

The Bone & Joint Journal



Supplementary Material

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Table i. International Classification of Diseases-10 Codes, Office of Population Censuses and Surveys codes, Healthcare Resource Groups, and costs of hospital admissions.

Reason for admission	ICD-10	OPCS	HRG	Day case cost, £	Inpatient cost (elective), £
ACL reconstruction (open)	M23.8 + M23.5 + T93.3	W74.2 +Z84.6+Z94.2 (or Z94.3) + Y65.8 + Z94.2 (or Z94.3)	HN23C Major knee procedures for non-trauma	2,656	4,772
ACL reconstruction (arthroscopic)	M23.8 + M23.5 + T93.3	W74.2 +Y76.7+Z84.6+Z94.2 (or Z94.3) + Y65.8 + Z94.2 (or Z94.3)	HN23C Major knee procedures for non-trauma	2,656	4,772
ACL reconstruction with medial/lateral meniscal repair and meniscectomy	M23.8 + M23.5 + T93.3	ACL reconstruction + W82.3 + Z94.2 (or Z94.3) + W82.2 + Z94.2 (or Z94.3)	HN22E Very major knee procedures for non-trauma	3,778	6,414
ACL operation but no reconstruction (ACL intact)	M23.8 + M23.5 + T93.3	W87.9 + Z94.2 (or Z94.3)	HN24C Intermediate knee procedures for non-trauma	1,901	3,523
Arthroscopic arthrolysis	M23.8 + M23.5	W85.8	HN25A Minor knee procedures for Non-trauma	1,650	2,262
Posterior cruciate ligament injury with medial/lateral meniscal repair	S83.5	W82.3 + Z94.2 (or Z94.3)	HT24C Intermediate knee procedures for trauma	2,261	3,909
Infection (cellulitis)	L03.1 + R22.4 + T81.4	-	JD07K Skin disorders without intervention	344*	1,658*

*Nonelective.

ACL, anterior cruciate ligament; HRG, Healthcare Resource Group; ICD, International Classification of Diseases; OPCS, Office of Population Censuses and Surveys Classification of Interventions and Procedures.

Table ii. Unit costs (UK 2019-20 £) of healthcare services.

Resource use type	Unit cost (£)	Source/details
GP – surgery*	39	Cost GP patient contact consultation: PSSRU 2019-20 (chapter 10, page 120). Average consultation length of 9.22 minutes. ¹
Theatre time (per minute)	16.49	Table R142X from Scottish cost tables 2019 (https://beta.isdscotland.org/find-publications-and-data/healthcare-resources/finance/scottish-health-service-costs)
GP – home*	90	Cost GP patient contact consultation (including qualification costs and direct care staff costs): PSSRU 2019-20 (chapter 10, page 120). Average consultation length of 9.22 minutes; ¹ assume average 12 minutes travel time for home visits: PSSRU 2009.
GP – telephone*	21	Cost GP patient contact consultation: PSSRU 2019-20 (chapter 10, page 124). Average consultation length of 5 minutes ¹
Physiotherapist, one to one	66.82	NHS Reference Cost schedule 2019-20, tab CHS, service code A08A1
Physiotherapist, group-based	65.34	NHS Reference Cost schedule 2019-20, tab CHS, service code A08AG
A&E	182.28	NHS Reference Cost schedule 2019-20, tab AE, weighted average of all attendances to a type 1 A&E unit with the exception of dental care and dead on arrival attendances.
Outpatient visit	122	NHS Reference Cost schedule 2019-20, tab total outpatient attendances, service code 110 (trauma & orthopaedics)
Acupuncture/ Chiropractor/Osteopath	99.18	Estimated as average of costs for acupuncture, chiropractor, and osteopath sessions. Acupuncture: NHS Reference Cost schedule 2019-20, tab OPROC, service code 191 (pain management), currency code AB23Z (£163.90) Chiropractor: assumed to cost the same as physiotherapy session (£66.82) Osteopath: assumed to cost the same as physiotherapy session (£66.82)

*Including direct care staff costs and including qualification costs.

A&E, accident and emergency; GP, general practitioner; PSSRU, Personal Social Services Research Unit.

