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Developing an exercise intervention to improve bone mineral density in traumatic amputees: protocol for a Delphi study

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ABSTRACT

Introduction Lower limb amputation results in reduced bone mineral density (BMD) on the amputated side. Exercise interventions have proven effective in improving BMD. However, such interventions have not been attempted in an amputee population. Exercises designed for people with intact limbs may not be suitable for amputees, due to joint loss and the mechanical interface between the exercise equipment and the femoral neck being mediated through a socket. Therefore, prior to intervention implementation, it would be prudent to leverage biomechanical knowledge and clinical expertise, alongside scientific evidence in related fields, to assist in intervention development. The objective of this study is to elicit expert opinion and gain consensus to define specific exercise prescription parameters to minimise/recover BMD loss in amputees.

Methods and analysis The Delphi technique will be used to obtain consensus among international experts; this will be conducted remotely as an e-Delphi process. 10–15 experts from ≥2 continents and ≥5 countries will be identified through published research or clinical expertise. Round 1 will consist of participants being asked to rate their level of agreement with statements related to exercise prescription to improve amputee BMD using a 5-point Likert Scale. Agreement will be deemed as ≥3 on the Likert Scale. Open feedback will be allowed in round 1 and any statement which less than 50% of the experts agree with will be excluded. Round 2 will repeat the remaining statements with the addition of any input from round 1 feedback. Round 3 will allow participants to reflect on their round 2 responses considering statistical representation of group opinion and whether they wish to alter any of their responses accordingly. Statements reaching agreement rates of 70% or above among the experts will be deemed to reach a consensus and will be implemented in a future exercise interventional trial.

Ethics and dissemination Ethical approval was received from Imperial College Research Ethics Committee (reference: 6463766). Delphi participants will be asked to provide digital informed consent. The findings will be disseminated through peer-reviewed publications.

STRENGTH AND LIMITATIONS OF THIS STUDY

- ⇒ Exercise prescription criteria to improve bone mineral density in amputees will be developed by an interdisciplinary expert panel using validated consensus methods.
- ⇒ Conducting the study remotely will facilitate accessibility and anonymity of participants' responses while reducing the effect of dominant individuals (bandwagon effect).
- ⇒ This technique will leverage expertise and use current best evidence in similar scientific and clinical fields to optimise the intervention design and maximise safety prior to implementation.
- ⇒ The views of the Delphi panellists may differ from experts who decline to participate and may not fully represent all experts in the field.
- ⇒ As the Delphi procedure is a consensus method, it will not create new direct evidence; therefore, further interventional work will be required to assess the accuracy of the consensus experimentally.

INTRODUCTION

Recent conflicts in Iraq and Afghanistan have resulted in many traumatic or surgical lower limb amputations.[1] The increased urbanisation of low-income and middle-income countries with concomitant increase in road traffic accidents also produced large numbers of amputations.[2] These injuries occur predominantly in males, with a mean age of 22 years in the military population, and not much older in civilians.[2 3] There is increasing evidence that lower limb amputation results in reduced bone mineral density (BMD) of the hip on the amputated side.[4] This can ultimately lead to osteoporosis, heightening the risk of hip fractures. Hip fractures cost over £1 billion per year in the UK. This risk is compounded by a higher falls risk in amputees.[5] Fractures can have serious implications on function, independence, employment and morbidity. Furthermore, this could have a disproportionate effect in amputees as it could compromise prosthetic usage. In a young, active population, the prospect of reduced independence and increased mortality is not acceptable and requires rigorous investigation and intervention.

During gait, unilateral amputees have higher muscle and joint forces in their intact limb.[6] The consequent lower loading in the amputated limb could precipitate progressive bone loss over the course of many remodelling cycles of the bone, resulting in localised unloading osteopenia/osteoporosis.[7] Furthermore, this increased loading on the healthy limb may contribute towards the increased rate of osteoarthritis in healthy limbs of amputees.[8] Therefore, altering biomechanical loading may reduce the risk of both localised unloading osteoporosis (affected limb) and osteoarthritis (intact limb) in the amputee population. Thus, any intervention to alter amputee BMD requires a biomechanically informed rationale.

