. cost-effective  ICER – cost per QALY gained, societal perspective: £7,909 (€8,078), i.e. cost-effective |
|  |  | Effect difference (95% CI)  QALY (0-1): 0.02 (-0.02 to 0.06) | | Cost difference (95% CI)  Healthcare perspective: £32 (-1 to 66) or €32 (-1 to 66)  Societal perspective: £158 (-398 to 716) or €160 (-407 to 731) | |
| ***Exercise therapy versus cognitive behavioural approach for chronic low back pain*** | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** |
|  |  | *Exercise therapy* | *CBA* | *Exercise therapy* | *CBA* |  |
| Critchley et al44 | Exercise therapy (n=72)  Cognitive behavioural approach (n=69) | Mean (SD) at 18 months  Disability (0-100):  28.3 (33.3)  Pain intensity (0-10): 3.2 (3.4)  QALY (0-1): 0.90 (0.37) | Mean (SD) at 18 months  Disability: 27.1 (37.1)  Pain intensity (0-10): 3.8 (3.8)  QALY (0-1): 1.00 (0.28) | Mean (SD) at 18 months  Healthcare perspective: £512 (1,406) or €523 (1,435) | Mean (SD) at 18 months  Healthcare perspective: £233 (273) or €227 (277) | ICER – cost per QALY lost, healthcare perspective: exercise therapy was dominated; CEAC, healthcare perspective: 35% at £30,000 (€34,278), i.e. exercise therapy was associated with higher costs and smaller effects than cognitive behavioural approach |
|  |  | Effect difference (95% CI) not reported  There were no significant differences between interventions for disability, pain intensity and QALY at 18 months (p>0.05) | | Costs difference (95% CI) not reported  There were no significant differences between interventions for costs at 18 months (p>0.05) | |
| Smeets et al50 | Exercise therapy (n=53)  Cognitive behavioural approach (n=58) | Mean (SD) at 12 months  Disability (0-24): 11.0 (4.8)    QALY (0-1): 0.69 (0.23) | Mean (SD) at 12 months  Disability (0-24): 10.6 (4.3)    QALY (0-1): 0.72 (0.20) | Mean (SD) at 12 months  Societal perspective: £24,029 (23,621) or €24,488 (23,999) | Mean (SD) at 12 months  Societal perspective: £17,761 (20,661) or €18,100 (21,055) | ICER not reported |
|  |  | Effect difference (95% CI) not reported | | Costs difference (95% CI) not reported | |

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| ***Exercise therapy versus different type of exercise for chronic neck pain*** | | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | | **ICER** |
|  |  | *Exercise therapy* | *Home exercise* | *Exercise therapy* | *Home exercise* | |  |
| Leininger et al36 | Home exercise (n=79)  Exercise therapy plus home exercise: (n=82) | Mean (SD) at 12 months  Pain intensity (0-10): 3.1 (1.9)  Disability (0-50): 17.2 (8.5)  QALY (SF-6D [0-1]): 0.80 (0.21)  QALY (EQ-5D [0-1]): 0.81 (0.99) | Mean (SD) at 12 months  Pain intensity (0-10): 3.2 (1.9)  Disability (0-50): 18.3 (8.8)  QALY (SF-6D [0-1]): 0.79 (0.22)  QALY (EQ-5D [0-1]): 0.82 (0.16) | Mean (SD) at 12 months  Healthcare perspective: £2,578 (508) or €2,670 (526)  Societal perspective:  £4,165 (1,450) or €4,314 (1,501) | Mean (SD) at 12 months  Healthcare perspective: £785 (282) or €813 (292)  Societal perspective: £2,325 (2,109) or €2,408 (1,706) | | *Exercise therapy versus home exercise*  ICER – cost per point reduction in pain intensity score, healthcare perspective: exercise therapy was associated with higher costs and smaller effect  ICER – cost per point deterioration in disability score, healthcare perspective: exercise therapy was associated with higher costs and smaller effect  ICER – cost per QALY lost (SF-6F), healthcare perspective: exercise therapy was associated with higher costs and smaller effect |
|  |  | Effect difference (95% CI)  Pain intensity: 0.2 (-0.2 to 0.5)  Disability: -0.2 (-1.9 to 1.6)  QALY (SF-6D [0-1]): -0.00 (-0.02 to 0.02)  QALY (EQ-5D [0-1]): -0.01 (-0.02 to 0.01) | | Costs difference (95% CI)  Healthcare perspective: £1,790 (1,603 to 1,965 to 1,603) or €1,853 (1,660 to 2,035)  Societal perspective: £1,836 (596 to 2,937) or €1,901 (617 to 3,043) | | |