Missing data

Missing data on patients' characteristics, EuroQol Five-dimension Five-level health index (EQ-5D-5L) and costs at baseline were imputed using unconditional mean imputation. Data on allocation to treatment arm and death were assumed to be complete. We examined patterns of missing data and their similarity between trial arms. In particular, we examined whether there was some evidence that the probability of data missing was conditional on baseline patients characteristics (age,

sex, Knee injury and Osteoarthritic Outcome Score (KOOS)) or on lagged outcomes (EQ-5D-5L utility). The association between the probability of data missing was estimated using logistic random-effects regressions. We used multiple imputation by chained equations to impute missing data on EQ-5D-5L utility scores and visual analogue scale (VAS) scores, and cost components, at each follow-up timepoint. Each missing value was imputed as a function of follow-up period, sex, age, recruitment site, treatment allocation, baseline EQ-5D data (score and VAS), baseline KOOS, physical activity prior to injury (as measured by the modified Tegner score), updated EQ-5D-5L score (utility and VAS) and costs (by category and payer - NHS or private). The imputation model was run separately by randomized treatment. We used predictive mean matching to create 30 imputed datasets (proportion of data missing across all time periods $\times 100$) with ten nearest neighbours.

Table iii. Missing data on self-reported resource use and EuroQol Five-dimension utility by treatment allocation in each follow-up period.

Follow-up	Resource use data, n (%)		EQ-5D data, n (%)	
	Surgical (n = 156)	Rehab (n = 160)	Surgical (n = 156)	Rehab (n = 160)
Baseline			156 (100)	159 (99)
6 mths	88 (56)	93 (58)	85 (54)	89 (56)
12 mths	87 (56)	78 (49)	84 (54)	75 (47)
18 mths	127 (81)	120 (75)	115 (74)	116 (73)

Self-reported healthcare resource use is classified as missing if resource use items are all missing.

EQ-5D, EuroQol five-dimension index.

Table iv. Response level data for EuroQol Five-dimension questionnaires at each follow-up time, by treatment allocation.

Follow-up	Surgical, n (%) (n = 156)					Rehabilitation, n (%) (n = 160)				
	M	SC	UA	PD	AD	M	SC	UA	PD	AD
Baseline										
Available data	156 (100)	156 (100)	156 (100)	156 (100)	156 (100)	159 (99)	159 (99)	159 (99)	159 (99)	159 (99)
No problems	46 (29)	101 (65)	17 (11)	14 (9)	60 (38)	40 (25)	106 (67)	21 (13)	12 (8)	68 (43)
Slight problems	53 (34)	29 (19)	40 (26)	53 (34)	43 (28)	51 (32)	36 (23)	49 (31)	51 (32)	48 (30)
Some problems	44 (28)	22 (14)	61 (39)	60 (38)	36 (23)	49 (31)	17 (11)	54 (34)	71 (45)	24 (15)
Severe problems	12 (8)	4 (3)	24 (15)	26 (17)	11 (7)	18 (11)	0 (0)	19 (12)	22 (14)	11 (7)
Extreme problems	1 (1)	0 (0)	14 (9)	3 (2)	6 (4)	1 (1)	0 (0)	16 (10)	3 (2)	8 (5)
6 mths										
Available data	85 (54)	85 (54)	85 (54)	85 (54)	85 (54)	90 (56)	90 (56)	89 (56)	90 (56)	90 (56)
No problems	39 (46)	65 (76)	19 (22)	10 (12)	36 (42)	42 (47)	74 (82)	23 (26)	18 (20)	37 (41)
Slight problems	32 (38)	11 (13)	35 (41)	45 (53)	32 (38)	30 (33)	10 (11)	24 (27)	34 (38)	31 (34)
Some problems	10 (12)	7 (8)	20 (24)	23 (27)	8 (9)	14 (16)	3 (3)	26 (29)	30 (33)	10 (11)
Severe problems	4 (5)	2 (2)	7 (8)	5 (6)	6 (7)	4 (4)	3 (3)	9 (10)	6 (7)	8 (9)
Extreme problems	0 (0)	0 (0)	4 (5)	2 (2)	3 (4)	0 (0)	0 (0)	7 (8)	2 (2)	4 (4)
12 mths										
Available data	84 (54)	85 (54)	85 (54)	85 (54)	85 (54)	76 (48)	76 (48)	76 (48)	76 (48)	75 (47)
No problems	59 (70)	79 (93)	45 (53)	25 (29)	53 (62)	56 (74)	70 (92)	39 (51)	21 (28)	38 (51)
Slight problems	21 (25)	6 (7)	30 (35)	47 (55)	19 (22)	9 (12)	4 (5)	16 (21)	40 (53)	21 (28)
Some problems	4 (5)	0 (0)	8 (9)	11 (13)	10 (12)	6 (8)	2 (3)	10 (13)	8 (11)	12 (16)
Severe problems	0 (0)	0 (0)	1 (1)	2 (2)	0 (0)	4 (5)	0 (0)	4 (5)	5 (7)	4 (5)
Extreme problems	0 (0)	0 (0)	1 (1)	0 (0)	3 (4)	1 (1)	0 (0)	7 (9)	2 (3)	0 (0)
18 mths										
Available data	116 (74)	116 (74)	115 (74)	116 (74)	116 (74)	116 (73)	116 (73)	116 (73)	116 (73)	116 (73)
No problems	89 (77)	105 (91)	65 (57)	37 (32)	72 (62)	77 (66)	99 (85)	54 (47)	28 (24)	67 (58)
Slight problems	17 (15)	7 (6)	28 (24)	51 (44)	21 (18)	21 (18)	10 (9)	21 (18)	56 (48)	30 (26)