Exercise interventions to increase BMD have been demonstrated to be successful in other fields: space flight,[9] postmenopausal women[10] and those recovering from anorexia.[11] Systematic reviews with meta-analyses have recommended specific exercise loading protocols to optimise BMD parameters.[10] However, exercise loading to reduce BMD loss in amputees has not been documented in the literature. Exercise in populations with intact limbs may not be suitable for amputees as the interface between the exercise equipment and the femoral neck is mediated non-physiologically through a socket or in some cases, an osseointegration implant. Therefore, biomechanical transmission of the load to the proximal femur requires careful consideration. Furthermore, the young age of many traumatic amputees[2 3] may allow and require more rigorous exercise interventions than previous interventions in older populations.[12] Despite the lack of empirical evidence on these interventions, anecdotally clinicians have been attempting to increase amputee BMD. Consequently, there is a pressing need to establish biomechanically driven loading parameters and determine the safety, success and feasibility of these interventions in a controlled and systematic fashion in amputees.

Exercise adaptations and progressive bone loss in amputees is likely to be different from other populations due to the offloading of the residual limb by the prosthetic socket design, reducing loading in the femoral neck, thus opening the way to novel interventions.[4] By implementing a biomechanically driven exercise intervention to focus on loading the femoral neck, direct recommendations could be disseminated on the success of exercise interventions prior to socket alteration. Altering socket type to increase femoral end-loading may result in secondary negative consequences, such as pain, discomfort and skin compromise. Without obtaining this insight regarding exercise interventions, the necessity of altering socket type to allow increased end-loading in the amputated limb will be unknown. This knowledge would improve amputee management, amputee and clinician education, and amputee rehabilitation.

However, prior to implementing any intervention, it would be clinically and scientifically prudent to leverage biomechanical knowledge and clinical expertise, alongside parallel scientific evidence in related fields, to assist in developing successful interventions and add to evidence-based practice. Delphi techniques have proven valuable in this phase as they generate knowledge that can provide insights into interventional parameters and potential effectiveness prior to implementation.[13] The objective of this study is to elicit expert opinion and gain consensus to define specific exercise prescription parameters to minimise/recover bone mineral loss in amputees.

METHODS AND ANALYSIS

Study design

An initial step of intervention development using the Delphi process is warranted to ascertain expert clinical and scientific consensus informing a future biomechanically underpinned intervention. Delphi processes have been implemented successfully in a variety of different clinical settings.[14–16] Therefore, prior to implementing an interventional study, current expert knowledge will be leveraged to ensure an optimal protocol with the available current evidence base and expertise through the Delphi process. This will allow specific questions to be answered regarding the exact parameters to include in the consequent study: what type of exercises should be used in the intervention, how frequently the intervention should occur, what intensity should the intervention be executed at and what should the duration of the intervention be?[17 18] Guidelines on conducting and reporting Delphi studies have been adhered to in the development of this protocol.[19]

Steering committee

A multidisciplinary steering group was formed to develop and conduct this Delphi procedure consisting of relevant disciplines (physiotherapy, exercise science, rheumatology, sports and exercise medicine, bioengineering, musculoskeletal biomechanics) and research expertise (quantitative methods, interventional trial development and implementation, longitudinal trial management, computational musculoskeletal and biomechanical modelling). Agreement was reached regarding inclusion and exclusion criteria of the expert committee, statement structure and analysis procedures, using previous Delphi studies and guidelines for guidance.[14–16 19 20]

Generation of the statement list

The statements were structured according to a well-established exercise science framework consisting of four domains of exercise prescription: frequency, intensity, time and type of exercise.[17 18] The parameters included in the questions were generated through the findings of systematic reviews, clinical trials and guidelines using exercise as a stimulus for bone mineral density.[9 10 21–24]

