

## Impact case study (REF3)

<b>Institution:</b> Teesside University		
<b>Unit of Assessment:</b> 3		
<b>Title of case study:</b> Transforming clinical guidelines and practice for the management of displaced proximal humerus fractures		
<b>Period when the underpinning research was undertaken:</b> 2009-2017		
<b>Details of staff conducting the underpinning research from the submitting unit:</b>		
<b>Name(s):</b>	<b>Role(s) (e.g. job title):</b>	<b>Period(s) employed by submitting HEI:</b>
Helen Handoll	Reader in Orthopaedics	Oct 2002 to Present
Nigel Hanchard	Reader in Orthopaedics	Jan 2000 to Oct 2016
Laura Denis	Clinical Trials Coordinator	Sep 2008 to Sep 2011
<b>Period when the claimed impact occurred:</b> 2016-2020		
<b>Is this case study continued from a case study submitted in 2014?</b> N		

**1. Summary of the impact (indicative maximum 100 words)**

The PROFHER trial (PROximal Fracture of the Humerus: Evaluation by Randomisation) was funded (c. GBP1,500,000) by the National Institute for Health Research (NIHR). The trial produced high-grade evidence that surgery did not improve patient-reported outcome (Oxford Shoulder Score) in adults up to two years after a displaced proximal humeral fracture, compared to conservative management (sling immobilisation). Furthermore, the health economics analysis showed that surgery was not cost-effective. The clinical- and cost-effectiveness findings formed the definitive evidence for the 2016 National Institute of Health and Care Excellence (NICE) guidelines for the treatment of these fractures: a strong recommendation was made for conservative management, as no additional benefit was indicated with surgery. A 2017 survey of UK National Health Service (NHS) specialist orthopaedic and trauma surgeons found that around half of respondents had changed practice based on the trial results by operating on fewer eligible patients, with greater confidence in treatment decision making. Around one-third of those who had not changed practice were already managing patients non-surgically. This group reported that the PROFHER trial findings provided evidence-based support for their treatment decisions and had also aided discussions with patients. The trial has also informed international practice, with examples from Denmark.

**2. Underpinning research (indicative maximum 500 words)**

Approximately 5% of fractures in adults in high income countries are those of the proximal humerus (top end of the upper arm bone), with over 700,000 occurring worldwide annually. Also called “broken shoulders”, these serious fractures occur mainly in older people. They are very painful and debilitating, often in the long-term. Most fractures are treated conservatively by immobilising the affected arm, such as with an arm sling, followed by physical exercises. Surgery typically involves fixation with a plate and screws, or partial or total joint replacement. Although surgery is indicated for very seriously disrupted fractures, prior to the PROFHER trial there was a trend for increased surgery in the largest subgroup of ‘displaced’ fractures; around 40% of the fracture population. Prior to the publication and incorporation of the PROFHER trial findings, a regularly updated Cochrane review conducted by Handoll et al. found insufficient evidence to inform on the use of surgery for these fractures. The review also noted several abandoned and under-recruited trials, illustrating the major challenges in conducting randomised trials on this topic.

Initiated by Teesside University (trial sponsor), a trial group of orthopaedic surgeons (lead applicant: Amar Rangan, James Cook University Hospital, Middlesbrough and Visiting Professor at Teesside University) and methodologists (University lead, Handoll; and members of the York Trials Unit, trial management) received NIHR funding to conduct the PROFHER trial (PROximal Fracture of the Humerus: Evaluation by Randomisation). The trial was registered on 25 March

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2008: <http://www.isrctn.com/ISRCTN50850043>. Handoll was the lead regarding co-ordinating and writing-up the various topic-specific and methodological aspects of the trial protocol, published in 2009 [3.1]. This contribution included working with physiotherapist Goodchild (formerly at James Cook University Hospital) and Hanchard (physiotherapist and Reader at Teesside University) to develop a patient information leaflet for initial self-care, as well as a physiotherapy protocol; rehabilitation aspects reported in [3.2]. Handoll was a core member of the trial management group. The PROFHER trial involved a substantial investment in terms of GBP1,500,000 funding through the NIHR and via contributions from hundreds of people, including surgeons and other clinicians at the participating sites.