Follow-up	Surgical, n (%) (n = 156)					Rehabilitation, n (%) (n = 160)				
	M	SC	UA	PD	AD	M	SC	UA	PD	AD
Some problems	8 (7)	4 (3)	14 (12)	24 (21)	13 (11)	14 (12)	6 (5)	27 (23)	24 (21)	14 (12)
Severe problems	2 (2)	0 (0)	5 (4)	3 (3)	7 (6)	3 (3)	1 (1)	11 (9)	6 (5)	0 (0)
Extreme problems	0 (0)	0 (0)	3 (3)	1 (1)	3 (3)	1 (1)	0 (0)	3 (3)	2 (2)	5 (4)

AD, anxiety/depression; M, mobility; PD, pain/discomfort; SC, self-care; UA, usual activities.

Table v. Odds ratios (proportional) comparing EuroQol Five-dimension responses by domain at each follow-up time, by treatment allocation.

Follow-up	Surgical, n (%) (n = 156)					Rehabilitation, n (%) (n = 160)					OR* (95% CI)				
	M	SC	UA	PD	AD	M	SC	UA	PD	AD	M	SC	UA	PD	AD
6 mths	85 (54)	85 (54)	85 (54)	85 (54)	85 (54)	90 (56)	90 (56)	89 (56)	90 (56)	90 (56)	1.16 (0.54 to 2.46)	1.44 (0.68 to 3.08)	0.73 (0.38 to 1.40)	1.17 (0.58 to 2.35)	0.82 (0.38 to 1.80)
12 mths	84 (54)	85 (54)	85 (54)	85 (54)	85 (54)	76 (48)	76 (48)	76 (48)	76 (48)	75 (47)	1.03 (0.54 to 1.99)	0.78 (0.31 to 1.91)	0.62 (0.31 to 1.25)	0.78 (0.40 to 1.52)	0.56 (0.20 to 1.57)
18 mths	116 (74)	116 (74)	115 (74)	116 (74)	116 (74)	116 (73)	116 (73)	116 (73)	116 (73)	116 (73)	0.65 (0.41 to 1.03)	0.59 (0.23 to 1.47)	0.53 (0.35 to 0.81)	0.73 (0.45 to 1.20)	0.94 (0.58 to 1.51)

*The difference is for surgical versus rehabilitation and based on an ordered logistic regression model of each treatment allocation against each EQ-5D domain adjusted for recruitment site and for the baseline level of the EQ-5D domain (as categorical variable). AD, anxiety/depression; CI, confidence interval; EQ-5D, EuroQol five-dimension index; M, mobility; OR, odds ratio; PD, pain/discomfort; SC, self-care; UA, usual activities.

Table vi. Data values for EuroQol Five-dimension utility for each follow-up period following multiple imputation.