Selection of international experts

Participants will be deemed suitable if they are seen as experts in a relevant field by the steering committee. Participants will be deemed as experts if they are:

1. Author of two or more English language peer-reviewed publications related to the domain (i.e., improving

bone mineral density) or constructs (i.e., exercise prescription).[15 16] And/or:

2. Have 5+ years of clinical experience of prescribing exercise interventions in amputees. Participants will be excluded if they do not have sufficient clinical or academic domain-specific knowledge or if they do not consent to participate. To form a representative international expert panel, we seek to include a diverse range of professions, research and clinical practice disciplines, countries, and backgrounds. Any expert who declines to participate will be asked to suggest a colleague with a similar background to replace them.[20] Furthermore, those who accepted the invitation will also be offered the opportunity to suggest peer recommendations to ensure no experts will be missed. We aim for a panel of 10–15 experts. As there are no explicit recommendations on Delphi sample size, we aimed for this sample as it is similar to previous Delphi studies,[16 25] and as within fields with limited experts, such as this field, strict inclusion criteria allow for effective and reliable utilisation of a moderate number of experts.[26] Experts from ≥2 continents and ≥5 countries will be identified to ensure internationalisation. We aim for at least 40% of the experts to either be practising clinically or have a clinical background and at least 40% from a scientific/engineering background.

Anonymity

The iterative nature of a Delphi technique means that participants are anonymous to each other, but not to the researcher, deemed quasi-anonymity.[27–29] At the completion of the process, participants will be offered the choice to remain anonymous to each other or to receive acknowledgement and give input to the future publication for their involvement.[27]

Delphi procedure

Each stage of the Delphi study will involve piloting the survey to a group of four to six postdoctoral researchers familiar with the disciplines to ensure comprehensibility of survey statements, correct survey set-up and accurate interpretation and analysis of data.[16] Construction, distribution and data collection will be conducted remotely as an e-Delphi using Microsoft Forms (Microsoft, Redmond, WA, USA).

Round one

Prior to round one, input on the question structure and content will be considered based on feedback from optional video calls offered to the invited expert participants and from the piloting phase to improve the clarity of statements and interpretation of responses.[16]

Round one will consist of participants being asked to rate their level of agreement with a statement using a five-point Likert Scale (0=Strongly disagree, 1=Disagree, 2=Neither agree nor disagree, 3=Agree, 4=Strongly agree). Agreement will be deemed as ≥3 on the Likert Scale. These questions will be split into four established domains related to exercise prescription: frequency, intensity, time and type. The first round will comprise an open-ended question at the end of each section for feedback from participants on improvements/modifications required for round two,[16] analysed using content analysis.[30] The answers to the statements will be analysed for percentage agreement, with those statements receiving less than 50% agreement among experts being excluded from progressing to round two[16] to reduce the list of items least likely to achieve consensus[31] and will result in a smaller number of statements in the final two rounds. This in turn will reduce the risk of fatigue and dropout in the Delphi expert participant panel. Each round will be open for 2 weeks, with a week between for analysis. If there has been no response in week one, participants will be reminded at the beginning of week two, and if there has still been no response, participants will receive a further personalised reminder on the final day to minimise attrition.

Round two

Round two will consist of the same statements as round one with any alterations to the statements (terminology, clarity, additional statements) based on round one feedback and the exclusion of any statement that failed to reach at least a 50% consensus from round one.[31] Other than the exclusion of questions from round one, no explicit feedback from group results of round one will be given in round two. Participants will again be asked to rate their level of agreement with a statement using a five-point Likert Scale (0=Strongly disagree, 1=Disagree, 2=Neither agree nor disagree, 3=Agree, 4=Strongly agree). These statements will again be split into four sections related to exercise prescriptions: frequency, intensity, time and type. One final open-ended question in round two will allow for additional comments/inputs to be added prior to the final third round. Round two statements will be analysed with descriptive statistics including measures of central tendencies (median), measure of distribution (interquartile range), alongside percentage agreement.[16]

