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Study Protocol

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Assessing functional recovery after total knee arthroplasty: a pilot study protocol to investigate the role of skeletal muscle regeneration

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Abstract

Total knee arthroplasty (TKA) is a widely performed procedure to relieve pain from advanced knee osteoarthritis. However, evidence suggests it may impair muscle physiology, leading to postoperative strength and functional deficits. The contribution of skeletal muscle's intrinsic regenerative capacity to these outcomes remains unclear, particularly that of satellite cells. By examining both the number and functional capacity of satellite cells, alongside longitudinal clinical assessments, this study will determine whether satellite cell quantity and regenerative potential are key determinants of postoperative recovery. This single-centre, prospective longitudinal pilot study will evaluate the role of satellite cells in quadriceps muscle regeneration following TKA. The primary outcome is quadriceps muscle strength, assessed using fixed dynamometry across the 12-month follow-up period. An intra-operative rectus femoris biopsy will assess muscle fibre structure, satellite cell content, and regenerative capacity using an innovative de novo myotube formation assay. Functional and patient-reported measures at baseline, 6 weeks, 6 months, and 12 months will include the five-repetition Sit-to-Stand test, near-infrared spectroscopy, and the Oxford Knee Score. The pilot will also evaluate feasibility of recruitment, data collection, and retention, with recruitment continuing until a minimum of 25 biopsy outcomes are consistent and reproducible. Statistical analyses will use multiple regression and linear mixed-effects models to explore associations between cellular markers and functional recovery. Patient and public involvement informed protocol development. The study may identify mechanisms and early biomarkers to guide personalised rehabilitation and improve post-TKA strength, mobility, and quality of life. Findings will be disseminated via scientific conferences and peer-reviewed journals.

Keywords: knee arthroplasty, muscle regeneration, osteoarthritis, satellite cells

INTRODUCTION

Knee osteoarthritis (KOA) is frequently associated with long-term deficits in skeletal muscle health, including reduction in muscle mass, strength losses, and impaired neuromuscular activity [1, 2]; leading to impaired functional mobility [3, 4]. KOA can develop as primary OA, driven by age-related degenerative changes and low-grade synovial inflammation that further perpetuate joint deterioration [5], or as secondary OA, arising from identifiable causes such as trauma, fracture, or mechanical instability. Post-traumatic abnormalities have been shown to predict poorer functional outcomes and increase susceptibility to secondary KOA [6]. Total knee arthroplasty (TKA) is a commonly performed procedure to improve these symptoms, although deficits in muscle health can persist and are often exacerbated during the acute postoperative phase [7, 8]. Postoperatively, reductions in quadriceps function can amount to ∼60% of preoperative strength [8] with the majority of muscle atrophy occurring within the first 2 weeks [2]. Over the next 6–12 months, quadriceps strength gradually improves to levels close to prior surgery levels, but it remains notably reduced compared to healthy individuals of the same age [4, 9]. This ongoing weakness is thought to be due to both reduced voluntary muscle activation and muscle atrophy. In the early phase post-TKA, and within the first month, the quadriceps weakness is primarily due to deficits in voluntary activation (i.e. muscle inhibition) [8]. However, by 1 year post-surgery, quadriceps strength is more closely linked to the cross-sectional area of the muscle as the voluntary activation deficits significantly diminish [10, 11]. Despite rehabilitation efforts to mitigate postoperative decline in skeletal muscle health to support joint function, deficits persist and progressively worsen, remaining evident even many years after TKA [12]. The causes of these longer-term deficits remain unexplained, with the regenerative potential of muscle

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largely being underexplored when trying to explain postoperative deficits following the procedure.