Follow-up	EQ-5D utility		
	Surgical (SE)	Rehabilitation (SE)	Difference (95% CI)*
6 mths	0.634 (0.028)	0.638 (0.028)	0.006 (-0.091 to 0.104)
12 mths	0.780 (0.018)	0.705 (0.025)	0.077 (0.008 to 0.146)
18 mths	0.770 (0.020)	0.724 (0.021)	0.048 (-0.019 to 0.116)

*Differences between treatment arms are obtained from multilevel mixed-effects models, adjusted for treatment allocation and EQ-5D utility at baseline; a time by treatment interaction was included in the model; the follow-up timepoint was used as a categorical variable; robust standard errors were used to account for clustering by site.

CI, confidence interval; EQ-5D, EuroQol five-dimension index; SE, standard error.

Table vii. Data values for costs for each follow-up period following multiple imputation.

Follow-up	NHS costs			Total healthcare costs (NHS + non-NHS)		
	Surgical (SE)	Rehabilitation (SE)	Difference (95% CI)*	Surgical (SE)	Rehabilitation (SE)	Difference (95% CI)*
6 mths	£2,306 (147)	£1,011 (92)	£1,295 (988 to 1,602)	£2,397 (148)	£1,084 (97)	£1,313 (969 to 1,657)
12 mths	£755 (103)	£805 (105)	-£51 (-371 to 269)	£796 (105)	£838 (108)	-£42 (-363 to 279)
18 mths	£129 (28)	£365 (71)	-£236 (-392 to -79)	£196 (38)	£452 (77)	-£256 (-434 to -79)

*Differences between treatment arms were obtained from multilevel mixed-effects models, adjusted for treatment allocation; a time by treatment interaction was included in the model; the follow-up time point was used as a categorical variable; robust standard errors were used to account for clustering by site.

Table viii. Baseline characteristics of participants according to allocated intervention groups broken down by those who completed follow-up before and after 23 March 2020, the start of the COVID-19 lockdown in the UK.

Characteristic	Before lockdown		After lockdown	
	Surgical (n = 80)	Rehabilitation (n = 79)	Surgical (n = 76)	Rehabilitation (n = 81)
Sex, n (%)				
Male	56 (70.0)	48 (60.8)	54 (71.1)	51 (63.0)
Female	24 (30.0)	31 (39.2)	22 (28.9)	30 (37.0)
Mean age at randomization, n; mean (SD)	80; 33.5 (9.8)	79; 32.5 (10.4)	76; 32.9 (10.3)	81; 33.2 (8.8)
KOOS4 at baseline, n; mean (SD)*				
Overall	80; 48.1 (20.6)	79; 44.0 (16.0)	76; 43.2 (19.0)	81; 42.8 (19.9)
Pain	79; 64.7 (21.0)	78; 60.1 (19.0)	76; 60.9 (20.0)	81; 50.1 (20.1)
Symptoms	79; 59.6 (22.7)	78; 55.5 (17.2)	76; 54.5 (20.8)	81; 53.7 (21.1)
ADL	79; 69.4 (23.3)	78; 69.0 (20.8)	76; 65.9 (22.0)	81; 67.0 (22.0)
Sport and recreation	79; 37.0 (29.1)	78; 34.6 (25.3)	76; 31.9 (24.9)	81; 32.3 (27.7)
QoL	79; 30.4 (19.8)	78; 26.6 (18.1)	76; 25.6 (20.6)	81; 26.1 (20.0)
Tegner Activity Scale before injury at baseline, n (%)				
Level 0 to 4	7 (8.7)	10 (10.1)	10 (13.2)	16 (19.8)
Level 5+	73 (91.3)	71 (89.9)	66 (86.8)	65 (80.2)
EQ-5D-5L, n; mean (SD)				
VAS	79; 64.6 (20.6)	79; 66.9 (19.7)	75; 63.8 (21.1)	78; 69.9 (21.4)
Index	80; 0.59 (0.25)	79; 0.58 (0.25)	76; 0.53 (0.26)	90; 0.56 (0.27)

*0 representing extreme problems and 100 representing no problems.

ADL, activities of daily living; EQ-5D, EuroQol five-dimension index; KOOS, Knee injury and Osteoarthritis Outcome Score; QoL, quality of life; SD, standard deviation; VAS, visual analogue scale.

