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Cost-effectiveness of surgery versus cast immobilization for adults with a bi-cortical fracture of the scaphoid waist: a within trial economic evaluation of the SWIFFT trial

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Abstract

Aims The Scaphoid Waist Internal Fixation for Fractures Trial (SWIFFT) was conducted to determine the optimal treatment pathway for adults with bi-cortical, undisplaced and minimally-displaced fractures of the scaphoid waist, comparing early surgical fixation with initial cast immobilisation, with immediate ~~urgent~~ surgical fixation offered ~~performed~~ in cases of confirmed non-union.

Methods A cost-effectiveness analysis was conducted to assess the relative merits of the treatment options. The differences in costs to the healthcare system and quality adjusted life years (QALYs) of the patients over the one year follow-up of the trial in the two treatment arms were estimated using regression methods.

Results Our base case analysis found patients randomised to early surgical fixation resulted in higher costs to the NHS, £1,295 more than the cast immobilisation arm, primarily due to the cost of the initial surgery. They had a marginally better quality of life over the period, of 0.0158 QALYs, however this was not statistically significant. The combined cost per additional QALY was £81,962, well above the accepted threshold for cost-effectiveness used in the UK and internationally. The probability of early surgery being cost-effective in this setting was only 5.6%.

Conclusions Consistent with the clinical findings of the SWIFFT trial these results indicate that initial cast immobilisation of minimally displaced scaphoid fractures, with immediate surgical fixation only offered in cases of confirmed non-union ~~initial cast immobilisation, with immediate urgent surgical fixation offered performed in cases of confirmed non-union~~, is the optimal treatment option, resulting in comparable patient outcomes whilst using less healthcare resources.

Introduction

Fractures of the scaphoid bone are common, with an estimated 7,265 in the United Kingdom (UK) per year, some 20% of all hand and arm fractures[1]. Often in young, active people, they account for about 90% of all carpal fractures[2]. Historically, treatment has been to immobilise the wrist in a plaster cast from the time of presentation, for up to ten weeks, to allow the bone to heal, with surgical intervention only considered if the fracture fails to unite. However, despite limited evidence, there is an increasing trend to immediately fix the fracture for all cases[3, 4].

The Scaphoid Waist Internal Fixation for Fractures Trial (SWIFFT) was conducted to compare the effectiveness of early surgical fixation with initial cast immobilisation. SWIFFT randomised 439 adults with bi-cortical, undisplaced and minimally-displaced (≤2mm) fractures of the scaphoid waist to receive early surgical fixation, or below elbow cast immobilisation, with ~~urgent~~ immediate surgical fixation offered ~~performed~~ in cases of confirmed ~~non-union~~ delayed union at 6 to 12 weeks. For trial research purposes, union was assessed using plain radiographs and CT scan at baseline and at 52 weeks, with routine radiographs at 6 weeks and 12 weeks. Union was determined at the point of complete disappearance of the fracture line on radiographs and bridging on CT scans, further details are published elsewhere[5].

The trial found no statistically significant difference between the two arms in the primary outcome measure, patient-rated wrist evaluation (PRWE)[5]. This finding led to the conclusion that this patient group should have initial cast immobilization, with suspected non-unions immediately fixed upon confirmation, a conclusion based on the perceived negative implications of primary surgery which entail no incremental clinical benefit. Full details of the SWIFFT trial design and clinical effectiveness results are published elsewhere[5-7].

However, a finding of no superiority of either treatment on the primary clinical outcome is insufficient to inform the optimal approach from a cost-effectiveness perspective, which incorporates a wider set of outcomes in the deliberative process. This study aims to address the question of cost-effectiveness of early surgical fixation with initial cast immobilisation through exploration of the within-trial cost and health related quality of life (HRQoL) consequences of the two treatment pathways.

The analysis has been conducted in keeping with best methodological practice, including the CHEERS checklist[8] and Glick et al.'s Economic Evaluation in Clinical Trials[9].

Patients and Methods

To inform the cost-effectiveness analysis data was collected and analysed from the SWIFFT trial on the patient HRQoL and costs associated with both arms of the trial. In line with current guidance

from the National Institute for Health and Care Excellence (NICE) for conducting such analysis[10] HRQoL was measured in terms of Quality Adjusted Life Years (QALYs), with costs estimated from a National Health Service (NHS) and personal social services (PSS) perspective at a 2017/18 price base. The analysis was conducted over the one-year timeframe of the trial, implying no need to discount future costs and QALYs.

The analysis consists of several elements: firstly, summaries of the unadjusted cost and HRQoL results are reported, secondly, regression analysis is conducted on both the cost and HRQoL results to control for observable differences in the two trial arm populations. Finally, the costs and HRQoL from the regression analyses are combined to explore the cost-effectiveness of the respective treatment modalities in terms of the incremental cost-effectiveness ratio (ICER). The ICER approach is used by NICE to assess the cost-effectiveness of an intervention under evaluation, with an ICER of between £20,000 and £30,000 per QALY considered to be cost-effective use of limited NHS resources[10].

The baseline analysis takes an intention to treat (ITT) approach, with imputation for missing data, and adjustment made for the difference in baseline HRQoL. This approach was taken to most reasonably reflect the clinical approach while adjusting for any observable biases in the trial data and adjusting for the missing data. We additionally present other regression analysis exploring the impact of not using imputed data, a per-protocol approach, and not adjusting for baseline HRQoL. We also present the results of a complete-case analysis, whereby the average costs and HRQoL of only those who returned all patient questionnaires are considered.

Additionally, non-parametric bootstrapping was conducted to inform an exploration of the uncertainty in which treatment is the cost-effective option and was used to populate a cost-effectiveness acceptability curve (CEAC). Details of how to interpret CEACs are available elsewhere[11].