Satellite cells are the resident muscle stems cells and have long been known to be necessary for muscle regeneration and repair as well as being involved in the hypertrophic process [13–19]. These cells are quiescent (dormant), mono-nucleated cells situated between the basal lamina and the sarcolemma of their associated muscle fibres. In adult muscles, they typically remain inactive but serve as a reserve cell population capable of activation and proliferation in response to injury, leading to the regeneration of muscle tissue and the production of additional satellite cells [20]. It has previously been demonstrated that satellite cell content may contribute to the extent of physical recovery following knee arthroplasty, whereby a strong correlation between satellite cell markers and lower limb power generation exists [21]. This preliminary cross-sectional study indicates that satellite cell content is a pre-determining factor for skeletal muscle regeneration and restorative function following TKA. However, the study's small sample size and reliance on isolated biological markers and a single strength test, oversimplify the complex nature of muscle regeneration, reducing the study's immediate clinical applicability. To this end, there is an urgent need to further explore the role of satellite cells in the physical recovery of patients following TKA, to determine whether there may be suitable interventions to identify those patients with reduced regenerative potential and also develop strategies to maximise muscle regeneration. Moreover, a multidisciplinary and integrative approach is required to further understand the cellular and molecular factors that contribute to muscle regeneration and function following TKA.

In this regard, this project proposes a highly novel approach using both *in vivo* and *in vitro* methodologies. Numerous studies have suggested that individuals with a higher number of satellite cells have greater potential for tissue regeneration and better recovery [22, 23]. This project aims to explore this hypothesis further by analysing tissue histology, focusing on muscle fibre size, type, and satellite cell count. However, satellite cell quantity does not necessarily reflect their functionality. To explore this, previous literature has investigated the role of satellite cells and their number in muscle regeneration in animal models [24, 25]. Due to the experimental models employed, these studies allow for the investigation of satellite cell kinetics; however, they do not fully reflect human muscle physiology. Therefore, in this study, an *in vitro* methodology will be used to isolate, culture, and assess muscle cell regeneration as a model of regenerative capacity. By assessing the functional recovery of patients with matched *in vitro* assays, we aim to determine whether satellite cell content and function contribute to *in vivo* functional outcomes. Despite obvious limitations, this approach provides a highly unique approach to investigate the role of satellite cells in skeletal muscle regeneration of patients undergoing TKA. Statistical modelling will assess the extent to which *in vivo* functional outcomes are associated with histological and cellular data in an attempt to uncover meaningful correlations which could serve as important findings for future interventional studies. The primary objective is to determine the association between satellite cell content/function and postoperative quadriceps strength recovery following TKA. Secondary objectives include exploring the relationships between histological, functional, and self-reported measures.

Hypothesis

Patients with greater preoperative satellite cell content and regenerative capacity will experience superior postoperative quadriceps strength recovery following TKA.

METHODS AND ANALYSIS

Study design and setting

This is a single-centre, prospective longitudinal observational pilot study using statistical modelling to identify whether relationships exist between functional measures and tissue structure/satellite cell content/*in vitro* variables post TKA. The study protocol will be prepared in accordance with STrengthening the Reporting of OBservational Studies in Epidemiology (STROBE) 2014 statement [26]. Figure 1 illustrates the patient flow through the pilot study and the timeline for enrolment, intervention and assessments, respectively.

Patients will be enrolled from the Department of Trauma and Orthopaedics at the Royal Free London NHS Foundation Trust, London, UK. This is a major teaching hospital and a member of the North Central London Elective Orthopaedic Network.

Recruitment

Patients with indications and consent for primary TKA will be recruited from the outpatient clinic lists of one consultant orthopaedic surgeon (NM), to control inter-surgeon variability. Patients will be approached during this clinic, ∼3 months prior to surgery. Screening is usually carried out by the consultant in charge, who will perform recruitment and surgery in the study. During the outpatient visit, the consultant will orally inform the eligible patients about the content of the study and the requirement for written informed consent following discussion about the details of the study. After this initial appointment and having read the participant information documentation, patients will have time to consider their participation and decide whether to proceed with surgery and join the study at preoperative assessment visit ∼6 weeks before surgery. Signed written informed consent will be collected if the patient agrees to participate. At this point, baseline measurements will be completed by an evaluator for those who decide to participate. Additional outcome measures will be assessed for the purposes of the study, existing pathways of care will be followed (One-stop clinic) and no additional burden (aside from time-outlined below) will be placed on the service or the patient.