Table ix. EuroQol Five-dimension utility and visual analogue scores by treatment allocation at each follow-up time point for patients who completed follow-up before and after 23 March 2020, the start of the COVID-19 lockdown in the UK (observed data without imputation for missing data)

Follow-up time	Surgical		Rehabilitation		Difference (95% CI)*
	n	Mean (SD)	n	Mean (SD)	
Completion of follow-up before 23 March 2020					
<i>EQ-5D utility</i>					
Baseline	80	0.589 (0.247)	79	0.580 (0.246)	
6 months	44	0.660 (0.231)	40	0.607 (0.257)	0.070 (-0.061 to 0.202)
12 mths	51	0.803 (0.138)	36	0.691 (0.237)	0.124 (0.066 to 0.183)
18 mths	60	0.784 (0.204)	54	0.710 (0.255)	0.079 (0.007 to 0.151)
<i>EQ-5D VAS</i>					
Baseline	79	64.6 (20.6)	79	66.9 (19.7)	
6 mths	44	72.2 (18.8)	40	64.3 (19.7)	6.7 (1.7 to 11.8)
12 mths	51	77.7 (15.3)	37	73.7 (19.9)	3.7 (-3.4 to 10.8)
18 mths	59	78.2 (16.0)	52	74.9 (16.3)	4.2 (-3.0 to 11.4)
Completion of follow-up after 23 March 2020					
<i>EQ-5D utility</i>					
Baseline	76	0.526 (0.255)	80	0.556 (0.272)	
6 mths	41	0.624 (0.233)	49	0.671 (0.280)	-0.038 (-0.139 to 0.064)
12 mths	33	0.747 (0.218)	39	0.766 (0.246)	0.004 (-0.098 to 0.106)
18 mths	55	0.747 (0.250)	62	0.737 (0.236)	0.020 (-0.065 to 0.106)
<i>EQ-5D VAS</i>					
Baseline	75	63.8 (21.1)	78	69.9 (21.4)	
6 mths	40	67.1 (16.9)	49	70.4 (18.6)	-0.6 (-7.4 to 6.3)
12 mths	33	72.0 (19.3)	38	78.1 (17.0)	-5.5 (-12.0 to 1.1)
18 mths	55	77.1 (16.8)	61	76.9 (16.2)	2.5 (-2.7 to 7.6)

* Differences between treatment arms obtained from multilevel mixed-effects models, adjusted for baseline utility, site, and treatment interaction with time, where the follow-up timepoint was used as a categorical variable.

CI, confidence interval; EQ-5D, EuroQol five-dimension index; SD, standard deviation; VAS, visual analogue scale.