All analyses were conducted in Stata version 16.1[12].

The SWIFFT trial

Details of the SWIFFT trial are published elsewhere[5, 6]. In brief, it was a multicentre, pragmatic, open-label, two-arm RCT with one year of follow-up, trial recruitment was undertaken from the orthopaedic departments of 30 NHS hospitals in England and one hospital in Wales, from 23rd July 2013 until 26th July 2016. A total of 439 adults (aged ≥16 years) with bi-cortical, undisplaced and minimally-displaced (≤2mm) fractures of the scaphoid waist were randomised to receive early percutaneous or open surgical fixation, or below elbow cast immobilisation for six to ten weeks, with ~~urgent~~ immediate surgical fixation offered ~~performed~~ in cases of confirmed non-union.

In addition to the clinical outcomes collected as part of the SWIFFT trial, such as PRWE, several variables were collected to inform the cost and HRQoL outcomes explored in this study, as detailed below. These were collected through a mix of patient questionnaires and routine hospital data extraction. All patient outcomes were collected at baseline, six, 12, 26, and 52 weeks.

Costs to the NHS and PSS

To determine the cost to the NHS and PSS of each treatment modality, data on the level of relevant resources used during the initial treatment and follow-up period, collected through SWIFFT, were combined with estimates of the unit cost of each resource. The resources used were determined by combining trial data on treatment modality (cast immobilisations, surgical fixations, and any imaging related to the original injury and within the 52 week follow-up), with patient reported interactions with primary and secondary care (reported by patient questionnaires at 6, 12, 26 and 52 weeks). The full list of categories included in the analysis and respective unit costs used are reported in Supplementary Appendix Table 1.

Interactions with the NHS and PSS for reasons unrelated to the original injury were requested as part of the patient questionnaires. This was to ensure patients separated interactions that were associated with the original wrist injury from those that were not, and to test whether there were imbalances in the unrelated healthcare needs in the two arms of the trial.

The cost of initial presentation with the injury, or any interim care that might have occurred upon initial presentation, were excluded from this analysis as occurring prior to enrolment onto the SWIFFT trial.

Patient health reported quality of life (HRQoL)

The EQ-5D-3L, NICE's preferred measure in cost-effectiveness analysis[10], was used to determine the HRQoL of patients throughout the 52 week trial follow-up. It consists of patient completed questions covering five dimensions of health: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression[13]. Using national preference weights it can be used to estimate a single score for patient HRQoL, ranging from -0.594 (worst response across all five dimensions) to 1 (best responses) for the UK[13], where 0 is equivalent to death, 1 represents perfect health, and negative scores are considered worse than death. The EQ-5D-3L preference scores for the five follow-up times were combined over the 52 week follow-up, using an area under the curve method, to estimate a patient level score for the full trial period, measured in terms of QALYs.

Missing data

A summary of the level of missing data at each follow-up time is reported in Supplementary Appendix Table 2, this highlights that returns of each questionnaire were reasonable for QoL and costs at each time-point varying from 0.5% to 36.4% missing. Despite the expectation of some level of attrition and missing data in any trial, and powering of the SWIFFT trial in accordance[6], its existence has the potential to bias the results of any subsequent analysis if it is caused by some underlying factors that are not controlled for. In addition to approaches such as complete case analysis, statistical imputation methods are available to address any potential imbalance in the observed data through imputation of the missing data[14].

An exploration of the missing data in the cost and EQ-5D-3L scores from the patient questionnaire responses at each follow-up point found that missingness was present and occurred at a greater level in the plaster cast arm. As a result, in addition to scenarios using only the returned patient questionnaires (the 'no imputation' scenarios in our analysis) ~~of complete case analysis~~, multiple imputation of missing data was conducted. Imputation was conducted simultaneously for all cost and EQ-5D-3L categories at each of the follow-up times, under the assumption that the data were missing at random (MAR)[14]. Missingness was assumed to depend on all other missing variables (i.e. costs and EQ-5D-3L score at each follow-up) as well as a number of baseline covariates: gender, whether the patient's dominant arm was injured, treatment allocation, and age. The variables were selected through clinical guidance provided by the trial steering committee. The imputation was run 36 times to be consistent with the largest proportion of missing data observed (36.4% in costs at 26 weeks in the plaster cast arm)[14].

Regression analysis

Despite the randomisation of patients in the SWIFFT trial, regression analysis is an important component in understanding the difference in the treatment specific costs and HRQoL as it allows for the controlling of any residual imbalances in the trial arms and gives a clearer understanding of what variables, beyond treatment allocation, drive the estimated costs and HRQoL[15].

Generalised linear regression models which contain the same variables but were estimated independently ~~Structurally consistent but independent generalised linear regression models~~ were estimated for HRQoL and costs over the 52 week trial period[15]. Following a pre-specified analysis plan the regression incorporated variables on treatment allocation, age, baseline fracture displacement (<1 mm/1-2 mm), and dominance of injured limb. An additional regression scenario was conducted which incorporated baseline EQ-5D-3L score as a variable for both the cost and HRQoL regressions to control for any difference in baseline score not controlled for by the other variables.

Results

Comparison of costs by treatment arm

Figure 1 reports the unadjusted average costs falling on the NHS and PSS for the two arms of the SWIFFT trial that were related to the scaphoid waist fracture. The patient-reported costs for each of the four follow-up time periods are represented by the bar charts, with the 95% confidence interval around the mean, provided by the error bars. The mean treatment specific costs that result from imaging, surgery, and casting are reported in the table embedded in Figure 1, alongside the associated 95% confident intervals. The treatment specific costs in the figure were calculated by multiplying the average frequency of the relevant clinical category per person recruited to each arm of the trial, taken from the SWIFFT trial data, by the unit costs reported in Supplementary Appendix Table 1.

