



■ TRAUMA

Economic outcomes associated with deep surgical site infection from lower limb fractures following major trauma

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Aims

This study aims to estimate economic outcomes associated with 30-day deep surgical site infection (SSI) from closed surgical wounds in patients with lower limb fractures following major trauma.

Methods

Data from the Wound Healing in Surgery for Trauma (WHiST) trial, which collected outcomes from 1,547 adult participants using self-completed questionnaires over a six-month period following major trauma, was used as the basis of this empirical investigation. Associations between deep SSI and NHS and personal social services (PSS) costs (£, 2017 to 2018 prices), and between deep SSI and quality-adjusted life years (QALYs), were estimated using descriptive and multivariable analyses. Sensitivity analyses assessed the impact of uncertainty surrounding components of the economic analyses.

Results

Compared to participants without deep SSI, those with deep SSI had higher mean adjusted total NHS and PSS costs (adjusted mean difference £1,577 (95% confidence interval (CI) -951 to 4,105); $p = 0.222$), and lower mean adjusted QALYs (adjusted mean difference -0.015 (95% CI -0.032 to 0.002); $p = 0.092$) over six months post-injury, but this difference was not statistically significant. The results were robust to the sensitivity analyses performed.

Conclusion

This study found worse economic outcomes during the first six months post-injury in participants who experience deep SSI following orthopaedic surgery for major trauma to the lower limb. However, the increase in cost associated with deep SSI was less than previously reported in the orthopaedic trauma literature.

Cite this article: *Bone Jt Open* 2022;3-5:398–403.

Keywords: Cost, Deep surgical site infection, Lower limb fracture

Introduction

Surgical site infection (SSI) is a serious complication of surgery, accounting for 20% of all hospital-acquired infections,¹ and is the most difficult to treat.² The 2019 UK Getting It Right First Time (GIRFT) SSI National Survey suggested that the overall SSI rate in orthopaedic surgery was 0.6% (95%CI 0.5% to 0.8%) among the 29 participating trusts.³ However, the SSI rates are much higher following orthopaedic trauma surgery,⁴ and especially in the context of major trauma where extensive local soft-tissue damage and systemic inflammatory responses greatly increase the risk of deep SSI.^{5,6}

A systematic review that used data from hospitals in Europe showed that the financial cost of surgery was consistently higher in patients with SSI compared to those without,⁷ while in England, the mean total cost among orthopaedic trauma patients who had a SSI was estimated to be approximately 2.9 times higher than those without a SSI.⁸ A more recent study by Parker et al⁹ demonstrated that deep SSI may lead to significantly increased economic costs and impaired health-related quality of life among patients with severe open fractures of the lower limb. However, there is no evidence of the economic impact of deep SSI in patients

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doi: 10.1302/2633-1462.35.BJO-2022-0033

Bone Jt Open 2022;3-5:398–403.

with closed surgical wounds following major trauma to their lower limbs.

The aim of this study was to explore the health economic implications of deep SSI in patients with closed surgical wounds associated with fractures following major trauma to their lower limbs.

Methods

This is a secondary data analysis from participants ($n = 1,547$) who took part in the Wound Healing in Surgery for Trauma (WHiST) trial,⁵ which has been approved by the UK National Research Ethics Committee (16/WM/0006). Full details of the trial methodology, clinical outcome measures, and response rates are reported elsewhere.^{5,6,10,11} In brief, participants with major trauma to the lower limb were eligible to take part if they had a fracture requiring surgical fixation following which the surgical wound could be closed primarily. Participants with open fractures that could not be closed primarily at the end of the first surgical wound debridement were excluded. The randomized trial compared two types of wound dressing. As there was no evidence of a difference in clinical outcomes, including the rate of deep SSI, between the two types of wound dressing, participants were combined into a single cohort for the purposes of this analysis.