The PROFHER trial recruited 250 adults from the orthopaedic departments (fracture clinics or wards) of 32 acute care UK NHS hospitals between September 2008 and April 2011 within 3 weeks of sustaining a displaced fracture of the proximal humerus. Patients were randomly assigned to surgery (fracture fixation or humeral head replacement) or non-surgical treatment (sling immobilization). Standard outpatient and community-based rehabilitation was provided to both groups. The primary outcome was the Oxford Shoulder Score – a patient-reported outcome with a range of 0-48, with higher scores indicating better outcomes – reported at 6, 12, and 24 months. The results showed no significant difference between groups for the mean Oxford Shoulder Score averaged over 2 years of follow-up (39.07 points for the surgical group vs 38.32 points for the nonsurgical group, a difference of 0.75 points [95% CI, -1.33 to 2.84 points]; P = 0.48). Also, there were no significant differences between groups in physical and mental health-related quality of life. The data did not support the trend of increased surgery for patients with displaced fractures of the proximal humerus.

Handoll was the lead author and responsible for the contents and structure of the comprehensive account of the trial published in the funder's journal [3.3] as well as in the leading medical journal, JAMA [3.4]. The health economic analysis was published separately and was centred on UK NHS costs [3.5]. A cost-utility analysis examined differences between surgery and non-surgery treatments in costs and quality adjusted life years (QALYs) at two years. The QALY is a commonly used metric in health economic analyses and combines quality and quantity of life into a single score. The QALY can be calculated using a utility value (quality of life) between 1 = perfect health and 0 = dead: a person living in perfect health for one year will have 1 QALY. Medical treatments are evaluated on a cost per QALY basis. The health economic analysis revealed that patients in the surgery group accumulated greater costs and slightly lower QALYs than patients randomised to non-surgery [3.5]. On average, the surgical intervention cost GBP1,758 more per patient. The probability of surgery being cost effective was less than 10% at the threshold used by NICE for 'willingness to pay' of GBP£20,000 per QALY. The analysis showed that surgical treatment is not cost effective for most displaced fractures of the proximal humerus involving the surgical neck in the United Kingdom's NHS. It was estimated that a 50% reduction in surgery would equate to an annual cost saving of GBP2,500,000 for NHS England.

In 2010, Handoll et al. successfully applied for additional funding to extend follow-up to five years. Oxford Shoulder Score data were available for 164, 155 and 149 participants at three, four and five years, respectively. There were no substantial differences between surgical and non-surgical treatment groups at each timepoint. The results at five years were consistent with those at two years [3.6]. Thus, overall, the results do not support the trend of increased surgery for patients with these fractures.

### **3. References to the research (indicative maximum of six references)**

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[3.1] Handoll H, Brealey S, Rangan A, Torgerson D, Dennis L, Armstrong A et al. 2009. Protocol for the ProFHER (PROximal Fracture of the Humerus: Evaluation by Randomisation) trial: a pragmatic multi-centre randomised controlled trial of surgical versus non-surgical treatment for proximal fracture of the humerus in adults. *BMC Musculoskeletal Disorders*. 10:140. <https://doi.org/10.1186/1471-2474-10-140>. Cited 35 times (Web of Science). Selected for REF2014 (95.5% 2\* and above).

[3.2] Handoll H, Goodchild L, Brealey S, Hanchard NCA, Jefferson L, Keding A, Rangan A. 2014. Developing, delivering and documenting rehabilitation in a multi-centre randomised

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controlled surgical trial: experiences from the ProFHER trial. *Bone and Joint Research*. 3:12, 335-40. <https://doi.org/10.1302/2046-3758.312.2000364>. Cited 6 times (Web of Science).