Based on clinic activity at the Royal Free Hospital orthopaedic service, we anticipate screening ∼8–10 patients per week who are scheduled for primary TKA. We expect that 3–4 patients per week will meet eligibility criteria and be approached for participation, with an estimated recruitment rate of 2–3 participants per week. A screening log will be kept to record all patients assessed for eligibility, including those excluded or declining participation, with reasons where available. This will support monitoring of recruitment feasibility and transparent reporting.

Sample size

Pilot studies are primarily intended to assess feasibility rather than test experimental hypotheses, so calculating precise sample sizes is not always necessary. Based on literature guidelines, Brown (1995), Billingham et al (2013), and Whitehead et al (2016), suggest a minimum of 30 samples per group to achieve sufficient statistical power, while Julious (2005) proposes that as few as 12 samples may be acceptable [27–30]. In this study, we aim to recruit 25–30 participants. Recruitment will continue until a minimum of 25 complete biopsy outcomes are consistent and reproducible, at which point the pilot will conclude. This approach identifies proof of concept, practical challenges, refines methods, and estimates sample size needs for future, larger studies.

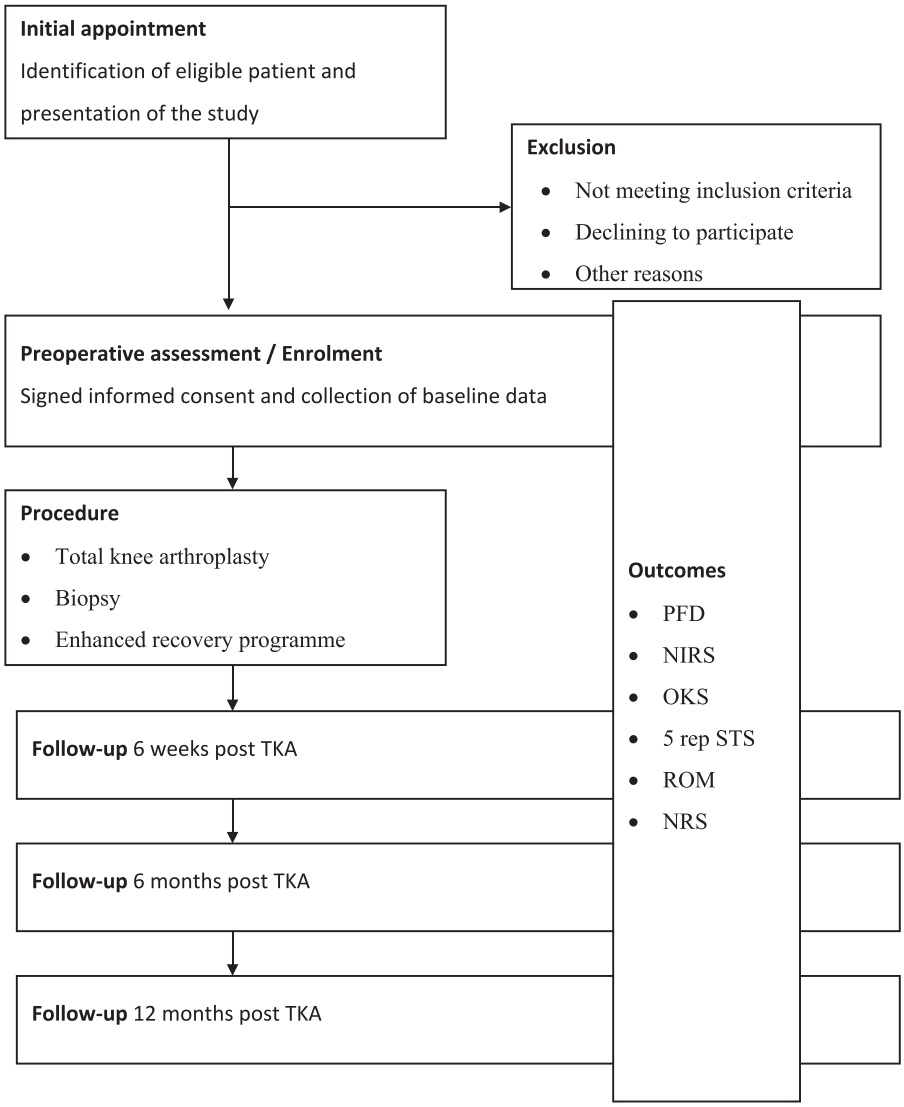

Figure 1: Flowchart of the study procedure. Abbreviations: TKA: Total Knee Arthroplasty; PFD: Portable Fixed Dynamometry; NIRS: Near-Infrared Spectroscopy; OKS: Oxford Knee Score; 5R-STS: Five Repetition Sit-to-Stand Test; ROM: Range of Motion; NRS: Numeric Rating Scale