Round three

Participants will be advised to reflect on their round two responses (each participant will be presented with their individual response) alongside statistical representation (percentage agreement) of group opinion for each question to inform their responses to round three and whether they wish to alter any of their round two responses accordingly.[15 16 19] This process may allow participants to realise disparities between them and the rest of the experts, to reconsider the evidence or to reflect on and re-evaluate their decision of each statement based on the group statistics.[15 16] Analysis of descriptive statistics will be performed as per round two. Statements reaching pre-defined criteria (ie, ≥ 70% of the expert group scoring their responses as ≥3 on the Likert Scale)[19 31] will be deemed to reach a consensus and will be implemented (where possible) in the exercise intervention.

Patient and public involvement

Three individuals with lower limb amputations formed a study patient and public involvement (PPI) group and were involved in the early conception of study design, and two individuals gave further detailed input based on their experience and preferences on the structure of the statements and the potential implementation of the intervention, with statements adapted accordingly. The Delphi expert participant panel will be given results from rounds two and three and will be invited to give input to obtain authorship on the results manuscript.

Ethics and dissemination

Ethical approval was received from Imperial College Research Ethics Committee, reference number 6463766.

Participants will be asked to give digital informed consent (online supplemental material) after reading a study information sheet, included within the invitation email. Participants will be free to withdraw at any time and without giving a reason. They can inform the investigators directly, or their withdrawal will be assumed from a lack of response to questions within the defined time frame for each round. Participants can stop being part of the study at any time (rounds one, two and three), without giving a reason, but the investigators will keep anonymised participant responses that already will have been used for some analysis (i.e., answers used in round one of the Delphi that may have resulted in a statement reaching <50% consensus and, therefore, being excluded from round two).

All data will be kept on an encrypted computer, in a locked office. Only the researchers will have access to the data which will be destroyed after 10 years.

We plan to disseminate the findings of this Delphi through peer-reviewed publications and international conference presentations. It is foreseen that the Delphi process and analysis will be completed by early 2024.

DISCUSSION

The present paper details the design of a study using the Delphi technique to design an exercise intervention aimed at improving bone mineral density in amputees. We aim to elicit opinion and obtain a consensus on the appropriate parameters of an exercise intervention to use within a consequent controlled interventional trial to investigate the effects of exercise on bone mineral density in amputees. The outcomes of these studies have the potential to improve exercise prescription in amputees and if the intervention is proven successful, may stabilise or improve bone mineral density and potentially reduce lifelong fracture risk within this population. The addition of a specific exercise loading programme to increase BMD in amputees seems particularly pertinent considering recent evidence that neither walking[7] nor sporting activity[32] appear enough to prevent hip demineralisation in amputees. The target of this work will be individuals who have suffered traumatic amputations, as those with cancer-related or dysvascular amputations[33] may require more individualised, adapted exercise regimes due to comorbidities.[34]

Using the Delphi technique where there is limited direct clinical knowledge of the effectiveness of an intervention may be valuable as the process can generate knowledge that may provide insights into interventional parameters and potential effectiveness prior to implementation.[13] This allows scientific, clinical and theoretical knowledge from relevant fields and interventions in other clinical populations[21–24] to be leveraged from experts to maximise the potential efficacy and safety of future interventions prior to design and implementation. Furthermore, the Delphi technique allows diverse participants from around the globe to participate and bring their expertise, facilitates participants to remain anonymous to one another, and prevents any social conformity to a dominant view (bandwagon effect).[19 27]

Previously, Delphi procedures have been used for exercise prescription in clinical conditions[35] including those with osteoporosis,[36] but none have been done to define a biomechanically driven loading intervention to increase bone mineral density in amputees, adding novelty to the literature. However, without direct interventional data of the effect of exercise on bone mineral density in amputees, the Delphi process cannot create new evidence for this but infer recommendations in amputees based on empirical data from exercise interventions on bone mineral density in other populations[9 21–24] and current scientific knowledge of the population in question.[4–6 8 37] Therefore, clinical recommendations on exercise interventions to increase bone mineral density in amputees will still require future rigorous, controlled, experimental trial data. There is also a recruitment challenge due to a limited number of experts in the area and the risk of these experts not agreeing to participate in the Delphi process or dropping out between rounds. The results of this Delphi will be used to design a feasibility interventional trial with the best available scientific knowledge available to optimise safety and maximise potential positive clinical outcomes in this population.

