■ TRAUMA

A feasibility study of standard dressings versus negative-pressure wound therapy in the treatment of adult patients having surgical incisions for hip fractures: the WHISH randomized controlled trial

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Aims

This study sought to compare the rate of deep surgical site infection (SSI), as measured by the Centers for Disease Control and Prevention (CDC) definition, after surgery for a fracture of the hip between patients treated with standard dressings and those treated with incisional negative pressure wound therapy (iNPWT). Secondary objectives included determining the rate of recruitment and willingness to participate in the trial.

Methods

The study was a two-arm multicentre randomized controlled feasibility trial that was embedded in the World Hip Trauma Evaluation cohort study. Any patient aged > 65 years having surgery for hip fracture at five recruitment centres in the UK was considered to be eligible. They were randomly allocated to have either a standard dressing or iNPWT after closure of the wound. The primary outcome measure was deep SSI at 30 and 90 days, diagnosed according to the CDC criteria. Secondary outcomes were: rate of recruitment; further surgery within 120 days; health-related quality of life (HRQoL) using the EuroQol five-level five-dimension questionnaire (EQ-5D-5L); and related complications within 120 days as well as mobility and residential status at this time.

Results

A total of 462 valid randomizations were carried out (232 and 230 in the standard dressing and iNPWT groups, respectively). In the standard dressing group, 14 of 218 patients (6.4%) developed deep SSI. In the iNPWT group, four of 214 patients (1.9%) developed deep SSI. This gives a total rate of SSI of 4.2% (95% confidence interval (CI) 2.7% to 6.5%). Patients and surgeons were willing to participate in the study with 462 patients being recruited from a possible 749 (62.3%).

Conclusion

The rate of deep SSI 30 days after surgery for a fracture of the hip was 4%, which makes a study comparing the clinical effectiveness of standard dressings and iNPWT feasible.

Cite this article: *Bone Joint J* 2021;103-B(4):755–761.

Introduction

The management of elderly patients with a hip fracture is one of the biggest challenges facing healthcare systems. There are 1.3 million hip fractures worldwide, and more than 60,000 in the UK every year.[1] The cornerstone of the acute care in these patients in high-income settings is the surgical management.[2] Surgery seeks to restore the patients' mobility as quickly as possible, and is used in more than 98% of patients with a hip fracture in the UK and other high-income settings.[2]

Given the high prevalence of comorbidity,[3,4] it is not surprising that complications commonly occur.[5] One of the most devastating complications is surgical site infection (SSI), which is associated with an increased length of stay in hospital and

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doi:10.1302/0301-620X.103B4.BJJ-2020-1603.R1 $2.00

Bone Joint J 2021;103-B(4):755–761.