Inclusion and exclusion criteria

Eligible participants will be adults undergoing primary TKA for KOA who can understand the study procedures and provide informed consent. Individuals will be excluded if they are undergoing revision TKA, receiving TKA for a non-OA diagnosis, or are unable to attend study visits or complete the required assessments.

Procedure

An experienced orthopaedic surgeon (NM), or a member of their surgical team under direct supervision, will perform all TKAs using the same type of prosthesis and a standardised medial parapatellar approach. Muscle biopsies will be taken intra-operatively (further details to follow). All participants will follow the same Enhanced Recovery Programme, which includes preoperative exercise, patient education, multimodal analgesia, and early mobilisation. Evaluations will be conducted preoperatively and at 6 weeks, 6 months, and 12 months postoperatively during routine outpatient clinical reviews at a local clinical testing facility within the Royal Free Hospital Trust (see Fig. 1).

Variables and outcomes

This study will employ a comprehensive outcome testing protocol combining patient-reported feedback and objective clinical assessments. The primary outcome will be the change in quadriceps strength measured by Portable Fixed Dynamometer (PFD) from baseline to 12 months. PFD is a cost-effective tool with excellent test–retest reliability (ICC > 0.90) and strong agreement with gold-standard isokinetic measures [31]. Secondary outcomes will include biopsy-derived satellite cell density/function. The Oxford Knee Score (OKS) will assess perceived joint function due to its strong reliability, sensitivity to change, and ease of use [32, 33]. Functional performance will be evaluated via the 5-repetition Sit-to-Stand (5R-STS) test, a quick and practical measure correlated with gait speed, balance, and fall risk, with established reliability (ICC = 0.89) [34]. Muscle mass will be estimated using Discrete Multi-wavelength Near-Infrared Spectroscopy (DMW-NIRS, FITTO), a portable, non-invasive alternative to DXA that enables real-time monitoring of muscle composition [35].

Range of motion will be assessed with a digital goniometer, offering improved accuracy and high inter- and intra-rater reliability (ICC > 0.95) over traditional tools [36]. Pain will be measured

using the Numeric Rating Scale, a simple yet robust tool with strong correlation to other validated pain scales [37].

Key confounders including age, sex, BMI, and preoperative physical activity levels will be recorded and adjusted for in statistical analyses to account for their potential influence on muscle regeneration and functional outcomes.

Muscle tissue collection and preparation for histology

Muscle biopsies will be taken intra-operatively from the distal quadriceps (Rectus Femoris - known to be impaired following TKA) by the same (NM) or nominated surgeon during the knee arthroplasty using the consultant's routine incision for TKA. The biopsy technique will be standardised, with the tissue sample being collected using a scalpel ~5 cm proximal to the superior pole of the patella. Biopsy samples will be acutely processed and stored as described by Martin et al 2013 for the purposes of cell isolation, and processed for histology as described by Maeo et al 2023 [38, 39].