Figure 1 here

The figure shows that, with the exception of surgery and casting costs, which were greater in the surgical fixation arm, there was no statistically significant difference between the treatments at any follow-up point or imaging costs.

Comparing the total costs for complete-case patients, i.e. those for whom we have no missing cost data, the average total cost for the surgical fixation arm was £2,350 (95% CI £2,164 to £2,536) and £727 (£496 to £958) for cast immobilisation over the 52 week trial period. However, these averages are based on a relatively small number of complete-case patient responses, 83 of 219 and 65 of 220 respectively, due to a large number of patients not completing one or more follow-up resource use questionnaires.

To address the issue of missing data and adjust for the impact of factors beyond treatment allocation on total costs, regression analysis was conducted on eight scenarios, the results of which are detailed in Supplementary Appendix Table 3. In all of the regressions surgical allocation was associated with a large and statistically significant increase in total healthcare cost, of between £1,228 and £1,770. The baseline analysis, of an intention to treat (ITT) approach with imputation for missing data and adjustment made for the difference in baseline HRQoL, estimated an addition cost of £1,295 from allocation to the surgical fixation arm.

Of the other regression variables included (~~surgical allocation,~~ HRQoL at baseline, fracture displacement, dominant wrist injured, and age), HRQoL at baseline was the only variable to achieved statistical significance in any of the scenarios, being associated with a reduction in the total cost, indicating a correlation between HRQoL and healthcare resource use. Fracture displacement resulted in an increase in costs in all of the scenarios, but never at a statistically significant level. Age and dominant wrist were found to neither have a consistent direction of impact on total cost, nor to reach statistical significance in any scenario.

The per-protocol regressions resulted in a higher cost difference due to treatment allocation as it removes the patients who cross-over from the analysis, and therefore have higher costs than their peers if they crossed over to surgery, or lower if they crossed over to casting.

An investigation into the number of interactions with the NHS which were unrelated to the patient's scaphoid fracture confirmed that there was no statistically significant difference between the trial arms (mean number of interactions: 5.65 for plaster immobilisation, 5.91 for surgical fixation; p = 0.828). This supports the assumption that unrelated NHS and PSS interactions can be excluded from the cost-effectiveness analysis and that the two arms are balanced in terms of unrelated care needs.

Comparison of quality of life by treatment arm

Figure **2** reports the unadjusted average patient reported HRQoL scores at each follow-up time for both treatment arms, using the UK EQ-5D-3L preference weights[16]. Scores at baseline were statistically similar but higher in the surgical fixation group. At 6 weeks HRQoL was better in the surgical fixation group, potentially as a result of the better baseline score, but the differences were neither maintained throughout the 52 weeks, nor statistically significant.

Taking a complete-case approach, the total HRQoL over the trial period was 0.832 QALYs (95% CI 0.806 to 0857) for surgical fixation and 0.814 QALYs (0.783 to 0.845) for cast immobilisation, indicating a larger HRQoL score in the surgical fixation arm, but not statistically significantly so. As with the complete-case cost analysis, this is based on a limited number of the total patient population.

Figure 2 here

Consistent with the approach taken to the cost analysis, the results of the eight HRQoL regressions are reported in Supplementary Table 4. HRQoL was found to be marginally better with surgical fixation in all of the regressions, but in contrast to the cost results, never reaching statistical significance.

As with the cost regressions, HRQoL at baseline was associated with a statistically significant increase in HRQoL for the full period in all of the analyses in which it was included. Furthermore, fracture displacement was associated with a lower quality of life in all of the scenarios, but never statistically significantly so at a 95% level. The injury of the dominant wrist did not have a consistent or statistically significant effect on HRQoL, and increased age was associated with a decrease in HRQoL, but again not to a statistically significant level.

Baseline cost-effectiveness results

A simple comparison of the complete-case cost and HRQoL scores for the two arms of the trial (i.e. excluding all of those who failed to return any of the patient questionnaires) results in the surgical fixation arm being associated with an average incremental cost of £1,623 and 0.018 additional QALYs, an ICER of £90,166/QALY. However, as discussed earlier, such an analysis fails to reflect the nature of the missing data, adjust for other underlying factors, and excludes a lot of data from patients who did not return one or more questionnaires.

Therefore, the base-case cost-effectiveness analysis uses the regression scenario which takes an ITT approach, with missing data imputed and adjustment made for the difference in baseline HRQoL. This scenario estimates that allocation to the surgical fixation arm was associated with an average incremental cost of £1,295 compared to the cast immobilisation arm. Surgical fixation allocation also implied 0.0158 more QALYs, implying a mean ICER of £81,962/QALY, well above the limits of what is considered to be a cost-effective use of NHS funding by NICE[10].

Our probabilistic sensitivity analysis, using non-parametric bootstrapping, estimated that even at the largest cost-effectiveness threshold considered appropriate by NICE, £30,000 per QALY gained, the probability of surgical fixation being cost effective is only 0.056. This is demonstrated in the CEAC given in

Figure 3, which shows that initial cast immobilisation is most likely to be the cost-effective treatment option for all thresholds considered reasonable in a UK setting.

Figure 3 here

Scenario analyses

reports the incremental costs and QALYs for all eight regression scenarios, drawn from the regression outputs reported in Supplementary Appendix Tables 3 and 4, alongside the respective ICERs. Across the difference scenarios the ICER for surgical fixation versus cast immobilisation is between £52,320/QALY and £135,085/QALY, consistently driven by the high incremental cost of surgery with small predicted HRQoL benefit. In all of these scenarios the ICER is above what is conventionally considered a cost-effective use of limited NHS resources in such a setting.