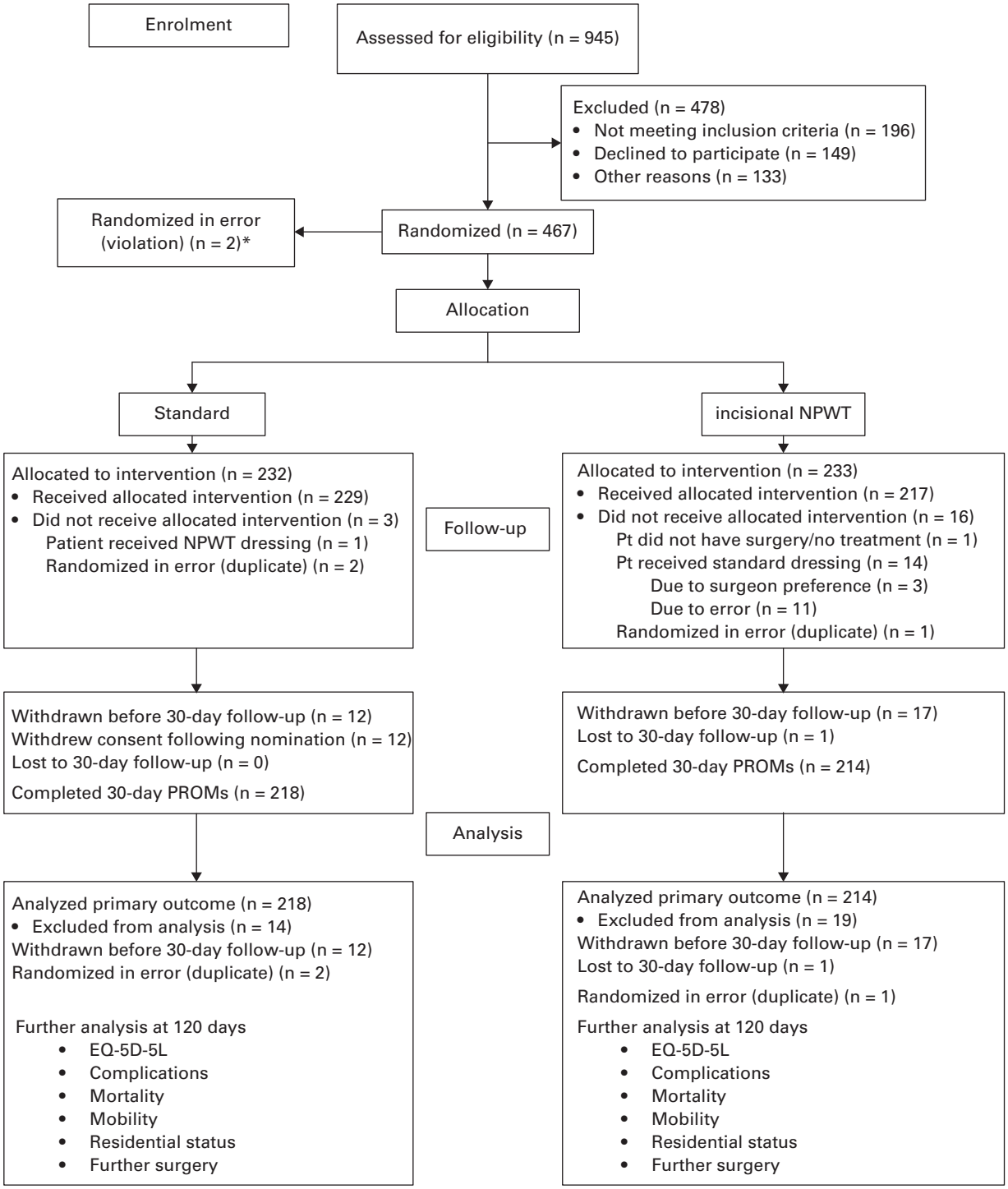

Fig. 1

Consolidated Standards of Reporting Trials (CONSORT) flow diagram outlining the process of participant identification and randomization. *Two patients were randomized in error (violation); these patients were randomized but had declined consent. These two randomizations are removed from the analyzed population. EQ-5D-5L, EuroQol five-level five-dimension questionnaire; NPWT, negative pressure wound therapy; PROM, patient-reported outcome measure; Pt, patient.

costs, and an increased rate of mortality of 20% one year post-operatively.[6] These consequences are well understood and the prevention of deep SSI is a major research priority.[7]

Wound management is an important component of reducing SSI. There is a growing body of evidence which suggests that the use of negative pressure wound therapy (NPWT) reduces the

risk of SSI.[8,9] Thus, a fully powered randomized controlled trial assessing the effectiveness of this form of treatment is required. Variations in the true rate of SSI, which has been reported to be between 1% and 9%, preclude an informed sample size calculation.[10,11]

Our aim was to compare the rate of SSI after surgery for a hip fracture in patients treated with standard dressings and NPWT.

Methods

Trial design summary. This study was part of the World Hip Trauma Evaluation (WHiTE) study.[12-19] It was approved by the UK National Research Ethics Service, who gave approval on 28 April 2017 (Oxford REC Committee C 17/ SC/0207);[20] full details are included in the published protocol.[21] The trial was overseen by independent steering and data and safety monitoring committees convened in Oxford, who were responsible for oversight of all WHiTE studies.

Consent. Patients with a hip fracture require surgery on the next available trauma operating list. All have received opiate analgesia. It is therefore understandable that most patients find the initial period of their treatment in hospital confusing and disorientating. Similarly, patients' next of kin, carers, and friends are often anxious at this time and may have difficulty taking in the large amounts of information that they are given about the injury and plan for treatment. It is often not possible for the patient or relative/carer (consultee) to review trial documentation, weigh the information, and give an informed decision about whether they wish to participate. The consent procedure for this trial reflected that of the surgery, with the clinical team assessing capacity before taking consent for the operation, and the assessment of capacity was then used to inform consent for the study. An appropriate method, in line with the Mental Capacity Act,[22] was then used to gain either prospective or retrospective consent from the patient or consultee by a Good Clinical Practice (GCP)-trained member of the local research team.