Effects on economic costs and health-related quality of life outcomes were compared between participants with a diagnosis of deep SSI and those without. Medical records were reviewed by an independent research associate who recorded deep SSI against the USA Centers for Disease Control and Prevention (CDC) criteria for the diagnosis of 'deep infection' within 30 days.¹² The criteria consisted of: 1) whether fluid was leaking from the wound which was pus; or, 2) fulfilment of at least one description from each of the following: i) the wound was gaping open (dehisced) or a surgeon had deliberately opened the wound, and ii) the area around the wound was painful or tender, or the participant had a fever higher than 38°C; or 3) whether there was any sign of abscess or infection on direct examination or imaging (e.g. ultrasound).¹²

Participant-reported health and personal social service (PSS) resources used due to the fracture were reported in trial case report forms, combined with trial participant completed questionnaires, at three and six months post-randomization, which had recall periods extending to hospital discharge and three months post-randomization, respectively. This included the primary admission: inpatient care consisting of hospitalization and further surgical procedures; readmissions; hospital outpatient care (i.e. visits to orthopaedic, pathology, radiology, physiotherapy, and emergency department clinics); community healthcare (i.e. contacts with general practitioners, practice nurses, district nurses, community

physiotherapists, and occupational therapists, and calls to NHS 111 or ambulance services); personal social services (contacts with meal-on-wheels, laundry, social worker, and care worker services); medications; aids and adaptations; direct non-medical costs (i.e. those associated with travel to health or social care settings, child care, and help with housework); as well as time off work due to the injury. Other than out-of-pocket medications, direct non-medical costs, and time off work due to the injury, the aforementioned resource categories were included in the base case analysis. Unit cost for the resource inputs have been reported elsewhere.^{13,14} Economic costs were estimated at 2017/18 prices.

Health-related quality of life (HRQoL) was measured using the EuroQol five-dimension five-level questionnaire (EQ-5D-5L)¹⁵ instrument at three and six months post-randomization. It was completed by the participants unless they did not have the capacity to do so; a proxy (usually the participant's carer) was used if participants were not able to complete this themselves. The EQ-5D-5L has five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), and five levels of severity for each dimension. Responses to the EQ-5D-5L were converted into multi-attribute utility scores comparable with those derived from the EQ-5D-3L instrument using the UK cross-walk value set developed by van Hout et al.¹⁶ Quality-adjusted life years (QALYs) were calculated as the area under the baseline-adjusted utility curve of the utility scores between baseline (estimated post-injury, taken at the point of study consent) and three months, as well as between baseline and six months, using the trapezoidal rule.¹⁷ No discounting was applied to either economic costs or QALY estimates as the study follow-up period was less than a year.

Statistical analysis. Economic costs and QALYs over three- and six-month periods of follow-up were summarized using descriptive statistics (i.e. independent-samples *t*-test). The adjusted mean total cost associated with readmissions, outpatient care, community healthcare, PSS services, aids and adaptations, medications, direct non-medical costs, and time off work due to the injury over six months was calculated using a two-part model to account for the skewed distribution of economic costs, as a high frequency of participants incurred zero or low costs, and a few participants incurred extremely high costs. This model had two stages: a logistic regression, in which the dependent variable (total cost) indicated presence of zero costs (yes, no); followed by a generalized linear model (GLM) with a γ distribution and log-link function for economic costs relating to participants with positive values. Covariates mirrored those used in previous analyses of this trial data,¹⁸ namely participant age at baseline, participant sex, randomized treatment, injury severity score, and wound closure. Due to the positively skewed nature of overall economic costs (encompassing costs of the

Table 1. Baseline characteristics of Wound Healing in Surgery for Trauma patients by deep surgical site infection status at 30 days.