Table 1: Surgical fixation incremental costs and HRQoL and ICERs for the regression scenarios, adjusted and unadjusted for baseline quality of life

	Scenario	Incremental cost	Incremental QALYs	ICER surgery versus cast
unadjusted	~~Complete case~~ No imputation[1] ITT	£1,580	0.0208	£75,962/QALY
	With MI ITT	£1,228	0.0182	£67,473/QALY
	~~Complete case~~ No imputation PP	£1,771	0.0257	£68,910/QALY
	With MI PP	£1,549	0.0173	£89,538/QALY
adjusted	~~Complete case~~ No imputation ITT	£1,308	0.0250	£52,320/QALY
	With MI ITT (base case)	£1,295	0.0158	£81,962/QALY
	~~Complete case~~ No imputation PP	£1,616	0.0238	£67,899/QALY
	With MI PP	£1,594	0.0118	£135,085/QALY

[1]No imputation in this context means only completed patient responses were included in the analyses, with all missing questionnaires dropped.
ITT – intention to treat, MI – multiple imputation, PP – per-protocol

Discussion

The results of this study provide further support to the ~~clinical~~ primary outcome findings of the SWIFFT trial[5], that initial cast immobilisation with fixation if non-union is detected is the optimal solution for patients with bi-cortical, undisplaced and minimally-displaced (≤2mm) fractures of the scaphoid waist. The clinical trial analysis finding of no statistically significant difference between the

two arms in the primary, PRWE, outcome measure is consistent with the findings of this analysis of no statistically significant increase in HRQoL in patients treated with initial surgical fixation. This study has further developed this result to demonstrate that this lack of patient health benefit is accompanied by a statistically significant increase in the cost of care falling on the NHS and PSS. Combined, these findings imply that the most cost-effective treatment pathway for this patient population is cast immobilisation with fixation if non-union is detected, as it achieves comparable patient outcomes for a lower level of expenditure which can be invested on patient care elsewhere. Furthermore, this study has highlighted that clinical factors such as the displacement of the fracture less than 2mm and injury to the dominant wrist, have no statistically significant impact on the HRQoL of the patient or the costs of care.

This study has a number of strengths both in terms of the analyses conducted and quality of the data. A key strength of the SWIFFT trial is its pragmatic multicentre randomised-controlled trial design, which provides robust, gold standard evidence in addition to reflecting actual practice in the NHS. In terms of the analyses conducted, the use of a wide range of scenario analyses, extensive and pre-agreed regression analysis, probabilistic sensitivity analysis, and missing data imputation facilitate an extensive exploration of the uncertainty and biasing factors that may impact the findings. The consistency with which the range of scenarios result in consistent conclusions about the optimal decision demonstrates the strength of the underlying SWIFFT trial data.

There are also some weaknesses in this study, ~~both~~ in terms of the data available, the analyses conducted and the relevance to the key stakeholders. Firstly, the reliance on patient reported outcomes is inevitably associated with a level of data missingness, as would be expected to occur in any study such as this. In the majority of the quality of life and resource use questionnaires missing data was reasonable, typically less than 75%, but in some resource use follow-up periods up to 36.4% missing from any single follow-up. While it is impossible to retrospectively determine why this occurred the relative length and complexity of the resource use questionnaire likely played a role. While the impact of the missing data is somewhat overcome through imputation and multiple regression analyses, it is never possible to be certain that the responses of those who did not complete the relevant questionnaire can be inferred from those who did. However, as the complete-case analysis, and all of the eight analyses conducted, resulted in initial cast immobilisation being the most cost-effective decision, we do not believe the level of missingness impacts the conclusion of this study.

Secondly, while the analysis has taken the methodological perspective recommended by NICE, the limited time horizon of one year, due to the length of the trial follow-up, inevitably has implications for the ability to inform lifetime cost-effectiveness analysis deliberations, as ultimately preferred by NICE. While the majority of related costs are likely to fall within the analysed period, some long-

term adverse events, such as osteoarthritis and surgical related complications, are likely to impact patient HRQoL in the long-term, but are outside the scope of this analysis. However, this robust analysis still represents an important addition to the decision-making process, for patients, clinicians, and commissioners. ~~While the NICE perspective excludes any costs which fall on patients and their families, either directly or indirectly, and other societal factors such as employment and carer burden, these may play a part in the decision making deliberations of patients and clinical staff. However, a secondary analysis of days of lost employment conducted as part of the SWIFFT trial found no statistically significant difference[5], indicating the impact of treatment pathway on wider factors may be limited.~~

Finally, the use of the EQ-5D-3L may be a weakness due to a lack of sensitivity of the measure to factors impacting patient HRQoL. A number of limitations of the EQ-5D-3L, including sensitivity to change in patient HRQoL, led to the development of an updated version of the questionnaire, the EQ-5D-5L[17]. However, at the time of commencement of the SWIFFT trial the updated version was not routinely available, and at the time of this analysis NICE recommends the use of EQ-5D-3L[18]. Similarly, as a generic measure of HRQoL, EQ-5D-3L is likely to be less sensitive to changes in this patient population than a disease specific measure, such as PRWE. However, the ability to derive QALY values with which to generalise cost-effectiveness results across settings is a significant strength of the EQ-5D-3L~~, and the consistent findings of this study to the SWIFFT clinical analysis of PRWE support the approach taken~~.