Eligibility. Eligible patients were aged > 65 years and having surgery for a hip fracture. Patients with an undisplaced intracapsular fracture treated with cannulated screws were excluded due to the small incisions needed for this procedure. A total of 462 patients were recruited successfully into the study between July 2017 and February 2018. Five were randomized in error and withdrawn (467 randomizations in total). Figure 1 outlines the Consolidated Standards of Reporting Trials (CONSORT) diagram.[23]

Allocation of treatment. A computer-generated randomization algorithm was created and delivered by the Oxford Clinical Trials Unit to ensure that the allocation sequence was concealed. The patients were allocated to treatment on a 1:1 basis, stratified by recruitment centre.

Standard care pathway. All patients received a general or regional anaesthetic. The operation followed standard clinical practice with relevant details recorded by the research team. Routine prophylactic antibiotics were given according to local hospital policy. This was either a single intraoperative dose (three centres) or multiple doses (two centres). All patients were assessed for venous thromboembolism prophylaxis according to local policy. At the end of the operation, the allocated dressing was applied to the wound.

Table I. Baseline patient and treatment characteristics by treatment group.

Characteristic	Standard dressing (n = 230)	iNPWT (n = 232)
Median age, yrs (IQR)	84.9 (77 to 89)	85.2 (77 to 90)
Sex, female:male, n (%)	168/62 (73/27)	160/72 (69/31)
ASA, n (%)[29]		
I	3 (1.4)	5 (2.3)
II	54 (24.5)	52 (23.4)
III	129 (58.6)	125 (56.3)
IV	33 (15.0)	40 (18)
V	1 (0.5)	0 (0.0)
Mean preop AMTS (SD)	8.0 (3.0)	7.4 (3.5)
Own home, n (%)	185 (85.6)	177 (82.3)
Residential care, n (%)	16 (7.4)	17 (7.9)
Nursing home, n (%)	10 (4.6)	19 (8.8)
Other, n (%)	5 (2.4)	2 (1.0)
Regular smoker, n (%)		
Yes	15 (7.0)	21 (10.0)
No	198 (93.0)	190 (90.0)
Diabetic, n (%)		
Yes	24 (12.6)	34 (18.9)
No	190 (87.4)	179 (81.1)

AMTS, Abbreviated Mental Test Score; ASA, American Society of Anesthesiologists; iNPWT, incisional negative pressure wound therapy; IQR, interquartile range.

The patients were not blinded to their treatment allocation as the dressings were clearly visible. In addition, the treating surgeons could not be blinded, but the surgical and healthcare team were not involved in any assessments relating to the trial and the primary outcome data were collected by independent research associates. All elements of postoperative care and rehabilitation were the same for all patients.

Standard dressings. For the standard dressing study arm, all recruitment centres used a sterile dressing sealed from external contamination. The precise details of the materials used in standard dressings depended on the routine local care.

Incisional negative pressure wound therapy pathway. The PICO dressing system (Smith & Nephew, London, UK) was used in the NPWT arm of the study. This involves a silicone contact layer with a silicon-based adhesive, an airlock layer, a superabsorbent layer, and a polyurethane (semipermeable) layer on top that makes the system showerproof while allowing water vapour to escape. A sealed tube connects the dressing to a built-in mini-pump that creates a partial vacuum (-80 mmHg of negative pressure) over the wound. This dressing was applied to the wound at the end of the operation according to the treating surgeon's normal practice and the manufacturer's instructions; any further dressing was recorded and followed the allocated treatment unless otherwise clinically indicated.

Outcomes. The addition of 90-day follow-up is a recent change in the CDC criteria. Therefore, to satisfy the criteria each patient was assessed at both 30 and 90 days.[24,25]

The rate of recruitment of patients, both in terms of eligibility and those who consented, or on whose behalf consent was provided, was recorded. The number of available patients and

proportion recruited is a feasibility parameter which will inform any definitive study.

Any further surgery to the hip within 120 days of the fracture was recorded from the patient and medical records.

Complications were recorded from a predefined list: wound infection; respiratory infection; urinary tract infection; venous thromboembolism; cerebrovascular accident; cardiac event; failure of fixation; dislocation; and blood transfusion. These were collected from the medical records and included if they were within 120 days of the fracture. A standard set of outcomes was recorded.[26] Death within 120 days was recorded from the medical records.

Health-related quality of life (HRQoL) was measured using the EuroQol five-level five-dimension questionnaire (EQ-5D-5L) at baseline and 120 days. The EQ-5D-5L is a validated self-administered patient-reported outcome measure consisting of five dimensions, each with five possible answers. Each combination of answers produces a health profile that can be converted into an estimated health utility score after applying a set of preference weights. A scoring that maps the EQ-5D-5L to EQ-5D-3L value sets was used as was the EuroQol calculator.[27,28] This score was completed either by the patient or a carer if they were unable to.