Characteristics	No deep SSI (n = 1,424)	Deep SSI (n = 95)
Deep infection at 90 days, n (%)		
No	1,069 (75.1)	0 (0)
Yes	55 (3.9)	95 (100)
Female, n (%)	547 (38.4)	29 (30.5)
Mean age, yrs (SE)	49.8 (0.53)	48.2 (2.07)
Race/ethnicity, n (%)		
White	1,262 (88.6)	91 (95.8)
Black African	27 (1.9)	0 (0)
Black Caribbean	15 (1.1)	0 (0)
Black (other)	6 (0.4)	0 (0)
Indian	18 (1.3)	0 (0)
Pakistani	21 (1.5)	0 (0)
Bangladeshi	4 (0.3)	0 (0)
Chinese	1 (0.1)	0 (0)
Other	49 (3.4)	2 (2.1)
Mean BMI, kg/m ² (SE)	26.4 (0.2)	28.1 (0.6)
Diabetes	131 (9.2)	12 (12.6)
Smoker	400 (28.1)	30 (31.6)
Alcohol consumption, n (%)		
0 to 7 units	967 (67.9)	46 (48.4)
8 to 14 units	99 (7)	8 (8.4)
15 to 21 units	189 (13.3)	22 (23.2)
> 21 units	123 (8.6)	15 (15.8)
Marital status, n (%)		
Single	491 (34.5)	29 (30.5)
Living with a partner	194 (13.6)	13 (13.7)
Married/ civil partner	488 (34.3)	30 (31.6)
Separated	31 (2.2)	5 (5.3)
Divorced	76 (5.3)	7 (7.4)
Widowed	109 (7.7)	9 (9.5)
Employment status, n (%)		
Full-time employed	557 (39.1)	36 (37.9)
Full-time student	38 (2.7)	1 (1.1)
Part-time employed	101 (7.1)	8 (8.4)
Retired/Homemaker/Inactive	373 (26.2)	27 (28.4)
Self-employed	132 (9.3)	14 (14.7)
Unemployed	165 (11.6)	5 (5.3)
Unpaid work	12 (0.8)	0 (0)
Qualification, n (%)		
None	562 (39.5)	36 (37.9)
Formal qualification(s) through training at work	244 (17.1)	22 (23.2)
Qualification (other than a degree) from college or university	328 (23.0)	19 (20.0)
Degree from college or university	213 (15.0)	12 (12.6)
Treatment allocation, n (%)		
NPWT	725 (50.9)	45 (47.4)
Standard dressing	699 (49.1)	50 (52.6)
Injury severity score, n (%)		
15 and below	1112 (78.1)	76 (80.0)
16 and above	312 (21.9)	19 (20.0)
Closed injury	252 (17.7)	30 (31.6)
Wound location, n (%)		
Femur	540 (37.9)	24 (25.3)

Continued

Table 1. Continued

Characteristics	No deep SSI (n = 1,424)	Deep SSI (n = 95)
Patella	20 (1.4)	2 (2.1)
Hip	257 (18)	12 (12.6)
Acetabulum	49 (3.4)	4 (4.2)
Tibia/ fibula	516 (36.2)	51 (53.7)
Foot	42 (2.9)	2 (2.1)
Wound location (side), n (%)		
Left	705 (49.5)	44 (46.3)
Right	717 (50.4)	51 (53.7)
Mechanism of injury, n (%)		
Low-energy fall	488 (34.3)	31 (32.6)
High-energy fall	264 (18.5)	18 (18.9)
Crush injury	28 (2.0)	2 (2.1)
Contact sports injury	20 (1.4)	2 (2.1)
Road traffic accident	526 (36.9)	36 (37.9)
Other	97 (6.8)	6 (6.3)
Other injuries (%)	813 (57.1)	55 (57.9)
Analgesia pre-injury (%)	265 (18.6)	17 (17.9)

NPWT, negative pressure wound therapy; SE, standard error; SSI, surgical site infection.

primary admission) with no zero values and a few participants incurring high costs, a GLM with log-link function and γ distribution was used to estimate the overall mean total costs. Covariates used to adjust the GLM mirrored those applied in the two-part model.

Linear regression models were estimated using ordinary least squares (OLS) to estimate the association between deep SSI infection and QALYs with the baseline EQ-5D utility score acting as an additional covariate for adjustment.

The base case analysis was conducted using multiple imputed data from an NHS and PSS perspective.¹⁹ Multiple imputation approaches of missing data in this dataset have previously been described,¹⁰ but for this analysis, we made an additional assumption that if one category of resource use within a participant questionnaire was completed (e.g. outpatient care) and if the others were not completed, values for resource use, and therefore economic costs, for incomplete resource categories were zero. All statistical analyses were conducted using Stata 17.

Sensitivity analysis. In order to ascertain the robustness of the results, several sensitivity analyses were performed. The 30-day CDC criterion to diagnose SSI was updated to 90 days² after trial recruitment had started, so a sensitivity analysis was performed for deep SSI up to 90 days. Specifically, the criteria for 90 days deep SSI was: 1) pus leaking from the wound; and 2) an increase in pain or discomfort in the area around the wound and one of the following: i) edges of any part of the wound had separated or gaped open, or ii) participant had further surgery because of their fracture and the operation note confirmed that this was for, or revealed, a deep infection.² In