The increasing trend to treat scaphoid fractures surgically as a first line has been observed both in the UK and in other developed healthcare systems[3, 4]. In this research we have demonstrated that the evidence does not vindicate this trend in terms of the cost-effectiveness of surgical fixation as a first line treatment. While this perspective excludes other factors that may play a part in the decision making deliberations, such as costs which fall on patients, and other factors such as employment and carer burden, a secondary analysis of days of lost employment conducted as part of the SWIFFT trial found no statistically significant difference[5], indicating the impact of treatment pathway on wider factors may be limited. Therefore, it is reasonable to conclude that ~~the finding that~~ the expected high cost of initial surgical fixation, intended to facilitate better patient health, does not appear to translate to significant HRQoL improvements for patients in the short-term, which has clear implications for the treatment of such injuries not just in the NHS but in other healthcare systems internationally.

References

1. Garala K, Taub N., Dias J. The epidemiology of fractures of the scaphoid. The Bone & Joint Journal. 2016;98-B(5):654-9.
2. Leslie IJ, Dickson RA. The fractured carpal scaphoid. Natural history and factors influencing outcome. J Bone Joint Surg Br. 1981 Aug;63-b(2):225-30. PubMed PMID: 7217146. Epub 1981/08/01. eng.
3. Dy CJ, Kazmers NH, Baty J, Bommarito K, Osei DA. An Epidemiologic Perspective on Scaphoid Fracture Treatment and Frequency of Nonunion Surgery in the USA. Hss j. 2018 Oct;14(3):245-50. PubMed PMID: 30258328. Pubmed Central PMCID: PMC6148584. Epub 2018/09/28. eng.
4. The NHS Information Centre. Hospital Episode Statistics for England. Inpatient statistics, 2005–09. Activity in English NHS Hospitals and English NHS commissioned activity in the independent sector. Leeds: The Health and Social Care Information Centre HES Analysis. 2010.
5. Dias J., Brealey S, Fairhurst C. Surgery compared with cast immobilization for adults with a bi-cortical fracture of the scaphoid waist (SWIFFT): a multicentre, pragmatic, open-label, parallel-group, two-arm randomised clinical trial. The Lancet. 2020;396(10248):390-401.
6. Dias J, Brealey S, Choudhary S, Cook L, Costa M, Fairhurst C, et al. Scaphoid Waist Internal Fixation for Fractures Trial (SWIFFT) protocol: a pragmatic multi-centre randomised controlled trial of cast treatment versus surgical fixation for the treatment of bi-cortical, minimally displaced fractures of the scaphoid waist in adults. BMC Musculoskelet Disord. 2016 Jun 4;17:248. PubMed PMID: 27260639. Pubmed Central PMCID: PMC4893284. Epub 2016/06/05. eng.
7. Dias J. Scaphoid Waist Internal Fixation for Fractures Trial (SWIFFT): a randomised controlled trial, economic evaluation and nested qualitative study of cast versus surgical fixation for the treatment of adult patients with a bi-cortical fracture of the scaphoid waist. NIHR HTA. 2020;24(52).
8. Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. BMJ : British Medical Journal. 2013;346:f1049.
9. Glick HA, Doshi JA, Sonnad SS, Polsky D. Economic evaluation in clinical trials: OUP Oxford; 2014.
10. NICE. Guide to the methods of technology appraisal 2013. NICE article [PMG9]. 2013.
11. Fenwick E, Marshall DA, Levy AR, Nichol G. Using and interpreting cost-effectiveness acceptability curves: an example using data from a trial of management strategies for atrial fibrillation. BMC Health Services Research. 2006 2006/04/19;6(1):52.
12. StataCorp. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC. 2019.
13. Dolan P, Gudex C, Kind P, Williams A. A social tariff for EuroQol: results from a UK general population survey. York Centre for Health Economics Discussion 1995;Sep; 138
14. Faria R, Gomes M, Epstein D, White IR. A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. Pharmacoeconomics. 2014;32(12):1157-70.
15. Briggs A, Sculpher M, Claxton K. Decision modelling for health economic evaluation: Oup Oxford; 2006.
16. Kind P. The EuroQoL instrument: an index of health-related quality of life. In: Spilker B, editor. Quality of Life and Pharmacoeconomics in Clinical Trials. Philadelphia: Lippincott-Raven. 1996.
17. Herdman M, Gudex C, Lloyd A, Janssen MF, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Quality of Life Research. 2011 2011/12/01;20(10):1727-36.
18. NICE. Position statement on use of the EQ-5D-5L value set for England. NICE: London. 2019.
19. NICE. NG38: Fractures (non-complex): assessment and management. NICE Guidelines. London: National Institute for Health and Care Excellence (NICE); 2016.
20. Department of Health and Social Care. Reference costs 2015 to 2016. Department of Health and Social Care: London. 2016.

21. Curtis LB, A. . Unit Costs of Health and Social Care 2016. Personal Social Services Research Unit, University of Kent, Canterbury. 2016.

