

## **Reply to Letter to Editor regarding “Development and delivery of the rehabilitation interventions for older adults with an ankle fracture in the AFTER trial”**

Thank you to X and colleagues for their considered reflections regarding our article describing the development and delivery of the AFTER interventions, and their kind comments about the robustness and transparent reporting of our intervention development process. Several of their reflections relate to the trial’s design (fully described in the published protocol[1]) and not the interventions per se, but we have tried to address these as well.

AFTER was a pragmatic randomised controlled trial (RCT) that compared ‘supervised rehabilitation’ (4-6 physiotherapy sessions) versus ‘self-directed rehabilitation’ (provision of a high-quality workbook to support self-management) for adults aged  $\geq 50$  years with an ankle fracture. A pragmatic trial asks if an intervention works in real-life clinical settings, whereas explanatory trials ask if interventions work under ideal conditions.[2] It was this pragmatic focus that underpinned the AFTER trial design and interventions.

X and colleagues raised valid concerns about possible contamination between treatment groups and use of out-of-trial physiotherapy by participants allocated to ‘self-directed rehabilitation’. We knew of these potential problems a-priori and indeed we highlighted the high rates of out-of-trial private physiotherapy as a key limitation of the EXACT trial[3] in our protocol[1] and intervention paper[4]. The AFTER protocol[1] describes our full strategy to mitigate for potential contamination and out-of-trial physiotherapy in the trial’s design, conduct, and analysis. Briefly, we notified General Practitioners (GPs) of their patient’s participation to reduce additional physiotherapy referrals by GPs, and we asked physiotherapists trained to deliver ‘supervised rehabilitation’ not to deliver or be involved in the rehabilitation of ‘self-directed rehabilitation’ participants. We also collected data on treatment crossovers and out-of-trial physiotherapy from sites and participant follow-up questionnaires and monitored this data in monthly trial meetings. Furthermore, the primary analysis will be by intention-to-treat but separate per-protocol and Complier Average Causal Effect analyses will examine the effect of treatment compliance on the results.

X and colleagues also suggested collecting a range of additional baseline data, apparently to enable the analysis of participants by specific subgroups. While some of this additional data is potentially of interest, it is very likely that collecting it would have been deemed too burdensome by some participants or the researchers recruiting them from busy UK National Health Service (NHS) fracture clinics. This could have compromised the trial’s delivery. Multiple subgroup analyses can also bring problems, for example with inadequate power and increased false positive rates from multiple testing[5].

Regarding the interventions, X and colleagues highlighted that differing levels of cognitive function, self-efficacy, and health literacy could lead to different levels of engagement with the paper or online workbooks. To be eligible, patients had to be able to adhere to the trial procedures. This includes having the cognitive capacity to follow ‘self-directed rehabilitation’. We also designed the paper and online workbooks to be easily understandable by older adults, and these were reviewed by patient partners similar in age to the AFTER

participants[4]. In the preceding AFTER pilot trial, participants interviewed in the embedded qualitative study also found the intervention workbooks valuable[6]. Furthermore, the main difference between the online and paper workbooks was the availability of exercise videos on the online version which we feel is unlikely to affect the trial results. We recognise that self-efficacy is important, so the Self-Efficacy Exercise Score was a trial outcome.

Given the trial's pragmatic focus, the interventions did not include formal psychological assessments or cognitive behavioural treatments because these would not be readily scalable across NHS physiotherapy departments. We believe that including these additional components would diminish the study's ecological validity. Indeed, we had to streamline the 'supervised rehabilitation' intervention for the definitive AFTER trial because it was judged too time consuming by the NHS physiotherapists who delivered it in the pilot[6]. Despite this, the intervention workbooks contain advice about the consequences of fear avoidance beliefs and behaviours and how participants can address these. The AFTER interventions also permitted physiotherapists to assess participants as per their normal practice, and provide any additional treatments judged clinically relevant once the core components of 'supervised rehabilitation' were delivered. This could include assessment for and addressing maladaptive beliefs and behaviours. Participants allocated to 'self-directed rehabilitation' did not have follow-up to reinforce the behaviour change techniques in this intervention because it was designed to enable participants to manage their recovery independently - as described in the intervention paper.

To conclude, AFTER is a pragmatic RCT designed to inform rehabilitation provision for people aged  $\geq 50$  years after ankle fracture treated in real world clinical settings. The results are anticipated in 2026. We are grateful for X and colleagues' comments - they raise several potential areas of future investigation, but perhaps in studies with a more explanatory approach.

- [1] Keene DJ, Achten J, Forde C, Png ME, Grant R, Draper K, et al. Effectiveness of supervised versus self-directed rehabilitation for adults aged 50 years and over with ankle fractures: protocol for the AFTER trial. *Bone Jt Open* 2024;5:499–513.
- [2] Loudon K, Treweek S, Sullivan F, Donnan P, Thorpe KE, Zwarenstein M. The PRECIS-2 tool: Designing trials that are fit for purpose. *BMJ* 2015;350:h2147.
- [3] Moseley AM, Beckenkamp PR, Haas M, Herbert RD, Lin CWC, Evans P, et al. Rehabilitation after immobilization for ankle fracture: The EXACT randomized clinical trial. *JAMA* 2015;314:1376–85.
- [4] Forde CP, Costa ML, Achten J, Grant R, Lamb SE, Keene DJ. Development and delivery of the rehabilitation interventions for older adults with an ankle fracture in the AFTER (Ankle Fracture Treatment Enhancing Rehabilitation) trial. *Physiotherapy* 2025;128.
- [5] Wang R, Lagakos SW, Ware JH, Hunter DJ, Drazen JM. Statistics in Medicine - Reporting of Subgroup Analyses in Clinical Trials. *N Engl J Med* 2007;357:2189–94.

- [6] Tutton E, Gould J, Lamb SE, Costa ML, Keene DJ. Experience of patients and physiotherapists within the after pilot randomised trial of two rehabilitation interventions for people aged 50 years and over post ankle fracture: A qualitative study. *BMJ Open* 2023;13.