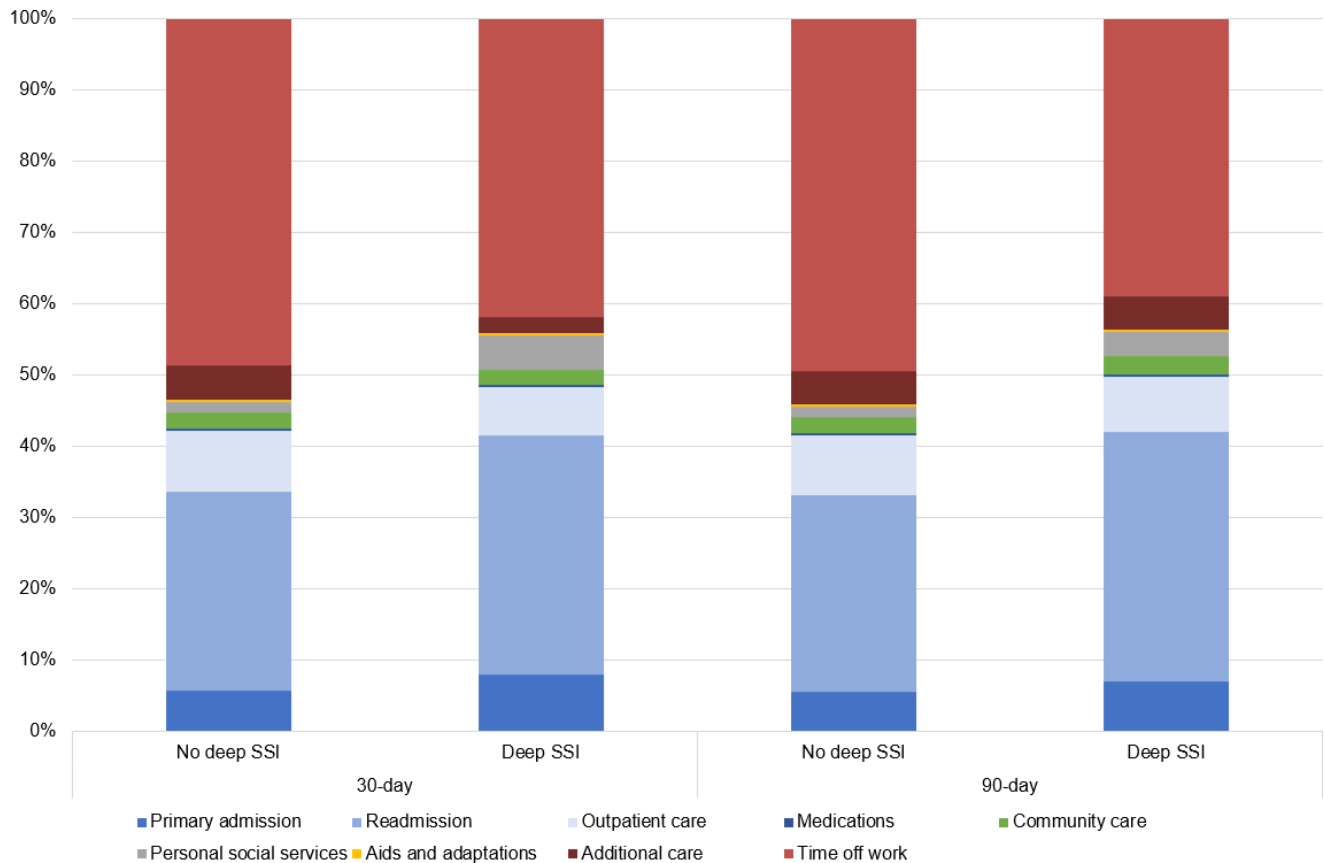


Fig. 1

Distribution of adjusted mean costs by resource category (%) over six months, by deep surgical site infection status at 30 days and 90 days. SSI, surgical site infection.

addition, economic costs were calculated from a societal perspective (including out-of-pocket medication expenses, direct non-medical costs, and economic values of time off work due to the injury), while a complete case analysis was also conducted.

Results

Baseline characteristics of the 1,519 participants from WHIST who provided data on deep SSI at 30 days are shown in Table I. The majority of the participants were male, did not have diabetes, were not regular smokers, and consumed 0 to 7 units of alcohol per week. The mean age and BMI of those without deep SSI was 49.8 years (standard error (SE) 0.5) and 26.4 kg/m² (SE 0.2), respectively, compared to a mean age of 48.2 years (SE 2.1) and a mean BMI of 28.1 kg/m² (SE 0.6) in those with deep SSI. There were 55 (3.9%) participants who did not have deep SSI by 30 days who went on to have deep infection by 90 days.