Data analysis

Data analysis will be conducted using R studio (*version* 4.4.2). Data will initially be assessed to verify normality assumptions, prior to conducting inferential statistics [40]. If data are not normally distributed or violate other statistical assumptions, non-parametric data analyses will be performed. If descriptive data analyses reveal outliers, these will be removed and reported accordingly. Changes in outcome scores across the four assessment time points will be analysed using paired analysis of variance, as an appropriate method for comparing means within the same group across different time points [41]. To examine the relationships between muscle strength, muscle mass, functional performance, and satellite cell content, the Pearson product–moment correlation coefficient will be calculated. Additionally, simple linear regression analysis will be performed to investigate these relationships. For a more comprehensive model, multiple linear regression will be employed using a stepwise selection approach. This method iteratively adds or removes predictors based on their statistical significance, allowing us to screen out non-significant variables effectively [42]. The stepwise model will ensure that predictors retained in the final model have a significant association with the response variable. A significance threshold of $P = 0.05$ will be used throughout the analysis, meaning results will be considered statistically significant if the p-value is less than or equal to 0.05. Effect sizes will be reported as appropriate (Cohen's d, R^2). Missing data will be managed using multiple imputation where suitable. Where feasible, analyses will also be stratified by key demographic factors (age, sex, BMI, preoperative activity) to explore subgroup differences in recovery.

Results will be reported according to STROBE flow diagram with full description of participant retention, missing data, and adverse events.

Data security

All participant data will be anonymised and stored on secure, password-protected servers in accordance with UK General Data Protection Regulation and institutional data governance policies [43]. Physical data, including biopsy samples, will be coded and stored in secure, access-controlled laboratory facilities. Only authorised and qualified study personnel will have access to identifiable information, which will be stored separately from research data [44].

Bias minimisation

To reduce selection bias, all consecutive eligible patients will be screened and documented in a screening log. Measurement and observer bias will be minimised by having all assessments performed by the same researcher (AB) using standardised protocols and calibrated equipment. A standardised surgical and rehabilitation pathway will limit performance bias. Detection bias will be reduced through blinded histological processing and satellite cell analyses. These measures ensure consistent and unbiased data collection and interpretation.

Research ethics approval

The study protocol will obtain ethical approval from the NHS Health Research Authority, ensuring that the pilot adheres to best practice ethical guidelines [45]. It will follow the Research Governance Framework for Health and Social Care and comply with the Data Protection Act 2018 [46]. Written informed consent from participants will be obtained before their inclusion in the study (Declaration of Helsinki, 2013). Participants will have the right to withdraw from the study at any time, without providing a reason, and their decision will not affect their standard of care. If a participant chooses to withdraw, any data collected up until the point of withdrawal may still be used for analysis unless the participant requests otherwise. The withdrawal process will be clearly explained to all participants, and they will be provided with contact details should they wish to discuss or initiate withdrawal from the study.

Impact and dissemination

Findings will be disseminated through conference presentations and publication in peer-reviewed journals. Results will inform a wider research programme aimed at improving functional recovery after TKA. Anonymised data will be shared via the UCL Research Data Repository in line with institutional policy. Outcomes will be communicated to local clinical teams, national collaborators, and patient-support organisations such as the Royal Free Charity and Versus Arthritis.

Anticipated limitations

The sample size is small and from a single centre, which may not reflect the broader demographic and clinical heterogeneity seen in larger cohorts such as the QPro-Gin study [47]. The absence of a control group prevents direct comparison with non-TKA or alternative rehabilitation cohorts. These limitations are common in early-phase mechanistic studies, as they emphasise feasibility over broad external validity. To mitigate these constraints, the study uses standardised assessments, consistent data collection procedures, and transparent reporting of recruitment, retention, and missing data. Findings will primarily inform methodological refinement and sample size estimation for future multi-centre studies with enhanced external validity.

CONFLICT OF INTEREST STATEMENT

None declared.

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REFERENCES

1. Franz A, Becker J, Behringer M, Mayer C, Bittersohl B, Krauspe R *et al.* Skeletal muscle health in osteoarthritis and total joint