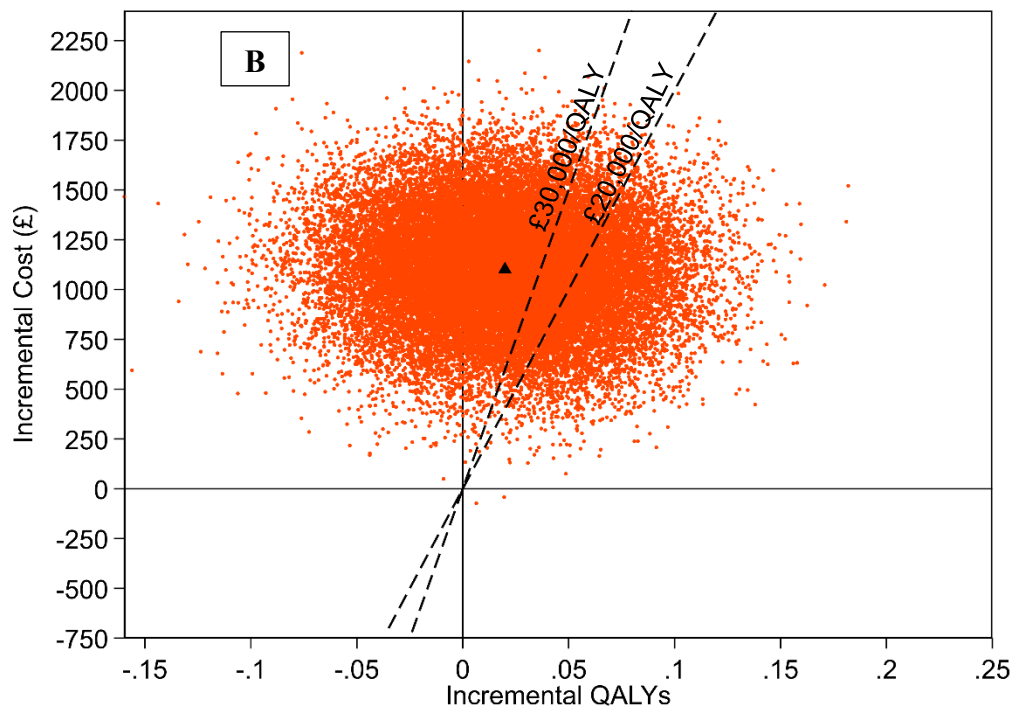
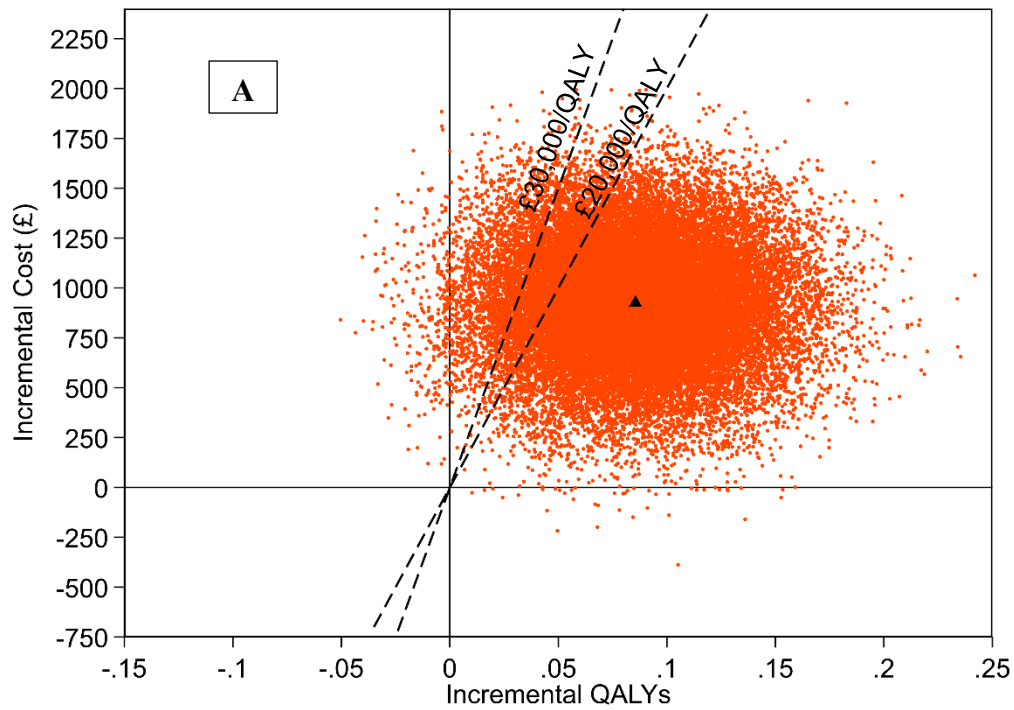


Fig a. Cost-effective scatter plot using a) only patients who completed the trial before the lockdown date of 23 March 2020 and b) those who completed the trial after 23 March 2020. Scatter plot of estimated joint density of incremental costs and quality-adjusted life years (QALYs) of surgical reconstruction relative to rehabilitation obtained by bootstrap re-sampling from each of the 30 imputed datasets, running the regression models on each bootstrapped dataset and extracting the estimated

incremental costs and QALYs. Dashed lines represent threshold values of £20,000 and £30,000 per QALY gained. Bootstrapped results falling below the lines are deemed cost-effective. From the bootstrapped results, we calculated the probability that surgical reconstruction was more cost-effective than rehabilitation for different threshold values per QALY gained.