Figure 1 shows the distribution of adjusted mean costs by resource category over six months by deep SSI status at 30 days and 90 days. Participants with deep SSI had a higher proportion of direct medical costs (i.e. those associated with the primary admission, readmissions,

outpatient care, and medications) than those without deep SSI at both 30 days (48.6% vs 42.5%) and 90 days (50.1% vs 41.9%).

Differences in economic outcomes among participants by deep SSI status are summarized in Table II for the base case analysis and for the sensitivity analyses. The mean adjusted total NHS and PSS cost during the first six months post-injury was £3,459.53 (SE 232.48) for those without deep SSI and £5,036.64 (SE 1,277.54) for those with deep SSI (mean adjusted difference £1,577.11 (95% CI -951.39 to 4,105.62); $p = 0.222$, independent-samples t -test). This difference was not statistically significant. In the base case analysis, mean adjusted QALYs accrued over six months post-injury were lower among those with deep SSI (0.181 (SE 0.008)) than those without deep SSI (0.196 (SE 0.002)) with a mean adjusted difference of -0.015 (95% CI -0.032 to 0.002; $p = 0.092$). Again, this difference was not statistically significant. Results remained robust in the sensitivity analyses when the 90-day deep infection definition was applied, when costs were estimated from a societal perspective, and when complete case analysis was applied.

Table II. Economic outcomes among participants by deep surgical site infection status.

Economic outcome	No deep infection; mean (SE)	Deep infection; mean (SE)	Mean adjusted difference (95% CI)	p-value*
Base case analysis†	n = 1,424	n = 95		
QALYs accrued over first 3 mths	0.064 (0.001)	0.060 (0.004)	-0.004 (-0.012 to 0.003)	0.290
QALYs accrued over 6 mths	0.196 (0.002)	0.181 (0.008)	-0.015 (-0.032 to 0.002)	0.092
Total costs incurred from 0 to 3 mths, £	2,197.85 (157.51)	3,229.61 (862.84)	1,031.76 (-684.41 to 2,747.93)	0.239
Total costs incurred from 0 to 6 months, £	3,459.53 (232.48)	5,036.64 (1,277.54)	1,577.11 (-951.39 to 4,105.62)	0.222
Sensitivity analysis: 90-day deep infection	n = 1,069	n = 150		
QALYs accrued over first 3 mths	0.065 (0.001)	0.061 (0.003)	-0.004 (-0.011 to 0.002)	0.185
QALYs accrued over 6 mths	0.200 (0.003)	0.185 (0.007)	-0.015 (-0.030 to 0.0002)	0.053
Total costs incurred from 0 to 3 mths, £	2,246.07 (191.28)	3,123.05 (688.62)	876.97 (-516.52 to 2,270.47)	0.217
Total costs incurred from 0 to 6 mths, £	3,560.74 (281.04)	4,697.09 (983.81)	1,136.34 (-841.63 to 3,114.32)	0.260
Sensitivity analysis: societal cost	n = 1,424	n = 95		
Total costs incurred from 0 to 3 mths, £	4,464.49 (251.06)	5,053.20 (1,076.12)	588.72 (-1,574.14 to 2,751.58)	0.594
Total costs incurred from 0 to 6 mths, £	7,310.23 (402.52)	9,038.48 (1,911.23)	1,728.25 (-2,098.25 to 5,554.75)	0.376
Sensitivity analysis: complete case	n = 408	n = 37		
QALYs accrued over first 3 mths	0.065 (0.001)	0.058 (0.005)	-0.007 (-0.017 to 0.003)	0.150
QALYs accrued over 6 mths	0.199 (0.004)	0.176 (0.013)	-0.023 (-0.051 to 0.004)	0.099
Total costs incurred from 0 to 3 mths, £	2,049.21 (209.62)	3,393.80 (1,204.88)	1,344.58 (-1,055.88 to 3,745.05)	0.272
Total costs incurred from 0 to 6 mths, £	3,388.64 (353.22)	5,670.34 (2,132.98)	2,281.70 (-1,929.52 to 6,492.92)	0.288

*Independent-samples *t*-test.