Figure and Table Legends

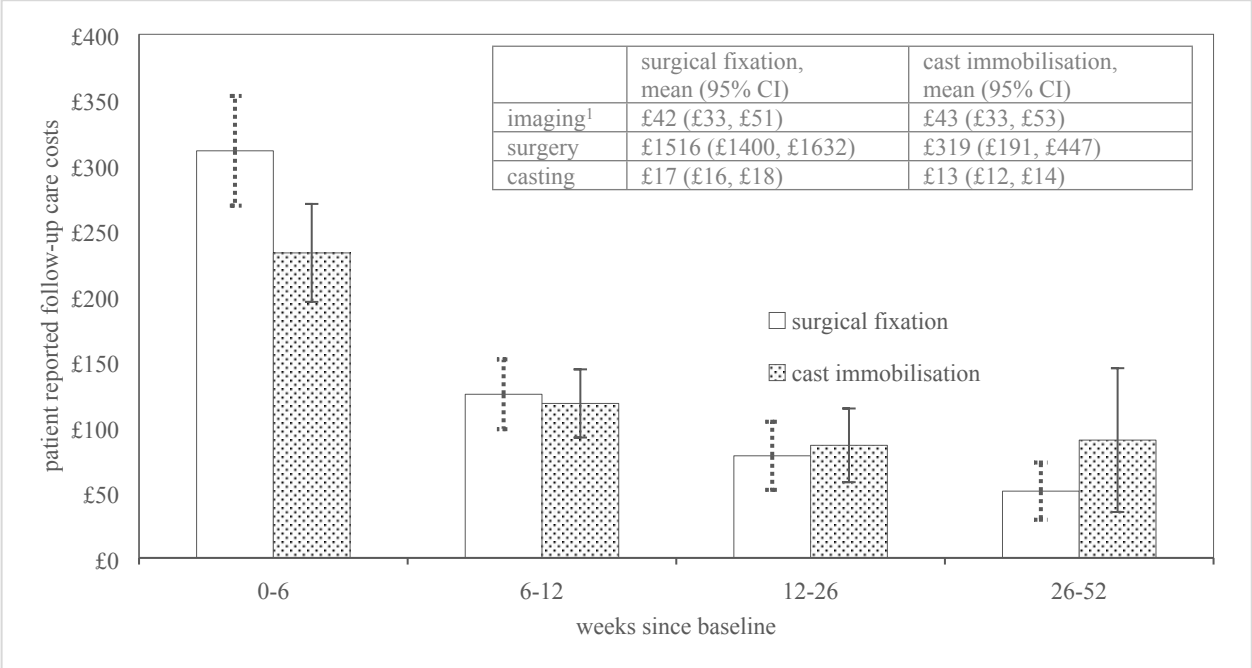
Figure 1: Within trial mean cost summary statistics, ~~complete case~~ without imputation

Figure 2: mean EQ-5D-3L scores at each follow-up time, error bars represent the 95% confidence interval, percentages report the level of missing data

Figure 3: Cost-effectiveness acceptability curve (CEAC) for the base-case analysis

Table 1: Surgical fixation incremental costs and HRQoL and ICERs for the regression scenarios, adjusted and unadjusted for baseline quality of life

Figure 1: Within trial mean cost summary statistics, ~~complete case~~ without imputation



	surgical fixation, mean (95% CI)	cast immobilisation, mean (95% CI)
imaging[1]	£42 (£33, £51)	£43 (£33, £53)
surgery	£1516 (£1400, £1632)	£319 (£191, £447)
casting	£17 (£16, £18)	£13 (£12, £14)

Error bars attached to each bar chart represent the 95% confidence interval (CI) for that follow-up period

[1]imaging consists of the average per patient costs for x-rays, T-scans, and MRIs, as reported in the clinical trial data, unit costs are reported in Supplementary Appendix Table 1

Figure 2: mean EQ-5D-3L scores at each follow-up time, error bars represent the 95% confidence interval, percentages report the level of missing data

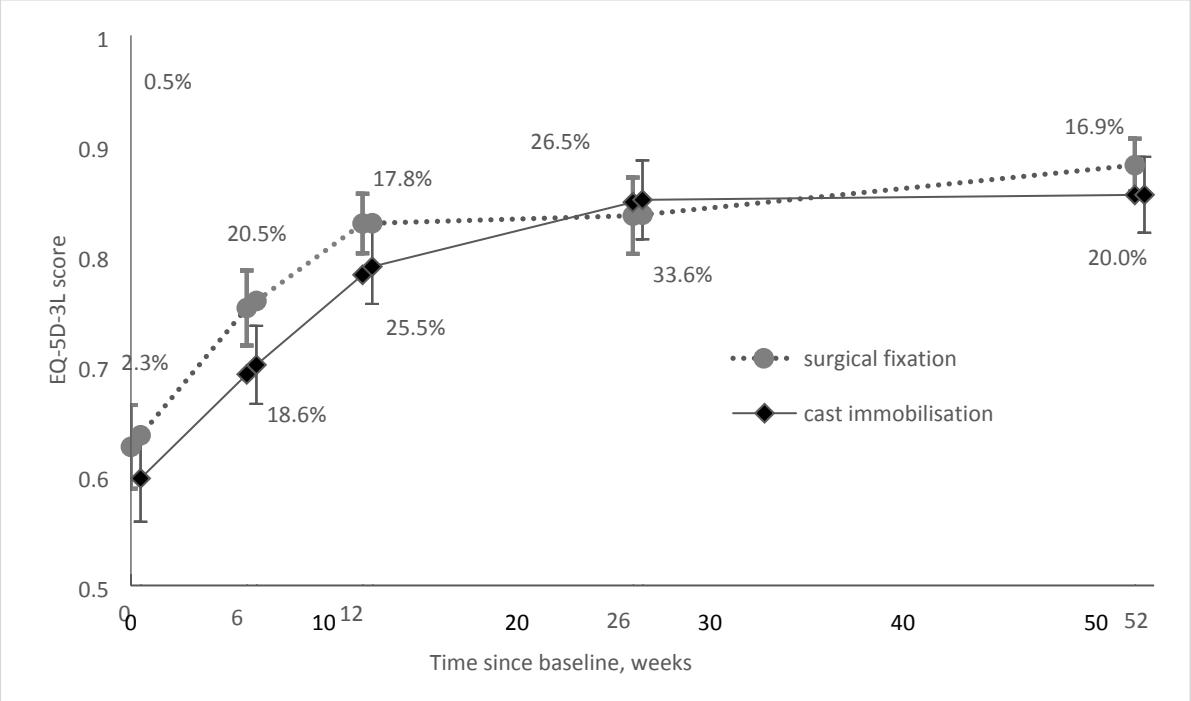
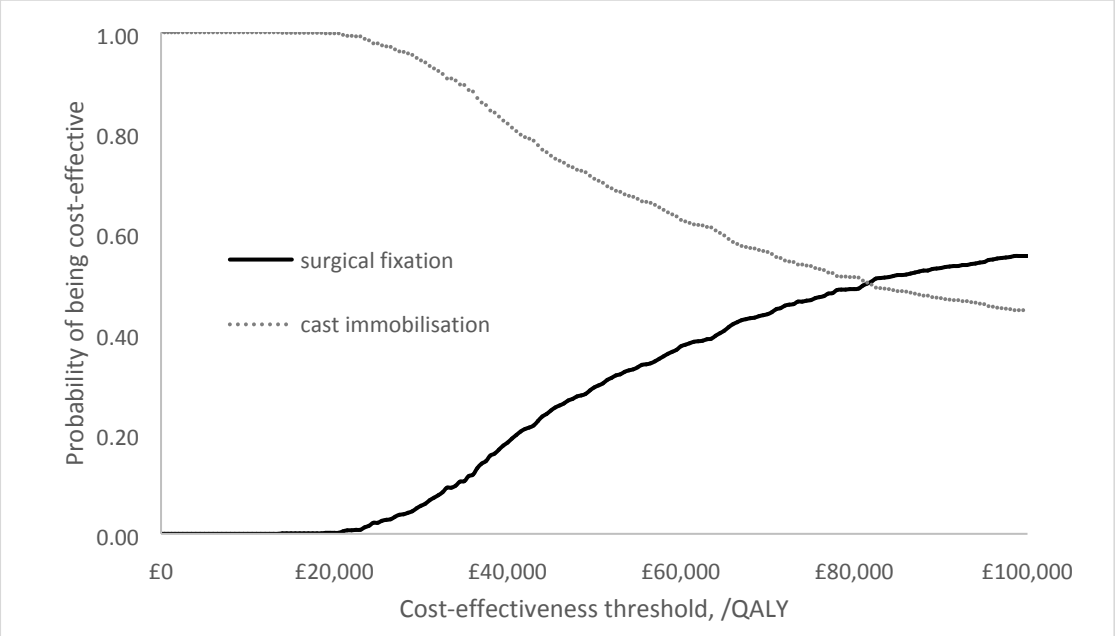