The mobility status pre-fracture and at 120 days was recorded. The possible responses for mobility were: freely mobile without aids; mobile outdoors with one aid; mobile outdoors with two aids or frame; some indoor mobility but never going outside without help; and no functional mobility (using lower limbs).

The residential status pre-fracture and at 120 days was recorded (Table I). The possible responses for residential status were: own home/sheltered housing; residential care; nursing home; rehabilitation unit; acute hospital; dead; and other.

Statistical analysis. Standard statistical summaries (means, SDs, medians, interquartile ranges (IQRs)) are reported for all discrete and continuous outcome measures. Baseline data (age and sex) were summarized to check comparability between treatment groups. No formal hypothesis testing was undertaken; according to the aims of this feasibility study, the analysis reports the rates of deep SSI overall and in the two treatment groups on an intention-to-treat basis at 30 and 90 days post-recruitment. Analysis of between-group rates of deep SSI was exploratory. Any between-group differences were 'post hoc' and were interpreted in this context. These differences were presented using descriptive statistics and appropriate measures of uncertainty (e.g. 95% confidence intervals (CIs)). All analyses were undertaken using Stata v15.1 (Stata Corp, College Station, Texas, USA). Binomial CIs were calculated using the Wilson method.[30]

Feasibility was shown if the rate of deep SSI was sufficiently high that a clinically important difference could be shown, and that the number of patients needed to do this would be realistic.

Results

There were 18 deep SSIs in 432 patients, giving an overall rate of 4.2% at 30 days (95% CI 2.7% to 6.5%). The rate of deep SSI at 30 days was 6.4% (14/218) in the standard dressing group and 1.9% (4/214) in the NPWT group (risk ratio 0.29; 95% CI 0.10 to 0.85) (Table II).

Table II. Baseline characteristics by treatment group.

Characteristic	Standard dressing (n = 230)	iNPWT (n = 232)	Total (n = 462)
Surgery < 36 hrs, n (%)	129 (56.1)	143 (61.6)	272 (58.9)
Operation, n (%)			
Hemiarthroplasty (cemented)	113 (49.3)	118 (51.1)	231 (50.2)
Hemiarthroplasty (uncemented)	2 (0.9)	3 (1.3)	5 (1.1)
Arthroplasty - THA (cemented)	11 (4.8)	9 (3.9)	20 (4.3)
Arthroplasty - THA (uncemented)	0 (0)	1 (0.4)	1 (0.2)
Arthroplasty - THA hybrid	15 (6.6)	13 (5.6)	28 (6.1)
Internal fixation - cannulated screws	2 (0.9)	5 (2.2)	7 (1.5)
Internal fixation - intramedullary nail	15 (6.6)	17 (7.4)	32 (7.0)
Internal fixation - sliding hip screw*	71 (31.0)	65 (28.1)	136 (29.6)
Surgeon grade, n (%)			
Consultant	153 (66.5)	156 (67.5)	309 (67.0)
ST3-ST8†	66 (28.7)	66 (28.6)	132 (28.6)
SAS	11 (4.8)	9 (3.9)	20 (4.3)
Other	0 (0.0)	0 (0.0)	0 (0.0)
Wound closure, n (%)			
Interrupted suture	26 (15.5)	16 (9.8)	42 (12.7)
Skin clips	25 (14.9)	26 (16.0)	51 (15.4)
Subcuticular suture	111 (66.1)	117 (71.8)	228 (68.9)
Other	6 (3.6)	4 (2.5)	10 (3.0)

*Within the sliding hip screw cohort were patients co-enrolled in another embedded trial, which included a similar device. All patients were classified as receiving a sliding hip screw.[17]
†ST3 denotes a training grade surgeon equivalent to resident.
iNPWT, incisional negative pressure wound therapy; SAS, Staff and Associate Specialist; THA, total hip arthroplasty.

The rate of deep SSI at 90 days was 6.4% (14/218) in the standard dressing group and 2.3% (5/214) in the NPWT group, and 4.4% overall (95% CI 2.8% to 6.8%).

When considered on a 'per protocol' basis, the rates of 30-day deep SSI were as follows: total rate of 15 SSIs in 307 patients, giving an overall rate of 4.6% at 30 days (95% CI 2.8% to 7.5%). The rate of deep SSI at 30 days was 6.5% (11/168) in the standard dressing group and 2.6% (4/156) in the NPWT group (risk ratio 0.39; 95% CI 0.13 to 1.20). The 'per protocol' rate of deep SSI at 90 days was 17 infections in 324 patients, a rate of 5.2% (95% CI 3.3% to 8.2%). By group, it was 7.7% (13/168) in the standard dressing group and 2.6% (4/156) in the NPWT group. All deep SSI outcome data are reported by group in Table III.

