Appendix H – Economic evidence tables

Study	Fernandez-Garcia 2021[31]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis (CUA) (health outcome: QALYs) **Study design:** Within-trial analysis (RCT- RATULS[88]) In a sensitivity analysis modelling was used to extrapolate results beyond trial follow-up. **Approach to analysis:** Analysis of individual level healthcare resource use and EQ-5D to estimate costs and QALYs over 6 months follow-up. Unit costs applied. Adjusted differences between groups were calculated using regression analysis incorporating randomised group, study centre, time since stroke, baseline utility	**Population:** Adults with moderate or severe upper limb functional limitation (Action Research Arm Test [ARAT] score 0–39) as a result of first-ever stroke that had occurred between 1 week and 5 years before randomisation. The median time from stroke to randomisation was 240 days (IQR 109–549 days), and participants had a mean ARAT score of 8.4 points (SD 11.8 points). A total of 409 out of 768 (53.3%) participants were receiving physiotherapy and/or occupational therapy at the time of randomisation. **Patient characteristics:** N = 768 Mean age = 61 years (SD 13.5 years) Male= 60.8%	**Total costs (mean per patient):** Intervention 1: £3785 (98.33% CI £2801 to £4770) Intervention 2: £5387 (98.33% CI £4777 to £5996) Intervention 3: £4451 (98.33% CI £3548 to £5354) **Incremental:** **2-1 (unadjusted as adjusted not reported):** £1601 (95% CI £706 to £2496) **3-1(adjusted):** £741 (98.33 CI –£461 to £1943) **3-2 (adjusted):** £741 (98.33 CI –£461 to £1943) **Currency & cost year:** 2018 UK pounds (£)	**QALYs (mean per patient):** Intervention 1: 0.21 (98.33% CI 0.19 to 0.23) Intervention 2: 0.21 (98.33% CI 0.19 to 0.23) Intervention 3: 0.23 (98.33% CI 0.21 to 0.24) **Incremental:** **2-1 (unadjusted):** 0.00 (95% CI -0.20 to 0.20) **3−1 (unadjusted):** 0.010 (98.33% CI -0.005 to 0.025) Note that adjusted QALY outcomes for each group were not reported, however authors reported that adjusted QALYs were lower.	**ICERs** Intervention 2 was dominated by intervention 3 due to higher costs and lower QALYs. Intervention 3 versus Intervention 1: £74,100 per QALY gained CI: NR Probability cost effective (£20K threshold): intervention 1 81%; intervention 2 0%; intervention 3 19%. **Analysis of uncertainty:** Scenario 1 examined the impact of assigning a value of zero to missing total healthcare costs, resulting in the ICER between EULT and usual care increasing to £172,000. Scenario 2 examined the possibility that those participants with missing total healthcare costs may have used some services and hence incurred some costs. This decreased the ICER between EULT and usual care to £50,000 with the probability of EULT being cost-effective at a £20,000 WTP threshold increasing to 27%.

(QALY analysis only) and baseline costs (cost analysis only) as explanatory variables. **Perspective:** UK NHS and PSS **Follow-up:** 6 months **Treatment effect duration:**[(a)] 6 months **Discounting:** NA	**Intervention 1:** Usual care (45 minutes with a physiotherapist or occupational therapist, 5 days a week) over 12 weeks. **Intervention 2:** Robot-assisted training (45 minutes per day, 3 times per week) plus usual care over 12 weeks. **Intervention 3:** Enhanced upper limb therapy (EULT) (45 minutes with a physiotherapist, 3 times per week) plus usual care over 12 weeks.	**Cost components incorporated:** Intervention costs, follow-up costs, primary care, therapy and community-based, services, secondary care, residential and nursing home care, social services, medication costs.		Scenario 3 increased the life span of the MIT-Manus robotic gym system from 5 to 7 years. This resulted in a reduction of the mean capital costs per patient and hence, in a lower mean total cost for the robot-assisted training group (£5085) compared with the base-case analysis (£5387). Robot-assisted training remained dominated by EULT and did not change the ICER from the base case results (£74,100). A secondary per-protocol within-trial cost-effectiveness analysis removed from the data set those participants who did not receive at least 20 sessions of therapy in the robot-assisted training and the EULT programme groups was also conducted. Usual care remained the least costly option, followed by EULT and robot-assisted training. The ICER between usual care and EULT was £68,000 and the probability of usual care being cost-effective at a £20,000 WTP threshold increased to 92%. Extrapolation of trial data on costs and effects to 12 months: The ICER for the comparison between EULT and usual care was £6,095, however there was only a 55% probability of EULT being considered cost-effective compared with usual care at the £20,000 WTP value. Robot-assisted training had no probability of being cost-effective at this WTP value.