Figure 3: Cost-effectiveness acceptability curve (CEAC) for the base-case analysis



Supplementary Appendix

Supplementary Table 1: Unit costs associated with within trial analysis

Stage	Cost item	Value	Source/assumption
Treatment and imaging	Cost of casts, both initial at diagnosis and additional casts	£10	*Consistent with NICE NG38.[1]* *Assumes costs of hospital attendance etc. are covered in patient reported activity.*
	Cost of primary surgery (patients randomised to surgical arm)	£1,632	Weighted average of adult HT44 (intermediate hand procedures for trauma, mapped from all open OPCS code), Reference Cost 2015/16[2]
	Cost of secondary surgery (repeat surgery for surgical arm and surgery for cast arm of trial)	£2,509	Weighted average of adult HT43 (Major hand procedures for trauma, mapped from all closed OPCS code), Reference Cost 2015/16[2]
	Cost per radiograph	£30	Reference Costs 15/16, DAPF, Direct Access Plain Film
	Cost per CT scans	£94	Reference Costs 15/16, RD20A, Computerised Tomography Scan of one area, without contrast, 19 years and over[2]
	Cost per MRI	£145	Reference Costs 15/16, RD01A, Magnetic Resonance Imaging Scan of one area, without contrast, 19 years and over[2]
Follow up care – from trial patient reported questionnaires, only for those 'about your wrist' rather than 'other reasons'	GP – at practice	£37	Based on estimates from PSSRU (11.7 minute consultation)[3]
	GP – at home	£74	Based on estimates from PSSRU (11.4 minute consultation plus 12 minute of travel)[3]
	GP – by phone	£22	Based on estimates from PSSRU (7.1 minute consultation)[3]
	Physiotherapist – at GP practice	£49	Reference cost 2015/16 A08A1 (physiotherapist, adult, one to one, community)[2]
	Nurse – at GP practice	£12	Based on estimates of duration of contact and cost per hour of face to face time from PSSRU [3]
	District/community nurse	£38	Reference Costs 15/16 (N02AF, district nurse, adult, face to face, community) [2]
	Occupational therapist	£79	Reference Costs 15/16 (A06A1, occupational therapist, adult, one to one, community) [2]
	Hospital – physiotherapist	£46	Reference Costs 15/16, WF01A, Non-Admitted Face to Face Attendance, Physiotherapy[2]
	Hospital – occupational therapist	£58	Reference Costs 15/16, WF01A, Non-Admitted Face to Face Attendance, Occupational therapist[2]
	Hospital – A&E	£157	Reference Costs 15/16, WF01B, Non-Admitted Face to Face Attendance, First, Accident & Emergency [2]
	Hospital – fracture clinic	£110	Reference Costs 15/16, WF01A, Non-Admitted Face to Face Attendance, Trauma and orthopaedics[2]
	Hospital – pain management clinic	£131	Reference Costs 15/16, WF01A, Non-Admitted Face to Face Attendance, Pain Management[2]
	Hospital – in patient stay	£269 per day	Weighted average of Reference Costs 15/16 HE41 hand fracture without intervention excess bed days[2]

1. NICE, *NG38: Fractures (non-complex): assessment and management*, in *NICE Guidelines*. 2016, National Institute for Health and Care Excellence (NICE): London.
2. Department of Health and Social Care, *Reference costs 2015 to 2016.* Department of Health and Social Care: London, 2016.
3. Curtis, L.B., A. , *Unit Costs of Health and Social Care 2016.* Personal Social Services Research Unit, University of Kent, Canterbury, 2016.