The patients recruited into the study were representative of the broader population of patients with hip fractures in terms of age, sex, and anaesthetic risk (Table I).[18] These characteristics were well balanced by the randomization process. Similarly, the surgical treatment was balanced between both study groups, and included a representative spread of arthroplasty and internal fixation by a mixture of training and consultant surgeons (Table II).

The process of recruitment is outlined in Supplementary Figure a. A total of 31 patients withdrew, of whom 30 did so prior to the collection of primary outcome data at 30 days.

Table III. Comparison of treatment groups on primary and secondary outcomes.

Outcome	Incisional negative pressure wound therapy		Standard dressing	
	Summary*	Total, n	Summary*	Total, n
30 days as randomized population (available cases), n (%)	4 (1.9)	214	14 (6.4)	218
30 days per protocol population (available cases), n (%)	4 (2.8)	144	11 (6.7)	163
90 days as randomized population (available cases), n (%)	5 (2.3)	214	14 (6.4)	218
Secondary outcomes				
Mortality, n (%)				
30 days	16 (7.4)	214	17 (7.8)	218
120 days	36 (17.0)	211	43 (19.9)	216
EQ-VAS (as randomized population, available cases), n (%)†				
Baseline	68.6 (20.0)	202	71.3 (19.1)	205
120 days	67.7 (22.3)	163	69.1 (21.4)	171
EQ-5D index (as randomized population, available cases), n (%)‡				
Baseline	0.69 (0.28)	201	0.73 (0.27)	206
120 days	0.46 (0.37)	206	0.48 (0.37)	209

*Summaries are n (%) for binary and mean (95% confidence interval) for continuous variables.
†EuroQol five-dimension questionnaire visual analogue scale range from 0 to 100, with higher scores indicating better quality of life.
‡EuroQol five-dimension questionnaire utility scores range from -0.594 to 1, with higher scores indicating better quality of life.Scores were converted to multi-attribute utility values using the crosswalk and EuroQol three-level five-dimension questionnairevalue sets.
EQ-5D, EuroQol five-dimension questionnaire; EQ-VAS, EuroQol visual analogue scale.

The main further surgical intervention was debridement of the wound (7/305 (2.3%)). Three patients underwent revision surgery within the 120-day follow-up period (3/313 (1.0%)).

There was a similar pattern of complications in the treatment groups. Most commonly, patients suffered from infection of the chest or urinary tract or required blood transfusion. Further data on complications, mobility, and residential status are reported in Supplementary Tables i to iii.

The mean EuroQol visual analogue scale (EQ-VAS) score was 69.1 (SD 21.4) in the standard dressing group (n = 171) and 67.7 (SD 22.3) in the NPWT group (n = 163). The mean EQ-5D index was 0.48 (SD 0.37) in the standard dressing group (n = 209) and 0.46 (SD 0.37) in the NPWT group (n = 206). All-cause mortality at 30 days was 33 patients out of a possible 432 (7.6%); there were 16 deaths in 214 patients (7.5%) in the standard dressing group and seven deaths in 218 patients (7.8%) in the NPWT group.

Discussion

The aims of this study were to assess each patient against the CDC criteria for deep SSI in those allocated to either standard dressings or NPWT in a randomized feasibility trial. Secondary aims were to understand recruitment and retention, and the nature of further surgery in patients with deep SSI. A total of 18 of 432 patients (4.2%) had a deep SSI at 30 days. Half of these patients (n = 9) underwent further surgery during the study period. The site study and clinical teams were able to recruit 462 patients over a six-month period. The feasibility objectives were met and a fully powered study comparing standard dressings with NPWT would be feasible based on these data.

A rate of deep SSI of 4.2% in patients undergoing surgery for a hip fracture is a critical benchmark metric for powering a full-scale randomized study looking at incisional NPWT (iNPWT) in these patients. If a reduction of 1.5% in the rate of SSI to 2.7% were sought, a total of 6,220 patients would be needed. This can be considered feasible on the basis of the rate of recruitment achieved in this study and the number of centres available to the WHiTE cohort. Given the profound consequences of deep SSI in patients with a hip fracture, such a study would be of value to patients and healthcare systems.