replacement therapy: effects of prehabilitation on muscular rehabilitation. *Dtsch Z Für Sportmed* 2019;**2019**:145–52. https://doi.org/10.5960/dzsm.2019.383.
2. Muyskens JB, Foote DM, Bigot NJ, Strycker LA, Smolkowski K, Kirkpatrick TK *et al.* Cellular and morphological changes with EAA supplementation before and after total knee arthroplasty. *J Appl Physiol* 2019;**127**:531–45. https://doi.org/10.1152/japplphysiol.00869.2018.
3. Mizner RL, Snyder-Mackler L. Altered loading during walking and sit-to-stand is affected by quadriceps weakness after total knee arthroplasty. *J Orthop Res* 2005;**23**:1083–90. https://doi.org/10.1016/j.orthres.2005.01.021.
4. Yoshida Y, Mizner RL, Ramsey DK, Snyder-Mackler L. Examining outcomes from total knee arthroplasty and the relationship between quadriceps strength and knee function over time. *Clin Biomech* 2008;**23**:320–8. https://doi.org/10.1016/j.clinbiomech.2007.10.008.
5. Belluzzi E, Olivotto E, Toso G, Cigolotti A, Pozzuoli A, Biz C *et al.* Conditioned media from human osteoarthritic synovium induces inflammation in a synoviocyte cell line. *Connect Tissue Res* 2019;**60**:136–45. https://doi.org/10.1080/03008207.2018.1470167.
6. Biz C, Maso G, Gambato M, Belluzzi E, Pozzuoli A, Favero M *et al.* Challenging surgical treatment of displaced articular tibial plateau fractures: do early knee radiographic features have a predictive value of the mid-term clinical functional outcomes? *Orthop Surg* 2019;**11**:1149–62. https://doi.org/10.1111/os.12577.
7. Dreyer HC, Strycker LA, Senesac HA, Hocker AD, Smolkowski K, Shah SN *et al.* Essential amino acid supplementation in patients following total knee arthroplasty. *J Clin Invest* 2013;**123**:4654–66. https://doi.org/10.1172/JCI70160.
8. Mizner RL, Petterson SC, Stevens JE, Vandenborne K, Snyder-Mackler L. Early quadriceps strength loss after total knee arthroplasty: the contributions of muscle atrophy and failure of voluntary muscle activation. *J Bone Jt Surg* 2005;**87**:1047–53. https://doi.org/10.2106/00004623-200505000-00016.
9. Meier W, Mizner R, Marcus R, Dibble L, Peters C, Lastayo PC. Total knee arthroplasty: muscle impairments, functional limitations, and recommended rehabilitation approaches. *J Orthop Sports Phys Ther* 2008;**38**:246–56. https://doi.org/10.2519/jospt.2008.2715.
10. Petterson SC, Barrance P, Marmon AR, Handling T, Buchanan TS, Snyder-Mackler L. Time course of quad strength, area, and activation after knee arthroplasty and strength training. *Med Sci Sports Exerc* 2011;**43**:225–31. https://doi.org/10.1249/MSS.0b013e3181eb639a.
11. Meier WA, Marcus RL, Dibble LE, Foreman KB, Peters CL, Mizner RL *et al.* The long-term contribution of muscle activation and muscle size to quadriceps weakness following total knee arthroplasty. *J Geriatr Phys Ther* 2009;**32**:35–8. https://doi.org/10.1519/00139143-200932020-00007.
12. LaStayo PC, Meier W, Marcus RL, Mizner R, Dibble L, Peters C. Reversing muscle and mobility deficits 1 to 4 years after TKA: a pilot study. *Clin Orthop Relat Res* 2009;**467**:1493–500. https://doi.org/10.1007/s11999-009-0801-2.
13. Crameri RM, Langberg H, Magnusson P, Jensen CH, Schrøder HD, Olesen JL *et al.* Changes in satellite cells in human skeletal muscle after a single bout of high intensity exercise. *J Physiol* 2004;**558**:333–40. https://doi.org/10.1113/jphysiol.2004.061846.