Data sources
Health outcomes: Within-trial analysis of RATULS trial[88] included in the clinical review. EQ-5D collected at baseline and at 3- and 6-months post-randomisation was used to calculate QALYs using the area under the curve method. **Quality-of-life weights:** Within-RCT analysis: EQ-5D-5L mapped to EQ-5D-3L, UK population valuation tariff. **Cost sources:** Resource use from within RCT. UK national unit costs applied.
Comments
Source of funding: National Institute for Health Research Health Technology Assessment Programme. **Limitations:** Within-trial analysis based on RATULS RCT and so only reflects this study and not the wider evidence base identified in the clinical review. **Other:** This study, as well as the RCT[88] that formed the basis of the analysis are also included as part of the evidence review for this guideline that assessed the clinical and cost-effectiveness of more intensive rehabilitation.
Overall applicability:[(b)] Directly applicable **Overall quality:**[(c)] Minor limitations

Abbreviations: SD = standard deviation; NR = not reported; ARAT = Action Research Arm Test; QALY=quality-adjusted life year; EULT = Enhanced upper limb therapy; IQR = Interquartile range.

a) *For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.*
b) *Directly applicable / Partially applicable / Not applicable*
c) *Minor limitations / Potentially serious Limitations / Very serious limitations*

Study	Remy-Neris 2021[49]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost-utility analysis (health outcome: QALYs) **Study design:** Within-trial analysis of an RCT (n=215) included in the clinical review (same paper) with no modelled extrapolation.	**Population:** Adults, 3 weeks to 3 months post-stroke, with a Fugl-Meyer Assessment (FMA) score of 10 to 40 points. **Patient characteristics:** Mean age (SD): 58 (13.63) years old Male: 65%	**Total costs (mean per patient):** Intervention 1: £45,843 (95% CI: £42,113 to £49,393; p=NR) Intervention 2: £45,744 (95% CI: £42,195 to £49,293; p=NR) Incremental (2−1): Saves £99 (95% CI: NR; p=0.99)	**QALYs (mean per patient (SD)):**[(c)] Intervention 1: 0.47 (0.26) Intervention 2: 0.48 (0.25) Incremental (2−1): 0.01 (95% CI: NR; p=0.87)	**ICER (Intervention 2 versus Intervention 1):** NR. Results suggested that the Exo group intervention dominates usual care (lower costs and higher QALYs), however total costs and QALY gains were not statistically significant between groups. Probability Intervention 2 cost effective (£20K/30K threshold): NR/NR **Analysis of uncertainty:**

Approach to analysis: Analysis of individual level healthcare resource use and EQ-5D to estimate costs and QALYs associated with self-rehabilitation (using a mechanized device) on post-stroke upper extremity impairment compared to those receiving control self-exercises. Unit costs applied. **Perspective:** French Health system **Follow-up:** 1 year **Treatment effect duration:**[(a)] 1 year **Discounting:** NA	**Intervention 1:** Control group (n=108) was provided with usual rehabilitation for 1 hour, 5 days per week plus an additional daily hour of self-rehabilitation (two 30-minute sessions) consisting of basic stretching and active exercises for 4 weeks. **Intervention 2:** The Exo group (n=107) was provided with usual rehabilitation for 1 hour, 5 days per week plus an additional daily hour of self-rehabilitation (two 30-minute sessions) consisting of gravity-supported, games-based training using an exoskeleton (Armeo®Spring) for 4 weeks.	**Currency & cost year:** 2018 euros converted to UK pounds (£)[(b)] **Cost components incorporated:** ArmeoSpring exoskeleton (device cost, 5-year linear depreciation, maintenance, and physical therapist for patient training). Resource use estimates included inpatient rehabilitation days, outpatient physiotherapy, GP and specialist consultations and transportation costs.		Results were robust to probabilistic sensitivity analysis, were uncertainty on the ICER was described using 1000 bootstrap replications on the cost-effectiveness plane.
Data sources				
Health outcomes: Within-trial analysis of a single-blind phase III RCT (same paper) included in the clinical review, where the primary outcome was the change in upper extremity impairment, measured using FMA UE scores collected at baseline and 4 weeks. Health-related quality of life was assessed using the EQ-5D-3L questionnaire at baseline and 1 year. Other secondary outcomes included FIM and SIS hand function. **Quality-of-life weights:** Within-trial analysis using EQ-5D-3L with French preference weights applied. **Cost sources:** References for cost sources were not reported, however the authors stated that data from both hospital and non-hospital resources were collected prospectively in the study case report form and patients' diaries. Hospitalisation costs were estimated from the average national severity-related group cost and average length of stay in rehabilitation per patient group. Repeated admissions during the 12 months after the initial intervention were also included in the cost computations using the same methodology.				
Comments				

Source of funding: The French Ministry of Health. **Limitations:** French healthcare system may not reflect current UK NHS context. French population valuation tariff was used to estimate QALYs but NICE reference case specifies that the UK tariff is preferred. Within-trial analysis based on a single-blind RCT, therefore results only reflect this study and not the wider evidence base identified in the clinical review. References for unit costs were not reported which limits interpretation of results for UK context. **Other:** None.

Overall applicability:[d] Partially applicable **Overall quality:**[e] Potentially serious limitations

Abbreviations: 95% CI= 95% confidence interval; EQ-5D-3L= EuroQol-5 Dimensions, three-level version (scale: 0.0 [death] to 1.0 [full health], negative values mean worse than death); FIM= functional independence measure (scale 0-18, higher values are better); FMA UE= Fugl-Meyer Assessment Upper Extremity (scale 0-66, higher scores are better); ICER= incremental cost-effectiveness ratio; NA= not applicable; NR= not reported; QALYs= quality-adjusted life years; RCT= randomised controlled trial; SIS hand function= stroke Impact Scale - hand function domain (scale 0-100, higher values are better).

a) For studies where the time horizon is longer than the treatment duration, an assumption needs to be made about the continuation of the study effect. For example, does a difference in utility between groups during treatment continue beyond the end of treatment and if so for how long.

b) Converted using 2018 purchasing power parities.[81] References for unit costs were not reported but 2018 was assumed based on the study completion date.

c) Mean difference taken from Figure 4 of guideline clinical review.

d) Directly applicable / Partially applicable / Not applicable

e) Minor limitations / Potentially serious limitations / Very serious limitations