The small numbers of patients in each group, lack of statistical power, and feasibility design of this study preclude a recommendation about clinical effectiveness based on these data.

The only previous study of iNPWT in the patients with a hip fracture compared the presence of seroma and dressing requirements,[31] and the results favoured the NPWT in reducing the size of the seroma.

Meta-analyses also suggested a treatment benefit for NPWT in many forms of surgery.[8,9] However, each group of patients may benefit differently as they will probably have different risks. Other large-scale studies of NPWT in major orthopaedic trauma have failed to show a clinically important difference in the rate of deep SSI.[32]

There were no substantial issues with the recruitment or retention of patients or the involvement of clinicians. The study centres had a high volume of eligible cases and any definitive study should be able to recruit a representative sample of patients in an appropriate timescale.

Further surgical procedures are a major determinant of cost and source of comorbidity. They remain an important component of any health economic analysis. That not all patients with deep SSI in this study had another operation may reflect the fact that some were deemed too high- risk for further surgery. This study only captured data up to 120 days postoperatively, in line with the framework of the cohort.[12] Any definitive study may benefit from a longer period of follow-up or the collection of more data in order to record information about further surgery for a longer period of time.

The core outcome data were successfully captured, and no difference was noted between treatment groups in terms of mortality and complications.

The collection of data about HRQoL will be crucial in informing the calculations of the cost-effectiveness of NPWT if clinical superiority was shown in a definitive trial.

While the sample size of 462 patients may be large for a feasibility study, it may still be relatively small to capture a 'rare' outcome. This is reflected in the broad CIs for both treatment groups and the total study population. The main strengths of the study relate to the inclusion of a highly representative series of patients, in particular with the inclusion of patients with cognitive impairment, who make up 40% of those with a hip fracture. These patients are difficult to include in randomized studies due to legal and practical issues. The situation of this feasibility trial within the WHiTE cohort made it possible to overcome these barriers, as there is notable expertise on this issue within the framework.[12]

The baseline characteristics of the patients included in the study demonstrate that they are representative of both the broader WHiTE cohort and similar national datasets such as the National Hip Fracture Database.[2]

This study had limitations. The inclusion of patients with cognitive impairment may have augmented the rate of withdrawal, as patients were recruited with the agreement of a consultee. For an outcome such as deep SSI, being able to account for each patient is critical due to the low rate of events relative to the study population. Methods such as multiple imputation are of limited value when dealing with these types of loss of data, as they propagate observed data and do not take into account any variation between the withdrawn and retained patients.

In conclusion, a definitive randomized clinical trial comparing standard dressings with NPWT in patients with a hip fracture is deemed to be feasible on the basis of the rate of deep SSI seen in these treatment groups. There were no major issues in recruitment, retention, or data capture. Given the devastating consequences of deep SSI for these patients, such a study should be considered a priority.

Take home message

- Prior to this study, there was uncertainty around the true event rate for surgical site infection (SSI) after hip fracture surgery.
- An overall rate of 4% in the hip fracture population undergoing surgery was found (6.4% in standard dressing group and 1.9% in the incisional negative pressure wound therapy (NPWT) group).
- Based on a 4% SSI event rate and other metrics such as rate of recruitment and willingness to participate, a definitive trial can be deemed feasible.

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Supplementary material

Figure a outlines the process of screening and recruitment. Tables i, ii, and iii summarize patient mobility at 120 days, complications reported by treatment arm, and residential status at 120 days, respectively.