14. Dreyer HC, Blanco CE, Sattler FR, Schroeder ET, Wiswell RA. Satellite cell numbers in young and older men 24 hours after eccentric exercise. *Muscle Nerve* 2006;**33**:242–53. https://doi.org/10.1002/mus.20461.
15. O'Reilly C, McKay B, Phillips S, Tarnopolsky M, Parise G. Hepatocyte growth factor (HGF) and the satellite cell response following muscle lengthening contractions in humans. *Muscle Nerve* 2008;**38**:1434–42. https://doi.org/10.1002/mus.21146.
16. Cermak NM, Snijders T, McKAY BR, Parise G, Verdijk LB, Tarnopolsky MA *et al.* Eccentric exercise increases satellite cell content in type II muscle Fibers. *Med Sci Sports Exerc* 2013;**45**:230–7. https://doi.org/10.1249/MSS.0b013e318272cf47.
17. Verdijk LB, Snijders T, Drost M, Delhaas T, Kadi F, Van Loon LJC. Satellite cells in human skeletal muscle; from birth to old age. *AGE.* 2014;**36**:545–57. https://doi.org/10.1007/s11357-013-9583-2.
18. Mackey AL, Andersen LL, Frandsen U, Sjøgaard G. Strength training increases the size of the satellite cell pool in type I and II fibres of chronically painful trapezius muscle in females. *J Physiol* 2011;**589**:5503–15. https://doi.org/10.1113/jphysiol.2011.217885.
19. Bellamy LM, Joanisse S, Grubb A, Mitchell CJ, McKay BR, Phillips SM *et al.* The acute satellite cell response and skeletal muscle hypertrophy following resistance training. *PloS One* 2014;**9**:e109739. https://doi.org/10.1371/journal.pone.0109739.
20. Morgan JE, Partridge TA. Muscle satellite cells. *Int J Biochem Cell Biol* 2003;**35**:1151–6. https://doi.org/10.1016/S1357-2725(03)00042-6.
21. Hamilton D, Gaston P, Simpson A. Patient muscle Satelite cell content is a potential biomarker for physical recovery and clinical outcome following Total knee arthroplasty. *Orthop Proc* 2016;**98-B**:32–2.
22. Petrella JK, Kim J, su, Mayhew DL, Cross JM, Bamman MM. Potent myofiber hypertrophy during resistance training in humans is associated with satellite cell-mediated myonuclear addition: a cluster analysis. *J Appl Physiol* 2008;**104**:1736–42. https://doi.org/10.1152/japplphysiol.01215.2007.
23. Snijders T, Nederveen JP, McKay BR, Joanisse S, Verdijk LB, Van Loon LJC *et al.* Satellite cells in human skeletal muscle plasticity. *Front Physiol* 2015;**6**:283. https://doi.org/10.3389/fphys.2015.00283.
24. Murphy MM, Lawson JA, Mathew SJ, Hutcheson DA, Kardon G. Satellite cells, connective tissue fibroblasts and their interactions are crucial for muscle regeneration. *Development.* 2011;**138**:3625–37. https://doi.org/10.1242/dev.064162.
25. Brooks MJ, Mohamed JS, Alway SE. Voluntary wheel running increases satellite cell abundance and improves recovery from disuse in gastrocnemius muscles from mice. *J Appl Physiol.* 2018;**124**:1616–28. https://doi.org/10.1152/japplphysiol.00451.2017.
26. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;**61**:344–9. https://doi.org/10.1016/j.jclinepi.2007.11.008.
27. Browne RH. On the use of a pilot sample for sample size determination. *Stat Med* 1995;**14**:1933–40. https://doi.org/10.1002/sim.4780141709.
28. Billingham SA, Whitehead AL, Julious SA. An audit of sample sizes for pilot and feasibility trials being undertaken in the United Kingdom registered in the United Kingdom clinical research network database. *BMC Med Res Methodol* 2013;**13**:104. https://doi.org/10.1186/1471-2288-13-104.