[3.3] Handoll H, Brealey S, Rangan A, Keding A, Corbacho B, Jefferson L, et al. 2015. The ProFHER (PROximal Fracture of the Humerus: Evaluation by Randomisation) trial – a pragmatic multicentre randomised controlled trial evaluating the clinical effectiveness and cost-effectiveness of surgical compared with non-surgical treatment for proximal fracture of the humerus in adults. *Health Technology Assessment*. 19:24. <https://doi.org/10.3310/hta19240>. Cited 40 times (Web of Science)

[3.4] Rangan A, Handoll H, Brealey S, Jefferson L, Keding A, Corbacho Martin B, Goodchild L, Chuang LH, Hewitt C, Torgerson D, for the PROFHER Trial Collaborators. 2015. Surgical vs nonsurgical treatment of adults with displaced fractures of the proximal humerus: The PROFHER randomized clinical trial. *JAMA*. 313: 10, 1037-1047. <https://doi.org/10.1001/jama.2015.1629>. Cited 167 times (Web of Science) and classified as a 'Highly Cited' paper in the top 1% for Clinical Medicine for the field and year. Selected for REF2021.

[3.5] Corbacho B, Duarte A, Keding A, Handoll H, Chuang LH, Torgerson D, Brealey S, Jefferson L, Hewitt C, Rangan A. 2016. Cost effectiveness of surgical versus nonsurgical treatment of adults with displaced fractures of the proximal humerus. Economic evaluation alongside the PROFHER TRIAL. *Bone and Joint Journal*. 98-B:2,152-9. <https://doi.org/10.1302/0301-620X.98B2.36614>. Cited 19 times (Web of Science)

[3.6] Handoll H, Keding A, Corbacho B, Brealey SD, Hewitt C, Rangan A. 2017. Five-year follow-up results of the PROFHER trial comparing operative and non-operative treatment of adults with a displaced fracture of the proximal humerus. *Bone and Joint Journal*. 99:3, 383-392. <https://doi.org/10.1302/0301-620X.99B3.BJJ-2016-1028>. Cited 37 times (Web of Science). Selected for REF2021.

The above research was underpinned by funding from a National Institute for Health Research grant. Chief Investigator: Rangan (University of York). Co-Investigator: Handoll. NIHR HTA. grid.451056.306/404/53. 2008-2016. *Pragmatic multi-centre randomised trial of surgical versus non-surgical treatment for proximal fracture of the humerus in adults*. 06/404/53. Contracting Organisation: Teesside University (Coordinator: Denis). Partners: James Cook University Hospital. GBP1,485,584.60 (includes extension for long-term follow-up). Handoll was employed as local lead and member of the core trial management team and Denis was the trial coordinator.

#### **4. Details of the impact (indicative maximum 750 words)**

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The PROFHER trial underpinned clinical guidelines and altered the practice of surgeons treating proximal fractures of the humerus. The trial findings provided the definitive evidence for treatment recommendations for these fractures in the UK National Institute of Health and Care Excellence (NICE) guideline NG38, 2016 [5.1]. Professionals and practitioners are expected to take NICE guidelines 'fully into account, alongside the individual needs, preferences and values of their patients or the people using their service' [5.1, p.19].

The full report for the assessment and management of non-complex fractures by NICE describes the trial (cited as Handoll et al. [3.3]) as 'a well conducted UK based trial', with the Guideline Development Group indicating that 'a strong recommendation should be made for the conservative approach as no additional benefit was indicated with surgery' [5.2, p.222]. As a result of this pivotal underpinning research, these new guidelines state specifically that 'for adults (skeletally mature) with displaced low energy proximal humerus fractures: offer non-surgical management for definitive treatment of uncomplicated injuries' [5.2, p.221].