| ***Exercise therapy versus different type of exercise for acute low back pain*** | | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** | |
|  |  | *General exercise* | *Yoga* | *General exercise* | *Yoga* |  | |
| Aboagye et al39 | Yoga (n=52)  Exercise therapy (n=52) | Mean (SD) at 12 months  QALY: 0.79 (0.13) | Mean (SD) at 12 months  QALY: 0.79 (0.14) | Mean (SD) at 12 months  Employer perspective: £435 or €482  Societal perspective: £3,215 or €3,558 | Mean (SD) at 12 months  Employer perspective: £251 or €266  Societal perspective: £1,779 or €1,969 | *Exercise therapy versus yoga*  ICER – cost per QALY lost, employer’s and societal perspective: cost-effective (<£10,064 [<€11,500]), exercise therapy showed higher costs and smaller effect than medical yoga (but not statistically significant) | |
|  |  | Effect difference (95% CI)  *Exercise therapy versus yoga*  QALY: -0.02 (-0.07 to 0.05) | | Costs difference  Employer perspective: £194 or €215  Societal perspective: £1,436 or €1,589 | |
| ***Exercise therapy versus different type of exercise for chronic low back pain*** | | | | | | | |
| **Study** | **Sample size** | **Effect** |  | **Costs** |  | **ICER** | |
|  |  | *General exercise* | *BGA* | *General exercise* | *BGA* |  | |
| Bello et al40 | Exercise therapy (n=40)  Behavioural graded activity (n=40) | Mean (SD) not reported | Mean (SD) not reported | Mean costs  Healthcare perspective: £614 or €687 | Mean costs  Healthcare perspective: £503 or €562 | ICER not reported  General exercise had similar effects and higher costs compared with behavioural graded activity | |
|  |  | Comparison of interventions showed no differences between groups for pain intensity and quality of life | |  | |  | |
|  |  | *Exercise therapy* | *Walking* | *Exercise therapy* | *Walking* |  | |
| Hurley et al48 | Exercise therapy (n=83)  Walking (n=82) | Mean (SD) at 12 months  Disability: 26.9 (17.8)  Pain intensity: 5.1 (3.0)  QALY: 0.62 (0.30) | Mean (SD) at 12 months  Disability: 26.7 (18.4)  Pain intensity: 4.2 (3.1)  QALY: 0.63 (0.31) | Mean total costs at 12 months  Healthcare perspective: £1,875 or €2,053 | Mean total costs at 12 months  Healthcare perspective: £1,090 or €1,194 | ICER not reported  Exercise therapy had similar effects and higher costs compared with walking | |
|  |  | Effect difference (95% CI)  *Walking versus exercise therapy*  Disability (0-100): -1.5 (-7.7 to 4.7)  Pain intensity: -0.6 (-1.6 to 0.5)  QALY: -0.02 (-0.13 to 0.10) | | Costs difference (95% CI) not reported | |
| Torstensen et al52 | Exercise therapy (n=71)  Walking (n=70) | Mean (SD) at 12 months  Pain intensity (0-10): 4.5 (2.4)  Disability (0-100): 44.1 (13.7) | Mean (SD) at 12 months  Pain intensity (0-10): 5.0 (2.8)  Disability (0-100): 50.6 (16.6) | Total direct costs at 15 months  Societal perspective: £840,511 or €943,025 | Total direct costs at 15 months  Societal perspective:  £945,696 or €1,061,039 | Exercise therapy was £105,185 (€118,013) less costly than walking at 15 months or £1,328 (€1,490) per patient | |
|  |  | Effect difference (95% CI) not reported  There were significant differences for disability at 12 months (p<0.05) in favour of exercise therapy  There were no significant differences between interventions for pain intensity at 12 months (p>0.05) | | Costs difference (95% CI) not reported | |

CEAC: cost-effectiveness acceptability curve; CI: confidence interval; EQ-5D: EuroQol five-dimension; ICER: incremental cost-effectiveness ratio; QALY: quality adjusted life year; SF-6D: Short Form six-dimension; SF-36: Short Form-36; BGA: behavioural graded activity; CBA: cognitive behavioural approach