Contributors Conception and design of the work: FPB, AMJB, ANB; drafting the work: FPB; Revising the work critically: FPB, AMJB, ANB; final approval of the version to be submitted: FPB, AMJB, ANB.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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REFERENCES

1 Edwards DS, Phillip RD, Bosanquet N, *et al*. What is the magnitude and long-term economic cost of care of the British military Afghanistan Amputee cohort *Clin Orthop Relat Res* 2015;473:2848–55.
2 Zafar SN, Canner JK, Nagarajan N, *et al*. Road traffic injuries: cross-sectional cluster randomized countrywide population data from 4 low-income countries. *Int J Surg* 2018;52:237–42.
3 Webster CE, Clasper J, Stinner DJ, *et al*. Characterization of lower extremity blast injury. *Mil Med* 2018;183:e448–53.
4 Kulkarni J, Adams J, Thomas E, *et al*. Association between amputation, arthritis and osteopenia in British male war veterans with major lower limb amputations. *Clin Rehabil* 1998;12:348–53.
5 Miller WC, Speechley M, Deathe B. The prevalence and risk factors of falling and fear of falling among lower extremity amputees. *Arch Phys Med Rehabil* 2001;82:1031–7.
6 Ding Z, Jarvis HL, Bennett AN, *et al*. Higher knee contact forces might underlie increased osteoarthritis rates in high functioning amputees: a pilot study. *J Orthop Res* 2021;39:850–60.
7 McMenemy L, Behan FP, Kaufmann J, *et al*. Association between combat-related traumatic injury and skeletal health: bone mineral density loss is localized and correlates with altered loading in amputees: the armed services trauma rehabilitation outcome (ADVANCE) study. *J Bone Miner Res* 2023;38:1227–33.
8 Lemaire ED, Fisher FR. Osteoarthritis and elderly amputee gait. *Arch Phys Med Rehabil* 1994;75:1094–9.
9 Sibonga J, Matsumoto T, Jones J, *et al*. Resistive exercise in astronauts on prolonged spaceflights provides partial protection against spaceflight-induced bone loss. *Bone* 2019;128.
10 Fratini A, Bonci T, Bull AMJ. Whole body vibration treatments in postmenopausal women can improve bone mineral density: results of a stimulus focussed meta-analysis. *PLoS One* 2016;11:e0166774.
11 Waugh EJ, Woodside DB, Beaton DE, *et al*. Effects of exercise on bone mass in young women with anorexia nervosa. *Med Sci Sports Exerc* 2011;43:755–63.
12 Massini DA, Nedog FH, de Oliveira TP, *et al*. The effect of resistance training on bone mineral density in older adults: a systematic review and meta-analysis. *Healthcare (Basel)* 2022;10:1129.
13 Niederberger M, Spranger J. Delphi technique in health sciences: a map. *Front Public Health* 2020;8:457.
14 Mendonça LDM, Schuermans J, Denolf S, *et al*. Sports injury prevention programmes from the sports physical therapist's perspective: an international expert Delphi approach. *Phys Ther Sport* 2022;55:146–54.
15 Smart KM, Blake C, Staines A, *et al*. Clinical indicators of 'nociceptive', 'peripheral neuropathic' and 'central' mechanisms of musculoskeletal pain. A Delphi survey of expert Clinicians. *Man Ther* 2010;15:80–7.
16 Lam KN, Heneghan NR, Mistry J, *et al*. Classification criteria for cervical radiculopathy: an international E-Delphi study. *Musculoskelet Sci Pract* 2022;61:102596.
17 Billinger SA, Boyne P, Coughenour E, *et al*. Does aerobic exercise and the FITT principle fit into stroke recovery *Curr Neurol Neurosci Rep* 2015;15:519.