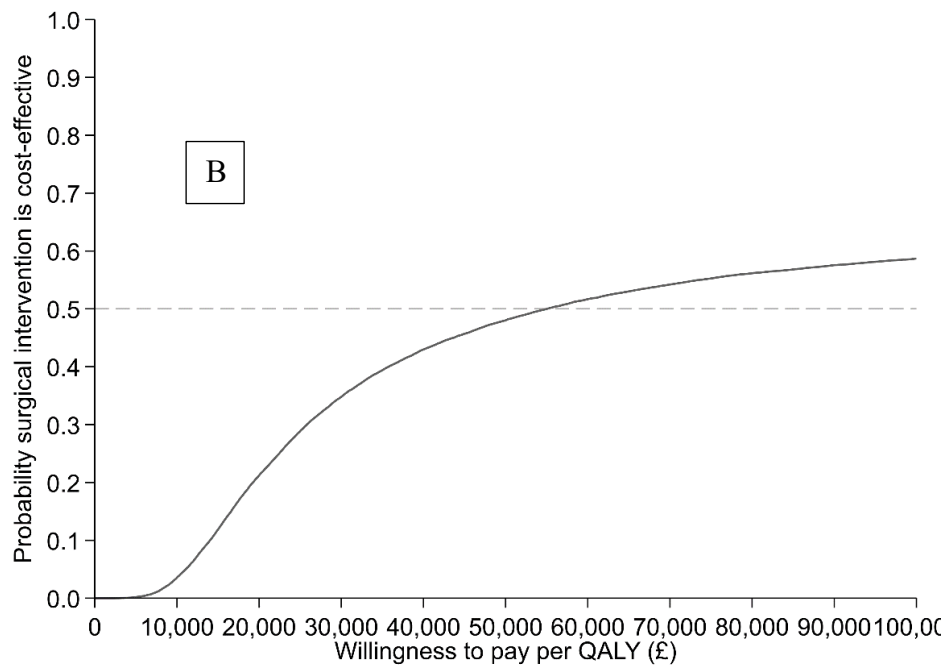
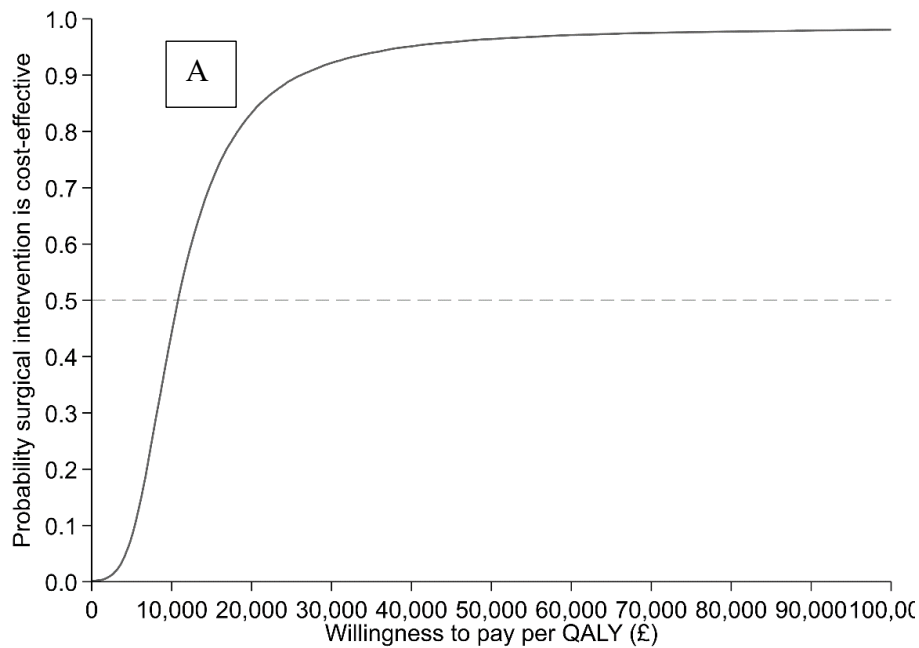


Fig b. Cost-effectiveness acceptability curve using a) only patients who completed the trial before the lockdown date of 23 March 2020 and b) those who completed the trial after 23 March 2020. These figures plot the probability (y-axis) that surgical reconstruction is cost-effective compared to rehabilitation for different willingness to pay thresholds per quality-adjusted life year (QALY) gain (x-axis). Probability captures the joint uncertainty in incremental costs and QALYs of surgical management compared to rehabilitation and was obtained by estimating the proportion of bootstrapped results that were cost-effective for each threshold value.

References

1. No authors listed. National Schedule of NHS Costs 2019/20 v2 2021. Department of Health. 2021. <https://www.england.nhs.uk/publication/2019-20-national-cost-collection-data-publication/> (date last accessed 2 November 2023).