References

1. **Falls and Fragility Fracture Audit Programme (FFFAP)**. National Hip Fracture Database (NHFD) annual report 2015. Royal College of Physicians: Falls and Fragility Fracture Audit Programme (FFFAP). 2015. https://www.nhfd.co.uk/2015report (date last accessed 16 February 2021).
2. **No authors listed**. National hip fracture database (NHFD) 2018 annual report. Royal College of Physicians. 2018. https://www.nhfd.co.uk/20/hipfractureR.nsf/docs/reports2018 (date last accessed 3 February 2021).
3. **Roche JJW**, **Wenn RT**, **Sahota O**, **Moran CG**. Effect of comorbidities and postoperative complications on mortality after hip fracture in elderly people: prospective observational cohort study. *BMJ*. 2005;331(7529):1374.
4. **Metcalfe D**, **Masters J**, **Delmestri A**, **et al**. Coding algorithms for defining Charlson and Elixhauser co-morbidities in Read-coded databases. *BMC Med Res Methodol*. 2019;19(1):115–121.
5. **Hansson S**, **Rolfson O**, **Åkesson K**, **Nemes S**, **Leonardsson O**, **Rogmark C**. Complications and patient-reported outcome after hip fracture. A consecutive annual cohort study of 664 patients. *Injury*. 2015;46(11):2206–2211.
6. **Edwards C**, **Counsell A**, **Boulton C**, **Moran CG**. Early infection after hip fracture surgery. *J Bone Joint Surg Br*. 2008;90-B(6):770–777.
7. **Fernandez MA**, **Arnel L**, **Gould J**, **et al**. Research priorities in fragility fractures of the lower limb and pelvis: a UK priority setting partnership with the James Lind alliance. *BMJ Open*. 2018;8(10):e023301.
8. **Hyldig N**, **Birke-Sorensen H**, **Kruse M**, **et al**. Meta-analysis of negative-pressure wound therapy for closed surgical incisions. *Br J Surg*. 2016;103(5):477–486.
9. **Webster J**, **Liu Z**, **Norman G**, **et al**. Negative pressure wound therapy for surgical wounds healing by primary closure. *Cochrane Database Syst Rev*. 2019;3(3):CD009261.
10. **Theodorides AA**, **Pollard TCB**, **Fishlock A**, **et al**. Treatment of post-operative infections following proximal femoral fractures: our institutional experience. *Injury*. 2011;42(Suppl 5):S28–S34.
11. **Westberg M**, **Snorrason F**, **Frihagen F**. Preoperative waiting time increased the risk of periprosthetic infection in patients with femoral neck fracture. *Acta Orthop*. 2013;84(2):124–129.
12. **Costa ML**, **Griffin XL**, **Achten J**, **et al**. World Hip Trauma Evaluation (WHiTE): framework for embedded comprehensive cohort studies. *BMJ Open*. 2016;6(10):e011679.
13. **Griffin XL**, **Achten J**, **Parsons N**, **Boardman F**, **Griffiths F**, **Costa ML**. The Warwick Hip Trauma Evaluation - an abridged protocol for the WHiTE Study: A multiple embedded randomised controlled trial cohort study. *Bone Joint Res*. 2012;1(11):310–314.
14. **Griffin XL**, **McArthur J**, **Achten J**, **Parsons N**, **Costa ML**. The Warwick Hip Trauma Evaluation One -an abridged protocol for the WHiTE One Study: An embedded randomised trial comparing the X-bolt with slidinghip screw fixation in extracapsular hip fractures. *Bone Joint Res*. 2013;2(10):206–209.
15. **Griffin XL**, **McArthur J**, **Achten J**, **Parsons N**, **Costa ML**. The Warwick Hip Trauma Evaluation Two -an abridged protocol for the WHiTE Two Study: An embedded randomised trial comparing the Dual-Mobility withpolyethylene cups in hip arthroplasty for fracture. *Bone Joint Res*. 2013;2(10):210–213.
16. **Griffin XL**, **Parsons N**, **McArthur J**, **Achten J**, **Costa ML**. The Warwick hip trauma evaluation one. A randomised pilot trial comparing the X-Bolt dynamic hip plating system with sliding hip screw fixation in complex extracapsular hip fractures. *WHiTE*. 2016;98-B(5):686–689.
17. **Griffin XL**, **Achten J**, **Sones W**, **Cook J**, **Costa ML**. Randomised controlled trial of the sliding hip screw versus X-Bolt dynamic hip plating system for the fixation of trochanteric fractures of the hip in adults: a protocol study for white 4 (WHiTE4). *BMJ Open*. 2018;8(1):e019944.
18. **Metcalfe D**, **Costa ML**, **Parsons NR**, **et al**. Validation of a prospective cohort study of older adults with hip fractures. *Bone Joint J*. 2019;101-B(6):708–714.
19. **Sims AL**, **Parsons N**, **Achten J**, **Griffin XL**, **Costa ML**, **Reed MR**. The world hip trauma evaluation study 3. *Bone Joint Res*. 2016;5(1):18–25.
20. **No authors listed**. IRAS Integrated Research Application System, version 5.18, 21/12/2020, IRAS Dataset version 3.5. The Health Research Authority (HRA). 2021. https://www.myresearchproject.org.uk/ (date last accessed 24 February 2021).
21. **Masters JPM**, **Achten J**, **Cook J**, **Dritsaki M**, **Sansom L**, **Costa ML**. Randomised controlled feasibility trial of standard wound management versus negative-pressure wound therapy in the treatment of adult patients having surgical incisions for hip fractures. *BMJ Open*. 2018;8(4):e020632.
22. **No authors listed**. Mental Capacity Act 2005. legislation.gov.uk. 2005. https://www.legislation.gov.uk/ukpga/2005/9/contents (date last accessed 16 February 2021).
23. **Rennie D**. CONSORT revised--improving the reporting of randomized trials. *JAMA*. 2001;285(15):2006–2007.
24. **Horan TC**, **Andrus M**, **Dudeck MA**. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control*. 2008;36(5):309–332.
25. **No authors listed**. Surgical site infection event (SSI). Centers for Disease Control and Prevention: National Healthcare Safety Network (NHSN). 2021. https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscssicurrent.pdf (date last accessed 4 February 2021).