18 Burnet K, Kelsch E, Zieff G, *et al*. How fitting is F.I.T.T.?: A perspective on a transition from the sole use of frequency, intensity, time, and type in exercise prescription. *Physiol Behav* 2019;199:33–4.
19 Jünger S, Payne SA, Brine J, *et al*. Guidance on conducting and reporting Delphi studies (CREDES) in palliative care: recommendations based on a methodological systematic review. *Palliat Med* 2017;31:684–706.
20 Slade SC, Dionne CE, Underwood M, *et al*. Standardised method for reporting exercise programmes: protocol for a modified Delphi study. *BMJ Open* 2014;4:e006682.
21 English KL, Downs M, Goetchius E, *et al*. High intensity training during spaceflight: results from the NASA sprint study. *NPJ Microgravity* 2020;6:21.
22 Zehnacker CH, Bemis-Dougherty A. Effect of weighted exercises on bone mineral density in post menopausal women. A systematic review. *J Geriatr Phys Ther* 2007;30:79–88.
23 Watson S, Weeks B, Weis L, *et al*. High-intensity resistance and impact training improves bone mineral density and physical function in postmenopausal women with osteopenia and osteoporosis: the LIFTMOR randomized controlled trial. *J Bone Miner Res* 2019;34:572.
24 Brooke-Wavell K, Skelton DA, Barker KL, *et al*. Strong, steady and straight: UK consensus statement on physical activity and exercise for osteoporosis. *Br J Sports Med* 2022;56:837–46.
25 Diamond IR, Grant RC, Feldman BM, *et al*. Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies. *J Clin Epidemiol* 2014;67:401–9.
26 Akins RB, Tolson H, Cole BR. Stability of response characteristics of a Delphi panel: application of bootstrap data expansion. *BMC Med Res Methodol* 2005;5:37.
27 Page A, Potter K, Clifford R, *et al*. Prescribing for Australians living with dementia: study protocol using the Delphi technique. *BMJ Open* 2015;5:e008048.
28 Hasson F, Keeney S, McKenna H. Research guidelines for the Delphi survey technique. *J Adv Nurs* 2000;32:1008–15.
29 Keeney S, Hasson F, McKenna H. Consulting the oracle: ten lessons from using the Delphi technique in nursing research. *J Adv Nurs* 2006;53:205–12.
30 Elo S, Kyngäs H. The qualitative content analysis process. *J Adv Nurs* 2008;62:107–15.
31 Heijboer WMP, Weir A, Delahunt E, *et al*. A Delphi survey and international E-survey evaluating the Doha agreement meeting classification system in groin pain: where are we 5 years later? *J Sci Med Sport* 2022;25:3–8.
32 Cavedon V, Sandri M, Peluso I, *et al*. Sporting activity does not fully prevent bone demineralization at the impaired hip in athletes with amputation. *Front Physiol* 2022;13:934622.
33 Dillingham TR, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. *South Med J* 2002;95:875–83.
34 Godlwana L, Stewart A, Musenge E. The effect of a home exercise intervention on persons with lower limb amputations: a randomized controlled trial. *Clin Rehabil* 2020;34:99–110.
35 Price J, Rushton A, Tyros V, *et al*. Consensus on the exercise and dosage variables of an exercise training programme for chronic non-specific neck pain: protocol for an international E-Delphi study. *BMJ Open* 2020;10:e037656.
36 Giangregorio LM, Papaioannou A, Macintyre NJ, *et al*. Too fit to fracture: exercise recommendations for individuals with osteoporosis or osteoporotic vertebral fracture. *Osteoporos Int* 2014;25:821–35.
37 Norvell DC, Czerniecki JM, Reiber GE, *et al*. The prevalence of knee pain and symptomatic knee osteoarthritis among veteran traumatic amputees and nonamputees. *Arch Phys Med Rehabil* 2005;86:487–93.