Handoll et al.'s health economic analysis [3.5] was the only research identified by the NICE Guideline Development Group comparing conservative treatment to surgery for cost-effectiveness, with this evidence 'assessed as directly applicable with minor limitations' [5.2, p. 223]. The results showed a slight increase in QALYs (0.01) for the conservative treatment group as well as a relative reduction in overall costs (GBP1,758 per patient). Therefore, the NICE Guideline Development Group concluded that the clinical effectiveness evidence was consistent

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with the cost effectiveness data and 'agreed that conservative treatment should be recommended for people with fractures of the proximal humerus' [5.2, p. 223].

Subsequently, Handoll et al. sought evidence of the influence of the PROFHER trial results on surgeons' clinical practice [5.3: selected for REF2021, cited 10 times on Web of Science]. They conducted a survey of UK NHS specialist orthopaedic and trauma surgeons, using a questionnaire piloted with six orthopaedic surgeons using a 'think aloud' process. The questionnaire was distributed online to surgeon members of the British Orthopaedic Association and British Elbow and Shoulder Society. Complete responses were obtained from 265 orthopaedic and trauma surgeons who treat patients with proximal humeral fractures. The results showed that around half (137/265) of respondents had changed practice entirely (n=90) or partly (n=47) based on the PROFHER trial results, by operating on fewer eligible patients [5.3]. A substantial number of this group of surgeons also reported that the PROFHER trial had given them greater confidence in making a decision to treat non-operatively (n=22) [5.3, p. 596]. Additional free-text feedback from surgeons included reduced concerns around liability as their practice was now evidence-based further to publication of the PROFHER trial [5.3, p. 596]. The evaluation also revealed that some surgeons used the trial findings to 'inform a patient-centred approach, for example, through discussions of treatment options with patients in light of the trial findings (21 cases)' [5.3, p. 596]. A total of 43 of the 128 respondents who had not changed practice were already managing patients without surgery, and a number of these reported that the PROFHER trial findings provided evidence-based support for their treatment decisions (n=19) and had also aided discussions with patients (n=9). Overall, the survey showed that high-grade evidence from definitive randomised clinical trials like PROFHER was the most important influence on surgeons' decisions to change practice [5.3].

Testimonials from two consultant surgeons in Denmark demonstrate that the PROFHER trial has had influence beyond the UK, with the trial shaping practice within their institutions to a non-operative approach to treating proximal fracture of the humerus [5.4, 5.5]. One testimonial pointed to national guidance in Denmark: 'we have agreed within the Danish Orthopaedic Society on a non-operative approach to most displaced proximal humeral fractures' [5.4].

In summary, the underpinning research – in the form of a pivotal randomised clinical trial – provided the definitive evidence for the NICE treatment recommendations for displaced proximal humerus fractures. The trial findings changed the practice of surgeons treating these fractures in the UK NHS and beyond, resulting in a reduction in unnecessary surgery and large potential cost savings.

### **5. Sources to corroborate the impact (indicative maximum of 10 references)**

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[5.1] NICE Guideline. National Institute for Health and Care Excellence. 2016. Fractures (non-complex): assessment and management. NICE guidelines [NG38] Published date: February 2016. Available at: <https://www.nice.org.uk/guidance/ng38>

[5.2] NICE Full Guideline. National Institute for Health and Care Excellence. 2016. Fractures (non-complex): assessment and management. NICE guidelines [NG38] (Fractures: diagnosis, management and follow-up of fractures). NICE Guideline NG38: Methods, evidence and recommendations. Available at: <https://www.nice.org.uk/guidance/ng38/evidence/full-guideline-pdf-2358460765>

[5.3] Survey. Jefferson L, Brealey S, Handoll H, Keding A, Kottam L, Sbizzera I, Rangan A. 2017. Impact of the PROFHER trial findings on surgeons' clinical practice: An online questionnaire survey. Bone and Joint Research. 6: 10, 590-599. <https://doi.org/10.1302/2046-3758.610.BJR-2017-0170>

[5.4] Signed Letter (pdf). Testimonial from surgeon at Zealand University Hospital, Denmark. Received on 25 September 2020.

[5.5] Signed Letter (pdf). Testimonial from surgeon at Aarhus University Hospital, Denmark. Received on 30 September 2020.