29. Whitehead AL, Julious SA, Cooper CL, Campbell MJ. Estimating the sample size for a pilot randomised trial to minimise the overall trial sample size for the external pilot and main trial for a continuous outcome variable. *Stat Methods Med Res* 2016;**25**:1057–73. https://doi.org/10.1177/0962280215588241.
30. Julious SA. Sample size of 12 per group rule of thumb for a pilot study. *Pharm Stat* 2005;**4**:287–91. https://doi.org/10.1002/pst.185.
31. Mentiplay BF, Perraton LG, Bower KJ, Adair B, Pua YH, Williams GP *et al.* Assessment of lower limb muscle strength and power using hand-held and fixed dynamometry: a reliability and validity study. *PloS One* 2015;**10**:e0140822. https://doi.org/10.1371/journal.pone.0140822.
32. Dawson J, Fitzpatrick R, Murray D, Carr A. Questionnaire on the perceptions of patients about total knee replacement. *J Bone Joint Surg Br* 1998;**80-B**:63–9. https://doi.org/10.1302/0301-620X.80B1.0800063.
33. Murray DW, Fitzpatrick R, Rogers K, Pandit H, Beard DJ, Carr AJ *et al.* The use of the Oxford hip and knee scores. *J Bone Joint Surg Br* 2007;**89-B**:1010–4. https://doi.org/10.1302/0301-620X.89B8.19424.
34. Bohannon RW. Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults. *J Strength Cond Res* 2011;**25**:3205–7. https://doi.org/10.1519/JSC.0b013e318234e59f.
35. Ferrari M, Muthalib M, Quaresima V. The use of near-infrared spectroscopy in understanding skeletal muscle physiology: recent developments. *Philos Trans R Soc Math Phys Eng Sci* 1955;**369**:4577–90. https://doi.org/10.1098/rsta.2011.0230.
36. Brosseau L, Balmer S, Tousignant M, O'Sullivan JP, Goudreault C, Goudreault M *et al.* Intra- and intertester reliability and criterion validity of the parallelogram and universal goniometers for measuring maximum active knee flexion and extension of patients with knee restrictions. *Arch Phys Med Rehabil* 2001;**82**:396–402. https://doi.org/10.1053/apmr.2001.19250.
37. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. *Pain.* 2011;**152**:2399–404. https://doi.org/10.1016/j.pain.2011.07.005.
38. Martin NRW, Passey SL, Player DJ, Khodabukus A, Ferguson RA, Sharples AP *et al.* Factors affecting the structure and maturation of human tissue engineered skeletal muscle. *Biomaterials.* 2013;**34**:5759–65. https://doi.org/10.1016/j.biomaterials.2013.04.002.
39. Maeo S, Balshaw TG, März B, Zhou Z, Haug B, Martin NRW *et al.* Long-term resistance trained human muscles have more fibers, more myofibrils, and tighter myofilament packing than untrained. *Med Sci Sports Exerc* 2024;**56**:1906–15. https://doi.org/10.1249/MSS.0000000000003495.
40. Mishra P, Pandey C, Singh U, Gupta A, Sahu C, Keshri A. Descriptive statistics and normality tests for statistical data. *Ann Card Anaesth* 2019;**22**:67–72. https://doi.org/10.4103/aca.ACA_157_18.
41. Sawyer SF. Analysis of variance: the fundamental concepts. *J Man Manip Ther* 2009;**17**:27E–38E. https://doi.org/10.1179/jmt.2009.17.2.27E.
42. Marill KA. *Advanced statistics:* linear regression, part II: multiple linear regression. *Acad Emerg Med* 2004;**11**:94–102. https://doi.org/10.1197/j.aem.2003.09.006.
43. FAIRsharing Team. FAIRsharing record for: UCL Research Data Policy. FAIRsharing; [cited 2025 July 2]. https://doi.org/10.25504/FAIRsharing.638f73
44. Tucker K, Branson J, Dilleen M, Hollis S, Loughlin P, Nixon MJ *et al.* Protecting patient privacy when sharing patient-level data from clinical trials. *BMC Med Res Methodol* 2016;**16**:77. https://doi.org/10.1186/s12874-016-0169-4.
45. NHS Health Research Authority. HRA approval. 2025 [cited 2025 July 4]. https://www.hra.nhs.uk/approvals-amendments/what-approvals-do-i-need/hra-approval/
46. NHS Health Research Authority. UK policy framework for health and social care research. 2023 [cited 2025 July 4]. https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/uk-policy-framework-health-social-care-research/uk-policy-framework-health-and-social-care-research/
47. Siviero P, Marseglia A, Biz C, Rovini A, Ruggieri P, Nardacchione R *et al.* Quality of life outcomes in patients undergoing knee replacement surgery: longitudinal findings from the QPro-gin study. *BMC Musculoskelet Disord* 2020;**21**:436. https://doi.org/10.1186/s12891-020-03456-2.

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