Supplementary Table 2: Missing data observed in patient reported questionnaires

	Surgical fixation (n=219)	Cast immobilisation (n=220)
QoL score baseline	5 (2.3%)	1 (0.5%)
QoL score 6 weeks	45 (20.5%)	41 (18.6%)
QoL score 12 weeks	39 (17.8%)	56 (25.5%)
QoL score 26 weeks	58 (26.5%)	74 (33.6%)
QoL score 52 weeks	37 (16.9%)	44 (20.0%)
Cost 6 weeks	51 (23.3%)	51 (23.2%)
Cost 12 weeks	54 (24.7%)	58 (26.4%)
Cost 26 weeks	66 (30.1%)	80 (36.4%)
Cost 52 weeks	45 (20.5%)	57 (25.9%)
Complete case	136 (62.1%)	155 (70.5%)

Supplementary Table 3: Cost regression results for the eight scenarios, adjusted and unadjusted for baseline quality of life, (p-values)

	Scenario	Regression constant	Surgical allocation	QoL at baseline	Fracture displacement	Dominant wrist injured	age
Unadjusted	~~Complete case~~ No imputation ITT	589.96 (0.120)	1,580.27 (0.000)***	N/A	180.06 (0.490)	-16.66 (0.934)	1.48 (0.833)
	With MI ITT	882.80 (0.002)**	1,228.13 (0.000)***	N/A	225.47 (0.168)	74.39 (0.622)	1.58 (0.767)
	~~Complete case~~ No imputation PP	678.06 (0.072)	1,770.87 (0.000)***	N/A	128.68 (0.595)	141.08 (0.467)	4.273 (0.535)
	With MI PP	799.81 (0.004)**	1,549.14 (0.000)***	N/A	190.84 (0.252)	86.87 (0.578)	2.716 (0.624)
Adjusted	~~Complete case~~ No imputation ITT	939.86 (0.001)***	1,308.11 (0.000)***	-530.67 (0.022)**	183.41 (0.223)	32.24 (0.804)	-0.08 (0.984)
	With MI ITT (base case)	1,160.66 (0.000)***	1,294.53 (0.000)***	-593.71 (0.015)**	212.60 (0.164)	1.856 (0.989)	0.19 (0.964)
	~~Complete case~~ No imputation PP	911.11 (0.002)**	1.615.50 (0.000)***	-519.08 (0.055)	143.33 (0.340)	-17.04 (0.904)	1.73 (0.692)
	With MI PP	1,091.85 (0.000)***	1,594.40 (0.000)***	-562.63 (0.036)**	173.21 (0.255)	-28.19 (0.841)	1.39 (0.764)

ITT – intention to treat, MI – multiple imputation, PP – per protocol, QoL – quality of life
Values in brackets are the p values for each coefficient
*p<0.05, **p<0.01, ***p<0.001

Supplementary Table 4: Quality of life regression output for the eight regression analyses, unadjusted and adjusted for baseline quality of life, (p-values)

	Scenario	Regression constant	Surgical allocation	QoL at baseline	Fracture displacement	Dominant wrist injured	age
Unadjusted	~~Complete case~~ No imputation[1] ITT	0.8162 (0.000)***	0.0208 (0.319)	N/A	-0.0283 (0.176)	-0.0285 (0.163)	-0.0011 (0.091)
	With MI ITT	0.8042 (0.000)***	0.0182 (0.304)	N/A	-0.0350 (0.047)*	-0.0399 (0.027)*	-0.0016 (0.010)*
	~~Complete case~~ No imputation PP	0.8112 (0.000)***	0.0257 (0.233)	N/A	-0.0342 (0.118)	-0.0348 (0.101)	-0.0012 (0.076)
	With MI PP	0.7984 (0.000)***	0.0173 (0.331)	N/A	-0.0423 (0.021)*	-0.0433 (0.018)*	-0.0015 (0.026)*
Adjusted	~~Complete case~~ No imputation ITT	0.6947 (0.000)***	0.0250 (0.289)	0.2895 (0.000)***	-0.0202 (0.371)	0.0046 (0.826)	-0.0020 (0.020)*
	With MI ITT (base case)	0.6733 (0.000)***	0.0158 (0.379)	0.2732 (0.000)***	-0.0261 (0.164)	0.0229 (0.203)	-0.0020 (0.005)**
	~~Complete case~~ No imputation PP	0.6761 (0.000)***	0.0238 (0.315)	0.3272 (0.000)***	-0.0168 (0.494)	0.0033 (0.884)	-0.0021 (0.018)*
	With MI PP	0.6690 (0.000)***	0.0118 (0.505)	0.2823 (0.000)***	-0.0265 (0.175)	0.0218 (0.227)	-0.0019 (0.009)**

ITT – intention to treat, MI – multiple imputation, PP – per protocol, QoL – quality of life
Values in brackets are the p values for each coefficient
*p<0.05, **p<0.01, ***p<0.001

CHEERS checklist—Items to include when reporting economic evaluations of health interventions

Section/item	Item No	Recommendation	Reported on page No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	1
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study.	2 and 3
		Present the study question and its relevance for health policy or practice decisions.	2 and 3
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	2 and 3
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	2 and 3
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	2 and 3
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	3
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	2
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	2
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	4
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	3
	11b	*Synthesis-based estimates*: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	N/A

Section/item	Item No	Recommendation	Reported on page No
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	3
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	2
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	N/A
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	N/A
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	4 and 5
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	4 and Supplementary appendix

Section/item	Item No	Recommendation	Reported on page No
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	6 and 7
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	9 and 10
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	N/A
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	N/A
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	10 and 11
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	1
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	1