†Refers to 30-day deep infection, analyzed from the NHS and personal social services perspective using imputed data.
CI, confidence interval; QALY, quality-adjusted life year; SE, standard error.

Discussion

This study of participants having orthopaedic trauma surgery found that those with deep SSI accrued higher economic costs and lower QALYs, on average, than those who did not have a deep SSI during the first 30 days after injury. Direct medical costs were the main cost driver among participants with deep SSI. This finding is consistent with previous studies that have demonstrated that patients with SSI incur higher economic costs and experience poorer health-related quality of life than people without SSI following their surgeries.⁷⁻⁹ However, in these participants with closed wounds following lower limb fracture surgery for major trauma, we find that the differences in economic outcomes were not statistically significant. Since this analysis includes a large number of participants with high levels of follow-up (around 85% at three months and around 90% at six months),¹⁴ it seems unlikely that this finding is due to lack of statistical power. More likely, it reflects changes in the management of deep SSI in orthopaedic trauma over time: rapid, definitive diagnosis and microbiology-guided treatment seemingly reducing the need for prolonged treatment of late presentation deep infection,²⁰⁻²⁶ and therefore reducing direct medical costs.

In an analogous analysis of participants with severe open fractures of the lower limb, we estimated significantly higher economic costs and lower QALYs in participants with deep SSI.⁶ However, in this study of participants whose wounds were closed primarily at the end of their first surgery, the increase in cost and reduction in QALYs were not statistically significant. This may be due to the

fact that the treatment of deep SSI in participants with severe open fractures is complicated by the frequent presence of soft-tissue grafts overlying the fracture.

A key strength of this study lies in the data collection processes adopted – resource use data were collected using participant questionnaires, and this allowed for the inclusion of costs, such as aids and adaptations at home, travel, childcare, help with housework required due to the open fracture, and time off work due to injury, that could not otherwise be collected using routine datasets or registry data. A key limitation is the constrained time horizon of six months, compared with the study by Parker et al⁹ where economic costs and QALYs were estimated over a 12-month time horizon. It is plausible that poorer economic outcomes related to deep SSI or its management continue to accrue over time.

In conclusion, our findings are indicative of poorer economic outcomes during the first six months post-injury in participants who experience deep SSI following orthopaedic surgery for major trauma to the lower limb, but the increase in costs was less than that reported in previous studies of orthopaedic trauma. These economic outcome estimates can be used to inform budgetary planning and modelling of economic outcomes in future studies.



Take home message

- Among participants with closed surgical wounds following major trauma to their lower limbs, those with deep surgical site infection (SSI) had higher total mean costs and lower mean quality-adjusted life years, from an NHS and personal social service perspective, than those without deep SSI, but this difference was not statistically significant.

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- S. Petrou: Supervision, Writing – review & editing.
- R. Knight: Data curation, Investigation, Writing – review & editing.
- J. Masters: Conceptualization, Writing – review & editing.
- J. Achten: Conceptualization, Resources, Writing – review & editing.
- M. L. Costa: Conceptualization, Investigation, Resources, Writing – original draft, Writing – review & editing.

Funding statement:

- The authors disclose receipt of the following financial or material support for the research, authorship, and/or publication of this article: this project was funded by the UK National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (HTA 14/192/14) and was supported by the NIHR Oxford Biomedical Research Centre. The funder has not been involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data, the preparation, review, or approval of the manuscript, nor in the decision to submit the manuscript for publication. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

ICMJE COI statement:

- M. L. Costa reports grants from NIHR HTA which relate to the publication of this article and reports other research grant funding to the University of Oxford from NIHR, EU, RCS England, and industry, all of which are unrelated to this article. R. Knight and M. E. Png report a grant from NIHR HTA, which is related to the publication of this article. J. Masters, J. Achten, R. Knight, and M. E. Png report no conflicts of interest.

Acknowledgements:

- We would like to acknowledge the UK Major Trauma Network and the National Institute for Health Research Clinical Research Network for supporting this study and all the collaborating investigators from the WHIST trial.

Ethical review statement:

- The Wound Healing in Surgery for Trauma has been previously approved by the UK National Research Ethics Committee (16/WM/0006).

Open access funding

- The authors confirm that the open access funding for this study was supplied by the NIHR Oxford Biomedical Research Centre.

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