26. **Haywood KL**, **Griffin XL**, **Achten J**, **Costa ML**. Developing a core outcome set for hip fracture trials. *Bone Joint J*. 2014;96-B(8):1016–1023.
27. **van Hout B**, **Janssen MF**, **Feng Y-S**, **et al**. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets. *Value Health*. 2012;15(5):708–715.
28. **No authors listed**. EQ-5D-5L | Valuation | Crosswalk Index Value Calculator. EuroQol. 2021. https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/crosswalk-index-value-calculator/ (date last accessed 4 February 2021).
29. **Saklad M**. Grading of patients for surgical procedures. *Anesthesiol*. 1941;2(5):281–284.
30. **Brown LD**, **Cai TT**, **Dasgupta A**. Interval Estimation for a Binomial Proportion. *Statistical Science*. 2001;16(2):101–133.
31. **Pauser J**, **Nordmeyer M**, **Biber R**, **et al**. Incisional negative pressure wound therapy after hemiarthroplasty for femoral neck fractures - reduction of wound complications. *Int Wound J*. 2016;13(5):663–667.
32. **Costa ML**, **Achten J**, **Knight R**, **et al**. Effect of incisional negative pressure wound therapy vs standard wound dressing on deep surgical site infection after surgery for lower limb fractures associated with major trauma: the WHIST randomized clinical trial. *JAMA*. 2020;323(6):519–526.

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J. Achten: Oversaw the conduct of the study, Critically revised the manuscript.
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Funding statement:
All decisions relating to the design, conduct, analysis, write-up, and publication of research are independent of each of these funders. Although none of the authors has received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article, benefits have been or will be received but will be directed solely to a research fund, foundation, educational institution, or other non- profit organization with which one or more of the authors are associated.

ICMJE COI statement:
J. Masters and J. Cook report institutional grants (paid to University of Oxford) from the Royal College of Surgeons of England/Dunhill Medical Trust research training fellowship, Smith & Nephew (device supply), and the NIHR Oxford Biomedical Research Centre (research infrastructure support), all related to this study. M. Costa reports institutional research grant funding (paid to University of Oxford) from the National Institute for Health Research (NIHR), the European Union (EU), the Royal College of Surgeons (RCS) England, and Smith & Nephew, not related to this study.

Acknowledgements:
We would like to acknowledge the members of the independent oversight committees: John Keating, NHS Lothian-Edinburgh (Chair Oversight Committee); Alan Johnstone, NHS Grampian-Aberdeen (Chair Data Safety and Monitoring Committee (DSMC)); Michael Dewey, Kings College London (Chair DSMC); Antony Johansen, Cardiff and Vale University Health board; Stuart White, Brighton and Sussex University Hospitals NHS Trust; May Cleary, University Hospital Waterford; Ada Keating, University of York.
We also acknowledge Dr Beverly Shirkey for support with the analysis.
The WHISH Trial Collaborators-Principle investigators and trainee Principle Investigators-will be named on PubMed under the WHISH study group.
We also acknowledge John McMaster and Katherine Butler, Oxford University Hospitals NHS Foundation Trust; Andrew Riddick, North Bristol NHS Trust; Iain McNamara, Rumina Begum, Alexander Durst, and Omar Toma, Norfolk and Norwich University Hospitals NHS Foundation Trust; Ben Ollivere, University of Nottingham; Mark Farrar and Arshad Iqbal, Poole Hospital NHS Foundation Trust.
We also acknowledge: site research associates Steven Barnfield, Ruth Halliday, Jessica Nightingale, Carolyn Colvin, Tracey Potter, Kathryn Lewis, and Martin Austin; and Central Study Team Lucy Sansom, Charlie Vicary, and Katy Mironov.

Ethical review statement:
Ethics and dissemination Oxford C Research Ethics Committee granted ethical approval on 28/04/2017, 17/ SC/0207. ISRCTN55305726.

This article was primary edited by J. Scott.